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Guidelines Breast
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FORSCHEN
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HEILEN

Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Duktales Carcinoma in situ (DCIS)

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

Prätherapeutische Abklärung suspekter Läsionen (BIRADS 4)			
	Oxford		
	LoE	GR	AGO
■ Mammographie	1b	B	++
■ Vergrößerungsaufnahmen von Mikroverkalkungen	4	C	++
■ Steigerung der Detektionsrate von G1/G2 DCIS durch digitale Mammographie (versus konventionell)	2b	B	+
■ Stereotaktische Stanzbiopsie / Vakuumbiopsie (VAB)	2b	B	++
■ Präparateradiographie	2b	B	++
■ Setzen eines Markierungsclips in der Biopsieregion, wenn die Läsion komplett entfernt wurde	5	D	++
■ MRT zur Festlegung der Ausdehnung	1b	B	+/-
■ Klinische Untersuchung	5	D	++
■ Feinnadelpunktion / duktale Lavage	5	D	-
■ Interdisziplinäre Tumorboard-Präsentation	5	D	++



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Mammographie

1. 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.



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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 Patientinnen aus der SEER data base**
- **Retrospektive Analyse**
- **Brustkrebspezifische Mortalität 3,3 %**
- **Erhöht bei jungen Frauen und schwarzer Rasse**
- **Patientinnen mit invasiven Rezidiven haben eine ungünstigere Prognose quoad vitam**
HR 18 (95%CI, 14,0–23,6)
- **Die Reduktion von invasiven Rezidiven durch Radiotherapie verbessert nicht das Überleben nach 10 Jahren**

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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Original Investigation

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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 [1 []	
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

- 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.


Generelle therapeutische Prinzipien

Exzision (BEO, Mastektomie) ist die therapeutische Basis für die Behandlung des DCIS.

Die adjuvante Therapie (Strahlentherapie, endokrine Therapie) muss mit der Patientin auf der Basis einer Risiko-Nutzen-Bewertung individuell erörtert werden.

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.



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Operative Maßnahmen zur Therapie des histologisch gesicherten DCIS I

	Oxford		
	LoE	GR	AGO
▪ Exzision (drahtmarkiert)	2b	B	++
▪ Flankierende Drahtmarkierung bei großen Läsionen	3a	C	+
▪ Präparatradiographie bei Drahtmarkierung	2b	B	++
▪ Intraoperative Sonographie (darstellbarer Befund)	3a	C	+/-
▪ Sofortige Nachresektion bei knappen Resektionsrändern (Präparateradiographie)	1c	B	++
▪ Intraoperative Schnellschnittdiagnostik (Einzelfall für Schnittländer)	3a	D	+/-
▪ Interdisziplinäre Tumorboard-Präsentation	2b	C	++

Offene Biopsien suspekter Läsionen (mammographische Mikrokalzifikationen, suspekter US, MRI etc.) ohne präoperative Stanzbiopsie sollten vermieden werden.

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

Operative Maßnahmen zur Therapie des histologisch gesicherten DCIS II			
	LoE	GR	AGO
▪ Histologisch freie Resektionsränder (pR0)	1a	A	++
▪ Multifokalität: BEO falls möglich (inkl. RT)	2b	B	+
▪ Nachresektion bei knappem Resektionsrand (< 2 mm im Paraffinschnitt)**	2b	C	+
▪ Mastektomie* (große Läsionen; keine sicheren Ränder im Nachresektat)	2a	B	++
▪ SNE beim DCIS			
▪ Mastektomie	3b	B	+
▪ BET	3b	B	-
▪ DCIS beim Mann	5	D	+/-
▪ Axilladisektion	2b	B	--
* Patientinnen mit einem tastbaren Tumor haben signifikant höhere Wahrscheinlichkeiten für eine okkulte Invasion (26%), Multizentrität und ein Lokalrezidiv. **besonders, wenn nicht nachbestrahlt wird			

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, 10 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.
3. De Lorenzi F, Di Bella J, Maisonneuve P et al. [Oncoplastic breast surgery for the management of ductal carcinoma in situ \(DCIS\): is it oncologically safe? A retrospective cohort analysis](#). Eur J Surg Oncol. 2018 Jul;44(7):957-962.

Axilladisektion

Prognostische Faktoren für das Auftreten eines ipsilateralen Rezidivs		
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		Oxford
		LoE
	▪ Resektionsränder	1a
	▪ Alter	1a
	▪ Größe	1a
	▪ Grading	1a
	▪ Komedonekrose	1a
	▪ Architektur	2b
	▪ Diagnostische Methode	1a
	▪ Fokalität	1a
	▪ HER2-Überexpression	1a
	▪ ER/PgR (positiv vs. negativ)	1a
	▪ (mod.) Van Nuys Prognose Index	2b
	▪ Palpables DCIS	2b
	▪ Palpabel + ER-, HER2, +Ki-67+	2b
	▪ DCIS-Score (9 gene recurrence score)	2b
	▪ MSKCC Nomogram	2b
	▪ Intrinsische Subgruppen (Luminal A,B, HER+, triple negativ)	2b

Resektionsränder

Residualer tumorassoziierter Mikrokalk

Alter

Größe

Grading

Komedonekrose

Architektur

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. 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

4. Farhat G, R Walker et al. (2010): "Changes in Invasive Breast Cancer and Ductal Carcinoma In Situ Rates in Relation to the Decline in Hormone Therapy Use" J Clin Oncol (28)
5. Pinder SE, C Duggan et al. A new pathological system for grading DCIS with improved prediction of local recurrence: results from the UKCCCR/ANZ DCIS trial. Br J Cancer 2010; 103: 94 – 100
6. Kerlikowske K, AM Molinaro et al. Biomarker Expression and Risk of Subsequent Tumors After Initial Ductal Carcinoma In Situ Diagnosis. J Natl Cancer Inst 2010; 102: 627 – 637
7. Rudloff U, LM Jacks et al. Normogram for Predicting the Risk of Local Recurrence After Breast-Conserving Surgery for Ductal Carcinoma In Situ. J Clin Oncol 2010; 28: 3762 – 3769
8. Cuzick J, I Sestak et al. Effect of Tamoxifen and radiotherapy in women with locally excised ductal carcinoma in situ: long-term results from the UK / ANZ DCIS trial. Lancet Oncol 2011; 12: 21- 29
9. Lari S, Kuerer HM. Review: Biological Markers in DCIS and Risk of Breast Recurrence: A Systematic Review. Journal of Cancer 2011; 2: 232-261
10. Harada S, Mick R, Roses R, et al. The significance of HER-2/neu Resceptor positivity and Immunophenotype in Ductal Carcinoma In Situ with Early Invasive Disease. J Surg Oncol 2011; 104: 458-465
11. Han K, Nofech-Mozes S, Narod S, et al. Expression of Her2neu in Ductal Carcinoma in situ is associated with Local Recurrence. Clinical Oncology 2011; 1-7 (epub ahead)
12. King TA, Sakr RA, Muhsen S, et al. Is there a Low-Grade Precursor Pathway in Breast Cancer? Ann Surg Oncol 2011;(epub ahead)
13. Chan P, Lim S. Predictors of Invasive Breast Cancer in Ductal Carcinoma In Situ initially diagnosed by Core Biopsy. Asian J Surg 2010; 33: 76-82
14. Liao N, Zhang GC, Liu YH, et al. HER2-positive status is an independent predictor for coexisting invasion of ductal carcinoma in situ of the breast presenting extensive DCIS component. Pathology Res Practice 2011; 207: 1-7
15. Dick AW, Sorbero MS, Ahrendt GM, et al. Comparative Effectiveness of Ductal Carcinoma In Situ Management and the Roles of margins and Surgeons. J natl Cancer Inst 2011; 103:92-104
16. Brennan ME, Turner RM, Ciatto S, et al. Ductal Carcinoma in Situ at Core-Needle Biopsy: Meta-Analysis of Underestimation and Predictors of Invasive Breast Cancer. Radiology 2011; 260: 119-128

17. Wang S, Shamliyan T, Virnig BA, et al. Tumor characteristics as predictors of local recurrence after treatment of ductal carcinoma in situ: a meta-analysis. *Breast Cancer Res Treat* 2011; 127: 1-14
18. Holmes P, Lloyd J, Chervoneva I, et al. Prognostic Markers and Long-Term Outcomes in Ductal Carcinoma In Situ of the Breast Treated With Excision Alone. *Cancer* 2011; 117: 3650-7
19. Visser LL, Elshof LE, Schaapveld M et al. Clinicopathological Risk Factors for an Invasive Breast Cancer [recurrence after Ductal Carcinoma In Situ-A Nested Case-Control Study](#). *Clin Cancer Res*. 2018 Aug 1;24(15):3593-3601.
20. Rakovitch E, Gray R, Baehner FL et al. [Refined estimates of local recurrence risks by DCIS score adjusting for clinicopathological features: a combined analysis of ECOG-ACRIN E5194 and Ontario DCIS cohort studies](#). *Breast Cancer Res Treat*. 2018 Jun;169(2):359-369

Diagnostische Methode

1. Han JS, Molberg KH, Sarode V. Predictors of Invasion and Axillary Lymph Node Metastasis in Patients with a Core Biopsy Diagnosis of Ductal carcinoma In Situ: An Analysis of 255 Cases. *The Breast Journal* 2011; 17: 223-229
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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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DCIS Strahlentherapie Statements


- **Strahlentherapie hat keinen Einfluss auf das Gesamtüberleben.**

LOE 1a
- **Strahlentherapie reduziert das ipsilaterale Lokalrezidivrisiko (invasiv und nicht-invasiv) um 50 %.**

LOE 1a
- **Das Vermeiden eines invasiven Rezidivs ist sehr wahrscheinlich nicht mit einem Überlebensvorteil verbunden.**

LOE 2b
- **Der absolute individuelle Benefit der Strahlentherapie ist vom individuellen Lokalrezidivrisiko abhängig.**
- **The number needed to treat (für jedes Auftreten eines In-Brust-Rezidivs) ist 9 (über alle Risikogruppen)**

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 Strahlentherapie

Oxford		
LoE	GR	AGO
1a	A	++
2b	B	--
3a	D	--
2b	D	+/-**
2b	D	--
2b	C	+/-
2b	C	-

Radiotherapie nach:

- **Brusterhaltender Operation (BEO) (gesamte Brust, WBI)**
- **Mastektomie**

Sonderformen der Radiotherapie:

- **Teilbrustbestrahlung**
- **Hypofraktionierte Radiotherapie**
- **Boost-RT des Tumorbettes**
 - Bei Patientinnen unter 45–50 Jahren
- **Intraoperative Strahlentherapie**

NW und Nachteile der Radiotherapie müssen gegenüber der erreichbaren Risikoreduktion abgewogen werden. Ein Verzicht auf eine Strahlentherapie nach BEO bedeutet ein erhöhtes lokales Rezidivrisiko ohne Einfluss auf das Überleben. Dieses gilt auch für Patientinnen mit günstigen prognostischen Faktoren (low-risk-Subgruppe; Level I-Evidenz): < 2,5 cm, low and intermediate nuclear grade, mammographisch entdeckt

** Analyse im Rahmen laufender Studien

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Mastektomie

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Sonderformen der Radiotherapie:

Teilbrustbestrahlung

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Hypofraktionierte Radiotherapie

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Boost-RT des Tumorbettes


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Intraoperative Strahlentherapie beim DCIS

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DCIS – Postoperative adjuvante Systemtherapie

- Postoperative endokrine Therapie hat keinen Einfluss auf das Gesamtüberleben. **LOE 1a**
- Postoperative endokrine Therapie kann einen geringen Effekt auf die ipsilateralen invasiven Rezidive haben. **LOE 1a**
- Endokrine Therapie hat einen Effekt auf die kontralaterale invasive Rezidivrate und die ipsilaterale und kontralaterale DCIS-Rezidivrate. **LOE 1a**
- The number needed to treat (für jedes In-Brust-Rezidiv) ist 15. **LOE 1a**



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DCIS - Postoperative adjuvante Systemtherapie

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

- **Tamoxifen (nur ER+) 20mg**
- **Tamoxifen (nur ER+) 5mg (Langzeitdaten fehlen)**
- **Aromataseinhibitor (nur ER+) bei postmenopausalen Patientinnen**
- **Trastuzumab (nur HER2+)**

• Indikation zur Therapie ist von Risikofaktoren, Nebenwirkungen und Patientinnenpräferenz abhängig.

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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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
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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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Behandlung des Lokalrezidivs des DCIS nach Tumorektomie

	Oxford LoE	GR	AGO
Nach vorangegangener Bestrahlung:			
▪ Einfache Mastektomie	3a	C	+
+ SNB	5	D	+
▪ Sekundärer brusterhaltende Operation	5	D	+/-
Ohne vorangegangene Bestrahlung			
▪ Therapieindikation wie bei primärer Erkrankung	3	C	++

Prognose für invasive Rezidive scheint besser zu sein als bei primären invasiven Karzinomen. Ca. 50% der Rezidive sind invasiv.

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