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Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Ductal Carcinoma in Situ (DCIS)



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Duktales Carcinoma in situ (DCIS)

- **Versionen 2002–2018:**
**Audretsch / Blohmer / Brunnert / Budach / Costa /
Fersis / Friedrich / Gerber / Hanf / Junkermann / Kühn /
Lux / Maass / Möbus /Mundhenke / Nitz / Oberhoff /
Scharl / Solomayer / Souchon / Thill / Thomssen / Wenz**

- **Version 2019:**
Bauerfeind / Schütz

Mammographie

Vergrößerungsaufnahmen von Mikroverkalkungen

Steigerung der Detektionsrate von G1/G2 DCIS durch digitale Mammographie (versus konventionell)

1. D’Orsi C: (2010) “Imaging for the Diagnosis and Management of Ductal Carcinoma In Situ” J Natl Cancer Inst Monogr (41) 214 – 217
2. Allegra CJ, Alberle DR, Ganschow P et al. National Institutes of Health State-of-the –Science Conference Statement: Diagnosis and Management of Ductal Carcinoma in Situ September 22-24,2009. JNCI 2009;102:161-169
3. Allen L, Lago_Toro C, Hughes JH et al. Is there a role for preoperative assessment of patients with DCIS? Ann Surg 2010; 17: 2395-2400
4. Farshid G, Sullivan T, Downey P et al. Independent predictors of breast malignancy in screen-detected microcalcifications: biopsy results in 2545 cases. Br J Cancer 2011; 105: 1669 – 1675
5. Hayward L, Oeppen RS, Grima AV, et al. The influence of clinicopathological features on the predictive accuracy of conventional breast imaging in determining the extent of screen-detected high-grade pure ductal carcinoma in situ. Ann R Coll Surg Engl 2011; 93:385-390

6. Lee RJ, Vallow LA, McLaughlin SA, Tzou KS, Hines SL, Peterson J et al. . Ductal carcinoma in situ of the breast. Int J Surg Oncol. 2012;2012:123549. doi:10.1155/2012/123549. Epub 2012 Jul 18.
7. Nederend J, Duijm LE, Louwman MW, et al. Impact of transition from analog screening mammography to digital screening mammography on screening outcome in The Netherlands: a population-based study. Ann Oncol. 2012 Dec;23(12):3098-103. doi: 10.1093/annonc/mds146. Epub 2012 Jun 27.
8. Badruddoja M. Ductal carcinoma in situ of the breast: a surgical perspective. Int J Surg Oncol. 2012;2012:761364. doi: 10.1155/2012/761364. Epub 2012 Sep 4.
9. Lynge E, Ponti A, James T, et al. ICSN DCIS Working group. Variation in detection of ductal carcinoma in situ during screening mammography: A survey within the International Cancer Screening Network. Eur J Cancer. 2014 Jan;50(1):185-92. doi: 10.1016/j.ejca.2013.08.013. Epub 2013 Sep 13.

Stereotaktische Stanzbiopsie / Vakuumbiopsie (VAB)

1. Houssami, N, D Ambrogetti et al. Accuracy of a Preoperative Model for Predicting Invasive Breast Cancer in Women with Ductal Carcinoma-in-situ on Vacuum-Assisted Core Needle Biopsy. Ann Oncol 2011;18(5):1364-71

Präparateradiographie

Setzen eines Markierungsclips in der Biopsieregion, wenn die Läsion komplett entfernt wurde

MRT zur Festlegung der Ausdehnung

1. Kim do, Y., W. K. Moon, et al. (2007). "MRI of the breast for the detection and assessment of the size of ductal carcinoma in situ." Korean J Radiol 8(1): 32-39.
2. Marcotte-Bloch, C., C. Balu-Maestro, et al. (2009). "MRI for the size assessment of pure ductal carcinoma in situ (DCIS): A prospective study of 33 patients." Eur J Radiol.
3. Neira, P., B. Aguirre, et al. (2009). "[Breast MRI--histologic correlation for ductal carcinoma in situ]." Radiologia 51(4): 396-402.
4. Onesti, J. K., B. E. Mangus, et al. (2008). "Breast cancer tumor size: correlation between magnetic resonance imaging and pathology

- measurements." *Am J Surg* 196(6): 844-848; discussion 849-850.
5. Schouten van der Velden, A. P., C. Boetes, et al. (2009). "Magnetic resonance imaging in size assessment of invasive breast carcinoma with an extensive intraductal component." *BMC Med Imaging* 9: 5.
 6. Schouten van der Velden, A. P., M. S. Schlooz-Vries, et al. (2009). "Magnetic resonance imaging of ductal carcinoma in situ: what is its clinical application? A review." *Am J Surg* 198(2): 262-269.
 7. Vag, T., P. A. Baltzer, et al. (2008). "Diagnosis of ductal carcinoma in situ using contrast-enhanced magnetic resonance mammography compared with conventional mammography." *Clin Imaging* 32(6): 438-442.
 8. Vanderwalde LH, Dang CM, Bresee C et al. Discordance between pathologic and radiologic tumor size on breast MRI may contribute to increased re-excision rates. *Am Surg* 2011; 77(10):1361-3.
 9. Itakura K, Lessing J, Sakata T, et al. The Impact of Preoperative Magnetic Resonance Imaging on Surgical Treatment and Outcomes for Ductal carcinoma In Situ. *Clin Breast Cancer* 2011; 11: 33-38.
 10. Mossa-Basha M, Fundaro GM, Shah BA, et al. Ductal carcinoma in Situ of the Breast: MR Imaging Findings with Histopathologica Correlation. *RadioGraphics* 2010; 30: 1673-1687
 11. Warner E, Causer PA, Wong J, et al. Improvement in DCIS Detection Rates by MRI over Time in a High Risk Breast Screening Study. *The Breast Journal* 2011; 17: 9-17
 12. Liu H, Peng W. MRI morphological classification of ductal carcinoma in situ correlating with different biological behavior. *Eur J Radiol.* 2012 Feb;81(2):214-7
 13. Stehouwer BL, Merckel LG, Verkooijen HM, et al. 3-T breast magnetic resonance imaging in patients with suspicious microcalcifications on mammography. *Eur Radiol.* 2013 Sep 29. [Epub ahead of print]
 14. Miyashita M, Amano G, Ishida T, et al. The clinical significance of breast MRI in the management of ductal carcinoma in situ diagnosed on needle biopsy. *Jpn J Clin Oncol.* 2013 Jun;43(6):654-63.
 15. Pilewskie M, Kennedy C, Shappell C, et al. Effect of MRI on the management of ductal carcinoma in situ of the breast. *Ann Surg Oncol.* 2013 May;20(5):1522-9. doi: 10.1245/s10434-012-2771-y. Epub 2012 Dec 7.
 16. Baur A, Bahrs SD, Speck S, et al. Breast MRI of pure ductal carcinoma in situ: sensitivity of diagnosis and influence of lesion characteristics. *Eur J Radiol.* 2013 Oct;82(10):1731-7.

17. A. Fancellu et al: Meta-analysis of the effect of preoperative breast MRI on the surgical management of ductal carcinoma in situ BJS 2015; 102:883-893
18. E.L. Voss et al: Benefits of preoperative MRI in breast cancer surgery studied in a large population-based cancer registry. BJS 2015: 102; 1649-1657.

Klinische Untersuchung

Feinnadelpunktion / duktale Lavage

Interdisziplinäre Tumorboard-Präsentation

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ▪ Mammography <ul style="list-style-type: none"> ▪ Magnification view of microcalcification ▪ Increase of detection rate of G1/G2 DCIS by full-field digital mammography (versus screen-film) ▪ Stereotactic core needle / vacuum biopsy (VAB) <ul style="list-style-type: none"> ▪ Specimen radiography ▪ Marker (Clip) left at biopsy site for localization if lesion is completely removed ▪ Assessment of extension <ul style="list-style-type: none"> ▪ MRI ▪ Clinical examination ▪ FNA / ductal lavage ▪ Interdisciplinary board presentation 	<p>1b 4 2b 2b 2b 5 1b 5 5 5</p>	<p>B C B B B D B D D D</p>	<p>++ ++ + ++ ++ ++ +/- ++ - ++</p>



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Mammographie

Li J, Zhang H, Jiang H, Guo X et al. [Diagnostic Performance of Digital Breast Tomosynthesis for Breast Suspicious Calcifications From Various Populations: A Comparison With Full-field Digital Mammography](#). Comput Struct Biotechnol J. 2018 Dec 20;17:82-89.


Präoperatives MRT hat keinen Einfluss auf die LRR und das OS

1. Vapiwala N, Hwang WT, Kushner CJ, et al. No impact of breast magnetic resonance imaging on 15-year outcomes in patients with ductal carcinoma in situ or early-stage invasive breast cancer managed with breast conservation therapy. Cancer. 2017;123(8):1324-1332.
2. Ryan R, Tawfik O, Jensen RA et al. . Current Approaches to Diagnosis and Treatment of Ductal Carcinoma In Situ and Future Directions. Prog Mol Biol Transl Sci. 2017;151:33-80.
3. Preibsch H, Beckmann J, Pawlowski J et al. [Accuracy of Breast Magnetic Resonance Imaging Compared to Mammography in the Preoperative Detection and Measurement of Pure Ductal Carcinoma In Situ: A Retrospective](#) _Radiol. 2018 Aug 24. pii: S1076-6332(18)30383-0.
4. So A, De La Cruz LM, Williams AD et al. [impact of preoperative magnetic resonance imaging and lumpectomy cavity shavings on re-](#)

[excision rate in pure ductal carcinoma in situ-A single institution's experience.](#) J Surg Oncol. 2018 Mar;117(4):558-566.

Molecular Subtyping

1. Nofech-Mozes S, Hanna W, Rakovitch E. [Molecular Evaluation of Breast Ductal Carcinoma in Situ with Oncotype DX DCIS.](#) Am J Pathol. 2018 Dec 31. pii: S0002-9440(18)30581-9.



Original Investigation

Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ

Steven A. Narod, MD, FRCPC; Javaid Iqbal, MD; Vasily Giannakeas, MPH; Victoria Sopik, MSc; Ping Sun, PhD

- **108,196 patients from the SEER data base**
- **Retrospective analysis**
- **Breast cancer specific mortality 3.3 %**
- **Increased in young women (< 35 years) and black ethnicity**
- **The risk of death increases after ipsilateral invasive recurrence HR 18 (95%CI, 14,0–23,6)**
- **Prevention of invasive recurrence by radiotherapy does not diminish mortality at 10 years**

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1. Steven A. Narod, MD, FRCPC; Javaid Iqbal, MD; Vasily Giannakeas, MPH; et al; JAMA Oncol. doi:10.1001/jamaoncol.2015.2510
Published online August 20, 2015.

Original Investigation						
Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ						
Steven A. Narod, MD, FRCPC; Javaid Iqbal, MD; Vasily Giannakeas, MPH; Victoria Sopik, MSc; Ping Sun, PhD						
Treatment	Cases, No	10-Year BCS Mortality (95%CI), %	Univariate HR (95% CI)	P Value	Multivariate ³ HR (95%)	P Value
Lumpectomy						
Without radiotherapy	19762	0.9 (0.7 - 1.1)	1 [Reference]		1 [Reference]	
With radiotherapy	42250	0.8 (0.7 - 1.0)	0.86 (0.67 - 1.10)	0.22	0.81 (0.63 - 1.04)	0.10
all	63319	0.8 (0.7 - 1.0)	1 [Reference]		1 [Reference]	
Unilateral mastectomy	19515	1.3 (1.1 - 1.5)	1.45 (1.18 - 1.79)	< 0.001	1.20 (0.96 - 1.50)	0.11


³ Adjusted for year of diagnosis, age of diagnosis, ethnicity, income, ER-status, tumor size and grade



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1. Steven A. Narod, MD, FRCPC; Javaid Iqbal, MD; Vasily Giannakeas, MPH; et al; JAMA Oncol. doi:10.1001/jamaoncol.2015.2510
Published online August 20, 2015.



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General Therapeutic Principles

Surgical excision (BCS, mastectomy) is the standard of treatment for DCIS.

Adjuvant treatment (radiotherapy, endocrine treatment) must be discussed with the patient individually. Adverse effects should be weighed against risk reduction.

1. Kirsty E. Stuart, Nehmat Houssami, Richard Taylor, et al. Long-term outcomes of ductal carcinoma in situ of the breast: a systematic review, meta-analysis and meta-regression analysis. *BMC Cancer* (2015) 15:890.
2. Katrina B. Mitchell and Henry Kuerer. Ductal Carcinoma In Situ: Treatment Update and Current Trends. *Curr Oncol Rep* (2015) 17: 48
3. Elizabeth M. Ward, Carol E. DeSantis, Chun Chieh Lin, et al. Cancer Statistics: Breast Cancer In Situ. *CA Cancer J Clin* 2015;65:481–495.
4. Benjamin D. Smith. When Is Good Enough Really Good Enough? Defining the Role of Radiation in Low-Risk Ductal Carcinoma In Situ. *J Clin Oncol* 2015; 33(7): 686 – 692.
5. Laura Esserman, Christina Yau. Rethinking the Standard for Ductal Carcinoma In Situ Treatment. *JAMA Oncology* Published online August 20, 2015.
6. Steven A. Narod, Javaid Iqbal, Vasily Giannakeas, et al. Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ. *JAMA Oncol*. doi:10.1001/jamaoncol.2015.2510 Published online August 20, 2015.
7. [Hamilton SN, Nichol A, Wai E et al. Local Relapse After Breast-Conserving Therapy Versus Mastectomy for Extensive Pure Ductal Carcinoma In Situ \$\geq 4\$ cm.](#) *Int J Radiat Oncol Biol Phys*. 2018 Sep 22. pii: S0360-3016(18)33801-X

8. Gradishar WJ, Anderson BO, Balassanian R et al. [Breast Cancer, Version 4.2017, NCCN Clinical Practice Guidelines in Oncology](#). J Natl Compr Canc Netw. 2018 Mar;16(3):310-320.

	Oxford		
	LoE	GR	AGO
▪ Excisional biopsy (wire guided)	2b	B	++
▪ Bracketing wire localization in large lesions	3a	C	+
▪ Specimen radiography	2b	B	++
▪ Intraoperative ultrasound (visible lesion)	3a	C	+/-
▪ Immediate re-excision for close margins (specimen radiography)	1c	B	++
▪ Intraoperative frozen section (in single cases for margin)	3a	D	+/-
▪ Interdisciplinary board presentation	2b	C	++

Open biopsy in suspicious lesions (mammographical microcalcifications, suspicious US, MRI etc.) without preoperative needle biopsy should be avoided



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Exzision (drahtmarkiert)

1. Houssami N, Ambrogetti D, Marinovich L et al. Accuracy of a preoperative model for predicting invasive breast cancer in women with ductal carcinoma in situ on vacuum assisted core needle biopsy. *Ann Surg Oncol* 2011;18(5):1364-71
2. Saadai P, Moezzi M et al. Preoperative and intraoperative predictors of positive margins after breast-conserving surgery: a retrospective review. *Breast Cancer* 2011; 18: 221-225
3. Kumar S, Sacchini V. The Surgical Management of Ductal Carcinoma In Situ. *The Breast Journal* 2010; 16: S 49-S52
4. Hwang ES. The Impact of Surgery on Ductal Carcinoma In Situ Outcomes: The Use of Mastectomy. *J Natl Cancer Inst Monogr* 2010; 41: 197-199.
5. Ryan R, Tawfik O, Jensen RA, et al. Current Approaches to Diagnosis and Treatment of Ductal Carcinoma In Situ and Future Directions. *Prog Mol Biol Transl Sci.* 2017;151:33-80.
6. Janssen NNY, van la Parra RFD, Loo CE et al. [Breast conserving surgery for extensive DCIS using multiple radioactive seeds.](#) *Eur J Surg Oncol.* 2018 Jan;44(1):67-73.

Flankierende Drahtmarkierung bei großen Läsionen

Präparatradiographie

1. Kuerer HM, Smith BD, Chavez-MacGregor M, et al. DCIS Margins and Breast Conservation: MD Anderson Cancer Center Multidisciplinary Practice Guidelines and Outcomes. J Cancer. 2017;8(14):2653-2662.

Ohne Einfluss auf NRR

1. DVerstehenden DPA, Keizer LGG, Schlooz-Vries MS, et al: Performance characteristics of specimen radiography for margin assessment for ductal carcinoma in situ: a systematic review. Breast Cancer Res Treat 2017;166:669–679.

„A literature search was conducted for diagnostic studies up to April 2017 concerning SR for intra-operative margin assessment of breast lesions with pure DCIS or with DCIS components. Studies reporting sensitivity and specificity calculated using final pathology report as reference test were included. Due to improved imaging technology, studies published more than 15 years ago were excluded. Methodological quality was assessed using quality assessment of diagnostic accuracy studies-2 checklist. Due to clinical and methodological diversity, meta-analysis was considered not useful.

Results Of 235 citations identified, 9 met predefined inclusion criteria and documented diagnostic efficacy data. Sensitivity ranged from 22 to 77% and specificity ranged from 51 to 100%. Positive predictive value and negative predictive value ranged from 53 to 100% and 32 to 95%, respectively. High or unclear risk of bias was found in reference standard in 5 of 9 studies. High concerns regarding applicability of index test were found in 6 of 9 studies.

Conclusions The present results do not support the routine use of intra-operative specimen radiography to reduce the rate of positive margins in patients undergoing breast-conserving surgery for pure DCIS or the DCIS component in invasive cancer. Future studies need to differentiate between initial and final specimen margin involvement. This could provide surgeons with a number needed to treat for a more applicable outcome.“

Intraoperative Sonographie (darstellbarer Befund)

1. Ahmed M, Douek M. Intra-operative ultrasound versus wire-guided localization in the surgical management of non-palpable breast cancers: systematic review and meta-analysis. *Breast Cancer Res Treat.* 2013; 140(3): 435-446.


Sofortige Nachresektion bei knappen Resektionsrändern (Präparateradiographie)

1. Thill M, Röder K, Diedrich K et al. Intraoperative assessment of surgical margins during breast conserving surgery of ductal carcinoma in situ by use of radiofrequency spectroscopy. *The Breast* 2011(11) 579-580
2. Guidroz JA, Larrieux G, Liao J et al. Sampling of secondary margins decreases the need for re-excision after partial mastectomy Surgery. 2011; 150: 802 – 809
3. Fisher CS, Klimberg S, Khan S, et al. Margin Index is not a reliable toll for predicting residual disease after breast- conserving surgery for DCIS. *Ann Surg Oncol* 2011; 18: 3155-3159
4. Kumar S, Sacchini V. the Surgical Management of Ductal Carcinoma In Situ. *The Breast Journal* 2010; 16: S49 – S52
5. Kennedy S, Geradts J, Bydlon T, et al. Optical breast cancer margin assessment: an observational study of the effects of tissue heterogeneity on optical contrast. *Breast Cancer Res* 2010
6. Javid SH, Anderson BO. Tailored Strategies for DCIS Management. *Oncology* 2011; 25 (9):861-3
7. Kulkarni S. Management of DCIS: A Work in Progress. *Oncology* 2011; 25 (9): 852-6
8. Thill M, Dittmer C, Baumann K, et al. MarginProbe®--final results of the German post-market study in breast conserving surgery of ductal carcinoma in situ. *Breast.* 2014 Feb;23(1):94-6. doi: 10.1016/j.breast.2013.11.002. Epub 2013 Dec 2.
9. Kuerer HM, Smith BD, Chavez-MacGregor M, et al. DCIS Margins and Breast Conservation: MD Anderson Cancer Center Multidisciplinary Practice Guidelines and Outcomes. *J Cancer.* 2017;8(14):2653-2662.

Intraoperative Schnellschnittdiagnostik

1. Kuerer HM, Smith BD, Chavez-MacGregor M et al. DCIS Margins and Breast Conservation: MD Anderson Cancer Center Multidisciplinary Practice Guidelines and Outcomes. *J Cancer.* 2017;8(14):2653-2662.
2. [Laws A](#), [Brar MS](#), [Bouchard-Fortier A](#), et al. [surgery for ductal carcinoma in situ.](#) *J Surg Oncol.* 2018 Dec;118(7):1205-1211.

Interdisziplinäre Tumorboard-Präsentation

		Oxford		
		LoE	GR	AGO
 <p>© AGO e. V. in der DGGG e. V. sowie in der DKG e. V.</p> <p>Guidelines Breast Version 2019.1</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	<ul style="list-style-type: none"> ▪ Histologically clear margins (R0) ▪ Multifocal DCIS: BCS if feasible ▪ Re-excision required for close margin \leq 2 mm in paraffin section)** ▪ Mastectomy* <ul style="list-style-type: none"> ▪ Large lesions confirmed by multiple biopsies; no clear margins after re-excision ▪ SNE* <ul style="list-style-type: none"> ▪ Mastectomy ▪ BCS ▪ In case of DCIS in the male breast ▪ ALND 			
		1a	A	++
		2b	B	+
		2b	C	+
		2a	B	++
		3b	B	+
		3b	B	-
		5	D	+/-
		2b	B	--
		* Patients who present with a palpable mass have a significantly higher potential for occult invasion (26%), multicentricity and local recurrence.		
	** Especially when a postoperative radiation therapy is not performed			

Histologisch freie Resektionsränder (pR0)

1. Lagios MD, Page DL, Silverstein MJ. Prospective study of wide excision alone for ductal carcinoma in situ of the breast. J Clin Oncol 2006;24:3809-11
2. MacAusland SG, Hepel JT, Chong FK, et al. An attempt to independently verify the utility of the Van Nuys Prognostic Index for ductal carcinoma in situ. Cancer 2007;110:2648-53
3. Macdonald HR, Silverstein MJ, Lee LA, et al. Margin width as the sole determinant of local recurrence after breast conservation in patients with ductal carcinoma in situ of the breast. Am J Surg 2006 192:420-2
4. Meijnen P, Oldenburg HS, Peterse JL, et al. Clinical outcome after selective treatment of patients diagnosed with ductal carcinoma in situ of the breast. Ann Surg Oncol 2007 Nov 7; [Epub ahead of print]
5. Lee RJ, Vallow LA, McLaughlin SA, et al. Ductal carcinoma in situ of the breast. Int J Surg Oncol. 2012;2012:123549. doi: 10.1155/2012/123549. Epub 2012 Jul 18.
6. Badruddoja M. Ductal carcinoma in situ of the breast: a surgical perspective. Int J Surg Oncol. 2012;2012:761364. doi: 10.1155/2012/761364. Epub 2012 Sep 4.
7. Hassani A, Griffith C, Harvey J. Size does matter: High volume breast surgeons accept smaller excision margins for wide local

excision--a national survey of the surgical management of wide local excision margins in UK breast cancer patients. Breast. 2013 Oct;22(5):718-22.

8. Morrow M., et al: Society of Surgical Oncology –American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery with Whole-Breast Irradiation in Ductal Carcinoma in Situ J CO 2016 34;33 :4040-4046

Multifokalität: BET falls möglich (inkl. RT)

1. Meijnen P, Bartelink H. Multifocal ductal carcinoma in situ of the breast: A contraindication for breast-conserving treatment? J Clin Oncol 2007;25:5548–5549
2. Rakovitch E, Pignol JP, Hanna W, et al. Significance of multifocality in ductal carcinoma in situ: outcomes of women treated with breast-conserving therapy. J Clin Oncol 2007;25:5591–5596

Nachresektion bei knappem Resektionsrand (< 2 mm im Paraffinschnitt)

1. Dunne, C., J. P. Burke, et al. (2009). "Effect of margin status on local recurrence after breast conservation and radiation therapy for ductal carcinoma in situ." J Clin Oncol 27(10): 1615-1620.
2. Van Cleef A, Altintas S, Huizing M et al. Current view on ductal carcinoma in situ and importance of the margin thresholds: A review. Facts Views Vis Obgyn. 2014;6(4):210-8.

**besonders wenn nicht nachbestrahlt wird

3. Kuerer HM, Smith BD, Chavez-MacGregor M et al. DCIS Margins and Breast Conservation: MD Anderson Cancer Center Multidisciplinary Practice Guidelines and Outcomes. J Cancer. 2017;8(14):2653-2662.
4. Morrow M. De-escalating and escalating surgery in the management of early breast cancer. Breast. 2017 Aug;34 Suppl 1:S1-S4.

„The panelists emphasized that clinical judgment is necessary to determine whether patients with negative margin widths less than 2 mm require re-excision based on the long-term rates of local control seen in National Surgical Adjuvant Breast and Bowel Project

(NSABP) trials, which used the negative margin definition of no ink on tumor [10] and on the results of the large single-institution study of Van Zee et al. [11] in which negative margin width was not a predictor of local recurrence in patients receiving radiotherapy after controlling for multiple clinical variables of interest. In the study of Van Zee et al., crude rates of local recurrence among the 2996 patients receiving radiotherapy were 10% for those with negative margins 2 mm or less in size, 7% for those with margins >2 mm, and 9% for margins >10 mm. Examples of factors to consider when deciding whether to re-excise a negative margin <2 mm include the extent of DCIS in proximity to the margin, which margin is close, the presence of residual calcifications on mammogram, the cosmetic impact of re-excision, and the patient's life expectancy."

Mastektomie* (große Läsionen; keine sicheren Ränder im Nachresektat)

1. Ringberg A, Nordgren H, Thorstensson S, et al. Histopathological risk factors for ipsilateral breast events after breast conserving treatment for ductal carcinoma in situ of the breast--results from the Swedish randomised trial. Eur J Cancer 2007;43:291-8
2. NCCN and National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Breast Cancer - Version V.1.2007.
3. Solin LJ. Is excision alone adequate treatment for low-risk ductal carcinoma-in-situ of the breast? J Clin Oncol 2006;24:1017-1019
4. Vargas C, Kestin L, Go N, et al. Factors associated with local recurrence and cause-specific survival in patients with ductal carcinoma in situ of the breast treated with breast-conserving therapy or mastectomy. Int J Radiat Oncol Biol Phys 2005;63:1514-21
5. Carlson, G. W., A. Page, et al. (2007). "Local recurrence of ductal carcinoma in situ after skin-sparing mastectomy." J Am Coll Surg 204(5): 1074-1078; discussion 1078-1080.
6. Rudloff U, E Brogi et al. (2010): "The Influence of Margin Width and Volume of Disease Near Margin on Benefit of Radiation Therapy for Women With DCIS Treated With Breast-Conserving Therapy" Ann Surg (251) 583 – 591
7. Polyak K. Molecular markers for the diagnosis and management of ductal carcinoma in situ. J Natl Cancer Inst Monogr 2010; 41: 210-213
8. Houssami N, Ambrogetti D, Marinovich L et al. Accuracy of a preoperative model for predicting invasive breast cancer in women with ductal carcinoma in situ on vacuum assisted core needle biopsy. Ann Surg Oncol 2011;18(5):1364-71

SNE*

1. Killelea BK, Long JB, Dang W, et al. [Associations Between Sentinel Lymph Node Biopsy and Complications for Patients with Ductal Carcinoma In Situ](#). Ann Surg Oncol. 2018 Jun;25(6):1521-1529.

Mastektomie

DCIS beim Mann

1. Chern J, Liao L, Baraldi R, et al. Case report: ductal carcinoma in situ in the male breast. Case Rep Radiol. 2012;2012:532527. doi: 10.1155/2012/532527. Epub 2012 Sep 26.

BET

1. Meijnen P, Oldenburg HS, Loo CE, et al. Risk of invasion and axillary lymph node metastasis in ductal carcinoma in situ diagnosed by core-needle biopsy. Br J Surg 2007;94:952-6
2. Miyake T, Shimazu K, Ohashi H, et al. Indication for sentinel lymph node biopsy for breast cancer when core biopsy shows ductal carcinoma in situ. The American Journal of Surgery 2011; 202: 59-65 :394095. doi: 10.5402/2012/394095. Epub 2012 May 14.
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Axilladisektion

	Oxford LoE
Resection margins	1a
Residual tumor-associated microcalcification	2b
Age	1a
Size	1a
Grading	1a
Comedo necrosis	1a
Architecture	2b
Method of diagnosis	1a
Focality	1a
(mod.) Van Nuys Prognostic Index	2b
Palpable DCIS	2b
Palpable + ER-, HER2+, Ki-67+	2b
HER2-Überexpression	1a
ER/PgR (positive vs. negative)	1a
DCIS-Score (9 Gene recurrence score)	2b
MSKCC Nomogram	2b
Intrinsic subtypes (luminal A, B, HER2+, triple negative)	2b

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Resektionsränder

Residualer tumorassoziierter Mikrokalk

Alter

Größe

Grading

Komedonekrose

Architektur

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Diagnostische Methode

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(mod.) Van Nuys Prognose Index und MSKCC Nomogramm

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Palpables DCIS

Palpabel + COX-2+p16+Ki-67+

Palpabel + ER-, HER2, +Ki-67+

HER2-Überexpression

ER/PgR (positiv vs. negativ)

DCIS-Score

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DCIS mit Mikroinvasion – Behandlung analog zum invasiven Karzinom

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Intrinsische Subgruppen (Luminal A,B, HER+, triple negativ)

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DCIS Radiotherapy Statements

- Radiotherapy has no impact on survival LOE 1a
- Radiotherapy reduces the risk of ipsilateral (invasive and non invasive) recurrences by 50 % LOE 1a
- Avoidance of invasive recurrence is probably not associated with survival benefit LOE 2b
- The absolute (individual) benefit of radiotherapy depends on the individual risk of local recurrence
- The number needed to treat (for ipsilateral breast recurrence) is 9 (over all risk groups)

El Hage Chehade H, Mokbel K. [Is Adjuvant Endocrine Therapy Indicated for DCIS Patients After Complete Surgical Excision?](#) Anticancer Res. 2018 Mar;38(3):1263-1266. Review.



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DCIS Radiotherapy

	Oxford		
	LoE	GR	AGO
Radiotherapy after:			
▪ Breast conserving surgery (BCS)	1a	A	++
▪ Mastectomy	2b	B	--
Modality:			
▪ Partial breast radiotherapy (PBI)	3a	D	--
▪ Hypofractionated radiotherapy regimens	2b	D	+/-**
▪ Radiotherapy boost on the tumor bed	2b	D	--
▪ Women younger than 45-50 years	2b	C	+/-
▪ Intraoperative Radiotherapy	2b	C	-

Side effects and disadvantages must be weighed against risk reduction. Omitting radiotherapy implies elevated risk for local recurrence without effect for overall survival even in the subset of „good risk“ patients. There remains a lack of level-1 evidence supporting the omission of adjuvant radiotherapy in selected low-risk cases: < 2.5 cm, low and intermediate nuclear grade, mammographically detected

** Analysis in ongoing trials

Radiotherapie nach: Brustershaltender Operation (BEO) (gesamte Brust, WBI)

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Teilbrustbestrahlung

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DCIS Postoperative Systemic Treatment - Statements

- **Postoperative endocrine treatment has no impact on survival** **LOE 1a**
- **Postoperative endocrine treatment may have a small effect on ipsilateral invasive recurrences** **LOE 1a**
- **Endocrine treatment for DCIS has an effect on contralateral invasive cancer and ipsilateral and contralateral DCIS** **LOE 1a**
- **The number needed to treat for any ipsilateral breast event is 15** **LOE 1a**



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DCIS Postoperative Systemic Treatment

Oxford		
LoE	GR	AGO
1a	A	+/-*
2b ^a	B	+/-*
1b	A	+/-*
5	D	--

- **Tamoxifen (only ER+) 20mg**
- **Tamoxifen (only ER+) 5mg (long-term data missing)**
- **Aromatase inhibitor (only ER+) in postmenopausal women only**
- **Trastuzumab (only Her2+)**

* Indication for treatment depends on risk factors, side effects and patient preference

Tamoxifen (nur ER+, nur BET)

1. Fisher B, Dignam J, Wolmark N, et al. Tamoxifen in treatment of intraductal breast cancer: National Surgical Adjuvant Breast and Bowel Project B-24 randomised controlled trial. *Lancet*. 1999 Jun 12;353(9169):1993-2000.
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AI (wenn postmenopausal und Kontraindikationen gegen Tamoxifen)

Andere endokrine Optionen Trastuzumab (nur HER2+)

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2. Siziopikou KP, Anderson SJ, Cobleigh MA et al. Preliminary results of centralized HER2 testing in ductal carcinoma in situ (DCIS): NSABP B-43. Breast Cancer Res Treat. 2013 Nov;142(2):415-21.
3. Richard G Margolese, Reena S Cecchini, Thomas B Julian, et al. Anastrozole versus tamoxifen in postmenopausal women with ductal carcinoma in situ undergoing lumpectomy plus radiotherapy (NSABP B-35): a randomised, double-blind, phase 3 clinical trial. www.thelancet.com Published online December 10, 2015
4. Patricia A Ganz, Reena S Cecchini, Thomas B Julian, et al. Patient-reported outcomes with anastrozole versus tamoxifen for postmenopausal patients with ductal carcinoma in situ treated with lumpectomy plus radiotherapy (NSABP B-35): a randomised, double-blind, phase 3 clinical trial. www.thelancet.com Published online December 10, 2015
5. John F Forbes, Ivana Sestak, Anthony Howell, et al. Anastrozole versus tamoxifen for the prevention of locoregional and contralateral

breast cancer in postmenopausal women with locally excised ductal carcinoma in situ (IBIS-II DCIS): a double-blind, randomized controlled trial. www.thelancet.com Published online December 11, 2015.

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Low dose Tamoxifen (5mg) in premalignant lesions


- **N=500**
 - **Follow up 5.69 years**
- DCIS (69%), LCIS (11%),
ADH (20%)

→ (R)


Tamoxifen 5 mg 3y

Placebo
- **EFS: TAM 5.5% (14/253) vs. PLAC 11.3% (28/247)**
 - **Severe adverse Event with same incidence**
 - **(Endometriumkarzinom TAM 1 vs. PLAC 0, thrombo-embolic event TAM1 vs. PLAC 1)**
 - **Adhärenz TAM 65% vs. PLAC 61%** DeCensi et al, SABCS 2018

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Therapy of Local DCIS Recurrence after Tumorectomy

Oxford			
LoE	GR	AGO	
After Radiation:			
■ Simple Mastectomy + SNB	3a 5	C D	+ +
■ Secondary breast conserving surgery	5	D	+/-
Without radiation after first tumorectomy			
■ Treatment like primary disease	3	C	++

Prognosis for invasive recurrences seems to be better than for primary invasive breast cancer. About 50% of recurrences are invasive.

Nach Radiatio

Einfache Mastektomie

+ SN B

1. Silverstein MJ, MD Lagios et al (1998): "Outcome After Invasive Local Recurrence in Patients With Ductal Carcinoma In Situ of the Breast" J Clin Oncol 16:1367-1373

Sekundäre Tumorektomie führt zu Rezidiven in bis zu 30 % der Fälle (NSABP B17)

1. Fisher ER, Dignam J, Tan-Chiu E et al. (1999): "Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) eight-year update of Protocol B-17: intraductal carcinoma" Cancer 86: 429 – 438

Keine Radiotherapie

Therapieindikation wie bei primär Erkrankung