Ductal Carcinoma in Situ (DCIS)
Ductal Carcinoma in Situ
DCIS

- **Version 2002:**
  Gerber

- **Versions 2003–2015:**
  Audretsch / Blohmer / Brunnert / Costa / Fersis / Friedrich / Hanf / Junkermann / Lux / Maass / Möbus / Nitz / Oberhoff / Scharl / Solomayer / Souchon / Thill / Thomssen

- **Version 2016:**
  Friedrich / Kühn
## Pretherapeutic Assessment of Suspicious Lesions (BIRADS IV)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Oxford / AGO Level</th>
<th>LoE / GR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mammography</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnification view of microcalcification</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>Increase of detection rate of G1/G2 DCIS by full-field digital mammography (versus screen-film)</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td><strong>Stereotactic core needle / vacuum biopsy (VAB)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specimen radiography</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>Marker (Clip) left at biopsy site for location if lesion is completely removed</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td><strong>Assessment of extension</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>3a</td>
<td>C</td>
</tr>
<tr>
<td>Clinical examination</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>FNA / ductal lavage</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>Interdisciplinary board presentation</td>
<td>5</td>
<td>D</td>
</tr>
</tbody>
</table>
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 database
- 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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cases, No</th>
<th>10-Year BCS Mortality (95% CI), %</th>
<th>Univariate HR (95% CI)</th>
<th>P Value</th>
<th>Multivariate(^3) HR (95%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lumpectomy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without radiotherapy</td>
<td>19762</td>
<td>0.9 (0.7 - 1.1)</td>
<td>1 [Reference]</td>
<td>1</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>With radiotherapy</td>
<td>42250</td>
<td>0.8 (0.7 – 1.0)</td>
<td>0.86 (0.67 – 1.10)</td>
<td>0.22</td>
<td>0.81 (0.63 – 1.04)</td>
<td>0.10</td>
</tr>
<tr>
<td>all</td>
<td>63319</td>
<td>0.8 (0.7 – 1.0)</td>
<td>1 [Reference]</td>
<td>1</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td><strong>Unilateral mastectomy</strong></td>
<td>19515</td>
<td>1.3 (1.1 – 1.5)</td>
<td>1.45 (1.18 – 1.79)</td>
<td>&lt; 0.001</td>
<td>1.20 (0.96 – 1.50)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

\(^3\) adjusted for year of diagnosis, age of diagnosis, ethnicity, income, ER-status, tumor size and grade
Decreasing Recurrence Rates for Ductal Carcinoma In Situ: Analysis of 2996 Women Treated with Breast-Conserving Surgery Over 30 Years

Preeti Subhedar, MD¹, Cristina Olcese, BS², Sujata Patil, PhD², Monica Morrow, MD, FACS¹, and Kimberly J. Van Zee, MS, MD, FACS¹

<table>
<thead>
<tr>
<th>Time period</th>
<th>5 year</th>
<th>10 year</th>
<th>HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1978-1998</td>
<td>19.1% (15.6 - 23.2%)</td>
<td>26% (22.0 - 30.7%)</td>
<td>1.0</td>
<td>----</td>
</tr>
<tr>
<td>1999-2010</td>
<td>8.9% (7.1 - 11.3%)</td>
<td>19% (14.9 - 23.1%)</td>
<td>0.59</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Breast Conserving Surgery and Radiotherapy

<table>
<thead>
<tr>
<th>Time period</th>
<th>5 year</th>
<th>10 year</th>
<th>HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1978-1998</td>
<td>6.4% (4.1 - 9.8%)</td>
<td>13% (9.3 - 17.1%)</td>
<td>1.0</td>
<td>----</td>
</tr>
<tr>
<td>1999-2010</td>
<td>4.9% (3.7 – 6.5 %)</td>
<td>11% (8.7- 14.2 %)</td>
<td>0.84</td>
<td>0.04</td>
</tr>
</tbody>
</table>
General Therapeutic Principles

Surgical excision (BCT, Mastectomy) is the therapeutic basis for the treatment of DCIS.

Adjuvant treatment (radiotherapy, hormonal treatment) must be discussed with the patient individually. Disadvantages must be balanced against risk reduction.
### Surgical Treatment for Histologically Proven DCIS I

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Oxford / AGO</th>
<th>LoE / GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excisional biopsy (wire guided)</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>Bracketing wire localization in large lesions</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>Specimen radiography</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>Intraoperative ultrasound (visible lesion)</td>
<td>3a</td>
<td>C</td>
</tr>
<tr>
<td>Immediate re-excision for close margins (specimen radiography)</td>
<td>1c</td>
<td>B</td>
</tr>
<tr>
<td>Intraoperative frozen section</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>Interdisciplinary board presentation</td>
<td>2b</td>
<td>C</td>
</tr>
</tbody>
</table>

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

- Histologically clear margins (R0)  2b C ++
- Multifocal DCIS: BCT if feasible  2b B +
- Re-excision required for close margin \(< \ 2 \text{ mm in paraffin section})  2b C +
- Mastectomy*
  - Large lesions confirmed by multiple biopsies; no clear margins after re-excision  2a B ++
- SNE*
  - BCT  3b B -
  - Mastectomy  3b B +
- ALND  2b B - -

* Patients who present with a palpable mass have a significantly higher potential for occult invasion (26%), multicentricity and local recurrence.
# DCIS – Prognostic Factors for the Incidence of Local- / Locoregional Recurrence

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

- Radiotherapy has no impact on survival

- Radiotherapy reduces the risk of local (invasive and non invasive) recurrences by 50 %

- Avoidance of invasive recurrence is probably not associated with survival benefit

- The absolute (individual) benefit of radiotherapy depends on the individual risk of local recurrence

- The number needed to treat (for any breast event) is 9 (over all risk groups)

LOE 1a

LOE 1a

LOE 2b
## DCIS Radiotherapy

**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

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

* Side effects and disadvantages of radiotherapy must be balanced 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
Cochrane Analysis
Radiation after Surgery (all/with Radiation after Breast Conserving Surgery)

Goodwin A, Parker S, Ghersi D, Wilcken N.
DCIS Postoperative Systemic Treatment - Statements

- Postoperative antihormonal treatment has no impact on survival  
  LOE 1a

- Postoperative antihormonal treatment may have a small effect on ipsilateral invasive recurrences  
  LOE 1a

- Antihormonal treatment for DCIS has an effect on contralateral invasive cancer and ipsilateral and contralateral DCIS  
  LOE 1a

- The number needed to treat for any breast event is 15  
  LOE 1a
Cochrane Analysis
Tamoxifen after DCIS (all/with Radiation)

Staley H, McCallum I, Bruce J.
Postoperative tamoxifen for ductal carcinoma in situ.

DCIS Postoperative Systemic Treatment

- **Tamoxifen (only ER+)**
  - Oxford / AGO LoE / GR: 1a A +/-*

- **Aromatase inhibitor (only ER+) in postmenopausal women only**
  - Oxford / AGO LoE / GR: 1b A +/-*

- **Trastuzumab (only Her2+)**
  - Oxford / AGO LoE / GR: 5 D --

*Indication for treatment depends on risk factors, side effects and patient preference*
Local Recurrence of DCIS after Tumorectomy w/o Irradiation

After radiation
- Simple mastectomy
  + SNB
- Second tumorectomy is followed by recurrences in up to 30% of patients (NSABP B17)

No radiation after first tumorectomy
- Treatment like primary disease

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

Oxford / AGO LOE / GR

3a C +
5 D +
5 D +/-
Ductal Carcinoma in Situ (DCIS) ((2/17))

No further information

No references
Pretherapeutic Assessment in Suspicious Lesions (BIRADS 4) (3/17)

Further information:
Alle Abstimmungen mit 100% Zustimmung

References:

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


- **Stereotaktische Stanzbiopsie / Vakuumbiopsie (VAB)**


- **Präparateradiographie**
- **Setzen eines Markierungscips in der Biopsieregion, wenn die Läsion komplett entfernt wurde**
- **MRT zur Festlegung der Ausdehnung**


- Klinische Untersuchung
- Feinnadelpunktion / duktale Lavage
- Interdisziplinäre Tumorboard-Präsentation
Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ (4-5/17)

No further information

Reference:

Steven A. Narod, MD, FRCPC; Javaid Iqbal, MD; Vasily Giannakeas, MPH; Victoria Sopik, MSc; Ping Sun, PhD; JAMA Oncol. doi:10.1001/jamaoncol.2015.2510 Published online August 20, 2015.
Decreasing Recurrence Rates for Ductal Carcinoma In Situ: Analysis of 2996 Women Treated with Breast-Conserving Surgery Over 30 Years (6/17)

No further information

Reference:

Preeti Subhedar, MD1, Cristina Olcese, BS1, Sujata Patil, PhD2, Monica Morrow, MD, FACS1, and Kimberly J. Van Zee, MS, MD, FACS1; Ann Surg Oncol (2015) 22:3273–3281
General Therapeutic Principles (7/17)

Further information:

Alle Abstimmungen mit 100% Zustimmung.

References:


5. Laura Esserman, Christina Yau. Rethinking the Standard for Ductal Carcinoma In Situ Treatment. JAMA Oncology Published online August 20, 2015.

**Surgical Treatment for Histologically Proven DCIS I (8/17)**

*Further information:*

Alle Abstimmungen mit 100% Zustimmung

*References:*

- **Exzision (drahtmarkiert)**

- **Flankierende Drahtmarkierung bei großen Läsionen**
  - **Präparatradiographie**
  - **Intraoperative Sonographie (darstellbarer Befund)**


- **Sofortige Nachresektion bei knappen Resektionsrändern (Präparateradiographie)**

- Intraoperative Schnellschnittdiagnostik
- Interdisziplinäre Tumorboard-Präsentation
Surgical Treatment for Histologically Proven DCIS II (9/17)

Further information:

Alle Abstimmungen mit 100% Zustimmung

References:

- **Histologisch freie Resektionsränder (pR0)**


- **Multifokalität: BET falls möglich (inkl. RT)**

Nachresektion bei knappem Resektionsrand (≤ 2 mm im Paraffinschnitt)


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


- SNE*
  - Mastektomie
  - DCIS beim Mann


- BET


- Axilladissektion
DCIS – Prognostic Factors for the Incidence of Local-/Locoregional Recurrence (10/17)

No further information

References:

- Resektionsränder
- Residualer tumorassoziierter Mikrokalk
- Alter
- Größe
- Grading
- Komedonekrose
- Architektur


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


Fokalität


(mod.) Van Nuys Prognose Index und MSKCC Nomogramm


7. Silverstein MJ, Lagios MD. Choosing Treatment for Patients With Ductal Carcinoma In Situ: Fine Tuning the University of Southern california/Van Nuys Prognostic Index. J natl Cancer Inst Monogr 2010; 41: 193-196

- Palpables DCIS
  - Palpabel + COX-2+p16+Ki-67+
  - Palpabel + ER-, HER2, +Ki-67+
  - HER2-Überexpression
  - ER/PgR (positiv vs. negativ)

- DCIS-Score

2. Sarah Patricia Cate, Alyssa Gillego, Manjeet Chadha, John Rescigno, Paul R. Gliedman, Ilana Kats, Susan K. Booolbol. Does the Oncotype DCIS score impact treatment decisions? J Clin Oncol 31, 2013 (suppl 26; abstr 91)
ductal carcinoma in situ patients with and without irradiation. SABCS 2015. S5-04


DCIS mit Mikroinvasion – Behandlung analog zum invasiven Karzinom


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


Radiotherapy Statements (11/17)

Further information:
Alle Abstimmungen mit 100% Zustimmung

References:
See next slides
DCIS Radiotherapy (12/17)

Further information:

Alle Abstimmungen mit 100% Zustimmung.

References:

Radiotherapie nach:

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


10. Schwartz GF, Solin LJ, Olivotto IA, Ernster VL, Pressman PI.
12. Impact of pathological characteristics on local relapse after breast-conserving therapy: a subgroup analysis of the EORTC boost versus no boost trial.


34. Australian New Zealand Clinical Trials Registry website. The Trans Tasman Radiation Oncology Group (TROG) 07.01: A randomised phase III study of radiodoses and fractionation schedules in non-low risk Ductal Carcinoma In


➤ Mastektomie

**Sonderformen der Radiotherapie:**

➢ Teilbrustbestrahlung


11. John Paul Einck, Steven E. Finkelstein, Ben Han, Robert Hong, Lydia T. Komarnicky, Robert R. Kuske, Sudha B. Mahalingam, Constantine Mantz, Serban Morcovescu, Stephen S. Nigh, Kerri L. Perry, Jon david Pollock, Jay E. Reiff, Daniel Scanderbeg, Jon F. Strasser, Catheryn M. Yashar, SAVI Collaborative Research Group; Department of Radiation Medicine and Applied Sciences, University of California, San Diego, La Jolla, CA; 21st Century Oncology of Arizona, Translational Research Center, Scottsdale, AZ; South Florida Radiation Oncology, LLC, Boynton Beach, FL; Virginia Hospital Center, Arlington, VA; Drexel University College of Medicine, Philadelphia, PA; Arizona Breast Cancer Specialists, Scottsdale, AZ; The Christ Hospital Cancer Center, Cincinatti, OH; 21st Century Oncology, Translational Research Consortium (TRC), Fort Myers, FL; Texas Oncology, Denton, TX; Northwest Community Hospital Cancer Services, Arlington Heights, IL; Kerri Perry, MD, Denton, TX; Schiffler Cancer Center, Wheeling, WV; Helen F. Graham Cancer Center - Christiana Care Health System, Newark, DE. Accelerated partial-breast irradiation using strut-based brachytherapy in ductal carcinoma in situ patients: A report on 321 patients with median 25-month follow-up. J Clin Oncol 31, 2013 (suppl 26; abstr 92)


Hypofractionierte Radiotherapie


Boost-RT des Tumorbettes


Bei Patientinnen unter 45-50 Jahren
Cochrane Analysis – Radiation after Surgery (13/17)

No further information

No references
No further information

References:

See next slides
Cochrane Analysis - Tamoxifen after DCIS (all/with radiation) (15/17)

No further information

Reference:

H. Staley, I. McCallum, J. Bruce. The Breast 23 (2014) 546e551
DCIS Postoperative Systemic Treatment (16/17)

Further information:

Alle Abstimmungen mit 100% Zustimmung

References:

➢ Tamoxifen (nur ER+, nur BET)


AI (wenn postmenopausal und Kontraindikationen gegen Tamoxifen)
Andere endokrine Optionen Trastuzumab (nur HER2+)


Local Recurrence of DCIS after Tumorectomy w/o Irradiation (17/17)

Further information and references:

Abstimmung:
Lokalrezidiv des DCIS nach Tumorektomie nach Radiatio:

Einfache Mastektomie
++ 4/19;
+ 15/19

Einfache Mastektomie + SNB:
++ 3/22
+ 14/22
+- 3/22
- 2/22
-- 0/22

Lokalrezidiv des DCIS nach Tumorektomie mit Radiotherapie

Therapieindikation wie bei primärer Erkrankung:
++ 10/21
+ 7/21
+- 1/21
- 1/21
-- 2/21

Nach Radiatio
➤ Einfache Mastektomie

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


   Keine Radiotherapie
   Therapieindikation wie bei primär Erkrankung