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Identification of occult breast lesions detected by magnetic resonance imaging with targeted ultrasound: A prospective study

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ABSTRACT

Objective: To verify the capacity of targeted ultrasound (US) to identify additional lesions detected on breast magnetic resonance imaging (MRI), but occult to initial mammography, US and clinical examinations.
Methods: This prospective study included 68 additional relevant breast lesions identified on MRI of 49 patients. As an inclusion criterion, breast US and mammography were required and performed up to six months before MRI. These lesions were then subjected to targeted "second-look" US up to 2 weeks after MRI, performed by one or two radiologists with expertise on breast imaging. Lesions were evaluated according to the established Breast Imaging Report and Data System (BI-RADS) lexicon.
Results: Targeted US identified 46/68 (67.6%) lesions revealed by MRI. No significant associations were observed between US identification and the type of lesion, dimensions, morphological characteristics and enhancement pattern according to MRI findings. Targeted US identified 100% of BI-RADS category 5 lesions, 90% of category 4 lesions, and just over 50% of category 3 lesions ($p < 0.05$). There was significant agreement ($p < 0.001$) between MRI and US BI-RADS classification for all three categories.
Conclusion: Targeted US can identify a large proportion of the lesions detected by breast MRI, especially those at high risk of malignancy, when performed by a professional with experience in both breast US and MRI.

1. Introduction

Breast magnetic resonance imaging (MRI) has gained importance in the last years due to its high sensitivity in detecting breast cancer. The frequency of additional malignant lesions revealed by MRI that were not identified by prior mammography and physical examination varies between 6% and 34% [1,2]. Although MRI has high sensitivity for detection of carcinoma (range 94–100%), it has a moderate specificity (range 37–97%), with great variation in the literature [3–5].

Because of its low specificity, MRI has a significant number of false-positive results. Thus, when a suspected abnormality is revealed by breast MRI only a percutaneous or surgical biopsy might be needed, to establish a reliable diagnosis [6]. However, MRI guided interventions are not widely available and are associated with high operating costs and procedure time [4]. On the other hand, ultrasound (US) has several advantages relative to MRI to guide percutaneous biopsies, including better access to certain areas of the breast and greater comfort for the patient [7].

Targeted US (also known as second-look US) can identify small cancers that lack the typical ultrasonographic characteristics of malignancy [8]. Some studies have evaluated the use of targeted US for the identification of additional MRI-detected lesions [8–17]. However, all published studies were retrospective and previous US examinations had only been performed in part of the patients, preventing the researchers from knowing whether lesions identified by MRI could have been found by an initial US [9,10,12–14,16,17].

The aim of this prospective study is to verify the capacity of targeted US to identify additional lesions detected on breast MRI, but occult to initial mammography, US and clinical examinations.

2. Patients and methods

2.1. Patients and lesions

After approval of the institution's Ethics Review Board, this prospective study included patients who performed breast MRI on

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a cancer center from April 2008 to November 2009. A total of 640 breast MRI exams were performed on the study period.

Overall, 68 additional relevant abnormalities identified on 49 patients were subjected to targeted US. As inclusion criteria, breast US and mammography were required and performed up to six months before MRI, in order to ensure a true second-look US evaluation. Patients' age ranged from 26 to 77 years (median, 49 years; mean, 50.57 years). Most common indications for breast MRI in these patients were inconclusive mammographic/sonographic findings (39.7%), screening (33.8%) and disease staging/surgical planning (13.2%). The abnormalities detected by MRI were evaluated according to the established American College of Radiology (ACR) Breast Imaging Report and Data System (BI-RADS) – MRI lexicon [6].

Targeted US exams were performed up to 2 weeks after MRI, by one or two radiologists with expertise on breast imaging. When two radiologists performed the exam, consensus results were obtained. An US finding was considered to correspond to the abnormality discovered by MRI if strict criteria were met with regard to its approximate size and similarity in shape and location. Lesions were located in three planes (axial, sagittal and coronal) on MRI to facilitate its location in the targeted US. Other references used to access location of lesion were the distance from the nipple and the skin, and proximity of other structures like cysts, vessels or breast implant. The US findings were analyzed according to the criteria suggested by Stavros et al. [18] and the final classification of lesions followed the ACR BI-RADS – US lexicon [6].

MRI was performed with a commercially available 1.5-T imaging system (Siemens Magnetom Symphony; Siemens Healthcare, Malvern, PA), by using a dedicated breast coil. The imaging protocol consisted of: (1) a sagittal T2-weighted Short Tau Inversion Recovery sequence; (2) an axial T1-weighted 3-D gradient echo; (3) an axial post-contrast, T1-weighted 3-D, fat-saturated gradient echo dynamic sequence before and four times after a rapid bolus injection of 0.1 mmol/L gadopentate dimeglumine (Magnevist; Schering, Berling, Germany) per kilogram of body weight, each with a 60 s temporal resolution; and (4) a sagittal high-resolution 3-D sequence. After the examination, the unenhanced images were subtracted from the post-contrast images.

US exams were performed with linear transducers (10–12 MHz; HDI 5000, TOSHIBA or Logiq 700; General Electric, Milwaukee, WI). The exam was directed to the location of the lesions revealed by MRI, and once found they were evaluated in the longitudinal, transversal, radial and antiradial axes.

Lesions were classified as benign or malignant based on histopathology, when available, or imaging follow-up. All lesions classified as BI-RADS 4 or 5 on MRI were submitted to percutaneous or surgical biopsy. BI-RADS 3 lesions that were not submitted to biopsy were followed with clinical examination, mammography and ultrasound or MRI (US for lesions identified on targeted US; MRI for lesions not identified on targeted US) for at least one year.

2.2. Statistical analysis

The descriptive patient and lesion data are presented as mean values, standard deviations, medians, and interquartile ranges. Absolute (n) and relative (%) frequencies were calculated for quantitative variables. Cohen's kappa coefficient was used to verify agreement between the examiners who performed the targeted US. The Mann–Whitney U test was used when only two groups were compared and a Kruskal–Wallis one-way analysis of variance (ANOVA) was used when more than two groups were compared. To verify the association between qualitative variables, the chi-square test or Fisher's exact test was used. For inferential analysis, a level of 5% ($\alpha = 0.05$) was considered significant and all tests were completed under a two-tailed hypothesis.

Table 1
Morphological characteristics and enhancement pattern of mass and non-mass findings detected by magnetic resonance imaging – MRI ($n = 68$).

Parameters	Descriptors	N	%
Mass			
Form	Round	17	32.1
	Oval	25	47.2
	Lobular	5	9.4
Margin	Smooth	43	81.1
	Irregular	10	18.9
Internal enhancement	Homogeneous	41	77.4
	Heterogeneous	11	20.8
	Peripheral	1	1.9
Contrast enhancement dymanic curve	Persistent	43	86.0
	Plateau	3	6.0
	Washout	4	8.0
Non-mass			
Distribution	Focal area	5	33.3
	Linear	4	26.7
	Ductal	1	6.7
	Segmental	3	20.0
	Regional	2	13.3
Internal enhancement	Homogeneous	5	33.3
	Heterogeneous	7	46.7
	Clumped	3	20.0

3. Results

Of 68 lesions identified on MRI, 53 (77.9%) were classified as masses and 15 (22.1%) as non-mass lesions. Dimensions ranged from 0.3 to 9.2 cm (median, 0.9 cm; mean, 1.4 cm). The frequencies of lesions according to type, morphological characteristics, enhancement pattern and BI-RADS categorization are presented in Tables 1 and 2.

Targeted US was performed by two radiologists in 63 lesions (93%) and interobserver agreement was considered good (kappa = 0.617; $p < 0.001$). Forty-six out of 68 lesions identified on MRI (67.6%) presented with a corresponding finding on targeted US. According to the BI-RADS – US lexicon, 27 (58.7%) lesions were classified as category 3, 16 (34.8%) as category 4, and 3 (6.5%) as category 5. No significant associations were observed between US identification and the type of lesion, dimensions, morphological characteristics and enhancement pattern according to MRI findings.

There was a significant association ($p = 0.025$) between the US findings and the BI-RADS – MRI lexicon classification (Table 2). Fig. 1 shows an example case in which a BI-RADS category 4 alteration was detected by breast MRI with a positive US correlation. A significant association was found between BI-RADS classification by MRI and US ($p < 0.001$) in all categories (Table 3).

Histological analysis of lesions classified as BI-RADS category 4 and 5 on MRI ($n = 22$) showed 17 (77.3%) benign lesions and 5 (22.7%) malignant lesions (Table 4). The two BIRADS category 4

Table 2
Correlation of BI-RADS categorization on magnetic resonance imaging (MRI) and targeted ultrasound result ($n = 68$).

BI-RADS – MRI	Targeted ultrasound		Total
	Negative	Positive	
Category 3	20 (43.6%)	26 (56.4%)	46 (100%)
Category 4	2 (10%)	18 (90%)	20 (100%)
Category 5	0	2 (100%)	2 (100%)

$p = 0.025$.