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Avoiding preoperative breast MRI when conventional imaging is sufficient to stage patients eligible for breast conserving therapy

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ABSTRACT

Aim: To determine when preoperative breast MRI will not be more informative than available breast imaging and can be omitted in patients eligible for breast conserving therapy (BCT).
Methods: We performed an MRI in 685 consecutive patients with 692 invasive breast tumors and eligible for BCT based on conventional imaging and clinical examination. We explored associations between patient, tumor, and conventional imaging characteristics and similarity with MRI findings. Receiver operating characteristic (ROC) analysis was employed to compute the area under the curve (AUC).
Results: MRI and conventional breast imaging were similar in 585 of the 692 tumors (85%). At univariate analysis, age ($p < 0.001$), negative preoperative lymph node status ($p = 0.011$), comparable tumor diameter at mammography and at ultrasound ($p = 0.001$), negative HER2 status ($p = 0.044$), and absence of invasive lobular cancer ($p = 0.005$) were significantly associated with this similarity. At multivariate analysis, these factors, except HER2 status, retained significant associations. The AUC was 0.68.
Conclusions: It is feasible to identify a subgroup of patients prior to preoperative breast MRI, who will most likely show similar results on conventional imaging as on MRI. These findings enable formulation of a practical consensus guideline to determine in which patients a preoperative breast MRI can be omitted.

1. Introduction

There is a persisting controversy about the role of contrast-enhanced magnetic resonance imaging (MRI) of the breast in patients with known breast cancer and eligible for breast conserving therapy (BCT). BCT includes limited surgery to excise the tumor and postoperative radiotherapy. Several studies demonstrated that MRI has superior sensitivity to detect invasive breast cancer compared to conventional imaging (mammography and ultrasound) and clinical breast examination (CBE) [1–4]. This sensitivity leads to improved definition of tumor extent [4,5]. As a result, MRI has been expected to increase complete resection rates, breast cancer control and cosmetic outcome, but these effects have not been demonstrated consistently.

Opponents of the routine use of preoperative breast MRI point at the risk of overdiagnosis and overtreatment, increase in cost, delay in surgery, increased patient anxiety, and the ability of adjuvant therapy to eradicate possible additional disease foci [2,6]. Conversely, it has been postulated that if lumpectomy margins need to be clear from microscopic disease in order to reduce the risk of local recurrence, small foci detected on MRI also need identification and excision [7].

The use of MRI in the preoperative staging of BCT is recommended by a number of studies [8,9], but remains controversial in others [2,6]. Meanwhile, preoperative breast MRI is increasingly used, and the need for clinical guidelines rises.

Parallel to the efforts to define the role of preoperative MRI in the ipsilateral breast, both the European Society of Breast Imaging, and the American College of Radiology (ACR) have recommended the use of MRI to screen the contralateral breast in patients with proven cancer [9,10]. More recently the European Society of Breast Cancer Specialists (EUSOMA) has published general recommendations for the application of breast MRI [11]. The authors acknowledged that preoperative MRI may have potential advantages for particular

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subgroups (e.g., patients with invasive lobular cancer and women at high risk for breast cancer), but recommended further research.

There is similarity between conventional imaging and MRI in approximately 85% of BCT patients [12–14]. So regardless which guidelines are used for preoperative breast MRI, the value of this technique can be disputed in this group of patients. If this group could be identified prior to the decision to perform the MRI, studies on MRI-detected additional disease could be powered more efficiently while reducing the number of clinical procedures and cost.

Our aim was to investigate clinical, pathological and imaging characteristics available prior to MRI to identify patients who are expected to have MRI findings similar to conventional imaging findings. Combined with existing knowledge on preoperative breast MRI we formulated practical guidelines to determine in which patients a preoperative breast MRI can be omitted.

2. Methods and materials

2.1. Patients

The cohort consisted of women with invasive breast cancer who participated in the MARGINS (*M*ulti-modality *A*nalysis and *R*adiogical Guidance *IN* breast con*S*erving therapy) study conducted at the Netherlands Cancer Institute, between 2000 and 2008. The aim of this single-institution study was to investigate the use of conventional imaging in combination with MRI to improve the assessment of extent and localization of the disease. In the MARGINS study, women with pathology-proven invasive breast cancer and eligible for BCT on the basis of conventional imaging and CBE were consecutively recruited for an additional preoperative breast MRI. Non-participants refused to undergo an additional MRI, could not be imaged by MRI prior to the scheduled surgery date (without treatment delay), or had contraindications for MRI, such as claustrophobia.

The MARGINS study was approved by the institutional review board and written informed consent of the participants was obtained.

Before MRI all patients underwent conventional imaging and CBE. Proof of malignancy was obtained by means of fine needle aspiration cytology (FNAC) and/or a core biopsy. Characteristics of the lesions at conventional imaging were assessed by radiologists experienced in breast imaging according to the ACR criteria [15].

2.2. Mammography

Initially mammography was done with a Trex LORAD MIV (Trex Medical Corporation, LORAD Division, Danbury, CT) or a Philips Mammo Diagnost 3000 (Philips Medical Systems, Best, The Netherlands) and Agfa HDR films. In 2004 we implemented digital mammography: Selenia (Hologic, 35 Crosby Drive, Bedford, MA). Both breasts were imaged in the cranio-caudal and medio-lateral oblique directions. Breast density was subdivided in 4 categories, representing ACR 1–4 (completely fatty to extremely dense) [15].

2.3. Ultrasound

Ultrasound was performed with a Kretz Voluson V730 (Kretztechnik, Zipf, Austria) and a Philips IU22 (Philips, Best, Netherlands). Ultrasound of the axilla was performed in all patients and an FNAC was done for proof of malignancy of suspicious lymph nodes [16].

2.4. MRI

MRI examinations were performed and interpreted as reported previously [17], initially using a 1.5-Tesla scanner (Magnetom, Siemens, Erlangen, Germany) and from April 2007 using a 3.0 Tesla scanner (Achieva Philips, Best, The Netherlands).

2.5. Guidelines for management of additional lesions on MRI

Additional lesions on MRI were defined as lesions in the vicinity of the index tumor, (multifocal tumor extent) and lesions in a different quadrant of the ipsilateral breast (multicentric tumor extent). Guidelines were established to handle additional lesions detected on MRI, aiming to minimize additional procedures and treatment changes due to benign findings. This approach has recently been described in more detail [17]. Briefly, for multifocal additional lesions (maximum diameter of volume including index tumor and additional lesion(s) <3 cm), surgery was done with larger wide-local excision margins. For multicentric additional lesions (>5 mm) attempts were made to obtain proof of malignancy by second-look targeted ultrasound and FNAC or core biopsy. If pathology confirmed malignant disease over a region too large to allow cosmetically acceptable BCT, a conversion to mastectomy was advised. If no pathology proof for multicentric additional lesions could be obtained prior to surgery, BCT was pursued and follow-up with MRI was advised. During the study period, MRI-guided biopsies were only occasionally done. Mastectomies, solely based on MRI findings were not performed. All findings were discussed preoperatively in a multidisciplinary team of breast cancer specialists. In the current study only primary and additional lesions with pathology proof of malignancy were included.

2.6. Pathology

Pathologists, experienced in breast cancer, assessed the specimens to report the margins, histological grade and type of the cancer. Excision specimens were handled according to a protocol adopted from Egan [18]. Briefly, each specimen was cut into 3–4 mm slices and fixed in 4% formalin overnight. Subsequently, a radiograph and a digital photo from the slices were obtained to correlate radiological and microscopic findings. Immunohistochemistry was used to assess estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2). Based on macroscopic, radiographic and MRI findings, samples were taken to enable adequate microscopic investigation of the lesions and their surroundings.

2.7. Statistical analysis

SPSS Version 20.0; SPSS Chicago, IL, was used to explore differences in patient and tumor characteristics between women with similar malignant findings and those with discordant malignant findings on preoperative breast MRI. Student's *t*-tests were performed for normally distributed continuous variables, and Mann–Whitney *U* and Fisher's exact test for the non-normally distributed ones. Multivariate analysis using logistic regression (LR) was performed to determine which factors were significant explanatory variables for additional disease. Backward LR using step-wise feature selection (f-to-entry: 0.05, f-to-remove: 0.10) was applied.

The following patient and tumor characteristics were entered into the multivariate analysis: age at diagnosis, preoperative lymph node metastasis (present/not present), ER status (positive/negative), PR status (positive/negative), HER2 status (positive/negative), invasive lobular cancer (ILC) (yes/no), breast density on mammography (ACR 1 and 2 versus 3 and 4), tumor

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