

Original article

The role of specimen radiography in breast-conserving therapy of ductal carcinoma in situ

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ARTICLE INFO

Article history:

Received 18 October 2015

Accepted 26 December 2015

Available online xxx

Keywords:

Breast cancer

Ductal carcinoma in situ

Specimen radiography

Breast-conserving therapy

Free surgical margin

ABSTRACT

Background: To assess the role of intraoperative specimen radiography (SR) and to define risk factors for positive margins in breast-conserving therapy (BCT) of ductal carcinoma in situ (DCIS).

Methods: In a retrospective study in calcification-associated DCIS treated with BCT between January 2009 and December 2011, digital mammographs and SR were reviewed and radiological margin width was determined. Clinical, radiological, and histological data were correlated with surgical histological data, and a histologically free margin of at least 2 mm was taken as evidence of successful BCT.

Results: 47/91 patients (51.6%) fulfilling the inclusion criteria had histologically involved surgical margins. Univariate analyses revealed DCIS size, mammographic extension of calcification, presence of comedo necrosis, negative progesterone receptor status, and a small radiological margin on SR to be risk factors for unsuccessful BCT. Receiver Operating Characteristic (ROC) analysis showed a radiological margin width of 4 mm to be optimal, with a sensitivity of 72.3% and specificity of 52.3%. The likelihood of surgical free margins was increased 2.9-fold with a radiological margin width ≥ 4 mm. On multivariate logistic regression analysis, only histological DCIS size >20 mm clearly emerged as an independent predictive factor for surgically involved margins ($p < 0.001$), while an SR margin <4 mm trended toward significance ($p = 0.066$).

Conclusions: SR is a reliable method for predicting free surgical margins in non-invasive breast cancer where a minimum radiological free margin of 4 mm is achieved. However, histological DCIS size remains the most important factor determining successful BCT.

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Introduction

Breast-conserving therapy (BCT), defined as lumpectomy with adjuvant radiation, is an established treatment for ductal carcinoma in situ (DCIS) [1–4]. In this treatment option one of the most important risk factors for local recurrence is a tumor-involved surgical margin [3,5–7]. Although DCIS is non-invasive and potentially curable by complete resection, achievement of this goal during a single operative session is challenging for the surgeon [8]. A surgical margin of ≥ 2 mm is generally accepted as sufficient and is recommended in the current German S3 guidelines [1,4,9–11]. Microscopic extension of DCIS to the specimen margin (<2 mm)

usually necessitates further resection. To avoid further surgery in cases of positive histological margins, the guidelines of the German Working Group of Gynecologic Oncology (AGO) recommend intraoperative margin assessment by specimen radiography (SR) and immediate re-excision in the event of close radiological margins [1,12–14]. However, the definition of a ‘safe’ radiological margin has yet to be established. In this retrospective study we set out to evaluate the factors associated with positive surgical margins and to study the role of SR. In particular, we sought to identify the radiological margin width that reduces the risk of involved surgical margins.

Patients and methods

The retrospective study included 132 patients with DCIS, treated between January 2009 and December 2011 in the Interdisciplinary Breast Center of the University Hospital in Rostock, Germany. Forty-

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one patients were excluded from the study because of missing images, absence of microcalcification or initial mastectomy (Fig. 1). Ninety-one women with DCIS treated by BCT remained for further analysis. After mammographic detection and diagnosis of DCIS by stereotactic vacuum biopsy, BCT guided by mammographic needle localization was performed. The whole lump from subcutaneous tissue to pectoralis fascia was removed with the aim of completely excising the area of microcalcification. The specimen was orientated with sutures for radiological and pathological analysis. Intraoperative ventro-dorsal radiographs of the surgical specimen were performed to verify that the microcalcification had been excised and to measure the radiological distance between microcalcification and surgical margin. Where SR was positive, immediate re-excision was performed. Histological analyses were conducted according to the interdisciplinary guidelines for the diagnosis and treatment of breast cancer [15]. Positive margin status was defined as the presence of DCIS less than 2 mm from the surgical margin. All mammographs and SRs were reviewed by an experienced breast radiologist (A.S.) and radiological specimen margins were measured (Fig. 2).

Statistics

Statistical analysis was carried out in collaboration with an independent statistician (Ä.G.) using the SPSS 20.0 software package

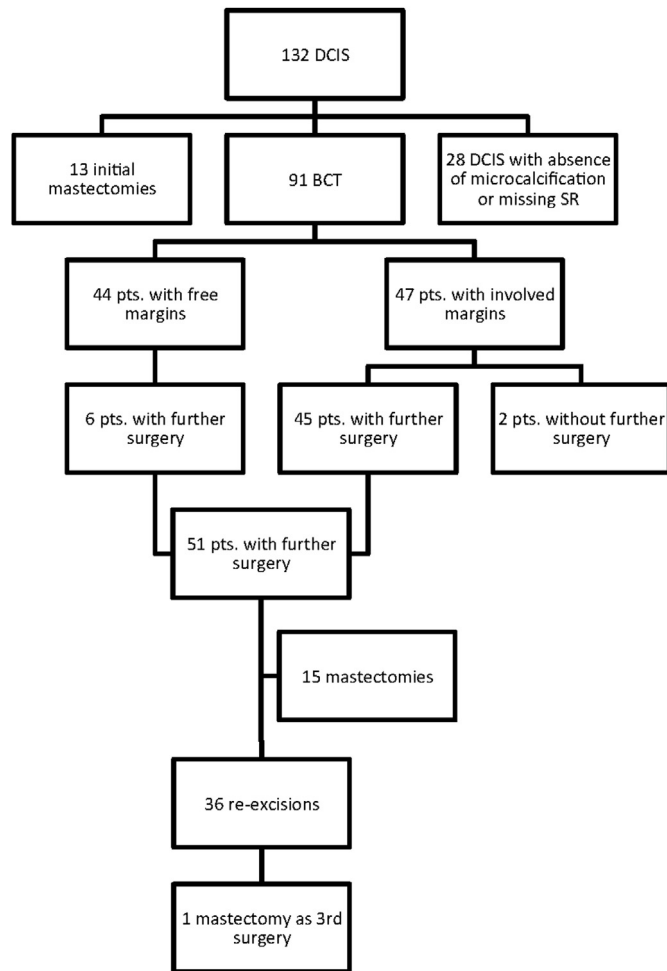


Fig. 1. Flow-chart of surgical procedures in 132 patients with diagnosed DCIS. DCIS, ductal carcinoma in situ; BCT, breast-conserving therapy; SR, specimen radiograph; pts, patients.

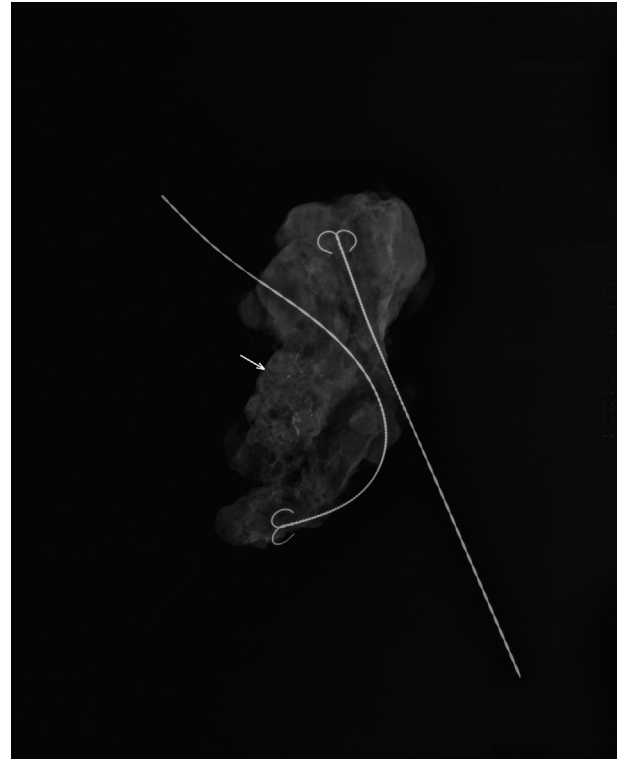


Fig. 2. Mammographic needle localization and specimen radiography (SR). Measurement of radiological margin width was taken from the nearest specimen margin (arrowhead).

(IBM Ehningen, Germany). Specimen histology was used as the gold standard for the definition of free margins. Descriptive statistics were computed, and included mean \pm standard deviation (SD) (median and range, where indicated) for continuous variables, and frequencies and relative percentages for categorical variables. Clinical, histological and radiological parameters were compared between patient groups using the t-test or chi-squared test and Fisher's exact test, respectively. In order to further evaluate the performance of SR in discriminating between free and involved surgical margins, a Receiver Operating Characteristic (ROC) analysis was performed to test the area under the curve (AUC) vs. 0.5. The logistic regression model was applied to assess the independence of involved surgical margins from prognostic factors. Odds ratios (ORs) and the respective 95% confidence intervals (CIs) were calculated. First, univariate analyses were performed to calculate unadjusted (unadj) ORs of potential predictors. Predictor candidates showing $p < 0.05$ on univariate analysis were entered into a subsequent multivariate regression model to calculate their adjusted (adj) ORs and the respective 95% CIs. For all tests $p < 0.05$ was considered to be statistically significant and all tests were two-tailed.

Results

Demographic data, radiological, surgical, and histological parameters

Clinical characteristics of the 91 patients, histological features of the specimens, and the surgical results of lumpectomy are shown in Table 1.

Forty-seven of 91 patients (51.6%) had involved or close histological margins of <2 mm. Forty-five of these received further

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