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# Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

## Duktales Carcinoma in situ (DCIS)



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# Duktales Carcinoma in situ (DCIS)

- **Versionen 2002–2019:**  
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Friedrich / Gerber / Hanf / Junkermann / Kühn / Lux / Maass / Möbus /  
Mundhenke / Nitz / Oberhoff / Scharl / Schütz / Solomayer / Souchon /  
Thill / Thomssen / Wenz
- **Version 2020:**  
Friedrich / Gerber

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



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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

Narod A. et al.: JAMA Oncol. 2015 Oct;1(7):888-96

- **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**

Narod SA, Iqbal J, Giannakeas V, Sopik V, Sun P.: [Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ](#). JAMA Oncol. 2015 Oct;1(7):888-96

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	Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ					
	Narod A. et al.: JAMA Oncol. 2015 Oct;1(7):888-96					
	Treatment	Cases, No	10-Year BCS Mortality (95%CI), %	Univariate HR (95% CI)	P Value	Multivariate <sup>3</sup> HR (95%)
	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)
	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)

Narod SA, Iqbal J, Giannakeas V, Sopik V, Sun P.: [Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ](#). JAMA Oncol. 2015 Oct;1(7):888-96

## Generelle therapeutische Prinzipien

**Exzision (BEO oder 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.



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.			

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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. 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. 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.
4. Hong YK, McMasters KM, Egger ME, Ajkay N: [Ductal carcinoma in situ current trends, controversies, and review of literature](#). Am J Surg. 2018 Nov;216(5):998-1003
5. 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.
6. 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.

### 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, 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.
2. 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.
3. Morrow M, Van Zee KJ, Solin LJ, Houssami N 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.](#) Ann Surg Oncol. 2016 Nov;23(12):3801-3810.

### Interdisziplinäre Tumorboard-Präsentation

# Operative Maßnahmen zur Therapie des histologisch gesicherten DCIS II

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	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	++
▪ SLNE			
▪ Mastektomie	3b	B	+
▪ BET	3b	B	--
▪ DCIS beim Mann	5	D	+/-
▪ Axilladisektion	2b	B	--

\* besonders, wenn nicht nachbestrahlt wird

\*\* Patientinnen mit einem tastbaren Tumor haben signifikant höhere Wahrscheinlichkeiten für eine okkulte Invasion (26%), Multizentrität und ein Lokalrezidiv.

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### Histologisch freie Resektionsränder (pR0)

1. 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.
2. 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.
3. 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.
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.

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

1. 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.
2. 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
3. Polyak K. Molecular markers for the diagnosis and management of ductal carcinoma in situ. J Natl Cancer Inst Monogr 2010; 41: 210-213
4. 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

#### SLNE\*

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.

2. [Hong YK](#), [McMasters KM](#), [Egger ME](#), [Ajay N](#): Ductal carcinoma in situ current trends, controversies, and review of literature. [Am J Surg](#). 2018 Nov;216(5):998-1003
3. [Karakatsanis A](#), [Hersi AF](#), [Pistiolis L](#): Effect of preoperative injection of superparamagnetic iron oxide particles on rates of sentinel lymph node dissection in women undergoing surgery for ductal carcinoma in situ (SentiNot study). [Br J Surg](#). 2019 May;106(6):720-728. doi: 10.1002/bjs.11110. Epub 2019 Mar 6.

### 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		
		Oxford LoE
<div>  <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2020.1D</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p> </div>	<ul style="list-style-type: none"> <li>Resektionsränder</li> <li>Alter</li> <li>Größe</li> <li>Grading</li> <li>Komedonekrose</li> <li>Diagnostische Methode</li> <li>Fokalität</li> <li>HER2-Überexpression</li> <li>ER/PgR (positiv vs. negativ)</li> <li>Residuelle Tumor-assoziierte Mikrokalzifikationen</li> <li>Architektur</li> <li>(mod.) Van Nuys Prognose Index</li> <li>Palpables DCIS</li> <li>Palpabel und ER-, HER2, +Ki-67+</li> <li>DCIS-Score (9 gene recurrence score)</li> <li>MSKCC Nomogram</li> <li>Intrinsische Subgruppen (Luminal A,B, HER+, triple negativ)</li> </ul>	<ul style="list-style-type: none"> <li>1a</li> <li>1a</li> <li>1a</li> <li>1a</li> <li>1a</li> <li>1a</li> <li>1a</li> <li>1a</li> <li>1a</li> <li>2b</li> <li>2b</li> <li>2b</li> <li>2b</li> <li>2b</li> <li>2b</li> <li>2b</li> </ul>

1. 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.
2. 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
3. [Cutuli B](#): Ductal carcinoma in situ in 2019: Diagnosis, treatment, prognosis. [Presse Med](#). 2019 Oct;48(10):1112-1122
4. [Badve SS](#), [Gökmen-Polar](#): Ductal carcinoma in situ of breast: update 2019. [Pathology](#). 2019 Oct;51(6):563-569.
5. Van Bockstal MR, Agahozo MC, Koppert LB: A retrospective alternative for active surveillance trials for ductal carcinoma in situ of the breast. [Int J Cancer](#). 2020 Mar 1;146(5):1189-1197
6. Solin LJ: [Management of Ductal Carcinoma In Situ \(DCIS\) of the Breast: Present Approaches and Future Directions](#). Curr Oncol Rep. 2019 Mar 5;21(4):33

### Diagnostische Methode

1. Park HS, Park S, Cho J, et al. Risk predictors of underestimation and the need for sentinel node biopsy in patients diagnosed with ductal carcinoma in situ by preoperative needle biopsy. J Surg Oncol. 2013 Mar;107(4):388-92. doi: 10.1002/jso.23273. Epub 2012 Sep 24.
2. Schulz S, Sinn P, Golatta M, et al. Prediction of underestimated invasiveness in patients with ductal carcinoma in situ of the breast on percutaneous biopsy as rationale for recommending concurrent sentinel lymph node biopsy. Breast. 2013 Aug;22(4):537-42.
3. Elshof LE, Schmidt MK, Rutgers EJ, et al. Cause-specific Mortality in a Population-based Cohort of 9799 Women Treated for Ductal Carcinoma In Situ. Ann Surg. 2017 Apr 3. doi: 10.1097/SLA.0000000000002239. [Epub ahead of print]
4. Punglia RS, Jiang W, Lipsitz SR, et al. Clinical risk score to predict likelihood of recurrence after ductal carcinoma in situ treated with breast-conserving surgery. Breast Cancer Res Treat. 2017 Oct 28. doi: 10.1007/s10549-017-4553-5. [Epub ahead of print]

### Fokalität

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

### (mod.) Van Nuys Prognose Index und MSKCC Nomogramm

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. Rudloff U, Jacks LM, Goldberg JL, et al. Nomogram for predicting the risk of local recurrence after breast conserving surgery for ductal carcinoma in situ. J Clin Oncol 2010; 28(23): 3762-9
3. Van Zee KJ, Patil S. Validation of a nomogram for predicting risk of local recurrence for ductal carcinoma in situ. J Clin Oncol 2012; 30(25): 3143-4.

4. Sweldens C, Peeters S, van Limbergen E, et al. Öokal relapse after breast-conserving therapy for ductal carcinoma in situ: a European single-center experience and external validation of the Memorial Sloan-Kettering Cancer Center DCIS nomogram. Cancer J 2014; 20(1): 1-7.

#### Palpables DCIS

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

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

HER2-Überexpression

ER/PgR (positiv vs. negativ)

#### DCIS-Score

1. Solin LJ, Gray R, Baehner FL, et al. A multigene expression assay to predict local recurrence risk for ductal carcinoma in situ of the breast. J Natl Cancer Inst. 2013 May 15;105(10):701-10.
2. Sarah Patricia Cate, Alyssa Gillego, Manjeet Chadha, et al. Does the Oncotype DCIS score impact treatment decisions? J Clin Oncol 31, 2013 (suppl 26; abstr 91)
3. Rakovitch E, Nofech-Mozes S, Hanna W et al. A large prospectively-designed study of the DCIS score. Predicting recurrence risk after local excision for ductal carcinoma in situ patients with and without irradiation. SABCS 2015. S5-04
4. Wood WC, Alvarado M, Buchholz DJ, et al. The current clinical value of the DCIS Score. Oncology (Williston Park). 2014 May;28 Suppl 2:C2, 1-8, C3.


#### DCIS mit Mikroinvasion – Behandlung analog zum invasiven Karzinom

1. Eng-Wong J, JP Costantino et al. The Impact of Systemic Therapy Following Ductal Carcinoma In Situ. J Natl Cancer Inst Monogr 2010; 41: 200 – 203
2. Ryan R, Tawfik O, Jensen RA, Anant S. Current Approaches to Diagnosis and Treatment of Ductal Carcinoma In Situ and Future Directions. Prog Mol Biol Transl Sci. 2017;151:33-80.



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

1. Noh JM, Lee J, Choi DH, et al. HER-2 overexpression is not associated with increased ipsilateral breast tumor recurrence in DCIS treated with breast-conserving surgery followed by radiotherapy. *Breast*. 2013 Oct;22(5):894-7.
2. Solin LJ.: Management of Ductal Carcinoma In Situ (DCIS) of the Breast: Present Approaches and Future Directions. *Curr Oncol Rep*. 2019 Mar 5;21(4):33. doi: 10.1007/s11912-019-0777-3.
3. Visser LL, Groen EJ, van Leeuwen FE, et al.: [Predictors of an Invasive Breast Cancer Recurrence after DCIS: A Systematic Review and Meta-analyses](#). *Cancer Epidemiol Biomarkers Prev*. 2019 May;28(5):835-845. doi: 10.1158/1055-9965.EPI-18-0976. Epub 2019 Apr 25.
4. Van Bockstal MR, Agahozo MC, Koppert LB, van Deurzen CHM. [A retrospective alternative for active surveillance trials for ductal carcinoma in situ of the breast](#). *Int J Cancer*. 2019 Apr 24. doi: 10.1002/ijc.32362. [Epub ahead of print]



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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)**

1. Bagenal J, Roche N, Ross G, Kirby A, Dodwell D: [Should patients with ductal carcinoma in situ be treated with adjuvant whole breast radiotherapy after breast conservation surgery?](#) BMJ. 2018 May 17;361:k1410. doi: 10.1136/bmj.k1410. Review.
2. Lebeau A, Kühn T.: [Updates in the treatment of ductal carcinoma in situ of the breast.](#) Curr Opin Obstet Gynecol. 2016 Feb;28(1):49-58.



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## DCIS

### adjuvante Strahlentherapie

	Oxford LoE	GR	AGO
<b>Radiotherapie nach:</b>			
▪ Brusterhaltender Operation (BEO) ; (gesamte Brust, WBI)	1a	A	++
▪ Mastektomie	2b	B	--
<b>Sonderformen der Radiotherapie:</b>			
▪ Teilbrustbestrahlung (DCIS < 3 cm)	2a	B	+/-
▪ Hypofraktionierte Radiotherapie	2b	D	+/-*
▪ Boost-RT des Tumorbettes	2b	D	--
▪ Bei Patientinnen unter 45–50 Jahren	2b	C	+/-
▪ Intraoperative Strahlentherapie	2b	C	-

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

#### Radiotherapie nach: Brusterhaltender Operation (BEO) (gesamte Brust, WBI)

1. EBCTCG Correa C et al. Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast. J Natl Cancer Inst Monogr. 2010 (41); 162 – 77
2. Abram Recht. Are the Randomized Trials of Radiation Therapy for Ductal Carcinoma in Situ Still Relevant? J Clin Oncol 2014; 32(22): 3588
3. Lawrence J. Solin, Robert Gray, Lorie L. Hughes et al. Surgical Excision Without Radiation for Ductal Carcinoma in Situ of the Breast: 12-Year Results From the ECOG-ACRIN E5194 Study. J Clin Oncol 2015; 33 (33):3938
4. Beryl McCormick, Kathryn Winter, Clifford Hudis, et al. RTOG 9804: A Prospective Randomized Trial for Good-Risk Ductal Carcinoma In Situ Comparing Radiotherapy With Observation. J Clin Oncol 2015; 33(7): 709
5. Garg PK, Jakhetiya A, Pandey R, et al. Adjuvant radiotherapy versus observation following lumpectomy in ductal carcinoma in-situ: A meta-analysis of randomized controlled trials. Breast J. 2017 Aug 22. doi: 10.1111/tbj.12889. [Epub ahead of print]
6. Giannakeas V, Sopik V, Narod SA. [Association of Radiotherapy With Survival in Women Treated for Ductal Carcinoma In Situ With Lumpectomy or Mastectomy](#). JAMA Netw Open. 2018 Aug 3;1(4):e181100.

### Mastektomie


1. Chadha M, Portenoy J, Boolbol SK, et al. Is there a role for postmastectomy radiation therapy in ductal carcinoma in situ? Int J Surg Oncol 2012;2012:423520. doi: 10.1155/2012/423520. Epub 2012 Jun 13.

### Teilbrustbestrahlung

1. [Whelan TJ](#), [Julian JA](#), [Berrang TS](#): External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): a randomised controlled trial. [Lancet](#). 2019 Dec 14;394(10215):2165-2172. doi: 10.1016/S0140-6736(19)32515-2.
2. Vicini FA, Cecchini RS, White JR et al.: [Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial](#). Lancet. 2019 Dec 14;394(10215):2155-2164

### Intraoperative Strahlentherapie beim DCIS

1. Banks A, Coronado G, Zimmerman R et al. [Breast conserving surgery with targeted intraoperative radiotherapy for the management of ductal carcinoma in situ](#). J Surg Oncol. 2018 Dec 27. doi: 10.1002/jso.25347. [Epub ahead of print]



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## DCIS – adjuvante Systemtherapie

<ul style="list-style-type: none"> <li>▪ <b>Adjuvante endokrine Therapie hat keinen Einfluss auf das Gesamtüberleben.</b></li> </ul>	<p><b>LOE 1a</b></p>
<ul style="list-style-type: none"> <li>▪ <b>Endokrine Therapie kann einen geringen Effekt auf die ipsilateralen invasiven und DCIS-Rezidive haben.</b></li> </ul>	<p><b>LOE 1a</b></p>
<ul style="list-style-type: none"> <li>▪ <b>Endokrine Therapie hat einen Effekt auf die kontralateralen invasiven und in-situ Karzinome</b></li> </ul>	<p><b>LOE 1a</b></p>
<ul style="list-style-type: none"> <li>▪ <b>The number needed to treat (für jedes In-Brust-Rezidiv) ist 15.</b></li> </ul>	<p><b>LOE 1a</b></p>

1. El Hage Chegade H, Mokbel K. [Is Adjuvant Endocrine Therapy Indicated for DCIS Patients After Complete Surgical Excision?](#) Anticancer Res. 2018 Mar;38(3):1263-1266.
2. [Johnston SR](#): Endocrine treatment for ductal carcinoma in situ: balancing risks and benefits. [Lancet](#). 2016 Feb 27;387(10021):819-21.
3. [Altundag K](#): Is it rational to extend the duration of preventive endocrine treatment in hormone receptor positive ductal carcinoma in situ? [J BUON](#). 2018 May-Jun;23(3):835.



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## DCIS – adjuvante Systemtherapie

Oxford		
LoE	GR	AGO
1a	A	+/-*
2b <sup>a</sup>	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.
2. Cuzick J, I Sestak et al. (2010): "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* (12) 21- 29
3. Wapnir IL, Dignam JJ, Fisher B, et al. Long-Term Outcomes of invasive ipsilateral breast tumor recurrences after lumpectomy in NSABP B-17 and B-24 randomized clinical trials for DCIS. *J Natl Cancer Inst* 2011; 103: 478-488
4. Staley H, McCallum I, Bruce J. Postoperative Tamoxifen for ductal carcinoma in situ: Cochrane systematic review and meta-analysis. *Breast*. 2014 Oct;23(5):546-51. doi: 10.1016/j.breast.2014.06.015. Epub 2014 Jul 9
5. 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.
6. [Johnston SR](#): Endocrine treatment for ductal carcinoma in situ: balancing risks and benefits. [Lancet](#). 2016 Feb 27;387(10021):819-21.
7. [Altundag K](#): Is it rational to extend the duration of preventive endocrine treatment in hormone receptor positive ductal carcinoma

in situ? [J BUON](#). 2018 May-Jun;23(3):835.

AI (wenn postmenopausal und Kontraindikationen gegen Tamoxifen)

1. Richard G Margoless, 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](http://www.thelancet.com) Published online December 10, 2015
2. 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](http://www.thelancet.com) Published online December 10, 2015
3. 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](http://www.thelancet.com) Published online December 11, 2015.
4. Wang L, Xia Y, Liu D, et al. Evaluating the efficacy of post-surgery adjuvant therapies used for ductal carcinoma (ca. in situ) patients: a network meta-analysis. *Oncotarget*. 2017;8(45):79257-79269.



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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 TAM 1 vs. PLAC 1)**
- **Adhärenz TAM 65% vs. PLAC 61%**

Lazzeroni M et al: Breast 2019

1. Lazzeroni M, Puntoni M, Provinciali N et al.: [Estimating the magnitude of clinical benefit of systemic therapy in patients with DCIS or pre-invasive disease of the breast](#). Breast. 2019 Nov;48 Suppl 1:S39-S43.
2. DeCensi A, Puntoni M, Guerrieri-Gonzaga A: [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.





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## Behandlung des Lokalrezidivs des DCIS nach Tumorektomie

Oxford		
LoE	GR	AGO

**Nach vorangegangener Bestrahlung:**

- Einfache Mastektomie  
+ SLNE 3a    C    +  
5    D    +
- Sekundäre 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