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Sensitivity of breast MRI for ductal carcinoma in situ appearing as microcalcifications only on mammography

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ABSTRACT

Purpose: This study aims to investigate sensitivity of breast magnetic resonance imaging (MRI) for mammographic microcalcifications-only ductal carcinoma in situ (DCIS), based on its histopathology and mammographic extent of microcalcifications.
Methods: Mammograms were reviewed to measure the extent of microcalcifications. Sensitivity of MRI was calculated in the overall study population and in groups differing for DCIS nuclear grade, microinvasivity, and microcalcifications' extent.
Results: Overall sensitivity of MRI was 78.3% for dynamic contrast enhanced and 66.7% for diffusion-weighted imaging and did not vary with nuclear grade and microinvasivity, while it increased with larger extent of microcalcifications (ExpB=1.063–1.046, *P*=.037–.013).
Conclusions: Mammographic extent of microcalcifications positively affects sensitivity of breast MRI.

1. Introduction

Ductal carcinoma in situ (DCIS) of the breast is characterized by a proliferation of malignant epithelial cells that line a terminal ductal-lobular unit without invasion through the basement membrane. According to the World Health Organization classification of tumors of the breast, DCIS can be classified into three grades: low, intermediate, and high [1]. Recent studies have defined breast cancer and DCIS as not one entity but as a spectrum of conditions that range from indolent to aggressive disease [2,3], stressing the complexity and controversy surrounding DCIS.

High-nuclear-grade DCIS has a greater risk of progression to invasive disease and local recurrence than intermediate- and low-nuclear-grade DCIS [4,5]. Since DCIS can be effectively treated with a complete local resection and adjuvant radiotherapy, usually advised to prevent recurrences, an accurate assessment of the extent of disease is essential to guide treatment [6]. A significantly superior ability of magnetic resonance imaging (MRI) to detect the presence and extent of DCIS in comparison to mammography or ultrasound (US) examinations has been demonstrated in literature [7]. However, use of breast MRI for the evaluation of disease extent in DCIS is not recommended by current EUSOMA (European Society of Breast Cancer Specialists) guidelines. Indeed, additional studies assessing the diagnostic role and performance of breast MRI for the diagnosis of DCIS are required to expand current indications [8].

Sensitivity of MRI for DCIS in relationship to tumor features such as nuclear grade [9,10] has been described in literature. Although prior works have investigated the relationship between presence of mammographic microcalcifications and sensitivity of breast MRI for DCIS [11–13], there are no studies focusing on the extent of mammographic microcalcifications as a parameter potentially affecting breast MRI diagnostic performance.

Accordingly, we sought to explore mammographic extent of microcalcifications as a parameter potentially affecting sensitivity of breast MRI for DCIS appearing as microcalcifications only at mammography. This could be helpful for the selection of patients that may benefit from breast MRI examinations for assessment of disease extent of histology-proven DCIS.

2. Materials and methods

2.1. Study population

A total of 232 consecutive patients that referred to our institution for mammography between March 2011 and November 2013 with evidence of suspicious or highly suspicious microcalcifications [Breast Imaging-Reporting and Data System (BI-RADS) 4–5 categories] [14] were recruited for this study. All of these patients underwent breast MRI at our institution prior to biopsy and surgery. The original study population was composed of 59 patients who had histological diagnosis

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of DCIS at biopsy. Three patients were excluded for motion artifacts degrading the quality of breast MRI examinations. Thus, the final study population included 56 patients with 60 distinct DCIS lesions appearing as microcalcifications only on mammography. Four patients had a bilateral DCIS. The histological diagnosis of DCIS was obtained on stereotactic-guided vacuum-assisted biopsy, using 11-gauge vacuum probes (Mammotome; Devicor Medical Products, Inc., Cincinnati, OH, USA) and confirmed at surgical specimens. All specimens were analyzed at our institution histopathology department. Pathology reports were reviewed to record DCIS grade (G1 low grade, G2 intermediate grade, G3 high grade) and presence or absence of foci of microinvasion.

The study cohort was grouped according to a positive or negative MRI examination into positive and negative MRI groups (PG and NG group, respectively). Two separate PG and NG were considered for dynamic contrast enhanced (DCE) and diffusion-weighted imaging (DWI) analyses. The study population was additionally grouped according to the nuclear grade in patients with non high grade DCIS histology (Group NHG, including patients with G1 and G2 DCIS) and patients with high-grade DCIS histology (Group HG, including subjects with G3 DCIS). Further stratification of patients was performed according to the presence or the absence of microinvasive foci. Accordingly, patients were grouped into microinvasive (MI) and nonmicroinvasive (NMI) histopathology groups.

This study was approved by our institutional review board and was conducted in accordance to the Declaration of Helsinki.

2.2. Mammography

Mammography was performed using both Senographe Essential ADS_56.12 (GE Healthcare, Milwaukee, WI, USA) and Heliantus (Metaltronica, Rome, Italy) digital mammography units. Patients underwent craniocaudal and mediolateral oblique views with lateral and magnified views, as necessary.

2.3. MRI protocol

All the examinations were achieved before stereotactic-guided breast biopsy to prevent postprocedural artifacts due to bleeding and edema. All patients were scanned in prone position using a 1.5-T MRI scanner (Signa Excite; GE Medical System, Milwaukee, WI, USA), with a 4-channel bilateral breast coil. For contrast administration, an intravenous cannula was placed in the cubital vein just before the investigation. During the examination, contrast agent (gadopentetate dimeglumine) was injected at a dose of 0.1 mmol/kg using a power injector at a flow rate of 2 ml/s, followed by a 20-ml saline flush. A written informed consent signed by each patient was obtained before examinations. For women in reproductive age, examination was performed between days 7 and 14 of the menstrual cycle, as appropriate.

The following sequences were acquired:

- *STIR (short-time inversion recovery) axial sequence* [repetition time (TR)=5900, echo time (TE)=68, echo train length=17, bandwidth=41–67, matrix=480×320, thickness=4 mm, interval=0, field of view (FOV)=32–34 cm, number of excitation (NEX)=1–2].
- *DWI axial sequence* [TR=5150, TE=min, frequency phase=96×96, matrix=96×96, thickness=4 mm, interval=0, FOV=32–34 cm, NEX=6]. DWI was acquired before dynamic sequences with a spin-echo echo-planar imaging sequence in the axial plane. Sensitizing diffusion gradients were applied sequentially in the x-, y-, and z-directions with *b*-values of 0 and 1000 s/mm^2.
- *Three-dimensional (3D) FSPGR (fast spoiled gradient echo) coronal sequence* [FA (flip angle)=15°, TR<30 ms, TE<5 ms, NEX=0.5, thickness=2–3 mm, interval=0, matrix=320×320, FOV=34–38 cm] before and five times after intravenous contrast agent administration.
- *3D FSPGR sagittal postcontrast fat-suppressed sequence* [TR<30, TE<5, FA=15°, matrix=288×288, thickness=2–3 mm, interval=0, FOV=22–26 cm, NEX=2].
- *3D FSPGR axial postcontrast fat-suppressed sequence* [TR<30, TE<5, FA=30°, matrix=512×256, thickness=2–3 mm, interval=0, FOV=34–38 cm, NEX=2].

Acquisition time of the complete MRI protocol was 18–20 min.

Dynamic images were transferred to a workstation (GE Advantage Windows 4.1) and postprocessed. Precontrast images of the dynamic series were subtracted from the postcontrast images to selectively highlight enhancing structures. Maximum intensity projection (MIP) and multiplanar reconstruction were performed.

Analysis of dynamic postcontrast sequences was performed using the "Functool" software able to show changes in signal intensity over time and for a given space point. A round-shaped region of interest (ROI) was placed over the enhancing lesions and a dynamic curve was obtained. DWI images postprocessing was also performed with the "ADC" tool, in order to obtain ADC maps.

2.4. Images analysis

2.4.1. Mammography

A radiologist with 10 years of experience in the field of breast imaging retrospectively reviewed all mammograms. For each case, microcalcifications with group, linear or segmental distribution belonging to categories 4 and 5 (suspicious and highly suspicious of malignancy, respectively) of the American College of Radiology (ACR) Breast Imaging-Reporting and Data System (BI-RADS) were identified on mammograms [14]. The site of suspicious microcalcifications on the affected breast was indicated using the quadrants notation. The extent of microcalcifications was evaluated and measured in the longest diameter on the unmagnified preoperative mammogram. The reader was free to choose any projection to measure the longest diameter of the suspicious microcalcifications.

2.4.2. Breast MRI

All MRI images were analyzed in consensus by two radiologists with 5 and 10 years of experience in breast imaging, respectively. Readers were blinded to the breast and quadrant affected by suspicious microcalcifications on mammograms.

Interpretation of DCE MRI images was based on morphology and kinetics of all enhancing lesions, according to the BI-RADS MRI lexicon as proposed by the ACR [15].

To obtain time–signal intensity curves, ROIs were placed above the area of the highest visual enhancement on images obtained during the last phases of contrast-enhanced dynamic imaging. Time–signal intensity curve patterns were classified into three types, associated with increasing probability of malignancy: type I, persistent, with small proportion of malignant lesions having this pattern (9%); type II, plateau, concerning for malignancy; and type III, washout, strongly suggestive of malignancy [16]. Although type I enhancing lesions have low probability of malignancy, available studies in literature have depicted DCIS as a non mass-like enhancement with delayed peak enhancement profiles [11]. Based on the supraindicated parameters, DCE MRI was considered positive when findings were referable as BI-RADS 3, 4, and 5 assessment categories according to the BI-RADS MRI lexicon [15], with patterns of kinetic curves not being a distinctive feature in imaging interpretation in the clinical setting of DCIS. All other enhancing lesions ratable as BI-RADS 2 were considered as benign findings.

On DWI images, lesions were identified based on the presence of hyperintensity corresponding to the site of the enhancing lesions at DCE MRI. For ADC measurements, diffusion-weighted images were postprocessed using the appropriate tool to obtain ADC maps; two ROIs were placed within an area corresponding to the hyperintensity observed on diffusion-weighted images, thus obtaining the resulting mean