Guidelines Breast
Version 2018.1

Ductal Carcinoma in Situ (DCIS)

Guidelines Breast
Version 2018.1

Ductal Carcinoma in Situ
DCIS

- **Versions 2002–2017:**
  Audretsch / Blohmer / Brunnert / Budach / Costa / Fersis / Friedrich / Gerber / Hanf / Junkermann / Kühn / Lux / Maass / Möbus / Nitz / Oberhoff / Scharl / Solomayer / Souchon / Thill / Thomssen

- **Version 2018:**
  Blohmer / Mundhenke / Wenz

Guidelines Breast
Version 2018.1

Pretherapeutic Assessment of Suspicious Lesions (BIRADS IV)

	Oxford LoE	Oxford GR	AGO
▪ **Mammography**	1b	B	++
▪ Magnification view of microcalcification	4	C	++
▪ Increase of detection rate of G1/G2 DCIS by full-field digital mammography (versus screen-film)	2b	B	+
▪ **Stereotactic core needle / vacuum biopsy (VAB)**	2b	B	++
▪ Specimen radiography	2b	B	++
▪ Marker (Clip) left at biopsy site for localization if lesion is completely removed	5	D	++
▪ **Assessment of extension**			
▪ MRI	1b	B	+/-
▪ **Clinical examination**	5	D	++
▪ **FNA / ductal lavage**	5	D	-
▪ **Interdisciplinary board presentation**	5	D	++

MRI and DCIS

Systematic review

Meta-analysis of the effect of preoperative breast MRI on the surgical management of ductal carcinoma *in situ*

A. Fancellu[1], R. M. Turner[2], J. M. Dixon[4], A. Pinna[1], P. Cottu[1] and N. Houssami[3]

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BJS 2015; **102**: 883–893

MRI and DCIS

- **9 Studies for this meta-analysis (7 Cohort, 2 randomized Studies)**
  that used MRI as a component of preoperative diagnostic
  evaluation.
- **4 Studies included both DCIS and invasive cancers.**
- **In 4 studies BEO was planned.**

MRI and DCIS

The present meta-analysis shows that preoperative MRI in women with DCIS is not associated with an improvement in surgical outcomes. MRI increases the initial rate of mastectomy, although the overall mastectomy rate is not significantly increased as a result of MRI. Importantly, this meta-analysis shows that preoperative MRI does not reduce the odds of having negative margins after BCS, nor does it reduce the odds of patients requiring reoperation for positive margins. On the basis of the collective evidence summarized in this meta-analysis, preoperative MRI does not improve the surgical treatment of women with DCIS of the breast.

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

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 [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

Ann Surg Oncol (2015) 22:3273–3281
DOI 10.1245/s10434-015-4740-8

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Decreasing Recurrence Rates for Ductal Carcinoma In Situ: Analysis of 2996 Women Treated with Breast-Conserving Surgery Over 30 Years

Preeti Subhedar, MD[1], Cristina Olcese, BS[1], Sujata Patil, PhD[2], Monica Morrow, MD, FACS[1], and Kimberly J. Van Zee, MS, MD, FACS[1]

Breast Conserving Surgery Alone

Recurrence rate (95 % confidence interval)

Time period	5 year	10 year	HR	P value
1978-1998	19.1 % (15.6 - 23.2 %)	26% (22.0 - 30.7%)	1.0	----
1999-2010	8.9 % (7.1 - 11.3 %)	19% (14.9 – 23.1%)	0.59	0.0002

Breast Conserving Surgery and Radiotherapy

Recurrence rate (95 % confidence interval)

Time period	5 year	10 year	HR	P value
1978-1998	6.4% (4.1- 9.8 %	13% (9.3 - 17.1 %)	1.0	----
1999-2010	4.9% (3.7 – 6.5 %)	11% (8.7- 14.2 %)	0.84	0.04

Guidelines Breast
Version 2018.1

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.

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Version 2018.1

Surgical Treatment for Histologically Proven DCIS I

	Oxford LoE	Oxford GR	Oxford AGO
▪ Excisional biopsy (wire guided)	2b	B	++
▪ Bracketing wire localization in large lesions	5	D	+
▪ 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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Version 2018.1

Surgical Treatment for Histologically Proven DCIS II

	Oxford LoE	Oxford GR	Oxford AGO
▪ Histologically clear margins (R0)	1a	A	++
▪ Multifocal DCIS: BCS if feasible	2b	B	+
▪ Re-excision required for close margin ≤ 2 mm in paraffin section)**	2b	C	+
▪ Mastectomy*			
▪ Large lesions confirmed by multiple biopsies; no clear margins after re-excision	2a	B	++
▪ SNE*			
▪ Mastectomy	3b	B	+
▪ BCS	3b	B	-
▪ In case of DCIS in the male breast	5	D	+/-
▪ ALND	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

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Version 2018.1

Prognostic Factors for an Ipsilateral Recurrence

	Oxford		
	LoE	GR	AGO
▪ Resection margins	1a	A	++
▪ Residual tumor-associated microcalcification	2b	C	++
▪ Age	1a	A	++
▪ Size	1a	A	++
▪ Grading	1a	A	++
▪ Comedo necrosis	1a	A	++
▪ Architecture	2b	C	+
▪ Method of diagnosis	1a	A	++
▪ Focality	1a	A	++
▪ (mod.) Van Nuys Prognostic Index	2b	C	+/-
▪ Palpable DCIS	2b	C	+/-
▪ Palpable + COX-2+, p16+, Ki-67+	2b	C	+/-
▪ Palpable + ER-, HER2+, Ki-67+	2b	C	+/-
▪ HER2-Überexpression	1a	B	+/-
▪ ER/PgR (positive vs. negative)	1a	B	+/-
▪ DCIS-Score	2b	C	+/-
▪ MSKCC Nomogram	2b	C	+/-
▪ DCIS with microinvasion – treatment in analogy to invasive breast cancer	3b	C	++
▪ Intrinsic subtypes (luminal A, B, HER2+, triple negative)	2b	C	-

Guidelines Breast
Version 2018.1

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)**

Guidelines Breast
Version 2018.1

DCIS Radiotherapy

	Oxford LoE	Oxford 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	+/-

* 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

Guidelines Breast
Version 2018.1

Cochrane Analysis Radiation after Surgery (all/with Radiation after Breast Conserving Surgery)

Goodwin A, Parker S, Ghersi D, Wilcken N.
Post-operative radiotherapy for ductal carcinoma in situ of the breast.
Cochrane Database Syst Rev. 2013 Nov 21;11:CD000563. doi: 10.1002/14651858.CD000563.pub7.

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Version 2018.1

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**

Cochrane Analysis Tamoxifen after DCIS (all/with Radiation)

Guidelines Breast
Version 2018.1

Staley H, McCallum I, Bruce J. Postoperative tamoxifen for ductal carcinoma in situ. Cochrane Database Syst Rev. 2012 Oct 17;10:CD007847. doi: 10.1002/14651858.CD007847.pub2.

Staley H, McCallum I, Bruce J. Postoperative Tamoxifen for ductal carcinoma in situ: Cochrane systematic review and metaanalysis. Breast. 2014 Oct;23(5):546-51. doi: 10.1016/j.breast.2014.06.015. Epub 2014 Jul 9.

Guidelines Breast
Version 2018.1

DCIS Postoperative Systemic Treatment

	Oxford LoE	Oxford GR	AGO
▪ Tamoxifen (only ER+)	1a	A	+/-*
▪ Aromatase inhibitor (only ER+) in postmenopausal women only	1b	A	+/-*
▪ Trastuzumab (only Her2+)	5	D	--

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

Guidelines Breast
Version 2018.1

Therapy of Local DCIS Recurrence after Tumorectomy

	Oxford LoE	Oxford GR	AGO
After Radiation:			
▪ Simple Mastectomy	3a	C	+
+ SNB	5	D	+
▪ Secondary tumorectomy is followed by recurrences in up to 30 % of patients (NSABP B17)	5	D	+/-
No 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.