

# Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

## Läsionen mit unsicherem biologischen Potenzial (B3)

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



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## Läsionen mit unklarem biologischen Potenzial (B3)

- **Versionen 2005–2019:**  
Albert / Audretsch / Brunnert / Ditsch / Fersis / Friedrich / Friederichs / Gerber / Huober / Kreipe / Nitz / Rody / Schreer / Sinn / Thomssen
- **Version 2020:**  
Fallenberg / Schmidt / Sinn

### Pubmed 2010-2020 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, Kubik-Huch RA, Munding A, Decker T, 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>
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## Pathologische Berichterstellung für minimalinvasive Biopsien

### B-Klassifikation\*

<b>B1</b> <b>B2</b> <b>B3</b> <b>B4</b> <b>B5</b>	<b>=</b> <b>=</b> <b>=</b> <b>=</b> <b>=</b>	<b>Normalgewebe oder nicht verwertbares Material</b> <b>Benigne Läsion</b> <b>Benigne Läsionen mit unsicherem biologischen Potenzial</b> <b>Malignitätsverdächtig</b> <b>Malignom</b> B5a: In-situ-Karzinom B5b: Invasives Karzinom B5c: Nicht zu entscheiden, ob invasiv oder in situ B5d: Malignom anderer Histogenese oder Metastase
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\*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.

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- Kreipe H-H, Höfler H, Lebeau A. Ergebnisse der Referenzpathologie im Mammographie-Screening. Pathologe. 2008 Oct 9;29(S2):178–80.
- 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.
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9. Wells, C. A. (2014). Pathology Update Breast Screening, pp. 1 - 48. Retrieved from <http://www.euref.org/european-guidelines>
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## Management nach minimalinvasiver Biopsie

Oxford		
LoE	GR	AGO
3a	C	++
3a	C	++
5	D	+

■ **Interdisziplinäre Konferenz:**

**Pathologie und Bildgebung konkordant?**


- ja: Vorgehen gemäß histologischem Typ
- nein: offene PE

Vakuumbiopsie (nach Stanzbiopsie)

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>
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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.



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## 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 duktolobulären 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 Mamma-Ca 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.ijssu.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
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11. Sinn HP, Flechtenmacher C, Aulmann S. Diagnostik benignen duktaler Epithelproliferationen der Mamma in der Stanzbiopsie. *Der Pathologe.* 2014;35(1):18-25. doi:10.1007/s00292-013-1886-7.



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## Strategie nach Diagnose einer ADH in der Biopsie

Oxford		
LoE	GR	AGO
3a	C	++
5a	C	+/-
3a	C	++

**ADH in Stanz-/ Vakuumbiopsie:**

- Offene Exzisionsbiopsie
- Offene Exzisionsbiopsie verzichtbar, wenn folgende Voraussetzungen erfüllt sind:
  - a) Kein radiologischer Herdbefund
  - b) Fokale Läsion (≤2 TDLU\*) in Vakuumbiopsie und
  - c) Suspekte Läsion in der Bildgebung komplett entfernt


**ADH im Resektionsrand in offener PE:**

- Keine Nachresektion, wenn die Veränderung ein intraduktales oder invasives Karzinom begleitet

\*TDLU = terminale duktilo-lobuläre Einheit (unit)

- 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>
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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>



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## 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 prä maligne 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.
  5. 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.
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Association of Surgical Oncology, 37(4), 279–289. <http://doi.org/10.1016/j.ejso.2011.01.009>

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6. 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. 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*. Springer International Publishing; 2016 Mar;23(3):722–8.



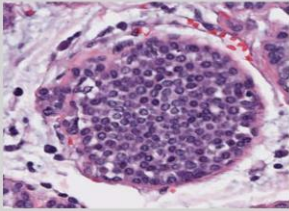
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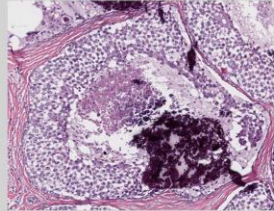
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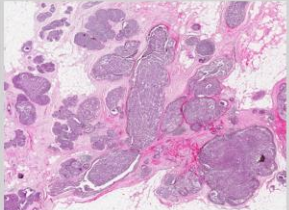
## Klassische LIN und Varianten der LIN (nicht-klassisches LCIS)



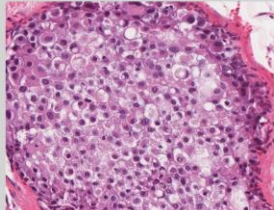
Klass. LIN



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>
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## 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.
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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.
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	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li><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, LIN mit Komedotypnekrosen, oder wenn Befund nach Korrelation mit der Bildgebung diskordant ist</li> </ul> </li> <li><b>LIN am Resektionsrand von BET</b> <ul style="list-style-type: none"> <li>Keine Nachresektion</li> </ul> </li> </ul> <p><b>Ausnahmen</b></p> <ul style="list-style-type: none"> <li>a) Pleomorphe, floride oder LIN mit Nekrosen</li> <li>b) Bildgebende Veränderung wurde nicht entfernt</li> </ul>	2b	C	++
	2b	C	++
	2a	C	++

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


- 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.
- 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.
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  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.
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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



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## 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 Mamma-Ca bei Vorliegen von ausgedehnten Kalzifikationen (auch wenn 75% verblieben nach Biopsie), Alter > = 57J., > 1cm in Bildgebung, > = 4 Foci.

### General

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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, Lehman CD. 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.

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# Strategie nach Diagnose einer FEA

		Oxford		
		LoE	GR	AGO
■ FEA in Stanz- / Vakuumbiopsie:				
■ Auf offene Biopsie kann verzichtet werden unter folgenden Voraussetzungen:		3b	C	+
a. Kleinherdiger Befund ( $\leq 2$ TDLU* in Vakuumbiopsie) <u>und</u>				
b. Entfernung oder weitgehend vollständige Entfernung der auffälligen Läsion in der Bildgebung				
■ Repräsentative offene Biopsie nur bei radiologisch ausgedehnten begleitenden Verkalkungen oder bei Diskordanz zum radiologischen Befund		5	C	+
■ FEA im Resektionsrand nach Exzisionsbiopsie:				
■ Keine Nachresektion, außer bei verbliebenem mammographischem Korrelat		3b	C	++
* TDLU = terminale duktulolobuläre Einheit				

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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.
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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.

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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.

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HEILEN

## Papillom

- **Umfasst:** Zentrales und peripheres Milchgangspapillom > 2 mm, Papillom mit Atypien (B3)
- **Abzugsgrenzen** von peripheren Mikropapillomen, von den TDLUs ausgehend, ≤ 2 mm, gelegentlich multipel
- Abzugsgrenzen 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).

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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> <li> <b>Multiple Papillome</b> <ul style="list-style-type: none"> <li>Offene Biopsie</li> </ul> </li> <li> <b>Atypisches Papillom in Stanz-/Vakuumbiopsie</b> <ul style="list-style-type: none"> <li>Offene Biopsie</li> </ul> </li> <li> <b>Papillom am Rand von Resektaten</b> <ul style="list-style-type: none"> <li>Keine verfügbaren Daten</li> </ul> </li> </ul>	3a	C	++
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## Radiäre sklerosierende Läsion (RS)


- **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%**

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 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2020.1D</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	Vorgehen bei radiärer Narbe, komplexer sklerosierender Läsion (CSL)		
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>■ Radiäre Narbe / CSL in Stanz- oder Vakuumbiopsie:             <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> </li> </ul>	5a	C	+
<ul style="list-style-type: none"> <li>■ Radiäre Narbe / CSL im Resektionsrand nach Exzisionsbiopsie:             <ul style="list-style-type: none"> <li>■ Keine Nachresektion</li> </ul> </li> </ul>	3b	C	++


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## 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.

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

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# Brustkrebs-Früherkennung: Follow-up nach B3-Läsionen für Frauen im Alter zwischen 50 und 69 Jahren

	Oxford		
	LoE	GR	AGO
■ FEA, Papillom ohne Atypien, RS, CSL			
■ Screening-Mammographie	5	C	++
■ LIN			
■ Kurative Mammographie (12 Monate)	3a	C	++
■ ADH			
■ Kurative Mammographie (12 Monate)	3a	C	++
■ Frauen mit LIN und ADH sind über ihr persönlich erhöhtes Brustkrebsrisiko zu informieren	3a	C	++

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## Prävention bei Läsionen mit unsicherem biologischen Potenzial (insbes. LIN, ADH)


	Oxford		
	LoE	GR	AGO
■ Tamoxifen 20mg für Frauen > 35 Jahre	1a	A	+/-
■ Low-dose Tamoxifen 5mg (3 Jahre)	2b	B	+/-
■ Aromataseinhibitor (Exemestan, Anastrozol) für postmenopausale Frauen	1b	A	+/-
■ Raloxifen für postmenopausale Frauen – Reduktion nur von invasivem Karzinom	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 years)

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## Low-dose Tamoxifen als Prophylaxe

- 500 Frauen ≤ 75 postoperativ mit intraepithelialer Neoplasie (ADH, LCIS, DCIS)
- Tamoxifen 5 mg/d für 3 Jahre vs. Placebo
- Brustkrebsereignisse: 14 vs. 28
  - invasiv: 11 vs. 19
  - HR 0,48; 95% CI 0,26-0,92; P = 0,02
- NNT 22
- PROM bis auf Hitzewallungen vergleichbar

DeCensi et al. J Clin Oncol 37:1629-1637, 2019

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.

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				Placebo	Verum
	Studienteil- nehmer	18.322			18.355
	Invasives Mammakarzinom	805			537
	ER-positiv	632			350
	ER-negativ	144			173
	Todesfälle durch Mammakarzinom	48			60
			Narod. JAMA Oncol 1:1033-4, 2015		

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