Ductal Carcinoma in Situ (DCIS)
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
## Pretherapeutic Assessment of Suspicious Lesions (BIRADS IV)

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

Systematic review

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

A. Fancellu¹, R. M. Turner², J. M. Dixon⁴, A. Pinna¹, P. Cottu¹ and N. Houssami³

¹Department of Clinical and Experimental Medicine, Unit of General Surgery 2, Clinica Chirurgica, University of Sassari, Sassari, Italy, ²School of Public Health and Community Medicine, The University of New South Wales, and ³Screening and Test Evaluation Programme, School of Public Health, Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia and ⁴Breakthrough Breast Cancer Research Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, UK

Correspondence to: Dr A. Fancellu, Department of Clinical and Experimental Medicine, Unit of General Surgery 2, Clinica Chirurgica, University of Sassari, Viale San Pietro 43, 07100 Sassari, Italy (e-mail: afancel@uniss.it)

_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

**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>Lumpectomy</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>1</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>1</td>
</tr>
<tr>
<td>Unilateral mastectomy</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, MD\textsuperscript{1}, Cristina Olcese, BS\textsuperscript{1}, Sujata Patil, PhD\textsuperscript{2}, Monica Morrow, MD, FACS\textsuperscript{1}, and Kimberly J. Van Zee, MS, MD, FACS\textsuperscript{1}

Breast Conserving Surgery Alone

Recurrence rate (95 % confidence interval)

<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

Recurrence rate (95 % confidence interval)

<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>
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

- Excisional biopsy (wire guided)  
  Oxford: 2b  
  LoE: B  
  AGO: ++

- Bracketing wire localization in large lesions  
  Oxford: 5  
  LoE: D  
  AGO: +

- Specimen radiography  
  Oxford: 2b  
  LoE: B  
  AGO: ++

- Intraoperative ultrasound (visible lesion)  
  Oxford: 3a  
  LoE: C  
  AGO: +/-

- Immediate re-excision for close margins (specimen radiography)  
  Oxford: 1c  
  LoE: B  
  AGO: ++

- Intraoperative frozen section (in single cases for margin)  
  Oxford: 3a  
  LoE: D  
  AGO: +/-

- Interdisciplinary board presentation  
  Oxford: 2b  
  LoE: C  
  AGO: ++

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)**
  - Oxford: 1a A ++

- **Multifocal DCIS: BCS if feasible**
  - Oxford: 2b B +

- **Re-excision required for close margin ≤ 2 mm in paraffin section)**
  - Oxford: 2b C +

- **Mastectomy**
  - Large lesions confirmed by multiple biopsies; no clear margins after re-excision
  - Oxford: 2a B ++

- **SNE**
  - **Mastectomy**
    - Oxford: 3b B +
  - **BCS**
    - Oxford: 3b B -
  - **In case of DCIS in the male breast**
    - Oxford: 5 D +/-

- **ALND**
  - Oxford: 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

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

* 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
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. 
DCIS Postoperative Systemic Treatment - Statements

- Postoperative endocrine treatment has no impact on survival \[ \text{LOE 1a} \]
- Postoperative endocrine treatment may have a small effect on ipsilateral invasive recurrences \[ \text{LOE 1a} \]
- Endocrine treatment for DCIS has an effect on contralateral invasive cancer and ipsilateral and contralateral DCIS \[ \text{LOE 1a} \]
- The number needed to treat for any ipsilateral breast event is 15 \[ \text{LOE 1a} \]

## DCIS Postoperative Systemic Treatment

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

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

- **Trastuzumab (only Her2+)**
  - Oxford: 5 D --

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

After Radiation:

- Simple Mastectomy
  + SNB

- Secondary 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.