

Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

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Ductal Carcinoma in Situ (DCIS)

Ductal Carcinoma in Situ DCIS

➤ **Version 2002:**
Gerber

➤ **Versions 2003–2016:**
**Audretsch / Blohmer / Brunnert / Costa /
Fersis / Friedrich / Hanf / Junkermann /
Kühn / Lux / Maass / Möbus / Nitz /
Oberhoff / Scharl / Solomayer / Souchon /
Thill / Thomssen**

➤ **Version 2017:**
Budach / Fersis

Pretherapeutic Assessment of Suspicious Lesions (BIRADS IV)

Further Information

References

	Oxford / AGO LoE / GR		
➤ Mammography			
➤ Magnification view of microcalcification	1b	A	++
➤ Increase of <u>detection rate</u> of G1/G2 DCIS by full-field digital mammography (versus screen-film)	4	C	++
➤ Stereotactic core needle / vacuum biopsy (VAB)			
➤ Specimen radiography	2b	B	+
➤ Marker (Clip) left at biopsy site for location if lesion is completely removed	2b	B	++
➤ Marker (Clip) left at biopsy site for location if lesion is completely removed	2b	B	++
➤ Marker (Clip) left at biopsy site for location 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	++

MRT und DCIS

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Studie	Anzahl Untersuchungen	Zuverlässigkeit (%)	Sensitivität (%)	Spezifität (%)
Gilles et al 1996	172	70	95	51
Westerhof et al 1998	63	56	45	72
Bazzocchi et al 2006	112	80	79	68
Kuhl et al 2007	75	-	88	-
Baur et al. 2013	58		79,3	

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References

„Ein negativer MRT-Befund kann nicht als Beweis für Gutartigkeit gewertet werden.“

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

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BJS 2015; **102**: 883–893

Further
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References

MRI and DCIS

- **9 Studien für diese Metaanalyse (7 Kohorten und 2 randomisierte Studien), die MRI im Rahmen der präoperativen Abklärung verwendet haben.**
- **4 Studien hatten sowohl DCIS als invasives Ca.**
- **In 4 Studien war BEO vorgesehen.**

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- **Adjusted odds ratios;**
Estimates of the effect of preoperative MRI on surgical outcomes in patients with ductal carcinoma in situ;

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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.

MRI and DCIS

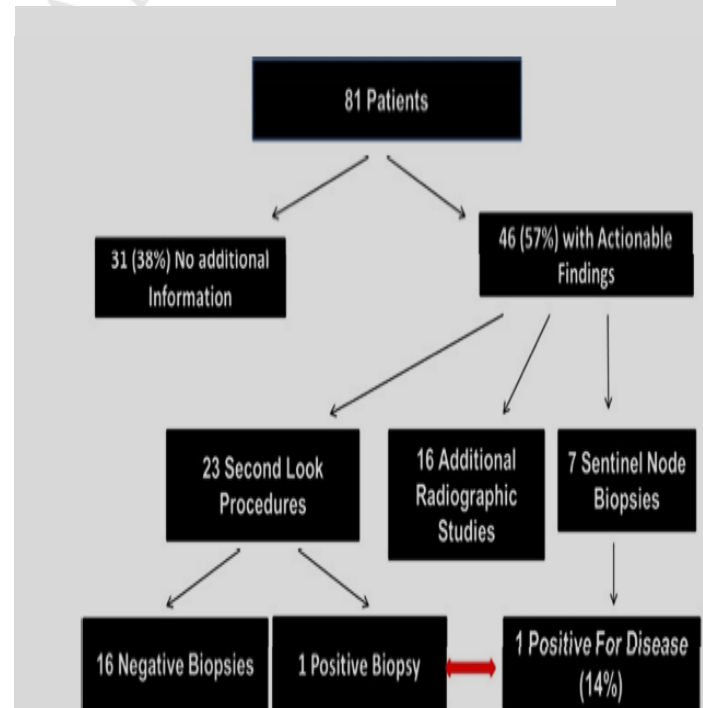
The True Impact of Breast MRI on the Management of In-Situ Disease: More is Not Better

Michael Lallemand MD*¹, Morgan Barron MD², Jason Bingham MD³, Andrew Mosier MD⁺⁴, Mark Hardin MD⁵, Vance Sohn MD⁶

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Over a seven year period, 93 patients were diagnosed with DCIS on percutaneous biopsy with no other indication for a breast MRI. Of these patients, 81 underwent an MRI preoperatively and comprised our patient cohort. Those that did not undergo an MRI were unable to do so either due to body habitus, anxiety, or the presence of an implantable pacemaker. In our patient cohort, 67 elected to undergo breast conservation therapy (BCT) and 14 decided to proceed with mastectomy. Of the BCT group, 8 required an additional procedure for positive margins (11.9%), four of whom chose to proceed with re-excision, while the remaining four were converted to mastectomy.



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MRI and DCIS

The True Impact of Breast MRI on the Management of In-Situ Disease: More is Not Better

Michael Lallemand MD^{*1}, Morgan Barron MD², Jason Bingham MD³, Andrew Mosier MD⁺⁴, Mark Hardin MD⁵, Vance Sohn MD⁶

Our data reveals that the routine use of MRI for DCIS did not change the overall clinical management in 88 of 89 patients (99%). Rather, it led to additional unnecessary studies and delayed time to definitive surgical therapy. Forty-six patients (57%) had a finding on MRI that prompted additional workup, including 17 additional biopsies, only one of which was positive.

At our institution, bilateral breast MRI is no longer routinely performed for patients being evaluated for DCIS. The impetus for this study was driven by the psychological distress that many patients felt by the time they needed to decide on a surgical treatment plan. Many felt overwhelmed and exhausted as they had already undergone numerous tests, biopsies, and delay to definitive therapy associated with the false positive findings on MRI. As stated, over half of the patients (57%) had a finding on MRI which prompted additional workup, including 16 negative biopsies. This study confirms that routine MRI is not useful to patients diagnosed with DCIS.

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

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- **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**

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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

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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, MD¹, Cristina Olcese, BS¹, Sujata Patil, PhD², Monica Morrow, MD, FACS¹,
and Kimberly J. Van Zee, MS, MD, FACS¹

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



General Therapeutic Principles

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

Adjuvant treatment (radiotherapy, endocrine treatment) must be discussed with the patient individually. Disadvantages must be balanced against risk reduction.

Surgical Treatment for Histologically Proven DCIS I

Further Information

References

Oxford / AGO LoE / GR

➤ 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	5	D	--
➤ Interdisciplinary board presentation	2b	C	++

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

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	Oxford / AGO LoE / GR		
➤ 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*	3b	B	+
➤ BCS	3b	B	-
➤ Mastectomy	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.

DCIS – Prognostic Factors for the Incidence of Ipsilateral Recurrence

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➤ 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/neu (positive vs. negative)	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	-

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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 any breast event) is 9 (over all risk groups)**

DCIS Radiotherapy

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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

Oxford / AGO LoE / GR

1a	A	+*
2b	B	--
3a	D	--
2b	D	-/+**
2b	D	--
2b	C	+/-

* 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)

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Goodwin A, Parker S, Gherzi 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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References

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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 breast event is 15** **LOE 1a**



Cochrane Analysis Tamoxifen after DCIS (all/with Radiation)

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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
meta-analysis. Breast. 2014 Oct;23(5):546-51. doi:
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DCIS Postoperative Systemic Treatment

**Oxford / AGO
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- | | | | |
|--|-----------|----------|-------------|
| ➤ 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**

Local Recurrence of DCIS after Tumorectomy w/o Irradiation

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After radiation

➤ **Simple mastectomy
 + SNB**

3a C +

5 D +

➤ **Second 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.

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References