

# Diagnosis and Treatment of Patients with early and advanced Breast Cancer



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## Ductal Carcinoma in Situ (DCIS)

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FORSCHEN  
LEHREN  
HEILEN

# Duktales Carcinoma in situ (DCIS)



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- **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**

# Pretherapeutic Assessment of Suspicious Lesions (BIRADS IV)

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

# 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**

# 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 <sup>3</sup> 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

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

# 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.**

# Surgical Treatment for Histologically Proven DCIS I

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

- **Excisional biopsy (wire guided)**
- **Bracketing wire localization in large lesions**
- **Specimen radiography**
- **Intraoperative ultrasound (visible lesion)**
- **Immediate re-excision for close margins (specimen radiography)**
- **Intraoperative frozen section (in single cases for margin)**
- **Interdisciplinary board presentation**

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

# Surgical Treatment for Histologically Proven DCIS II

	Oxford		
	LoE	GR	AGO
■ Histologically clear margins (R0)	1a	A	++
■ Multifocal DCIS: BCS if feasible	2b	B	+
■ Re-excision required for close margin ( $\leq 2$ 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



# Prognostic Factors for an Ipsilateral Recurrence

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	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

# DCIS Radiotherapy Statements

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- **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)**

# DCIS Radiotherapy

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

## Radiotherapy after:

- **Breast conserving surgery (BCS)**
- **Mastectomy**

## Modality:

- **Partial breast radiotherapy (PBI)**
- **Hypofractionated radiotherapy regimens**
- **Radiotherapy boost on the tumor bed**
  - **Women younger than 45-50 years**
- **Intraoperative Radiotherapy**

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

# 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**

# DCIS Postoperative Systemic Treatment

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

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

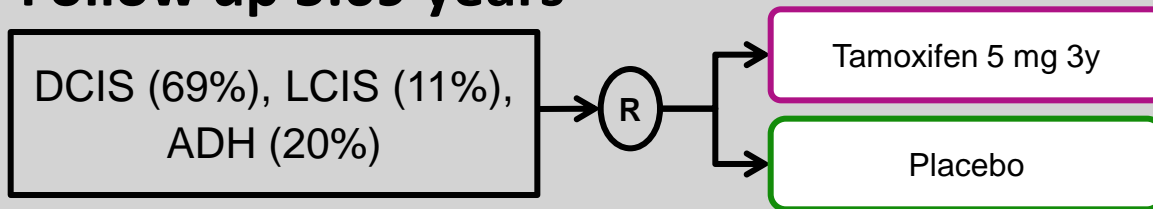
\* Indication for treatment depends on risk factors, side effects and patient preference

# Low dose Tamoxifen (5mg) in premalignant lesions

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- **N=500**
- **Follow up 5.69 years**



- **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

# Therapy of Local DCIS Recurrence after Tumorectomy



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## After Radiation:

- **Simple Mastectomy  
+ SNB**
- **Secondary breast conserving surgery**

## Without radiation after first tumorectomy

- **Treatment like primary disease**

	Oxford		
	LoE	GR	AGO
	<b>3a</b>	<b>C</b>	<b>+</b>
	<b>5</b>	<b>D</b>	<b>+</b>
	<b>5</b>	<b>D</b>	<b>+/-</b>
	<b>3</b>	<b>C</b>	<b>++</b>

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