



Clinical Implications of Growth Pattern and Extension of Tumor-Associated Intraductal Carcinoma of the Breast

Holm Eggemann,¹ Thomas Kalinski,² Anna K. Ruhland,¹ Tanja Ignatov,¹
Serban Dan Costa,¹ Atanas Ignatov¹

Abstract

Tumor specimens from 410 patients with primary invasive breast cancer were investigated to identify the clinically relevant features of tumor-associated intraductal component (IDC) surrounding invasive breast cancer. A tumor-associated IDC associated with invasive tumor was mostly localized between the tumor and nipple. Thus, segmental resection of breast tissue is suggested.

Introduction: The goal of the present study was to identify the clinically relevant features of tumor-associated intraductal component (IDC) surrounding invasive breast cancer. **Patients and Methods:** The tumor specimens from 410 patients with primary invasive breast cancer were investigated. The distance between the surgical margins and tumor edge (invasive and intraductal areas) was measured prospectively. **Results:** Of the 410 investigated patients, 395 were eligible for analysis. An IDC was observed in 241 specimens (61.0%) and was associated with a younger age at diagnosis, postmenopausal status, and positive estrogen receptor, progesterone receptor, and human epidermal growth factor 2 (HER2) expression status. Most cases with tumor-associated ductal carcinoma in situ (DCIS) were found in the upper-outer quadrants of the breasts. An extended intraductal component (EIC) tended to be present in the outer and lower quadrants of the breasts. In the study cohort of 187 patients with tumor-associated DCIS, 1496 surgical margins were investigated. IDC was associated with invasive tumor growth predominantly in the nipple direction. The nipple-associated growth of DCIS correlated with patient age > 40 years, tumor size ≤ 2 cm, poor histologic differentiation of the noninvasive and invasive components, and positive estrogen and progesterone receptor status and negative HER2 status. **Conclusions:** Our data provide evidence that in patients with primary breast cancer, the EIC areas will be mostly segmentally localized between the invasive tumor and the nipple. Therefore, if EIC is present or assumed, surgery should consist of segmental resection of the breast tissue, at least in patients with breast cancer who are > 40 years old, with a tumor size of < 2 cm, and with hormone receptor-positive and HER2-negative, poorly differentiated tumors.

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Introduction

During the past 2 decades, breast-conserving surgery (BCS) has become the standard operative treatment of early invasive breast

H.E. and T.K. contributed equally to this study.

¹Department of Obstetrics and Gynecology, University Clinic Magdeburg, Magdeburg, Germany

²Institute of Pathology, University Clinic Magdeburg, Magdeburg, Germany

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Address for correspondence: Atanas Ignatov, MD, PhD, Department of Obstetrics and Gynecology, University Clinic Magdeburg, Gerhart-Hauptmann Strasse 35, Magdeburg 39108 Germany

E-mail contact: atanas.ignatov@gmail.com

cancer.¹ Because close and positive surgical margins are associated with an increased risk of local recurrence, tumor-free resection margins during BCS must be achieved. The incidence of inadequate resection margins has been reported to range from 5% to 60% and will be increased if an extensive intraductal component (EIC) is present.²⁻⁴ Because a tumor-associated intraductal component (IDC) is a risk factor for local recurrence,^{4,5} with an increasing incidence reported,⁶ complete removal of an EIC in BCS is mandatory. A few retrospective analyses have shown that pure DCIS grows in a segmental direction in a pyramid-like shape.^{7,8} A similar growth pattern has been described when a tumor-associated EIC is present.⁹⁻¹² A predominant extension toward the nipple area has been proposed,¹² and this was also observed in patients with pure

Growth Pattern of DCIS

DCIS.^{8,11} Very recently, we have found that segmental resection in the mammillary direction will be associated with a lower rate of positive surgical margins compared with simple lumpectomy.¹³ The concept of BCS for a case of an EIC and the selection of the patients who will benefit from segmental resection should be addressed.

The present study was undertaken to identify the clinically relevant features of breast cancer associated with noninvasive IDC (defined as intraductal carcinoma in situ or lobular carcinoma in situ).

Patients and Methods

Patients

The present trial was designed as a retrospective, single-institution study. All 410 patients with primary invasive breast cancer (IBC) diagnosed at our institution from January 2011 to May 2014 were evaluated for eligibility. Of these patients, 15 were excluded because of incomplete histologic findings (Figure 1). Thus, 395 patients with IBC were eligible. Of these patients, 187 (47.3%) had ductal carcinoma in situ (DCIS). To investigate the growth pattern of DCIS in more details 208 patients were excluded because: 76 had no intraductal component (IDC), 41 had undergone neoadjuvant chemotherapy, 41 had a multicentric or multifocal tumor, 37 had undergone only diagnostic core needle biopsy followed by neoadjuvant therapy without surgery at the closing date of the study, and 7 had only lobular carcinoma with lobular carcinoma in situ. All patients underwent preoperative mammography, breast ultrasonography, and core needle biopsies. Patient age; menopausal status; estrogen receptor (ER) status; progesterone receptor (PR) status; human epidermal growth factor 2 (HER2); Ki-67; tumor size; tumor grade; histologic type; lymph node status; grade, type, and size of the IDC; and tumor localization were assessed. The patient characteristics were collected from the

institutional data bank and are summarized in Table 1. The research and ethical committee of Otto-von-Guericke University (Magdeburg, Germany) approved the present study.

Surgical Margins

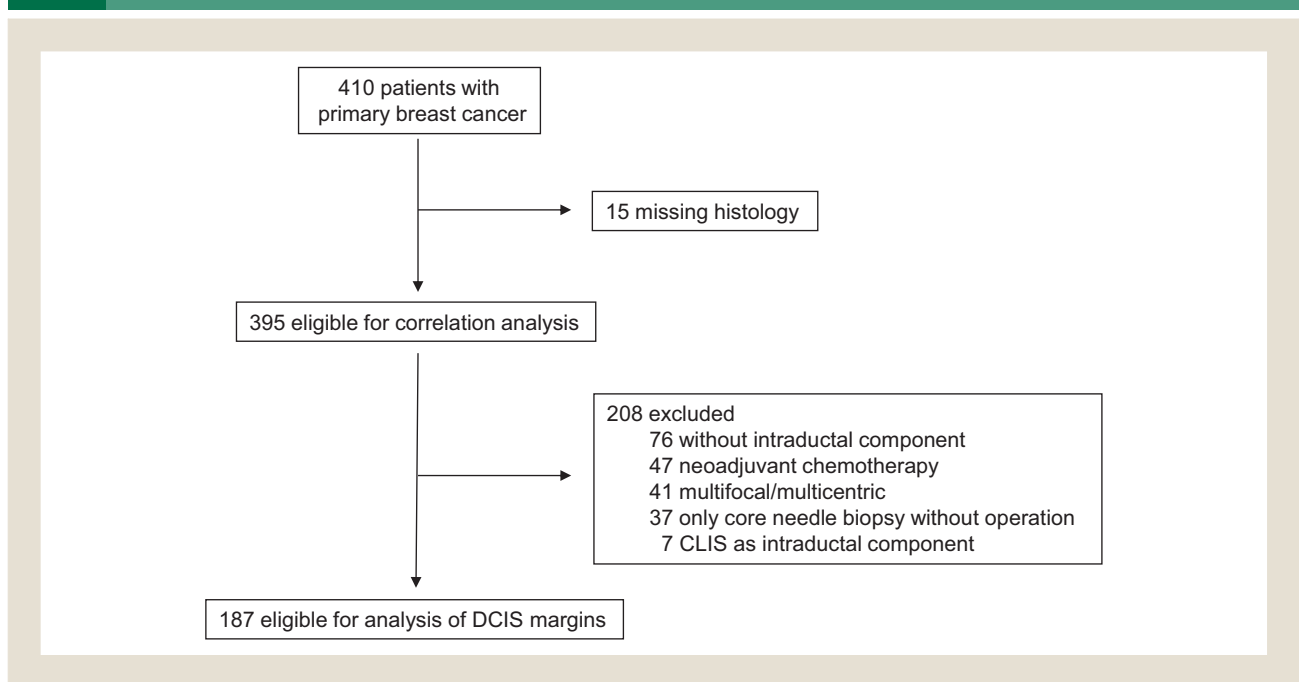
The tumor size and extent of the IDC were assessed in millimeters. The resection margins were prospectively analyzed at the primary diagnosis. The distance between the resection margin and the edge of the invasive component and IDC was measured by the pathologist in millimeters. This distance was measured in all directions: cranial, caudal, lateral, medial, ventral, dorsal, and toward the nipple. In the present study, special attention was given to the tissue area situated peripherally (ie, not between the tumor and nipple; we termed it the “antinipple direction”). Next, the distance between the IBC and IDC was calculated. Patients with lobular carcinomas were excluded from the present study. An EIC was considered present when the DCIS had extended beyond the margin of the infiltrating component at least in 1 direction. DCIS tumors with focal invasion were also classified as having an EIC.

The primary outcome of the present study was to estimate the pattern and magnitude of the extension of the IDC. The secondary outcome was the identification of prognostic factors for the EIC.

Statistical Analysis

The statistical calculations were performed using SPSS, version 21.0 (SPSS, Chicago, IL). The correlation between the surgical margins and the clinical and pathologic variables was tested using Fisher’s exact test or χ^2 test. Analysis of variance was used to compare the mean and median values of the nonparametric variables. The results were considered statistically significant if they reached $P < .05$. All P values were 2-sided.

Figure 1 Flow Chart of Study Design



Abbreviations: CLIS = lobular carcinoma in situ; DCIS = ductal carcinoma in situ.

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