



© AGO e. V.  
in der DGGG e. V.  
sowie  
in der DKG e. V.


Guidelines Breast  
Version 2022.1D

FORSCHEN  
LEHREN  
HEILEN

## Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

### **Läsionen mit unsicherem biologischen Potenzial (B3)**

**(ADH, LIN, FEA, Papillom, Radiäre Narbe)**



© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2022.1D

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN

## Läsionen mit unklarem biologischen Potenzial (B3)

- **Versionen 2005–2021:**  
**Albert / Audretsch / Brunnert / Ditsch / Fallenberg / Fersis / Friedrich / Friedrichs / Gerber / Huober / Kreipe / Nitz / Maass / Rody / Schmidt / Schreer / Sinn / Thomssen**
- **Version 2022:**  
**Bauerfeind / Kreipe**

### Pubmed 2010-2021 queries

#### Lobular neoplasia (114 Results)

(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh]) AND ("2012/01/01"[dp] : "2020/01/01"[dp]) AND ("lobular neoplasia"[ti] OR "lobular intraepithelial neoplasia"[ti] OR "atypical lobular hyperplasia"[ti] OR "lobular carcinoma in situ"[ti] OR "LIN"[ti] OR "ALH"[ti] OR "LCIS"[ti]) AND ("english"[la] OR "german"[la])

#### Atypical ductal hyperplasia (71 Results)

(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh]) AND ("2012/01/01"[dp] : "2020/01/01"[dp]) AND ("atypical ductal hyperplasia"[ti] OR "atypical hyperplasia"[ti] OR "ADH"[ti]) AND ("english"[la] OR "german"[la])

#### Flat epithelial atypia (45 Results)

(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh])

AND ("2012/01/01"[dp] : "2020/01/01"[dp]) AND ("flat epithelial atypia"[ti] OR "columnar cell"[ti] OR "FEA"[ti]) AND ("english"[la] OR "german"[la])

#### Papilloma (183 Results)

(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh]) AND ("2012/01/01"[dp] : "2020/01/01"[dp]) AND ("papilloma"[ti] OR "papillary"[ti]) AND ("english"[la] OR "german"[la]) NOT virus[Title]

#### Radial scar (17 Results)

(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh]) AND ("2012/01/01"[dp] : "2020/01/01"[dp]) AND ("radial scar"[ti] OR "complex sclerosing lesion"[ti] OR "radial sclerosing lesion"[ti]) AND ("english"[la] OR "german"[la])

#### National and international guidelines

1. AWMF, Deutschen Krebsgesellschaft e.V. und Deutschen Krebshilfe e.V. (Hrsg.). Interdisziplinäre S3-Leitlinie für die Diagnostik, Therapie und Nachsorge des Mammakarzinoms. Langversion 4.0, Aktualisierung 2017 <http://www.leitlinienprogramm-onkologie.de/leitlinien/mammakarzinom/>
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Breast cancer. Version 1. 2020.
3. National Comprehensive Cancer Network (NCCN). Breast Cancer Screening and Diagnosis. Version 1.2019
4. Rageth CJ, O'Flynn EAM, Pinker K, et al. Second International Consensus Conference on lesions of uncertain malignant potential in the breast (B3 lesions). Breast Cancer Res Treat. 2019 Apr;174(2):279–96.
5. Scottish Intercollegiate Guidelines Network (SIGN) (2013) SIGN 134 • Treatment of primary breast cancer. <http://www.sign.ac.uk/pdf/SIGN134.pdf>
6. World Health Organization: WHO Classification of Tumours of the Breast. Lokuhetty D, White VA, Watanabe R, Cree IA (Hrsg.) 2019.



© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2022.1D

www.ago-online.de

## Pathologische Berichterstellung für minimalinvasive Biopsien

### B-Klassifikation\*

**B1 = Normalgewebe oder nicht verwertbares Material**

**B2 = Benigne Läsion**

**B3 = Benigne Läsionen mit unsicherem biologischen Potenzial**

**B4 = Malignitätsverdächtig**

**B5 = Malignom**

**B5a: In-situ-Karzinom**


**B5b: Invasives Karzinom**

**B5c: Nicht zu entscheiden, ob invasiv oder in situ**

**B5d: Malignom anderer Histogenese oder Metastase**

\* AWMF, Deutschen Krebsgesellschaft e.V. und Deutschen Krebshilfe e.V. (Hrsg.). Interdisziplinäre S3-Leitlinie für die Diagnostik, Therapie und Nachsorge des Mammakarzinoms. Langversion 4.0, Aktualisierung 2017

1. The Royal College of Pathologists. Guidelines for non-operative diagnostic procedures and reporting in breast cancer [Internet]. United Kingdom: National ...; 2016. Available from: <https://www.rcpath.org/profession/publications/cancer-datasets.html>
2. Ellis IO, Humphreys S, Michell M et al. Best Practice No 179. Guidelines for breast needle core biopsy handling and reporting in breast screening assessment. Vol. 57, Journal of clinical pathology. 2004. pp. 897–902.
3. Wells C (ed.) (2006) Quality assurance guidelines for pathology: Cytological and histological non-operative procedures. In: European guidelines for quality assurance in breast cancer screening and diagnosis. Perry N, Broeders M, de Wolf C, Törnberg S, Holland R, Koch von F, editors. Luxembourg: Office for Official Publications of the European Communities, ISBN 92-79-01258-4 pp. 221-256 Retrieved from <http://www.euref.org/european-guidelines>
4. Wells, C. A. (2014). Pathology Update Breast Screening, pp. 1 - 48. Retrieved from <http://www.euref.org/european-guidelines>
5. World Health Organization: WHO Classification of Tumours of the Breast. Lokuhetty D, White VA, Watanabe R, Cree IA (Hrsg.) 2019.

 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.  Guidelines Breast Version 2022.1D  www.ago-online.de FORSCHEN LEHREN HEILEN</p>	<h2 style="text-align: center; color: green;">B3-Läsionen</h2> <ol style="list-style-type: none"> <li><b>1. Läsionen mit erhöhtem Risiko eines assoziierten DCIS oder invasiven Karzinoms</b> <ul style="list-style-type: none"> <li>▪ Atypische duktale Hyperplasie (ADH) bzw. atypische Epithelproliferation vom duktalem Typ (in Abhängigkeit von der Ausdehnung ggf. B4)</li> <li>▪ Flache epitheliale Atypie (FEA)</li> <li>▪ Lobuläre Neoplasie (LIN; LN; in älterer Nomenklatur zusammengefasst jetzt unterteilt in ALH und LCIS), klassischer und nicht-klassischer Typ</li> <li>▪ Atypische apokrine Adenose</li> </ul> </li> <li><b>2. Potenziell heterogene Läsionen mit Risiko eines unvollständigen Sampling</b> <ul style="list-style-type: none"> <li>▪ Zellreiche fibroepitheliale Läsion oder Phylloides tumor ohne Malignitätsverdacht</li> <li>▪ Intraduktales Papillom ohne / mit Atypien, nicht sicher vollständig entfernt (bei Atypien in Abhängigkeit von der Ausdehnung ggf. B4)</li> <li>▪ Radiäre Narbe bzw. komplexe sklerosierende Läsion (Ausnahme: wenn radiäre Narbe nicht Ursache der radiologischen Veränderung: B2)</li> <li>▪ Hämangiom</li> </ul> </li> <li><b>3. Seltene Veränderungen</b> <ul style="list-style-type: none"> <li>▪ Adenomyoepitheliom, Mikrogländuläre Adenose, Mukozelenartige Läsion, Noduläre Faszitis, Fibromatose vom Desmoidtyp, unklare Spindelzellläsion</li> </ul> </li> </ol>
---	--

1. AWMF, Deutschen Krebsgesellschaft e.V. und Deutschen Krebshilfe e.V. (Hrsg.). Interdisziplinäre S3-Leitlinie für die Diagnostik, Therapie und Nachsorge des Mammakarzinoms. Langversion 4.0, Aktualisierung 2017 <http://www.leitlinienprogramm-onkologie.de/leitlinien/mammakarzinom/>
2. The Royal College of Pathologists. Guidelines for non-operative diagnostic procedures and reporting in breast cancer [Internet]. United Kingdom: National ...; 2016. Available from: <https://www.rcpath.org/resourceLibrary/g150-non-op-reporting-breast-cancer-screening-jun16-pdf.html>
3. Ellis IO, Humphreys S, Michell M et al. Best Practice No 179. Guidelines for breast needle core biopsy handling and reporting in breast screening assessment. Vol. 57, Journal of clinical pathology. 2004. pp. 897–902.
4. Hayes BD, Quinn CM. Pathology of B3 lesions of the breast. Diagnostic Histopathology. Elsevier Ltd; 2009 Oct 1;15(10):459–69.
5. Kreipe H-H, Höfler H, Lebeau A. Ergebnisse der Referenzpathologie im Mammographie-Screening. Pathologe. 2008 Oct 9;29(S2):178–80.
6. Rageth CJ, O'Flynn EAM, Pinker K et al. Second International Consensus Conference on lesions of uncertain malignant potential in the breast (B3 lesions). Breast Cancer Res Treat. 2019 Apr;174(2):279–96.
7. Rakha, E. A., Lee, A. H. S. et al (2011). Characterization and outcome of breast needle core biopsy diagnoses of lesions of uncertain malignant potential (B3) in abnormalities detected by mammographic screening. International Journal of Cancer, 129(6), 1417–1424. <http://doi.org/10.1002/ijc.25801>

8. Wells C (ed.) (2006) Quality assurance guidelines for pathology: Cytological and histological non-operative procedures. In: European guidelines for quality assurance in breast cancer screening and diagnosis. Perry N, Broeders M, de Wolf C, Törnberg S, Holland R, Koch von F, editors. Luxembourg: Office for Official Publications of the European Communities, ISBN 92-79-01258-4 pp. 221-256 Retrieved from <http://www.euref.org/european-guidelines>
9. Wells, C. A. (2014). Pathology Update Breast Screening, pp. 1 - 48. Retrieved from <http://www.euref.org/european-guidelines>
10. World Health Organization: WHO Classification of Tumours of the Breast. Lokuhetty D, White VA, Watanabe R, Cree IA (Hrsg.) 2019.
11. Bachert S, Jen S, Denison C et al. :Breast lesions associated with mammographic architectural distortion: a study of 588 core needle biopsies Dec 29. 2021 doi: 10.1038/s41379-021-00996-3. Online ahead of print.


Management nach minimalinvasiver Biopsie			
	Oxford		
	LoE	GR	AGO
■ Interdisziplinäre Konferenz: Pathologie und Bildgebung konkordant?			
■ ja: Vorgehen gemäß histologischem Typ	3a	C	++
■ nein: offene PE	3a	C	++
Vakuumbiopsie (nach Stanzbiopsie)	5	D	+

1. Atkins KA, Cohen MA, Nicholson B et al.: Atypical lobular hyperplasia and lobular carcinoma in situ at core breast biopsy: use of careful radiologic-pathologic correlation to recommend excision or observation. Radiology. 2013 Nov;269(2):340-7.
2. AWMF, Deutschen Krebsgesellschaft e.V. und Deutschen Krebshilfe e.V. (Hrsg.). Interdisziplinäre S3-Leitlinie für die Diagnostik, Therapie und Nachsorge des Mammakarzinoms. Langversion 4.0, Aktualisierung 2017 <http://www.leitlinienprogramm-onkologie.de/leitlinien/mammakarzinom/>
3. Calhoun, B. C., & Collins, L. C. (2016). Recommendations for excision following core needle biopsy of the breast: a contemporary evaluation of the literature. Histopathology, 68(1), 138–151. <http://doi.org/10.1111/his.12852>
4. Hayes BD, O'Doherty A, Quinn CM. Correlation of needle core biopsy with excision histology in screen-detected B3 lesions: the Merrion Breast Screening Unit experience. J Clin Pathol. 2009 Dec 1;62(12):1136–40.
5. Houssami N et al: Borderline breast core needle histology: predictive values for malignancy in lesions of uncertain malignant potential (B3). Br J Cancer 2007; 96:1253-1257
6. 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 Jun;3(3):492-9
7. Morrow, M., Schnitt, S. J., & Norton, L. (2015). Current management of lesions associated with an increased risk of breast cancer. Nature Reviews. Clinical Oncology, 12(4), 227–238. <http://doi.org/10.1038/nrclinonc.2015.8>
8. Neal L, Sandhu NP, Hieken TJ et al.: Diagnosis and management of benign, atypical, and indeterminate breast lesions detected on

core needle biopsy. Mayo Clin Proc. 2014 Apr;89(4):536-47

9. Rageth CJ, O'Flynn EA, Comstock C et al. First International Consensus Conference on lesions of uncertain malignant potential in the breast (B3 lesions). Breast Cancer Res Treat. Springer US; 2016 Sep;159(2):203–13.
10. Saladin C, Haueisen H, Kampmann G et al. Lesions with unclear malignant potential (B3) after minimally invasive breast biopsy: evaluation of vacuum biopsies performed in Switzerland and recommended further management. Acta Radiol. 2016 Jul;57(7):815–21.
11. Sinn HP, Flechtenmacher C, Aulmann S. Diagnostik benigner duktaler Epithelproliferationen der Mamma in der Stanzbiopsie. Der Pathologe. Springer Berlin Heidelberg; 2014 Feb;35(1):18–25.
12. Thomas PS. Diagnosis and Management of High-Risk Breast Lesions. J Natl Compr Canc Netw. 2018 Nov;16(11):1391–6.
13. Mod Pathol





© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2022.1D

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN

## Atypische duktale Hyperplasie (ADH)

- **Synonyme:** Atypische intraduktale Epithelproliferation, atypische epitheliale Proliferation vom duktalem Typ (ADP)
- **Definition:** Atypische intraduktale Proliferation mit zytologischen und strukturellen Merkmalen eines gut differenzierten DCIS, wie Ausbildung starrer Brücken oder Mikropapillen, häufig gut erkennbaren Zellgrenzen und höchstens zwei ganz von atypischen Epithelproliferaten ausgefüllten Gängen. Die Summe der Durchmesser aller betroffenen Lumina in einer duktulolobulären Einheit (TDLUs) nicht mehr als 2 mm. Proliferationen größer 2 mm oder mehr als zwei komplett ausgefüllte Gänge werden als DCIS (low-grade) bezeichnet.
- **Indikator- / Vorläuferläsion:** Ipsi- und kontralateral erhöhtes Brustkrebsrisiko: RR 3 - 5-fach nach 10 Jahren.
- Besonders hohes Risiko für MaCa bei zusätzlich BIRADS IV/V und hohem Brustvolumen.


1. Calhoun BC, Collins LC. Recommendations for excision following core needle biopsy of the breast: a contemporary evaluation of the literature. *Histopathology*. 2016;68(1):138-151. doi:10.1111/his.12852.
2. Co M, Kwong A, Shek T. Factors affecting the under-diagnosis of atypical ductal hyperplasia diagnosed by core needle biopsies - A 10-year retrospective study and review of the literature. *Int J Surg*. 2018;49:27-31. doi:10.1016/j.ijsu.2017.11.005.
3. Clauser P, Marino MA, Baltzer PAT, Bazzocchi M, Zuiani C. Management of atypical lobular hyperplasia, atypical ductal hyperplasia, and lobular carcinoma in situ. *Expert Rev Anticancer Ther*. 2016;16(3):335-346. doi:10.1586/14737140.2016.1143362
4. Degnim AC, Dupont WD, Radisky DC et al. Extent of atypical hyperplasia stratifies breast cancer risk in 2 independent cohorts of women. *Cancer*. 2016 Oct;122(19):2971-8.
5. Ellis IO. Intraductal proliferative lesions of the breast: morphology, associated risk and molecular biology. *Mod Pathol*. 2010 May 1;23 Suppl 2:S1-7.
6. Kader T, Hill P, Rakha EA, Campbell IG, Gorringer KL. Atypical ductal hyperplasia: update on diagnosis, management, and molecular landscape. *Breast Cancer Res*. 2018;20(1):39-11. doi:10.1186/s13058-018-0967-1.
7. Hartmann LC, Degnim AC, Santen RJ et al. Atypical hyperplasia of the breast--risk assessment and management options. *N Engl J Med*. 2015;372(1):78-89. doi:10.1056/NEJMSr1407164.
8. Howard-Mcnatt M. Atypical Ductal Hyperplasia: What Is the Current Risk for Developing Breast Cancer? *JAMA Oncol*. 2017;3(1):20-

21. doi:10.1001/jamaoncol.2016.3136.
9. Kader T, Hill P, Rakha EA, Campbell IG, Gorringer KL. Atypical ductal hyperplasia: update on diagnosis, management, and molecular landscape. *Breast Cancer Res.* 2018;20(1):39–11. doi:10.1186/s13058-018-0967-1.
10. Racz JM, Degnim AC. When Does Atypical Ductal Hyperplasia Require Surgical Excision? *Surg Oncol Clin N Am.* 2018;27(1):23-32. doi:10.1016/j.soc.2017.07.011.
11. Sinn HP, Flechtenmacher C, Aulmann S. Diagnostik benigner duktaler Epithelproliferationen der Mamma in der Stanzbiopsie. *Der Pathologe.* 2014;35(1):18-25. doi:10.1007/s00292-013-1886-7.

Strategie nach Diagnose einer ADH in der Biopsie			
	Oxford		
	LoE	GR	AGO
<b>ADH in Stanz- / Vakuumbiopsie:</b>			
▪ Offene Exzisionsbiopsie	3a	C	++
▪ Offene Exzisionsbiopsie verzichtbar, wenn folgende Voraussetzungen erfüllt sind:	5a	C	+/-
a) Kein radiologischer Herdbefund			
b) Fokale Läsion ( $\leq 2$ TDLU*) in Vakuumbiopsie und			
c) Suspekte Läsion in der Bildgebung komplett entfernt			
<b>ADH im Resektionsrand in offener PE:</b>			
▪ Keine Nachresektion, wenn die Veränderung ein intraduktales oder invasives Karzinom begleitet	3a	C	++
* TDLU = terminale duktulo-lobuläre Einheit (unit)			

1. Allison, K. H., Rendi, M. H. et al. (2016). Histological features associated with diagnostic agreement in atypical ductal hyperplasia of the breast: illustrative cases from the B-Path study. *Histopathology*, 69(6), 1028–1046. <http://doi.org/10.1111/his.13035>
2. Hartmann, L. C., Degnim, A. C., Santen et al. (2015). Atypical hyperplasia of the breast--risk assessment and management options. *The New England Journal of Medicine*, 372(1), 78–89. <http://doi.org/10.1056/NEJMSr1407164>
3. Hayes B et al: Correlation of needle core biopsy with excision histology in screen-detected B3 lesions: the Merrion Breast Screening Unit experience. *J Clin Pathol* 2009; 62:1136-1140.
4. Houry, T., Chen, X., Wang, D. et al. (2015). Nomogram to predict the likelihood of upgrade of atypical ductal hyperplasia diagnosed on a core needle biopsy in mammographically detected lesions. *Histopathology*, 67(1), 106–120. <http://doi.org/10.1111/his.12635>
5. Lewin AA, Mercado CL. Atypical Ductal Hyperplasia and Lobular Neoplasia: Update and Easing of Guidelines. *Am J Roentgenol*. December 2019;1-11. doi:10.2214/AJR.19.21991.
6. Li, S., Liu, J., Yang, Y et al. (2014). Impact of atypical hyperplasia at margins of breast-conserving surgery on the recurrence of breast cancer. *Journal of Cancer Research and Clinical Oncology*, 140(4), 599–605. <http://doi.org/10.1007/s00432-014-1597-3>
7. McGhan, L. J., Pockaj, B. A., Wasif, N. et al. (2012). Atypical ductal hyperplasia on core biopsy: an automatic trigger for excisional biopsy? *Annals of Surgical Oncology*, 19(10), 3264–3269. <http://doi.org/10.1245/s10434-012-2575-0>
8. Menes TS, Rosenberg R, Balch S et al.: Upgrade of high-risk breast lesions detected on mammography in the Breast Cancer Surveillance Consortium. *Am J Surg*. 2014 Jan;207(1):24-31.

9. Mesurolle, B., Perez, J. C. H., Azzumea, F. et al. (2014). Atypical ductal hyperplasia diagnosed at sonographically guided core needle biopsy: frequency, final surgical outcome, and factors associated with underestimation. *American Journal of Roentgenology*, 202(6), 1389–1394. <http://doi.org/10.2214/AJR.13.10864>
10. Racz JM, Degnim AC (2018) When Does Atypical Ductal Hyperplasia Require Surgical Excision? *Surg Oncol Clin N Am*. 27:23-32. doi: 10.1016/j.soc.2017.07.011.
11. Sutton T, Farinola M, Johnson N, Garreau JR (2018) Atypical ductal hyperplasia: Clinicopathologic factors are not predictive of upgrade after excisional biopsy. *Am J Surg*. pii: S0002-9610(18)31431-4. doi: 10.1016/j.amjsurg.2018.12.020. [Epub ahead of print]
12. Youn, I., Kim, M. J., Moon, H. J. et al. (2014). Absence of Residual Microcalcifications in Atypical Ductal Hyperplasia Diagnosed via Stereotactic Vacuum-Assisted Breast Biopsy: Is Surgical Excision Obviated? *Journal of Breast Cancer*, 17(3), 265–269. <http://doi.org/10.4048/jbc.2014.17.3.265>
13. Yu, C.-C., Ueng, S.-H., Cheung, Y.-C. et al. (2015). Predictors of Underestimation of Malignancy after Image-Guided Core Needle Biopsy Diagnosis of Flat Epithelial Atypia or Atypical Ductal Hyperplasia. *The Breast Journal*, 21(3), 224–232. <http://doi.org/10.1111/tbj.12389>.
14. Michaels AY, Ginter PS, Dodelzon K, et al. High Risk Lesions by MRI Guided Core Biopsy: Upgrade Rates of Surgical Excision and Implications for Management *AJR Am J Roentgenol*. 2021 Mar;216(3):622-632
15. Lucioni M, Rossi C, Lomoro P, et al. positive Predictive Value for Malignancy of uncertain malignant Potential (B3) Lesions diagnosed on vacuum Assisted Biopsy (VAB): is Surgery Still recommended? *Eur Radiol*. 2021 Feb;31(2):920-927.



© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.  
Guidelines Breast  
Version 2022.1D

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN

## Lobuläre intraepitheliale Neoplasie (LIN)

- Umfasst:
  - Atypische lobuläre Hyperplasie (ALH)
  - Klassisches lobuläres Carcinoma in situ (klassische LIN)
  - Nicht-klassisches lobuläres Carcinoma in situ (nicht-klassische LIN)
- Eine Einteilung in LIN 1 - 3 ist prognostisch nicht ausreichend validiert
- Nicht-klassische LIN (pleomorphe LIN, floride LIN) werden als prämaligne klassifiziert → B5a
- Indikator- / Vorläufer-Läsion:  
Ipsi- und kontralateral erhöhtes Brustkrebsrisiko:  
7-fach nach 10 Jahren

1. Wen HY, Brogi E. Lobular Carcinoma In Situ. Surg Pathol Clin. 2018 Mar;11(1):123–45.
2. Pinder SE, Shaaban AM. In situ lobular proliferations of the breast. Diagnostic Histopathology. Elsevier Ltd; 2018 Feb 1;24(2):58–63.
3. Ginter PS, D'Alfonso TM. Current Concepts in Diagnosis, Molecular Features, and Management of Lobular Carcinoma In Situ of the Breast With a Discussion of Morphologic Variants. Arch Pathol Lab Med. 2017 Dec;141(12):1668–78.
4. Pravettoni G, Yoder WR, Riva S et al.: Eliminating "ductal carcinoma in situ" and "lobular carcinoma in situ" (DCIS and LCIS) terminology in clinical breast practice: The cognitive psychology point of view. Breast. 2016 Feb;25:82–5.
5. Calhoun BC, Collins LC. Recommendations for excision following core needle biopsy of the breast: a contemporary evaluation of the literature. Histopathology. 2016 Jan;68(1):138–51.
6. Ginter, P. S., & D'Alfonso, T. M. (2017). Current Concepts in Diagnosis, Molecular Features, and Management of Lobular Carcinoma In Situ of the Breast With a Discussion of Morphologic Variants. Archives of Pathology & Laboratory Medicine, 141(12), 1668–1678. <http://doi.org/10.5858/arpa.2016-0421-RA>
7. Hussain, M., & Cunnick, G. H. (2011). Management of lobular carcinoma in-situ and atypical lobular hyperplasia of the breast--a review. European Journal of Surgical Oncology : the Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology, 37(4), 279–289. <http://doi.org/10.1016/j.ejso.2011.01.009>
8. Hwang, H., Sullivan, M. E., & Susnik, B. (2010). Lobular neoplasia. Diagnostic Histopathology, 16(7), 337–344. <http://doi.org/10.1016/j.mpdhp.2010.03.016>

9. Jorns, J., Sabel, M. S., & Pang, J. C. (2014). Lobular neoplasia: morphology and management. *Archives of Pathology & Laboratory Medicine*, 138(10), 1344–1349. <http://doi.org/10.5858/arpa.2014-0278-CC>
10. Pinder S, Provenzano E, Reis-Filho J. Lobular in situ neoplasia and columnar cell lesions: diagnosis in breast core biopsies and implications for management. *Pathology*. 2007 Mar 31;39(2):208–16.
11. Sinn, H. P., Helmchen, B., Heil, J. et al. (2014). Lobuläre Neoplasie und invasives lobuläres Mammakarzinom. *Der Pathologe*, 35(1), 45–53. <http://doi.org/10.1007/s00292-013-1840-8>

Statement: Indicator-/ precursor lesion

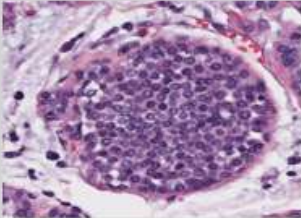
1. Ansquer Y, Delaney S, Santulli P et al. Risk of invasive breast cancer after lobular intra-epithelial neoplasia: review of the literature. *Eur J Surg Oncol*. 2010 Jul;36(7):604–9.
2. Chuba PJ, Hamre MR, Yap J, et al. Bilateral risk for subsequent breast cancer after lobular carcinoma-in-situ: analysis of surveillance, epidemiology, and end results data. *J Clin Oncol*. 2005 Aug 20;23(24):5534–41.
3. Nakhli 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*. Springer International Publishing; 2016 Mar;23(3):722–8.



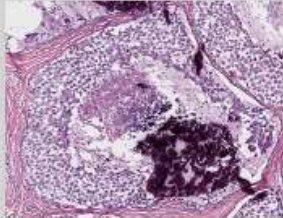
© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DGK e.V.  
Guidelines Breast  
Version 2022.1D

www.ago-online.de

## Klassische LIN und Varianten der LIN (nicht-klassisches LCIS)



**Klass. LIN**



**LIN mit Komedonekrose**




**Floride LIN**



**Pleomorphe LIN**

1. Brogi, E., Murray, M. P., & Corben, A. D. (2010). Lobular carcinoma, not only a classic. *Breast Journal*, 16 Suppl 1, S10–4.  
<http://doi.org/10.1111/j.1524-4741.2010.00994.x>
2. Ginter, P. S., & D'Alfonso, T. M. (2017). Current Concepts in Diagnosis, Molecular Features, and Management of Lobular Carcinoma In Situ of the Breast With a Discussion of Morphologic Variants. *Archives of Pathology & Laboratory Medicine*, 141(12), 1668–1678.  
<http://doi.org/10.5858/arpa.2016-0421-RA>
3. Jorns, J., Sabel, M. S., & Pang, J. C. (2014). Lobular neoplasia: morphology and management. *Archives of Pathology & Laboratory Medicine*, 138(10), 1344–1349. <http://doi.org/10.5858/arpa.2014-0278-CC>
4. Shin SJ, Lal A, De Vries S et al.: Florid lobular carcinoma in situ: molecular profiling and comparison to classic lobular carcinoma in situ and pleomorphic lobular carcinoma in situ. *Hum Pathol*. 2013;44(10):1998-2009.
5. Sinn, H. P., Helmchen, B., Heil, J. et al. (2014). Lobuläre Neoplasie und invasives lobuläres Mammakarzinom. *Der Pathologe*, 35(1), 45–53. <http://doi.org/10.1007/s00292-013-1840-8>





© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.  
Guidelines Breast  
Version 2022.1D

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN

## LIN mit hohem Risiko

- **Nicht-klassisches LCIS:**
  - Pleomorphes LCIS: höhergradige zelluläre Atypien, häufig Befall der Gänge mit Komedotyp-Nekrosen und Mikroverkalkungen
  - Florides LCIS: Befall zahlreicher Läppchen mit maximaler Distension bis Konfluenz und Übergreifen auf Duktuli und benachbarter TDLU
- **Mikroinvasion bei ILC\*:**
  - klass. LCIS: n = 11
  - florides LCIS: n = 4
  - pleomorphes LCIS: n = 1

\* Ross DS. Am J Surg Pathol 2011 35: 750–6.

### Statement: Pleomorphic lobular carcinoma in situ (PLCIS)

1. Nakhli F, Harrison BT, Giess CS, et al. Evaluating the Rate of Upgrade to Invasive Breast Cancer and/or Ductal Carcinoma In Situ Following a Core Biopsy Diagnosis of Non-classic Lobular Carcinoma In Situ. *Ann Surg Oncol*. 2019;26(1):55-61. doi:10.1245/s10434-018-6937-0.
2. Desai AA, Jimenez RE, Hoskin TL, Day CN, Boughey JC, Hieken TJ. Treatment Outcomes for Pleomorphic Lobular Carcinoma In Situ of the Breast. *Ann Surg Oncol*. 2018;25(10):3064-3068. doi:10.1245/s10434-018-6591-6.
3. Guo T, Wang Y, Shapiro N, Fineberg S. Pleomorphic Lobular Carcinoma in Situ Diagnosed by Breast Core Biopsy: Clinicopathologic Features and Correlation With Subsequent Excision. *Clinical breast cancer*. 2018;18(4):e449-e454. doi:10.1016/j.clbc.2017.10.004.
4. Altundag K. Uncertainties in the management of pleomorphic lobular carcinoma in situ of the breast still remain. *J BUON*. 2018;23(1):273. doi:10.1016/j.clbc.2017.10.004.
5. De Brot M, Koslow-Mautner S, Muhsen S, et al. Pleomorphic lobular carcinoma in situ of the breast: a single institution experience with clinical follow-up and centralized pathology review. *Breast Cancer Res Treat*. 2017;165(2):411-420. doi:10.1007/s10549-017-4334-1.
6. Flanagan MR, Rendi MH, Calhoun KE et al.: Pleomorphic Lobular Carcinoma In Situ: Radiologic-Pathologic Features and Clinical Management. *Ann Surg Oncol*. 2015;22(13):4263-4269. doi:10.1245/s10434-015-4552-x.
7. Khoury T, Karabakhtsian RG, Mattson D, et al. Pleomorphic lobular carcinoma in situ of the breast: clinicopathological review of 47



cases. *Histopathology*. 2014;64(7):981-993. doi:10.1111/his.12353.

8. Masannat YA, Bains SK, Pinder SE, et al. Challenges in the management of pleomorphic lobular carcinoma in situ of the breast. *Breast*. 2013;22(2):194-196. doi:10.1016/j.breast.2013.01.003.

#### Statement: Florid lobular carcinoma in situ (FLCIS)

1. Singh K, Paquette C, Kalife ET, et al. Evaluating agreement, histological features, and relevance of separating pleomorphic and florid lobular carcinoma in situ subtypes. *Hum Pathol*. 2018;78:163-170. doi:10.1016/j.humpath.2018.04.026.
2. Graziano L, Bitencourt AGV, Guatelli CS, et al. Lobular Carcinoma in Situ with Atypical Mass Presentation: a Case Report. *Rev Bras Ginecol Obstet*. 2016;38(2):112-116. doi:10.1055/s-0035-1571174.
3. Calhoun BC, Collins LC. Recommendations for excision following core needle biopsy of the breast: a contemporary evaluation of the literature. *Histopathology*. 2016;68(1):138-151. doi:10.1111/his.12852.
4. Shin SJ, Lal A, De Vries S, et al. Florid lobular carcinoma in situ: molecular profiling and comparison to classic lobular carcinoma in situ and pleomorphic lobular carcinoma in situ. *Hum Pathol*. 2013;44(10):1998-2009. doi:10.1016/j.humpath.2013.04.004.
5. Christiano JG, Duncan LD, Bell JL. Lobular carcinoma in situ of the breast presenting as a discrete mass. *Am Surg*. 2012;78(1):E38-E40.
6. Bagaria SP, Shamonki J, Kinnaird M, et al. The florid subtype of lobular carcinoma in situ: marker or precursor for invasive lobular carcinoma? *Ann Surg Oncol*. 2011;18(7):1845-1851. doi:10.1245/s10434-011-1563-0.
7. Ross DS, Hoda SA. Microinvasive (T1mic) lobular carcinoma of the breast: clinicopathologic profile of 16 cases. *The American journal of surgical pathology*. 2011;35(5):750-756. doi:10.1097/PAS.0b013e318212acd3.
8. Alvarado-Cabrero I, Picón Coronel G, Valencia Cedillo R, et al. Florid lobular intraepithelial neoplasia with signet ring cells, central necrosis and calcifications: a clinicopathological and immunohistochemical analysis of ten cases associated with invasive lobular carcinoma. *Arch Med Res*. 2010;41(6):436-441. doi:10.1016/j.arcmed.2010.08.010.

#### Statement: Lobular carcinoma in situ with microinvasion

1. Nemoto, T., Castillo, N., Tsukada, Y et al. (1998). Lobular carcinoma in situ with microinvasion. *Journal of Surgical Oncology*, 67(1), 41–46.
2. Howat AJ, Armour A, Ellis IO. Microinvasive lobular carcinoma of the breast. *Histopathology*. 2000;37(5):477-478.
3. Ross, D. S., & Hoda, S. A. (2011). Microinvasive (T1mic) lobular carcinoma of the breast: clinicopathologic profile of 16 cases. *The American Journal of Surgical Pathology*, 35(5), 750–756. <http://doi.org/10.1097/PAS.0b013e318212acd3>

Strategie nach Diagnose einer LIN			
	Oxford		
	LoE	GR	AGO
<b>LIN in Stanz- / Vakuumbiopsie</b> <ul style="list-style-type: none"> <li>Keine weitere Abklärung bei isoliertem oder inzidentellem Befund einer LIN (klassisches LCIS) mit Befall von <math>\leq 3</math> TDLU (terminale duktulolobuläre Einheit) in Vakuumbiopsie und Konkordanz mit der Bildgebung.</li> <li>Offene Exzisionsbiopsie bei pleomorpher LIN, florider LIN (LIN3), LIN mit Komedytypnekrosen, oder wenn Befund nach Korrelation mit der Bildgebung diskordant ist.</li> </ul>	2b	C	++
<b>LIN am Resektionsrand von BET</b> <ul style="list-style-type: none"> <li>Keine Nachresektion.</li> </ul>	2a	C	++
<b>Ausnahmen</b> <ul style="list-style-type: none"> <li>a) Pleomorphe, floride oder LIN mit Nekrosen</li> <li>b) Bildgebende Veränderung wurde nicht entfernt</li> </ul>			

#### LIN in core- / vacuum-assisted biopsy (LoE 2b)

1. Lewin AA, Mercado CL. Atypical Ductal Hyperplasia and Lobular Neoplasia: Update and Easing of Guidelines. *Am J Roentgenol*. 2020;214(2):265-275. doi:10.2214/AJR.19.21991.
2. Hoffman DI, Zhang PJ, Tchou J. Breast-conserving surgery for pure non-classic lobular carcinoma in situ: A single institution's experience. *Surgical Oncology*. 2019;28:190-194. doi:10.1016/j.suronc.2019.01.009.
3. Taylor LJ, Steiman J, Schumacher JR et al.: Surgical Management of Lobular Carcinoma In Situ: Analysis of the National Cancer Database. *Ann Surg Oncol*. 2018;25(8):2229-2234. doi:10.1245/s10434-018-6495-5.
4. Schmidt H, Arditi B, Wooster M, et al. Observation versus excision of lobular neoplasia on core needle biopsy of the breast. *Breast Cancer Res Treat*. 2018;168(3):649-654. doi:10.1007/s10549-017-4629-2.
5. Racz JM, Carter JM, Degnim AC. Lobular Neoplasia and Atypical Ductal Hyperplasia on Core Biopsy: Current Surgical Management Recommendations. *Ann Surg Oncol*. 2017;24(10):2848-2854. doi:10.1245/s10434-017-5978-0.
6. El-Khoury M, Sanchez LM, Lalonde L, et al. Is the outcome at surgery different when flat epithelial atypia and lobular neoplasia are found in association at biopsy? *Br J Radiol*. 2017;90(1072):20160750. doi:10.1259/bjr.20160750.
7. Fives C, O'Neill CJ, Murphy R, et al. When pathological and radiological correlation is achieved, excision of fibroadenoma with lobular neoplasia on core biopsy is not warranted. *Breast*. 2016;30:125-129. doi:10.1016/j.breast.2016.09.006.
8. Susnik B, Day D, Abeln E, et al. Surgical Outcomes of Lobular Neoplasia Diagnosed in Core Biopsy: Prospective Study of 316 Cases.

*Clinical breast cancer*. 2016;16(6):507-513. doi:10.1016/j.clbc.2016.06.003.

9. Calhoun BC, Collie AMB, Lott-Limbach AA, et al. Lobular neoplasia diagnosed on breast Core biopsy: frequency of carcinoma on excision and implications for management. *Ann Diagn Pathol*. 2016;25:20-25. doi:10.1016/j.anndiagpath.2016.07.009.
10. Sen LQC, Berg WA, Hooley RJ, et al. Core Breast Biopsies Showing Lobular Carcinoma In Situ Should Be Excised and Surveillance Is Reasonable for Atypical Lobular Hyperplasia. *Am J Roentgenol*. 2016;207(5):1132-1145. doi:10.2214/AJR.15.15425.
11. Obeng-Gyasi S, Ong C, Hwang ES. Contemporary management of ductal carcinoma in situ and lobular carcinoma in situ. *Chin Clin Oncol*. 2016;5(3):32. doi:10.21037/cco.2016.04.02.
12. Khoury T, Kumar PR, Li Z, et al. Lobular neoplasia detected in MRI-guided core biopsy carries a high risk for upgrade: a study of 63 cases from four different institutions. *Mod Pathol*. 2016;29(1):25-33. doi:10.1038/modpathol.2015.128.
13. Calhoun BC, Collins LC. Recommendations for excision following core needle biopsy of the breast: a contemporary evaluation of the literature. *Histopathology*. 2016;68(1):138-151. doi:10.1111/his.12852.
14. Renshaw AA, Gould EW. Long term clinical follow-up of atypical ductal hyperplasia and lobular carcinoma in situ in breast core needle biopsies. *Pathology*. 2016;48(1):25-29. doi:10.1016/j.pathol.2015.11.015.
15. Nakhli 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*. November 2015. doi:10.1245/s10434-015-4922-4.
16. Chester R, Bokinni O, Ahmed I, Kasem A. UK national survey of management of breast lobular carcinoma in situ. *Ann R Coll Surg Engl*. 2015;97(8):574-577. doi:10.1308/rcsann.2015.0037.
17. Allen S, Levine EA, Lesko N, Howard-Mcnatt M. Is Excisional Biopsy and Chemoprevention Warranted in Patients With Atypical Lobular Hyperplasia on Core Biopsy? *Am Surg*. 2015;81(9):876-878.
18. Morrow M, Schnitt SJ, Norton L. Current management of lesions associated with an increased risk of breast cancer. *Nat Rev Clin Oncol*. 2015;12(4):227-238. doi:10.1038/nrclinonc.2015.8.
19. Jorns J, Sabel MS, Pang JC. Lobular neoplasia: morphology and management. *Arch Pathol Lab Med*. 2014;138(10):1344-1349. doi:10.5858/arpa.2014-0278-CC.
20. Parkin CKE, Garewal S, Waugh P, et al. Outcomes of patients with lobular in situ neoplasia of the breast: the role of vacuum-assisted biopsy. *Breast*. 2014;23(5):651-655. doi:10.1016/j.breast.2014.06.016.
21. Meroni S, Stefano M, Bozzini AC, et al. Underestimation rate of lobular intraepithelial neoplasia in vacuum-assisted breast biopsy. *Eur Radiol*. 2014;24(7):1651-1658. doi:10.1007/s00330-014-3132-y.
22. Buckley ES, Webster F, Hiller JE et al: A systematic review of surgical biopsy for LCIS found at core needle biopsy - do we have the

answer yet? *Eur J Surg Oncol*. 2014;40(2):168-175. doi:10.1016/j.ejso.2013.10.024.

23. Atkins KA, Cohen MA, Nicholson B, et al., Atypical lobular hyperplasia and lobular carcinoma in situ at core breast biopsy: use of careful radiologic-pathologic correlation to recommend excision or observation. *Radiology*. 2013;269(2):340-347. doi:10.1148/radiol.13121730.
24. D'Alfonso TM, Wang K, Chiu Y-L, Shin SJ. Pathologic upgrade rates on subsequent excision when lobular carcinoma in situ is the primary diagnosis in the needle core biopsy with special attention to the radiographic target. *Arch Pathol Lab Med*. 2013;137(7):927-935. doi:10.5858/arpa.2012-0297-OA.
25. Hall FM. Lobular neoplasia: what does it mean and how should it be treated? *Am J Roentgenol*. 2013;200(5):W538. doi:10.2214/AJR.12.10123.
26. Murray MP, Luedtke C, Liberman L et al.: Classic lobular carcinoma in situ and atypical lobular hyperplasia at percutaneous breast core biopsy: outcomes of prospective excision. *Cancer*. 2013;119(5):1073-1079. doi:10.1002/cncr.27841.
27. Lewis JL, Lee DY, Tartter PI. The significance of lobular carcinoma in situ and atypical lobular hyperplasia of the breast. *Ann Surg Oncol*. 2012;19(13):4124-4128. doi:10.1245/s10434-012-2538-5.
28. Niell B, Specht M, Gerade B, Rafferty E. Is excisional biopsy required after a breast core biopsy yields lobular neoplasia? *Am J Roentgenol*. 2012;199(4):929-935. doi:10.2214/AJR.11.8447.
29. Shah-Khan MG, Geiger XJ, Reynolds C et al.: Long-term follow-up of lobular neoplasia (atypical lobular hyperplasia/lobular carcinoma in situ) diagnosed on core needle biopsy. *Ann Surg Oncol*. 2012;19(10):3131-3138. doi:10.1245/s10434-012-2534-9.
30. Shehata MN, Rahbar H, Flanagan MR et al. Risk for Upgrade to Malignancy After Breast Core Needle Biopsy Diagnosis of Lobular Neoplasia: A Systematic Review and Meta-Analysis. *J Am Coll Radiol*. 2020;17:1207-1219
31. Lee J, Ku GY, Lee H, et al. Lobular Carcinoma in Situ preoperative Biopsy and the Rate of Upgrade Cancer Res Treat. 2021 Dec 21. doi: 10.4143/crt.2021.864. Online ahead of print.
32. Karimi Z, Phillips J, Brook A, et al. Upgrade rates of pure radiology pathology concordant lobular neoplasia diagnosed on breast core needle biopsy: is surgical excision warranted? *Acad Radiol*. 2021 Oct 23:S1076-6332
33. Laws A, Katlin F, Nakhliis F, et al. Atypical lobular hyperplasia and classic lobular carcinoma in situ can safely be managed without surgical excision. *Ann Surg Oncol*. 2021 Sep 23. doi: 10.1245/s10434-021-10827-z. Online ahead of print. PMID: 34554341
34. van Maaren MC, Ávila AO, van Manen JG, et al. Trends in incidence treatment survival and subsequent breast cancer in lobular carcinoma in situ in the Netherlands : a population based analysis Breast. 2021 Oct;59:376-382.
35. Kunjummen J, Rodriguez K, Newell MS, et al. Management of Lobular neoplasia Found on Core Needle Biopsy Performed for Calcifications using precise Radiologic Pathologic Correlation. *AJR Am J Roentgenol*. 2021 Jun;216(6):1476-1485

LIN accompanying intraductal or invasive carcinoma in patients with BCT (LoE 2a)

1. Ciocca R: Presence of lobular carcinoma in situ does not increase recurrence in patients treated with breast-conserving therapy. Ann Surg Oncol 2008; 15:2263-2271



© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.  
Guidelines Breast  
Version 2022.1D

www.ago-online.de  
FORSCHEN  
LEHREN  
HEILEN

## Flache epitheliale Atypie (FEA)

- **Synonyme:** Kolumnarzellhyperplasie mit Atypien, Kolumnarzellmetaplasie mit Atypien
- **Differenzialdiagnose:**
  - ADH unterscheidet sich durch in das Ganglumen hineinreichende oder ausfüllende Epithelproliferate mit kribriformer oder mikropapillärer Architektur → **B3**
  - DCIS vom Clinging-Typ (clinging carcinoma G2 / G3) muss als intraduktales Karzinom eingestuft werden → **B5a**
- **Markerläsion:**  
FEA ist häufig mit Mikrokalk assoziiert und es besteht ein Zusammenhang mit dem Auftreten einer FEA und der Entdeckung von ADH und low-grade DCIS. Gehäuftes Vorkommen in dichter Brust (OR 1.3)  
Hohes Risiko für assoziiertes MaCa bei Vorliegen von ausgedehnten Kalzifikationen (auch wenn 75 % verblieben nach Biopsie), Alter > = 57 J., > 1cm in Bildgebung, > = 4 Foci.

### General

1. Racz JM, Carter JM, Degnim AC. Challenging Atypical Breast Lesions Including Flat Epithelial Atypia, Radial Scar, and Intraductal Papilloma. *Ann Surg Oncol*. 2017;24(10):2842-2847. doi:10.1245/s10434-017-5980-6.
2. Noël J-C, Buxant F, Engohan-Aloghe C. Immediate surgical resection of residual microcalcifications after a diagnosis of pure flat epithelial atypia on core biopsy: a word of caution. *Surgical Oncology*. 2010;19(4):243-246. doi:10.1016/j.suronc.2009.08.002.
3. Moinfar F. Flat ductal intraepithelial neoplasia of the breast: a review of diagnostic criteria, differential diagnoses, molecular-genetic findings, and clinical relevance--it is time to appreciate the Azzopardi concept! *Arch Pathol Lab Med*. 2009;133(6):879-892.
4. Böcker W, Hungermann D, Tio J, Weigel S, Decker T. Flache epitheliale Atypie. *Der Pathologe*. 2009;30(1):36-41. doi:10.1007/s00292-008-1123-y.
5. Turashvili G, Hayes M, Gilks B, Watson P, Aparicio S. Are columnar cell lesions the earliest histologically detectable non-obligate precursor of breast cancer? *Virchows Arch*. 2008;452(6):589-598.
6. Lerwill MF. Flat epithelial atypia of the breast. *Arch Pathol Lab Med*. 2008;132(4):615-621. doi:10.1043/1543-2165(2008)132[615:FEAOTB]2.0.CO;2.
7. Feeley L, Quinn C. Columnar cell lesions of the breast. *Histopathology*. 2008;52(1):11-19. doi:10.1111/j.1365-2559.2007.02890.x.
8. Pinder SE, Reis-Filho JS. Non-operative breast pathology: columnar cell lesions. *J Clin Pathol*. 2007;60(12):1307-1312. doi:10.1136/jcp.2006.040634.

Statement: Marker Lesion

1. Lamb LR, Bahl M, Gadd MA, et al. Flat Epithelial Atypia: Upgrade Rates and Risk-Stratification Approach to Support Informed Decision Making. *J Am Coll Surg*. 2017;225(6):696-701. doi:10.1016/j.jamcollsurg.2017.08.022.
2. Said SM, Visscher DW, Nassar A, et al. Flat epithelial atypia and risk of breast cancer: A Mayo cohort study. *Cancer*. 2015;121(10):1548-1555. doi:10.1002/cncr.29243.
3. Verschuur-Maes AHJ, Witkamp AJ et al.: Progression risk of columnar cell lesions of the breast diagnosed in core needle biopsies. *Int J Cancer*. 2011;129(11):2674-2680. doi:10.1002/ijc.25926.

Strategie nach Diagnose einer FEA			
	Oxford		
	LoE	GR	AGO
<b>FEA in Stanz- / Vakuumbiopsie:</b> <ul style="list-style-type: none"> <li>Offene Exzisionsbiopsie</li> <li>Auf offene Biopsie kann verzichtet werden unter folgenden Voraussetzungen: <ul style="list-style-type: none"> <li>Kleinerherdiger Befund (<math>\leq 2</math> TDLU* in Vakuumbiopsie) <u>und</u></li> <li>Entfernung oder weitgehend vollständige Entfernung der auffälligen Läsion in der Bildgebung (<math>\geq 90\%</math>)</li> </ul> </li> </ul>	2b	B	+
	2b	B	+
<b>FEA im Resektionsrand nach Exzisionsbiopsie:</b> <ul style="list-style-type: none"> <li>Keine Nachresektion, außer bei verbliebenem mammographischem Korrelat</li> </ul>	3b	C	++

\* TDLU = terminale duktulolobuläre Einheit

1. Grabenstetter A, Brennan S, Salagean ED et al.: Flat Epithelial Atypia in Breast Core Needle Biopsies With Radiologic-Pathologic Concordance: Is Excision Necessary? *The American journal of surgical pathology*. 2020;44(2):182-190. doi:10.1097/PAS.0000000000001385.
2. Alencherry E, Goel R, Gore S, et al. Clinical, imaging, and intervention factors associated with the upgrade of isolated flat epithelial atypia. *Clin Imaging*. 2019;54:21-24. doi:10.1016/j.clinimag.2018.11.008.
3. McCroskey Z, Sneige N, Herman CR, et al. Flat epithelial atypia in directional vacuum-assisted biopsy of breast microcalcifications: surgical excision may not be necessary. *Mod Pathol*. 2018;31(7):1097-1106. doi:10.1038/s41379-018-0035-5.
4. Chan PMY, Chotai N, Lai ES, et al. Majority of flat epithelial atypia diagnosed on biopsy do not require surgical excision. *Breast*. 2018;37:13-17. doi:10.1016/j.breast.2017.10.005.
5. Schiaffino S, Gristina L, Villa A, et al. Flat epithelial atypia: conservative management of patients without residual microcalcifications post-vacuum-assisted breast biopsy. *Br J Radiol*. 2018;91(1081):20170484. doi:10.1259/bjr.20170484.
6. Samples LS, Rendi MH, Frederick PD, et al. Surgical implications and variability in the use of the flat epithelial atypia diagnosis on breast biopsy specimens. *Breast*. 2017;34:34-43. doi:10.1016/j.breast.2017.04.004.
7. El-Khoury M, Sanchez LM, Lalonde L et al.: Is the outcome at surgery different when flat epithelial atypia and lobular neoplasia are found in association at biopsy? *Br J Radiol*. 2017;90(1072):20160750. doi:10.1259/bjr.20160750.
8. Acott AA, Mancino AT. Flat epithelial atypia on core needle biopsy, must we surgically excise? *Am J Surg*. 2016;212(6):1211-1213.




doi:10.1016/j.amjsurg.2016.09.019.

9. Berry JS, Trappey AF, Vreeland TJ, et al. Analysis of Clinical and Pathologic Factors of Pure, Flat Epithelial Atypia on Core Needle Biopsy to Aid in the Decision of Excision or Observation. *J Cancer*. 2016;7(1):1-6. doi:10.7150/jca.12781.
10. Maeda I, Kanemaki Y, Tozaki M, et al. Positive predictive value for malignancy of pure flat epithelial atypia diagnosis by percutaneous needle biopsy of the breast: management of FEA in ultrasonography. *Breast Cancer*. 2015;22(6):634-640. doi:10.1007/s12282-014-0530-6.
11. Yu C-C, Ueng S-H, Cheung Y-C, et al. Predictors of underestimation of malignancy after image-guided core needle biopsy diagnosis of flat epithelial atypia or atypical ductal hyperplasia. *Breast Journal*. 2015;21(3):224-232. doi:10.1111/tbj.12389.
12. Calhoun BC, Sobel A, White RL, et al. Management of flat epithelial atypia on breast core biopsy may be individualized based on correlation with imaging studies. *Mod Pathol*. 2015;28(5):670-676. doi:10.1038/modpathol.2014.159.
13. Dialani V, Venkataraman S, Frieling G et al.: Does isolated flat epithelial atypia on vacuum-assisted breast core biopsy require surgical excision? *Breast Journal*. 2014;20(6):606-614. doi:10.1111/tbj.12332.
14. Prowler VL, Joh JE, Acs G, et al. Surgical excision of pure flat epithelial atypia identified on core needle breast biopsy. *Breast*. 2014;23(4):352-356. doi:10.1016/j.breast.2014.01.013.
15. Villa A, Chiesa F, Massa T, et al. Flat epithelial atypia: comparison between 9-gauge and 11-gauge devices. *Clinical breast cancer*. 2013;13(6):450-454. doi:10.1016/j.clbc.2013.08.008.
16. Ceugnart L, Doualliez V, Chauvet MP, et al. Pure flat epithelial atypia: is there a place for routine surgery? *Diagn Interv Imaging*. 2013;94(9):861-869. doi:10.1016/j.diii.2013.01.011.
17. Becker AK, Gordon PB, Harrison DA, et al. Flat Ductal Intraepithelial Neoplasia 1A Diagnosed at Stereotactic Core Needle Biopsy: Is Excisional Biopsy Indicated? *Am J Roentgenol*. 2013;200(3):682-688. doi:10.2214/AJR.11.8090.
18. Khoumais NA, Scaranelo AM, Moshonov H, et al. Incidence of breast cancer in patients with pure flat epithelial atypia diagnosed at core-needle biopsy of the breast. *Ann Surg Oncol*. 2013;20(1):133-138. doi:10.1245/s10434-012-2591-0.
19. Biggar MA, Kerr KM, Erzetich LM, Bennett IC. Columnar cell change with atypia (flat epithelial atypia) on breast core biopsy-outcomes following open excision. *Breast Journal*. 2012;18(6):578-581. doi:10.1111/tbj.12039.
20. Bianchi S, Bendinelli B, Castellano I, et al. Morphological parameters of flat epithelial atypia (FEA) in stereotactic vacuum-assisted needle core biopsies do not predict the presence of malignancy on subsequent surgical excision. *Virchows Arch*. 2012;461(4):405-417. doi:10.1007/s00428-012-1279-y.
21. Uzoaru I, Morgan BR, Liu ZG, et al. Flat epithelial atypia with and without atypical ductal hyperplasia: to re-excise or not. Results of a 5-year prospective study. *Virchows Arch*. 2012;461(4):419-423. doi:10.1007/s00428-012-1312-1.

22. Verschuur-Maes AHJ, Witkamp AJ, de Bruin PC et al.: Progression risk of columnar cell lesions of the breast diagnosed in core needle biopsies. *Int J Cancer*. 2011;129(11):2674-2680. doi:10.1002/ijc.25926.
23. Peres A, Barranger E, Becette V et al.: Rates of upgrade to malignancy for 271 cases of flat epithelial atypia (FEA) diagnosed by breast core biopsy. *Breast Cancer Res Treat*. 2011;133(2):659-666. doi:10.1007/s10549-011-1839-x.
24. Rajan S, Sharma N, Dall BJG, Shaaban AM. What is the significance of flat epithelial atypia and what are the management implications? *J Clin Pathol*. 2011;64(11):1001-1004. doi:10.1136/jclinpath-2011-200176.
25. Noske A, Pahl S, Fallenberg E, et al. Flat epithelial atypia is a common subtype of B3 breast lesions and is associated with noninvasive cancer but not with invasive cancer in final excision histology. *Hum Pathol*. 2010;41(4):522-527. doi:10.1016/j.humpath.2009.09.005.
26. Graesslin O, Antoine M, Chopier J, et al. Histology after lumpectomy in women with epithelial atypia on stereotactic vacuum-assisted breast biopsy. *Eur J Surg Oncol*. 2010;36(2):170-175. doi:10.1016/j.ejso.2009.09.002.
27. Ingegnoli A, d'Aloia C, Frattaruolo A, et al. Flat epithelial atypia and atypical ductal hyperplasia: carcinoma underestimation rate. *Breast Journal*. 2010;16(1):55-59. doi:10.1111/j.1524-4741.2009.00850.x.
28. Aroner SA, Collins LC, Schnitt SJ et al.: Columnar cell lesions and subsequent breast cancer risk: a nested case-control study. *Breast Cancer Res*. 2010;12(4):R61. doi:10.1186/bcr2624.
29. Hayes BD, O'Doherty A, Quinn CM. Correlation of needle core biopsy with excision histology in screen-detected B3 lesions: the Merrion Breast Screening Unit experience. *J Clin Pathol*. 2009;62(12):1136-1140. doi:10.1136/jcp.2009.067280.
30. Piubello Q, Parisi A, Eccher A, Barbazeni G, Franchini Z, Iannucci A. Flat epithelial atypia on core needle biopsy: which is the right management? *Am J Surg Pathol*. 2009;33(7):1078-1084. doi:10.1097/PAS.0b013e31819d0a4d.
31. Chivukula M, Bhargava R, Tseng G, Dabbs DJ. Clinicopathologic implications of "flat epithelial atypia" in core needle biopsy specimens of the breast. *Am J Clin Pathol*. 2009;131(6):802-808. doi:10.1309/AJCPLDG6TT7VAHPH.
32. Jara-Lazaro AR, Tse GM-K, Tan PH. Columnar cell lesions of the breast: an update and significance on core biopsy. *Pathology*. 2009;41(1):18-27. doi:10.1080/00313020802563486.
33. Eby PR, Ochsner JE, Demartini WB et al.: Is surgical excision necessary for focal atypical ductal hyperplasia found at stereotactic vacuum-assisted breast biopsy? *Ann Surg Oncol*. 2008;15(11):3232-3238. doi:10.1245/s10434-008-0100-2.
34. Boulos FI, Dupont WD, Simpson JF, et al. Histologic associations and long-term cancer risk in columnar cell lesions of the breast: a retrospective cohort and a nested case-control study. *Cancer*. 2008;113(9):2415-2421. doi:10.1002/cncr.23873.
35. Collins LC, Achacoso NA, Nekhlyudov L, et al. Clinical and pathologic features of ductal carcinoma in situ associated with the presence of flat epithelial atypia: an analysis of 543 patients. *Mod Pathol*. 2007;20(11):1149-1155.

36. RA Wahab, SJ Lee MF Mulligan et al.: Upgrade Rate of Pure Flat Epithelial Atypia Diagnosed at Core Needle Biopsy: A Systematic Review and Meta-Analysis. Radiol Imaging Cancer 2021 Jan 22;3(1):e200116. doi: 10.1148/rycan.2021200116. eCollection 2021 Jan



© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DGK e.V.  
Guidelines Breast  
Version 2022.1D

www.ago-online.de

## Papillom

---

- **Umfasst:** Zentrales und peripheres Milchgangspapillom > 2 mm, Papillom mit Atypien (B3)
- **Abzugrenzen** von peripheren Mikropapillomen, von den TDLUs ausgehend, ≤ 2 mm, gelegentlich multipel
- Abzugrenzen vom Papillom mit DCIS, vom intraduktalen papillären Karzinom und dem gekapselten papillären Karzinom
- **Vorläufer-Läsion:**  
Assoziation mit in situ- oder invasiven Karzinomen (bis zu 6 % ohne Atypie bei konkordanter Bildgebung, bis 30 % mit Atypie), erhöhtes ipsilaterales Karzinomrisiko (bis zu 4,6 % und bis zu 13 % bei atypischen Papillomen).

1. World Health Organization: WHO Classification of Tumours of the Breast. Lokuhetty D, White VA, Watanabe R, Cree IA (Hrsg.) 2019.
2. Tse GM. Papillary lesions of the breast. *Diagnostic Histopathology*. 2018;24(2):64-70. doi:10.1016/j.mpdhp.2017.12.005.
3. Rakha EA, Ellis IO. Diagnostic challenges in papillary lesions of the breast. *Pathology*. 2018;50(1):100-110. doi:10.1016/j.pathol.2017.10.005.
4. Racz JM, Carter JM, Degnim AC. Challenging Atypical Breast Lesions Including Flat Epithelial Atypia, Radial Scar, and Intraductal Papilloma. *Ann Surg Oncol*. 2017;24(10):2842-2847. doi:10.1245/s10434-017-5980-6.
5. Agoumi M, Giambattista J, Hayes MM. Practical Considerations in Breast Papillary Lesions: A Review of the Literature. *Arch Pathol Lab Med*. 2016;140(8):770-790. doi:10.5858/arpa.2015-0525-RA.
6. Saladin C, Haueisen H, Kampmann G, et al. Lesions with unclear malignant potential (B3) after minimally invasive breast biopsy: evaluation of vacuum biopsies performed in Switzerland and recommended further management. *Acta Radiol*. 2016;57(7):815-821. doi:10.1177/0284185115610931.
7. Ni Y-B, Tse GM. Pathological criteria and practical issues in papillary lesions of the breast - a review. *Histopathology*. 2016;68(1):22-32. doi:10.1111/his.12866.
8. Länger F, Hille-Betz U, Kreipe H-H. Papilläre Läsionen der Mamma. *Der Pathologe*. 2014;35(1):36-44. doi:10.1007/s00292-013-1839-1.

Vorgehen nach Diagnose eines Papilloms			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>▪ <b>Solitäres Papillom ohne Atypien in Stanz- / Vakuumbiopsie</b> <ul style="list-style-type: none"> <li>▪ Keine weiteren Maßnahmen, wenn Biopsie ausreichend repräsentativ (100 mm<sup>2</sup>) und keine Diskordanz zur Bildgebung</li> </ul> </li> </ul>	2b	C	+
<ul style="list-style-type: none"> <li>▪ <b>Multiple Papillome</b> <ul style="list-style-type: none"> <li>▪ Offene Biopsie</li> </ul> </li> </ul>	3a	C	++
<ul style="list-style-type: none"> <li>▪ <b>Atypisches Papillom in Stanz- / Vakuumbiopsie</b> <ul style="list-style-type: none"> <li>▪ Offene Biopsie</li> </ul> </li> </ul>	3a	C	++
<ul style="list-style-type: none"> <li>▪ <b>Papillom am Rand von Resektaten</b> <ul style="list-style-type: none"> <li>▪ Keine verfügbaren Daten</li> </ul> </li> </ul>			

1. MacColl C, Salehi A, Parpia S et al.: Benign breast papillary lesions diagnosed on core biopsy: upgrade rate and risk factors associated with malignancy on surgical excision. *Virchows Arch.* 2019;475(6):701-707. doi:10.1007/s00428-019-02626-5.
2. Symbol B, Ricci A. Management of intraductal papilloma without atypia of the breast diagnosed on core biopsy: Size and sampling matter. *Breast Journal.* 2018;24(5):738-742. doi:10.1111/tbj.13052.
3. Crown A, Scovel L, Deal S et al.: Clinical and radiological follow-up rather than excisional biopsy is reasonable after complete papilloma excision at the time of core needle biopsy. *Breast Journal.* 2018;24(5):841-842. doi:10.1111/tbj.13058.
4. Khan S, Diaz A, Archer KJ, et al. Papillary lesions of the breast: To excise or observe? *Breast Journal.* 2018;24(3):350-355. doi:10.1111/tbj.12907.
5. Calhoun BC. Core Needle Biopsy of the Breast: An Evaluation of Contemporary Data. *Surg Pathol Clin.* 2018;11(1):1-16. doi:10.1016/j.path.2017.09.001.
6. Ahn SK, Han W, Moon H-G, et al. Management of benign papilloma without atypia diagnosed at ultrasound-guided core needle biopsy: Scoring system for predicting malignancy. *Eur J Surg Oncol.* 2018;44(1):53-58. doi:10.1016/j.ejso.2017.10.214.
7. Tran H-T, Mursleen A, Mirpour S et al.: Papillary Breast Lesions: Association with Malignancy and Upgrade Rates on Surgical Excision. *Am Surg.* 2017;83(11):1294-1297.
8. Armes JE, Galbraith C, Gray J, Taylor K. The outcome of papillary lesions of the breast diagnosed by standard core needle biopsy within a BreastScreen Australia service. *Pathology.* 2017;49(3):267-270. doi:10.1016/j.pathol.2016.12.346.

9. Moon SM, Jung HK, Ko KH et al.: Management of Clinically and Mammographically Occult Benign Papillary Lesions Diagnosed at Ultrasound-Guided 14-Gauge Breast Core Needle Biopsy. *J Ultrasound Med*. 2016;35(11):2325-2332. doi:10.7863/ultra.15.11049.
10. Jorns JM. Papillary Lesions of the Breast: A Practical Approach to Diagnosis. *Arch Pathol Lab Med*. 2016;140(10):1052-1059. doi:10.5858/arpa.2016-0219-RA.
11. Tatarian T, Sokas C, Rufail M, et al. Intraductal Papilloma with Benign Pathology on Breast Core Biopsy: To Excise or Not? *Ann Surg Oncol*. 2016;23(8):2501-2507. doi:10.1245/s10434-016-5182-7.
12. Kim S-Y, Kim E-K, Lee HS, et al. Asymptomatic Benign Papilloma Without Atypia Diagnosed at Ultrasonography-Guided 14-Gauge Core Needle Biopsy: Which Subgroup can be Managed by Observation? *Ann Surg Oncol*. 2016;23(6):1860-1866. doi:10.1245/s10434-016-5144-0.
13. Nakhli F, Ahmadiyah N, Lester SC et al.: Papilloma on core biopsy: excision vs. observation. *Ann Surg Oncol*. 2015;22(5):1479-1482. doi:10.1245/s10434-014-4091-x.
14. Glenn ME, Throckmorton AD, Thomison JB et al.: 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.
15. Yamaguchi R, Tanaka M, Tse GM, et al. Management of breast papillary lesions diagnosed in ultrasound-guided vacuum-assisted and core needle biopsies. *Histopathology*. 2015;66(4):565-576. doi:10.1111/his.12477.
16. Wang H, Tsang P, D'Cruz C, Clarke K. Follow-up of breast papillary lesion on core needle biopsy: experience in African-American population. *Diagn Pathol*. 2014;9(1):86. doi:10.1186/1746-1596-9-86.
17. McGhan LJ, Pockaj BA, Wasif N et al.: Papillary lesions on core breast biopsy: excisional biopsy for all patients? *Am Surg*. 2013;79(12):1238-1242.
18. Nayak A, Carkaci S, Gilcrease MZ, et al. Benign papillomas without atypia diagnosed on core needle biopsy: experience from a single institution and proposed criteria for excision. *Clinical breast cancer*. 2013;13(6):439-449. doi:10.1016/j.clbc.2013.08.007.
19. Shamonki J, Chung A, Huynh KT, et al. Management of papillary lesions of the breast: can larger core needle biopsy samples identify patients who may avoid surgical excision? *Ann Surg Oncol*. 2013;20(13):4137-4144. doi:10.1245/s10434-013-3191-3.
20. McGhan LJ, Pockaj BA, Wasif N et al.: Papillary lesions on core breast biopsy: excisional biopsy for all patients? *Am Surg*. 2013;79(12):1238-1242.
21. Wiratkapun C, Keeratitragoon T, Lertsithichai P, Chanplakorn N. Upgrading rate of papillary breast lesions diagnosed by core-needle biopsy. *Diagn Interv Radiol*. 2013;19(5):371-376. doi:10.5152/dir.2013.017.
22. Swapp RE, Glazebrook KN, Jones KN, et al. Management of benign intraductal solitary papilloma diagnosed on core needle biopsy. *Ann Surg Oncol*. 2013;20(6):1900-1905. doi:10.1245/s10434-012-2846-9.

23. Maxwell AJ, Mataka G, Pearson JM. Benign papilloma diagnosed on image-guided 14 G core biopsy of the breast: effect of lesion type on likelihood of malignancy at excision. *Clin Radiol*. 2013;68(4):383-387. doi:10.1016/j.crad.2012.06.136.
24. Kibil W, Hodorowicz-Zaniewska D, Popiela TJ, Kulig J. Vacuum-assisted core biopsy in diagnosis and treatment of intraductal papillomas. *Clinical breast cancer*. 2013;13(2):129-132. doi:10.1016/j.clbc.2012.09.018.
25. Koo JS, Han K, Kim MJ et al.: Can additional immunohistochemistry staining replace the surgical excision for the diagnosis of papillary breast lesions classified as benign on 14-gage core needle biopsy? *Breast Cancer Res Treat*. 2013;137(3):797-806. doi:10.1007/s10549-012-2403-z.
26. Wen X, Cheng W. Nonmalignant breast papillary lesions at core-needle biopsy: a meta-analysis of underestimation and influencing factors. *Ann Surg Oncol*. 2013;20(1):94-101. doi:10.1245/s10434-012-2590-1.
27. Fu CY, Chen TW, Hong ZJ, et al. Papillary breast lesions diagnosed by core biopsy require complete excision. *Eur J Surg Oncol*. 2012;38(11):1029-1035. doi:10.1016/j.ejso.2012.08.019.
28. Holley SO, Appleton CM, Farria DM, et al. Pathologic outcomes of nonmalignant papillary breast lesions diagnosed at imaging-guided core needle biopsy. *Radiology*. 2012;265(2):379-384. doi:10.1148/radiol.12111926.
29. Shouhed D, Amersi FF, Spurrier R, et al. Intraductal papillary lesions of the breast: clinical and pathological correlation. *Am Surg*. 2012;78(10):1161-1165.
30. Brennan SB, Corben A, Liberman L, et al. Papilloma diagnosed at MRI-guided vacuum-assisted breast biopsy: is surgical excision still warranted? *Am J Roentgenol*. 2012;199(4):W512-W519. doi:10.2214/AJR.12.8750.
31. Destounis S, Seifert P, Somerville P, et al. Underestimation of papillary breast lesions by core biopsy: correlation to surgical excision. *Breast Cancer*. 2012;21(2):128-134. doi:10.1007/s12282-012-0361-2.
32. Jakate K, De Brot M, Goldberg F, et al. Papillary lesions of the breast: impact of breast pathology subspecialization on core biopsy and excision diagnoses. *The American journal of surgical pathology*. 2012;36(4):544-551. doi:10.1097/PAS.0b013e318243fa00.
33. Lu Q, Tan EY, Ho B, Chen JJC, Chan PMY. Surgical excision of intraductal breast papilloma diagnosed on core biopsy. *ANZ J Surg*. 2012;82(3):168-172. doi:10.1111/j.1445-2197.2011.05969.x.
34. Rizzo M, Linebarger J, Lowe MC, et al. Management of papillary breast lesions diagnosed on core-needle biopsy: clinical pathologic and radiologic analysis of 276 cases with surgical follow-up. *J Am Coll Surg*. 2012;214(3):280-287. doi:10.1016/j.jamcollsurg.2011.12.005.
35. Polat DS, Knippa EE, Ganti R et al. Benign breast papillomas without atypia diagnosed with core needle biopsy: Outcome of surgical excision and imaging follow-up. *Eur J Radiol*. 2020;131:109237. doi: 10.1016/j.ejrad.2020.109237
36. S A Rahbar, S Sack, K E Larson, et al. Multidisciplinary Review of Intraductal Papilloma of the Breast can Identify Patients who may

Omit Surgical Excision *Ann Surg Oncol* 2021 Oct;28(10):5768-5774.

37. A. Beck, SL Fu, J Liao et al.: Risk management recommendations and patient acceptance vary with high-risk breast lesions *Am J Surg*. 2022 Jan;223(1):94-100.
38. Nakhli F, Baker GM, Pilewskie M, Gelman R, Calvillo KZ, Ludwig K, McAuliffe PF, Willey S, Rosenberger LH, Parker C, Gallagher K, Jacobs L, Feldman S, Lange P, DeSantis SD, Schnitt SJ, King TA The Incidence of Adjacent Synchronous Invasive carcinoma and /or DCIS in Patients with intraductal Papilloma without Atypia on Core Biopsy. Results from a Prospective Multiinstitutional Registry (TBCRC 034) *Ann Surg Oncol*. 2021 May;28(5):2573-2578.
39. Lee SJ, Wahab RA, Sobel LD et al.: Analysis of 612 Benign Papillomas Diagnosed at Core Biopsy: Rate of Upgrade to Malignancy, Factors Associated With Upgrade, and a Proposal for Selective Surgical Excision *AJR* 2021; 217:1299–1312



© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2022.1D

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN

## Radiäre sklerosierende Läsion

- **Benigne pseudoinfiltrierende Läsion mit zentralem fibroelastischem Kern und radiärem Aufbau.**
- **Beinhaltet:**
  - radiäre Narbe
  - komplexe sklerosierende Läsion (> 1 cm)
- **Zusätzlicher Risikofaktor bei Pat. mit benignen Epithelhyperplasien (proliferierender Mastopathie)**
- **Risiko für Upgrade in offener PE nach Diagnose einer radiär-sklerosierenden Läsion in der Stanzbiopsie in Abhängigkeit der Größe der Nadel (CNB) bzw. Methode (VAB) und zusätzlicher Atypie: 1–18 %**

1. Rakha E, Beca F, D'Andrea M, et al. Outcome of radial scar/complex sclerosing lesion associated with epithelial proliferations with atypia diagnosed on breast core biopsy: results from a multicentric UK-based study. *J Clin Pathol.* 2019;72(12):800-804. doi:10.1136/jclinpath-2019-205764.
2. Farshid G, Buckley E. Meta-analysis of upgrade rates in 3163 radial scars excised after needle core biopsy diagnosis. *Breast Cancer Res Treat.* 2019;174(1):165-177. doi:10.1007/s10549-018-5040-3.
3. Chou WYY, Veis DJ, Aft R. Radial scar on image-guided breast biopsy: is surgical excision necessary? *Breast Cancer Res Treat.* 2018;170(2):313-320. doi:10.1007/s10549-018-4741-y.
4. Salemis NS, Katikaridis I, Birpanagos C, et al. Complex radial sclerosing lesion of the breast-A great cancer mimicker. *Breast Journal.* 2018;24(3):408-410. doi:10.1111/tbj.12917.
5. Racz JM, Carter JM, Degnim AC. Challenging Atypical Breast Lesions Including Flat Epithelial Atypia, Radial Scar, and Intraductal Papilloma. *Ann Surg Oncol.* 2017;24(10):2842-2847. doi:10.1245/s10434-017-5980-6.
6. Ferreira AI, Borges S, Sousa A, et al. Radial scar of the breast: Is it possible to avoid surgery? *Eur J Surg Oncol.* 2017;43(7):1265-1272. doi:10.1016/j.ejso.2017.01.238.
7. Donaldson AR, Sieck L, Booth CN, et al. Radial scars diagnosed on breast core biopsy: Frequency of atypia and carcinoma on excision and implications for management. *Breast.* 2016;30:201-207. doi:10.1016/j.breast.2016.06.007.
8. Leong RY, Kohli MK, Zeizafoun N et al.: Radial Scar at Percutaneous Breast Biopsy That Does Not Require Surgery. *J Am Coll Surg.*

2016;223(5):712-716. doi:10.1016/j.jamcollsurg.2016.08.003.

9. Kalife ET, Lourenco AP, Baird GL, et al. Clinical and Radiologic Follow-up Study for Biopsy Diagnosis of Radial Scar/Radial Sclerosing Lesion without Other Atypia. *Breast Journal*. 2016;22(6):637-644. doi:10.1111/tbj.12645.
10. Hooda S, Li Z. Surgical excision outcome after radial scar without atypical proliferative lesion on breast core needle biopsy: a single institutional analysis. *Ann Diagn Pathol*. 2016;21:35-38. doi:10.1016/j.anndiagpath.2015.11.004.
11. Li Z, Ranade A, Zhao C. Pathologic findings of follow-up surgical excision for radial scar on breast core needle biopsy. *Hum Pathol*. 2016;48:76-80. doi:10.1016/j.humpath.2015.06.028.
12. Matrai C, D'Alfonso TM, Pharmer L.: Advocating Nonsurgical Management of Patients With Small, Incidental Radial Scars at the Time of Needle Core Biopsy: A Study of 77 Cases. *Arch Pathol Lab Med*. 2015;139(9):1137-1142. doi:10.5858/arpa.2014-0550-OA.
13. Conlon N, D'Arcy C, Kaplan JB, et al. Radial Scar at Image-guided Needle Biopsy: Is Excision Necessary? *The American journal of surgical pathology*. 2015;39(6):779-785. doi:10.1097/PAS.0000000000000393.
14. Dominguez A, Durando M, Mariscotti G, et al. Breast cancer risk associated with the diagnosis of a microhistological radial scar (RS): retrospective analysis in 10 years of experience. *Radiol Med*. 2015;120(4):377-385. doi:10.1007/s11547-014-0456-2.
15. Nassar A, Connors AL, Celik B et al.: Radial scar/complex sclerosing lesions: a clinicopathologic correlation study from a single institution. *Ann Diagn Pathol*. 2015;19(1):24-28. doi:10.1016/j.anndiagpath.2014.12.003.
16. Aroner SA, Collins LC, Connolly JL, et al. Radial scars and subsequent breast cancer risk: results from the Nurses' Health Studies. *Breast Cancer Res Treat*. 2013;139(1):277-285. doi:10.1007/s10549-013-2535-9.
17. Andacoglu O, Kanbour-Shakir A, Teh Y-C, et al. Rationale of excisional biopsy after the diagnosis of benign radial scar on core biopsy: a single institutional outcome analysis. *Am J Clin Oncol*. 2013;36(1):7-11. doi:10.1097/COC.0b013e3182354a3f.
18. Tóth D, Sebő É, Sarkadi L, et al.: Role of core needle biopsy in the treatment of radial scar. *Breast*. 2012;21(6):761-763. doi:10.1016/j.breast.2012.02.009.
19. Bianchi S, Giannotti E, Vanzì E, et al. Radial scar without associated atypical epithelial proliferation on image-guided 14-gauge needle core biopsy: analysis of 49 cases from a single-centre and review of the literature. *Breast*. 2012;21(2):159-164. doi:10.1016/j.breast.2011.09.005.
20. Morgan C, Shah ZA, Hamilton R, et al. The radial scar of the breast diagnosed at core needle biopsy. *Proc (Bayl Univ Med Cent)*. 2012;25(1):3-5.
21. Bunting DM, Steel JR, Holgate CS, Watkins RM. Long term follow-up and risk of breast cancer after a radial scar or complex sclerosing lesion has been identified in a benign open breast biopsy. *Eur J Surg Oncol*. 2011;37(8):709-713. doi:10.1016/j.ejso.2011.04.011.
22. Eusebi V, Millis RR. Epitheliosis, infiltrating epitheliosis, and radial scar. *Semin Diagn Pathol*. 2010;27(1):5-12.

doi:10.1053/j.semdp.2009.12.008.

23. Loane J. Benign sclerosing lesions of the breast. *Diagnostic Histopathology*. 2009;15(8):395-401. doi:10.1016/j.mpdhp.2009.05.003.
24. Manfrin E, Remo A, Falsirollo F et al.: Risk of neoplastic transformation in asymptomatic radial scar. Analysis of 117 cases. *Breast Cancer Res Treat*. 2008;107(3):371-377. doi:10.1007/s10549-007-9569-9.
25. Douglas-Jones AG, Denson JL, Cox AC et al.: Radial scar lesions of the breast diagnosed by needle core biopsy: analysis of cases containing occult malignancy. *J Clin Pathol*. 2007;60(3):295-298. doi:10.1136/jcp.2006.037069.
26. Doyle E, Banville N, Quinn C, et al. Radial scars/complex sclerosing lesions and malignancy in a screening programme: incidence and histological features revisited. *Histopathology*. 2007;50(5):607-614
27. Sanders ME, Page DL, Simpson JF et al.: Interdependence of radial scar and proliferative disease with respect to invasive breast carcinoma risk in patients with benign breast biopsies. *Cancer*. 2006;106(7):1453-1461. doi:10.1002/cncr.21730.

Vorgehen bei radiärer Narbe, komplexer sklerosierender Läsion (CSL)			
	Oxford		
	LoE	GR	AGO
<b>▪ Radiäre Narbe / CSL in Stanz- oder Vakuumbiopsie:</b> <ul style="list-style-type: none"> <li>▪ Auf offene Biopsie kann verzichtet werden, wenn Läsion klein (<math>\leq 5</math> mm) oder in der Vakuumbiopsie bereits vollständig oder weitgehend vollständig enthalten</li> </ul>	5a	C	+
<b>▪ Radiäre Narbe / CSL im Resektionsrand nach Exzisionsbiopsie:</b> <ul style="list-style-type: none"> <li>▪ Keine Nachresektion</li> </ul>	3b	C	++



1. Rakha E, Beca F, D'Andrea M, et al. Outcome of radial scar/complex sclerosing lesion associated with epithelial proliferations with atypia diagnosed on breast core biopsy: results from a multicentric UK-based study. *J Clin Pathol*. 2019;72(12):800-804. doi:10.1136/jclinpath-2019-205764.
2. Farshid G, Buckley E. Meta-analysis of upgrade rates in 3163 radial scars excised after needle core biopsy diagnosis. *Breast Cancer Res Treat*. 2019;174(1):165-177. doi:10.1007/s10549-018-5040-3.
3. Chou WYY, Veis DJ, Aft R. Radial scar on image-guided breast biopsy: is surgical excision necessary? *Breast Cancer Res Treat*. 2018;170(2):313-320. doi:10.1007/s10549-018-4741-y.
4. Salemis NS, Katikaridis I, Birpanagos C et al.: Complex radial sclerosing lesion of the breast-A great cancer mimicker. *Breast Journal*. 2018;24(3):408-410. doi:10.1111/tbj.12917.
5. Racz JM, Carter JM, Degnim AC. Challenging Atypical Breast Lesions Including Flat Epithelial Atypia, Radial Scar, and Intraductal Papilloma. *Ann Surg Oncol*. 2017;24(10):2842-2847. doi:10.1245/s10434-017-5980-6.
6. Ferreira AI, Borges S, Sousa A, et al. Radial scar of the breast: Is it possible to avoid surgery? *Eur J Surg Oncol*. 2017;43(7):1265-1272. doi:10.1016/j.ejso.2017.01.238.
7. Donaldson AR, Sieck L, Booth CN, Calhoun BC. Radial scars diagnosed on breast core biopsy: Frequency of atypia and carcinoma on excision and implications for management. *Breast*. 2016;30:201-207. doi:10.1016/j.breast.2016.06.007.
8. Leong RY, Kohli MK, Zeizafoun N et al.: Radial Scar at Percutaneous Breast Biopsy That Does Not Require Surgery. *J Am Coll Surg*.

2016;223(5):712-716. doi:10.1016/j.jamcollsurg.2016.08.003.

9. Kalife ET, Lourenco AP, Baird GL, Wang Y. Clinical and Radiologic Follow-up Study for Biopsy Diagnosis of Radial Scar/Radial Sclerosing Lesion without Other Atypia. *Breast Journal*. 2016;22(6):637-644. doi:10.1111/tbj.12645.
10. Hooda S, Li Z. Surgical excision outcome after radial scar without atypical proliferative lesion on breast core needle biopsy: a single institutional analysis. *Ann Diagn Pathol*. 2016;21:35-38. doi:10.1016/j.anndiagpath.2015.11.004.
11. Li Z, Ranade A, Zhao C. Pathologic findings of follow-up surgical excision for radial scar on breast core needle biopsy. *Hum Pathol*. 2016;48:76-80. doi:10.1016/j.humpath.2015.06.028.
12. Matrai C, D'Alfonso TM, Pharmer L et al.:Advocating Nonsurgical Management of Patients With Small, Incidental Radial Scars at the Time of Needle Core Biopsy: A Study of 77 Cases. *Arch Pathol Lab Med*. 2015;139(9):1137-1142. doi:10.5858/arpa.2014-0550-OA.
13. Conlon N, D'Arcy C, Kaplan JB, et al. Radial Scar at Image-guided Needle Biopsy: Is Excision Necessary? *The American journal of surgical pathology*. 2015;39(6):779-785. doi:10.1097/PAS.0000000000000393.
14. Dominguez A, Durando M, Mariscotti G, et al. Breast cancer risk associated with the diagnosis of a microhistological radial scar (RS): retrospective analysis in 10 years of experience. *Radiol Med*. 2015;120(4):377-385. doi:10.1007/s11547-014-0456-2.
15. Nassar A, Connors AL, Celik B et al.: Radial scar/complex sclerosing lesions: a clinicopathologic correlation study from a single institution. *Ann Diagn Pathol*. 2015;19(1):24-28. doi:10.1016/j.anndiagpath.2014.12.003.
16. Aroner SA, Collins LC, Connolly JL, et al. Radial scars and subsequent breast cancer risk: results from the Nurses' Health Studies. *Breast Cancer Res Treat*. 2013;139(1):277-285. doi:10.1007/s10549-013-2535-9.
17. Andacoglu O, Kanbour-Shakir A, Teh Y-C, et al. Rationale of excisional biopsy after the diagnosis of benign radial scar on core biopsy: a single institutional outcome analysis. *Am J Clin Oncol*. 2013;36(1):7-11. doi:10.1097/COC.0b013e3182354a3f.
18. Tóth D, Sebő É, Sarkadi L et al.: Role of core needle biopsy in the treatment of radial scar. *Breast*. 2012;21(6):761-763. doi:10.1016/j.breast.2012.02.009.
19. Bianchi S, Giannotti E, Vanzi E, et al. Radial scar without associated atypical epithelial proliferation on image-guided 14-gauge needle core biopsy: analysis of 49 cases from a single-centre and review of the literature. *Breast*. 2012;21(2):159-164. doi:10.1016/j.breast.2011.09.005.
20. Morgan C, Shah ZA, Hamilton R, et al. The radial scar of the breast diagnosed at core needle biopsy. *Proc (Bayl Univ Med Cent)*. 2012;25(1):3-5.
21. Bunting DM, Steel JR, Holgate CS, Watkins RM. Long term follow-up and risk of breast cancer after a radial scar or complex sclerosing lesion has been identified in a benign open breast biopsy. *Eur J Surg Oncol*. 2011;37(8):709-713. doi:10.1016/j.ejso.2011.04.011.
22. Eusebi V, Millis RR. Epitheliosis, infiltrating epitheliosis, and radial scar. *Semin Diagn Pathol*. 2010;27(1):5-12.

doi:10.1053/j.semdp.2009.12.008.

23. Loane J. Benign sclerosing lesions of the breast. *Diagnostic Histopathology*. 2009;15(8):395-401. doi:10.1016/j.mpdhp.2009.05.003.
24. Manfrin E, Remo A, Falsirollo F et al.: Risk of neoplastic transformation in asymptomatic radial scar. Analysis of 117 cases. *Breast Cancer Res Treat*. 2008;107(3):371-377. doi:10.1007/s10549-007-9569-9.
25. Douglas-Jones AG, Denson JL, Cox AC et al.: Radial scar lesions of the breast diagnosed by needle core biopsy: analysis of cases containing occult malignancy. *J Clin Pathol*. 2007;60(3):295-298. doi:10.1136/jcp.2006.037069.
26. Doyle E, Banville N, Quinn C, et al. Radial scars/complex sclerosing lesions and malignancy in a screening programme: incidence and histological features revisited. *Histopathology*. 2007;50(5):607-614
27. Sanders ME, Page DL, Simpson JF et al.: Interdependence of radial scar and proliferative disease with respect to invasive breast carcinoma risk in patients with benign breast biopsies. *Cancer*. 2006;106(7):1453-1461. doi:10.1002/cncr.21730.
28. Kraft E, Limberg JN, Dodelzon K, Newman LA, Simmons R, Swistel A, Ginter PS, Marti JL. Radial Scars and Complex Sclerosing Lesions of the Breast: Prevalence of Malignancy and Natural History Under Active Surveillance of the Breast: *Ann Surg Oncol*. 2021 Sep;28(9):5149-5155. doi: 10.1245/s10434-021-09713-5. Epub 2021 Mar 5. PMID: 3366681

© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.  
Guidelines Breast  
Version 2022.1D

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN

## Management Radial Scar

- “When RS (radial scar) is associated to atypia (such as flat epithelial atypia (FEA), atypical ductal (ADH), or lobular neoplasia (classical LN)), management can the same as recommended in cases of atypia alone.”

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN


Rageth CJ, O’Flynn EAM, Pinker K et al.: Second International Consensus Conference on lesions of uncertain malignant potential in the breast (B3 lesions). Review, Breast Cancer Res Treat, 2018, doi: 10.1007/s10549-018-05071-1

1. Rageth CJ, O’Flynn EAM, Pinker K et al.: Second International Consensus Conference on lesions of uncertain malignant potential in the breast (B3 lesions). Review, Breast Cancer Res Treat, 2018, doi: 10.1007/s10549-018-05071-1

Brustkrebs-Früherkennung: Follow-up nach B3-Läsionen für Frauen im Alter zwischen 50 und 69 Jahren			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>■ <b>FEA, Papillom ohne Atypien, Radiäre sklerosierende Läsion, CSL</b> <ul style="list-style-type: none"> <li>■ Screening-Mammographie</li> </ul> </li> <li>■ <b>LIN</b> <ul style="list-style-type: none"> <li>■ Kurative Mammographie (12 Monate)</li> </ul> </li> <li>■ <b>ADH</b> <ul style="list-style-type: none"> <li>■ Kurative Mammographie (12 Monate)</li> <li>■ Frauen mit LIN und ADH sind über ihr persönlich erhöhtes Brustkrebsrisiko zu informieren</li> </ul> </li> </ul>	5	C	++
	3a	C	++
	3a	C	++
	3a	C	++

1. Whiffen A: Predictors of Breast Cancer Development in Women with Atypical Ductal Hyperplasia and Atypical Lobular Hyperplasia. Ann Surg Oncol. 2010 Sep 28. [Epub ahead of print]
2. Weir R: Risk factors for breast cancer in women:a systematic review of the literature. Christchurch: New Zealand Health Technology Assessment (NZHTA); 2007.
3. Chuba PJ: Bilateral Risk for Subsequent Breast Cancer After Lobular Carcinoma-In-Situ: Analysis of Surveillance, Epidemiology, and End Results Data. Journal of Clinical Oncology 2005; 23(24):5534-5541
4. Degnim A: Stratification of breast cancer risk in women with atypia: A Mayo Cohort Study. JCO 2007; 25(19):2671-2677.
5. Youk J: Sonographically guided 14-gauge core needle biopsy of breast mass: A review of 2.420 cases with long-term follow-up. AJR 2007; 190:202-207
6. NCCN, National Comprehensive Cancer Network: Breast cancer screening and diagnosis V.1.2010, ed 2010. USA, NCCN, 2010
7. O'Connor A: Decision aids for people facing health treatment or screening decisions (Review). The Cochrane Library 2009;(4):1-35





© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.  
Guidelines Breast  
Version 2022.1D

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN

## Prävention bei B3 Läsionen mit erhöhtem Risiko eines DCIS oder invasiven Karzinoms

	Oxford		
	LoE	GR	AGO
▪ <b>Tamoxifen 20 mg für Frauen &gt; 35 Jahre</b>	1a	A	+/-
▪ <b>Low-dose Tamoxifen 5 mg (3 Jahre) unabh. vom Menopausenstatus</b>	2b	B	+/-
▪ <b>Aromataseinhibitor (Exemestan, Anastrozol) für postmenopausale Frauen</b>	1b	A	+/-
▪ <b>Raloxifen für postmenopausale Frauen – Reduktion nur von invasivem Karzinom</b>	1b	A	+/-*

**Eine präventive Medikamentenbehandlung sollte nur nach ausführlicher individueller Beratung angeboten werden: Der Netto-Benefit ist stark abhängig vom Risikostatus, Lebensalter und vorbestehenden Risiken für Nebenwirkungen.**

\* Risiko entsprechend der Definition des NSABP P1-trial (1,66 % in 5 Jahren)

1. Fischer B: Tamoxifen for the prevention of breast cancer: current status of the national surgical adjuvant breast and bowel project P-1 study. J Natl Cancer Inst 2005, 97:1652-1662
2. Cuzick J: Long-term results of tamoxifen prophylaxis for breast cancer - 96 months follow-up of the randomized IBIS-I trial. J Natl Cancer Inst 2007; 99:272-282.
3. Goss PE, Ingle JN, Alés-Martínez JE et al.: Exemestane for breast-cancer prevention in postmenopausal women. N Engl J Med. 2011 Jun 23;364(25):2381-91.
4. Maunsell E, Goss PE, Chlebowski RT et al.: Quality of life in MAP.3 (Mammary Prevention 3): a randomized, placebo-controlled trial evaluating exemestane for prevention of breast cancer. J Clin Oncol. 2014 May 10;32(14):1427-36.
5. Cuzick J, Sestak I, Forbes JF et al.: Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial *Lancet* 2014; 383: 1041–48
6. DeCensi A, Puntoni M, Guerrieri-Gonzaga A et al.: Randomized Placebo Controlled Trial of Low-Dose Tamoxifen to Prevent Local and Contralateral Recurrence in Breast Intraepithelial Neoplasia. J Clin Oncol. 2019 Jul 1;37(19):1629-1637. doi: 10.1200/JCO.18.01779. Epub 2019 Apr 11.
7. US Preventive Services Task Force, Owens DK, Davidson KW et al.: Medication Use to Reduce Risk of Breast Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2019 Sep 3;322(9):857-867. doi: 10.1001/jama.2019.11885.
8. Lazzeroni M, Puntoni M, Provinciali N et al.: Estimating the magnitude of clinical benefit of systemic therapy in patients with DCIS or

pre-invasive disease of the breast. *Breast*. 2019 Nov;48 Suppl 1:S39-S43. doi: 10.1016/S0960-9776(19)31121-X.

9. Flanagan MR, Zabor EC, Stempel M et al.: Chemoprevention Uptake for Breast Cancer Risk Reduction Varies by Risk Factor. *Ann Surg Oncol*. 2019 Jul;26(7):2127-2135. doi: 10.1245/s10434-019-07236-8. Epub 2019 Feb 27.
10. Marmor S, Jerome-D'Emilia B, Begun JW et al.: Trends in lobular carcinoma in situ management: endocrine therapy use in California and New Jersey. *Cancer Causes Control*. 2019 Feb;30(2):129-136. doi: 10.1007/s10552-019-1126-4. Epub 2019 Jan 17.
11. Narod, *JAMA Oncol*. 2015 Nov;1(8):1033-4. doi: 10.1001/jamaoncol.2015.2247
12. Lewin AA, Mercado CL. Atypical Ductal Hyperplasia and Lobular Neoplasia: Update and Easing of Guidelines. *AJR Am J Roentgenol*. 2020; 214:265-275