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Guidelines Breast
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Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Läsionen mit unsicherem biologischen Potenzial (B3)

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



Läsionen mit unklarem biologischen Potenzial (B3)

- **Versionen 2005–2020:**

Albert / Audretsch / Brunnert / Ditsch / Fallenberg / Fersis / Friedrich / Friederichs / Gerber / Huober / Kreipe / Nitz / Rody / Schmidt / Schreer / Sinn / Thomssen

- **Version 2021:**

Kreipe / Maass

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.
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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>
6. World Health Organization: WHO Classification of Tumours of the Breast. Lokuhetty D, White VA, Watanabe R, Cree IA (Hrsg.) 2019.



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
 - BSa: In-situ-Karzinom
 - BSb: Invasives Karzinom
 - BSc: Nicht zu entscheiden, ob invasiv oder in situ
 - BSd: 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>
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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>
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B3-Läsionen

- 1. Läsionen mit erhöhtem Risiko eines assoziierten DCIS oder invasiven Karzinoms**
 - Atypische duktale Hyperplasie (ADH) bzw. atypische Epithelproliferation vom duktalem Typ (in Abhängigkeit von der Ausdehnung ggf. B4)
 - Flache epitheliale Atypie (FEA)
 - Lobuläre Neoplasie (LIN; LN; in älterer Nomenklatur zusammengefasst jetzt unterteilt in ALH und LCIS), klassischer und nicht-klassischer Typ
 - Atypische apokrine Adenose
- 2. Potenziell heterogene Läsionen mit Risiko eines unvollständigen Sampling**
 - Zellreiche fibroepitheliale Läsion oder Phylloides tumor ohne Malignitätsverdacht
 - Intraduktales Papillom ohne /mit Atypien, nicht sicher vollständig entfernt (bei Atypien in Abhängigkeit von der Ausdehnung ggf. B4)
 - Radiäre Narbe bzw. komplexe sklerosierende Läsion (Ausnahme: wenn radiäre Narbe nicht Ursache der radiologischen Veränderung: B2)
 - Hämangiom
- 3. Seltene Veränderungen**
 - Adenomyoepitheliom, Mikroglanduläre Adenose, Mukozelenartige Läsion, Noduläre Faszitis, Fibromatose vom Desmoidtyp, unklare Spindelzellläsion

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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.
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Management nach minimalinvasiver Biopsie

- **Interdisziplinäre Konferenz:
Pathologie und Bildgebung konkordant?**
 - ja: Vorgehen gemäß histologischem Typ
 - nein: offene PE
- Vakuumbiopsie (nach Stanzbiopsie)**

Oxford		
LoE	GR	AGO
3a	C	++
3a	C	++
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
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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
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 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 benignen duktalen 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 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.ijso.2017.11.005.
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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.
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8. Howard-Mcnatt M. Atypical Ductal Hyperplasia: What Is the Current Risk for Developing Breast Cancer? *JAMA Oncol*. 2017;3(1):20-

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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
ADH in Stanz-/ Vakuumbiopsie:			
▪ Offene Exzisionsbiopsie	3a	C	++
▪ Offene Exzisionsbiopsie verzichtbar, wenn folgende Voraussetzungen erfüllt sind:	5a	C	+/-
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:	3a	C	++
▪ Keine Nachresektion, wenn die Veränderung ein intraduktales oder invasives Karzinom begleitet			

*TDLU = terminale dukto-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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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 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.
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2. 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>
3. Hwang, H., Sullivan, M. E., & Susnik, B. (2010). Lobular neoplasia. Diagnostic Histopathology, 16(7), 337–344.

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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.



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>
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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.
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.

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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.
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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.
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8. Alvarado-Cabrero I, Picón Coronel G, Valencia Cedillo R, Canedo N, Tavassoli FA. 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
<ul style="list-style-type: none"> LIN in Stanz- / Vakuumbiopsie <ul style="list-style-type: none"> Keine weitere Abklärung bei isoliertem oder inzidentellem Befund einer LIN (klassisches LCIS) mit Befall von ≤ 3 TDLU (terminale duktilolobuläre Einheit) in Vakuumbiopsie und Konkordanz mit der Bildgebung Offene Exzisionsbiopsie bei pleomorpher LIN, florider LIN (LIN3), LIN mit Komedynekrosen, oder wenn Befund nach Korrelation mit der Bildgebung diskordant ist LIN am Resektionsrand von BET <ul style="list-style-type: none"> Keine Nachresektion 	2b	C	**
Ausnahmen <ul style="list-style-type: none"> a) Pleomorphe, floride oder LIN mit Nekrosen b) Bildgebende Veränderung wurde nicht entfernt 	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.
- 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.
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- El-Khoury M, Sanchez LM, Lalonde L, Trop I, David J, Mesurolle B. 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.
- 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.
- Susnik B, Day D, Abeln E, et al. Surgical Outcomes of Lobular Neoplasia Diagnosed in Core Biopsy: Prospective Study of 316 Cases.

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 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.
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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, Rao S. 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.
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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.
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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

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 DGFB e. V.
in der DGK e. V.

Guidelines Breast
Version 2021.10

www.ago-online.de

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 > = 57J., > 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.
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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.
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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, 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.
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
<ul style="list-style-type: none"> FEA in Stanz- / Vakuumbiopsie: <ul style="list-style-type: none"> Auf offene Biopsie kann verzichtet werden unter folgenden Voraussetzungen: <ol style="list-style-type: none"> Kleinherdiger Befund (≤ 2 TDLU* in Vakuumbiopsie) und 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 	3b	C	+
<ul style="list-style-type: none"> FEA im Resektionsrand nach Exzisionsbiopsie: <ul style="list-style-type: none"> Keine Nachresektion, außer bei verbliebenem mammographischem Korrelat 	3b	C	++

* TDLU = terminale duktuolobuläre 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.
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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.
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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.
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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.
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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).

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Vorgehen nach Diagnose eines Papilloms

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> • Solitäres Papillom ohne Atypien in Stanz-/Vakuumbiopsie <ul style="list-style-type: none"> • Keine weiteren Maßnahmen, wenn Biopsie ausreichend repräsentativ (100 mm²) und keine Diskordanz zur Bildgebung 	3a	C	+
<ul style="list-style-type: none"> • Multiple Papillome <ul style="list-style-type: none"> • Offene Biopsie 	3a	C	++
<ul style="list-style-type: none"> • Atypisches Papillom in Stanz-/Vakuumbiopsie <ul style="list-style-type: none"> • Offene Biopsie 	3a	C	++
<ul style="list-style-type: none"> • Papillom am Rand von Resektaten <ul style="list-style-type: none"> • Keine verfügbaren Daten 			


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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%**

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FÜR DIE SENOLOGIE
UND DIE BRUSTKREBSKRANKHEIT

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Vorgehen bei radiärer Narbe, komplexer sklerosierender Läsion (CSL)

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

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The slide features a logo in the top left corner with the letters 'AGO' and a stylized 'S' below it. The main title 'Management Radial Scar' is centered at the top in a green font. A horizontal line separates the title from the main content area. On the left side, there is a vertical text block containing the AGO logo, the text 'AGO e. V.', 'in der DGGG a.V.', 'in der DGG a.V.', 'Guidelines Breast', and 'Version 2021.10'. Below this is the website 'www.ago-online.de' and the text 'FÜR DIE DGGG a.V.', 'FÜR DIE DGG a.V.', 'FÜR DIE DGG'. The main content area contains a single bullet point: '• "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."'. At the bottom of the slide, there is a reference: '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'.

Management Radial Scar

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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"> FEA, Papillom ohne Atypien, Radiäre sklerosierende Läsion, CSL <ul style="list-style-type: none"> Screening-Mammographie 	5	C	++
<ul style="list-style-type: none"> LIN <ul style="list-style-type: none"> Kurative Mammographie (12 Monate) 	3a	C	++
<ul style="list-style-type: none"> ADH <ul style="list-style-type: none"> Kurative Mammographie (12 Monate) 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

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FÜR GYNEKOLOGIE UND
GEBURTSHILFE
UND GYNÄKOLOGIE

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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UND IHRER ANGEHÖRIGEN

Tamoxifen Chemoprevention— End of the Road?

	Placebo	Verum
Studienteilnehmer	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

Narod, JAMA Oncol. 2015 Nov;1(8):1033-4. doi: 10.1001/jamaoncol.2015.2247