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Predictive values of BI-RADS® magnetic resonance imaging (MRI) in the detection of breast ductal carcinoma *in situ* (DCIS)

Gustavo Machado Badan (MD PhD, student)[b,*], Sebastião Piato (MD PhD)[a], Décio Roveda Júnior (MD PhD)[b], Eduardo de Faria Castro Fleury (MD PhD)[b]

[a] *Mastology Division—Gynecology and Obstetrics Department, Brazil*
[b] *Breast Imaging Service of Radiology Depatment—Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, SP, Brazil*

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ABSTRACT

Purpose: The purpose of this study was to evaluate BI-RADS indicators in the detection of DCIS by MRI.
Materials and methods: Prospective observational study that started in 2014 and lasted 24 months. A total of 110 consecutive patients were evaluated, who presented with suspicious or highly suspicious microcalcifications on screening mammography (BI-RADS categories 4 and 5) and underwent stereotactic-guided breast biopsy, having had an MRI scan performed prior to biopsy.
Results: Altogether, 38 cases were characterized as positive for malignancy, of which 25 were DCIS and 13 were invasive ductal carcinoma cases. MRI had a sensitivity of 96%; specificity of 75.67%; positive predictive value (PPV) for DCIS detection of 57.14%; negative predictive value (NPV) in the detection of DCIS of 98.24%; and an accuracy of 80.80%.
Conclusion: BI-RADS as a tool for the detection of DCIS by MRI is a powerful instrument whose sensitivity was higher when compared to that observed for mammography in the literature. Likewise, the PPV obtained by MRI was higher than that observed in the present study for mammography, and the high NPV obtained on MRI scans can provide early evidence to discourage breast biopsy in selected cases.

1. Introduction

DCIS is a type of non-invasive malignant neoplasm of the breast characterized by the proliferation of malignant epithelial cells in the terminal ductal lobular unit, with no evidence of invasion of the basement membrane. If detected before invasion occurs, the chances of cure reach about 100% [1,2].

Considered a precursor of invasive carcinoma, its clinical manifestations vary considerably, with the possibility that those of a low-nuclear grade remain silent for a long period of time or even never disseminate from the duct, while those of high-grade exhibit an elevated mitotic index and, in 30–50% of cases, progress to invasive carcinoma [3].

The factors associated with the progression of DCIS to invasive breast cancer are poorly understood. Many studies on this subject focus on the role of the molecular and genetic alterations in neoplastic epithelial cells. However, emerging evidence suggests that the transition from DCIS to invasive cancer is strongly dependent upon alterations in the microenvironment. The role of myoepithelial cells, responsible for the synthesis and maintenance of the basal membrane and stromal cells (fibroblasts and myofibroblasts) that stimulate tumor growth and stromal angiogenesis should be emphasized [4].

Its main presentation is in the form of clustered microcalcifications seen on mammography, which helped to establish it as the method of choice for breast cancer screening [5].

After the introduction of mammographic screening, the detection of DCIS has increased from 2% to 20% of all diagnosed cases [6,7], thus contributing to the reduction of the mortality rate for breast cancer [7–9]. However, only 75% of all DCIS cases present with calcifications [10], and the sensitivity of mammography ranges from 27 to 80% [6,11,12].

Along with the technological development came an interest in using other imaging detection methods. The sensitivity of MRI in diagnosing invasive carcinoma ranges from 86 to 96% [13,14] and a series of studies has demonstrated a sensitivity of 35–100% in detecting DCIS by using the method [12,15–29].

Due to the wide variation in sensitivity rates observed in the literature and to the fact that, as far as we know, there are no studies demonstrating the performance of other BI-RADS indicators in

* Corresponding author at: Rua Loureiro da Cruz, 121-Aclimação, CEP: 01529-020, São Paulo, SP, Brazil.
E-mail address: gustavobadan@hotmail.com (G.M. Badan).

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evaluating DCIS by MRI, it is appropriate to verify these indicators in patients participating in a screening program at a teaching hospital.

Given that MRI allows the functional evaluation of lesions through enhancement of the cells after the injection of the paramagnetic contrast and it is known that DCIS progresses as increases its nuclear grade, with increased permeability of the basement membrane and protease in its pathophysiology [28,30], it is expected that the vast majority of high grade DCIS is characterized by the method.

The purpose of this study was thus to evaluate the sensitivity, specificity, predictive values, and accuracy of BI-RADS system in the detection of DCIS by MRI.

2. Material and methods

2.1. Sampling

This was a prospective and observational study, approved by the Institution's Research Ethics Committee and carried out in the Diagnostic Imaging Department. A total of 110 consecutive patients were evaluated for 24 months, starting May 2014; they presented with suspicious or highly suspicious microcalcifications on screening mammography (BI-RADS categories 4 and 5) and underwent stereotactic-guided breast biopsy, having had an MRI scan performed prior to biopsy. The cases with histological results indicative of high-risk lesions for malignancy, i.e. atypical ductal hyperplasia (ADH) or positive for malignancy, were referred to surgery.

Excluded from the study were 6 cases of patients who did not undergo biopsy or failed to comply with the follow-up procedures. Two other cases were excluded due to the fact that the patients underwent MRI scanning only after biopsy, hence at odds with the study methodology; and still another three cases were eliminated because their surgical results were unavailable. There remained 99 cases that met the inclusion criteria.

Cases that were negative for malignancy were followed up with mammography at return visits. The median follow-up time was 20 months (with a minimum of 12 and a maximum of 24 months). True negatives were those cases presenting with stability of the lesion, as recommended by the BI-RADS [31].

The average interval between the completion of mammography and breast MRI was 21 days (range 3–60 days).

2.2. Mammography technique

Bilateral mammograms were performed on a full-field digital mammography system (DR), Selenia/Lorad (Hologic, Bedford, U.S.), with standard mediolateral oblique and craniocaudal views and digital magnification of microcalcification areas.

2.3. Breast MRI technique

Breast MRI examinations were performed with the patient in the prone position on a 1.5 T machine using a dedicated 4-channel breast coil (MRI Philips Anchieva, Eindhoven, the Netherlands). The examination consists of protocol sequences for conventional breast MRI investigation, including dynamic sequence acquisition coupled with image subtraction and 3D reconstruction.

Image acquisition includes axial T1-weighted sequences with fat subtraction and short T1 inversion recovery (STIR), followed by T2 SPAIR, right and left sagittal T2 sequences without fat suppression, axial dynamic study divided into 5 stages with images being acquired every 60 s after paramagnetic contrast agent administration. The contrast used was Gadovist® gadolinium at a dose of 0.1 ml/kg (Bayer Schering Pharma AG, Berlin, Germany), administered intravenously, often in "bolus", which could be followed by saline injection or not. Finally, the subtraction of post-contrast and pre-contrast series is performed.

2.4. Interpretation of mammograms and breast MRI scans

Mammograms and breast MRI scans were interpreted by two radiologists specializing in breast imaging with over 10 years' experience. Image interpretation was carried out by correlating clinical data and other imaging studies, when available, as recommended by the BI-RADS.

Imaging scans were acquired from the communication system (PACS, AGFA HealthCare, Mortsel, Belgium) with high resolution monitors being used for issuing reports – 5 megapixel monitors for mammograms and 3 megapixel monitors for breast MRI scans (BARCO N.V., Kortrijk, Belgium), with software that permits the optimization of digital imaging parameters.

Their corresponding reports were issued according to the fifth edition of the BI-RADS (1–negative radiologic findings; 2–benign findings; 3–probably benign findings, with recommendation for reassessment at 6 months; 4–suspicious findings; and 5–highly suspicious findings, with recommendation for histological correlation).

Only cases of microcalcifications detected on mammograms were of interested to us and were classified according to their morphology (round, amorphous; coarse heterogeneous; fine pleomorphic; fine linear branching) and distribution (diffuse; regional; grouped; linear; and segmental) as recommended by BI-RADS. Those classified as BI-RADS 4 and 5 were selected and sent for biopsy, regardless of the findings featured in their corresponding breast MRI scans.

2.5. Biopsy methods

Microcalcification biopsies were stereotactic-guided and performed on a dedicated table with a high-resolution digital camera (Lorad Multicare Platinum, Hologic, Bedford, U.S.). The success of the procedure was confirmed by the presence of microcalcifications on radiographs of the fragments, thus ensuring that the target had been correctly reached.

The protocol used at our department uses needles for vacuum-assisted biopsies (VAB) for cases of microcalcifications with less than one centimeter (cm) in extent. We used 9-gauge needles (Suros System, Hologic, Bedford, U.S.). Those cases involving microcalcifications greater than one centimeter in length underwent core biopsy by using 12-gauge needles (SACN, Biopsy Needle, Medical Device Technologies) coupled to an automated biopsy gun (Magnum, BARD, Covington, U.S.) with advancement of 2.2 cm.

2.6. Analysis of breast MRI findings

For each case, the presence or absence of findings on breast MRI scans with regard to the topography of microcalcifications as characterized by mammography was reported. All lesions showing enhancement after the administration of the contrast agent were classified as mass or non-mass like enhancements (NMLE); and their morphological and kinetic features were described according to the BI-RADS lexicon. The mass were reported according to their shape (oval, round or irregular), margins (circumscribed, irregular or spiculated) and internal enhancement pattern (homogeneous, heterogeneous and peripheral enhancement), while NMLE were classified according to their distribution (diffuse, regional, segmental, linear, focal) and internal enhancement pattern (homogeneous, heterogeneous or "clumped"). Electronic calipers, with the help of appropriate software, were used for on-screen measurements of the lesions.