Breast Magnetic Resonance Imaging in microcalcifications
BI-RADS 3 and 4

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Purpose

Magnetic resonance imaging (MRI) is an imaging method that has developed significantly lately because of the advantages over other imaging techniques, such as its ability to use different planes, absence of ionizing radiation, low invasiveness, contrast with low allergenic potential and a sequence design which is faster and more useful for diagnosis.

It has long been used successfully in two main aspects: for assessing the integrity and morphology of breast implants (without contrast), and for the assessment and monitoring of Breast Cancer (with gadolinium intravenous contrast).

Regarding this last primary utility, there are some basic guidelines for MRI, some more accepted than others. For example, it is traditionally used mainly for monitoring postoperative breast or screening in high-risk populations, preoperative assessment of Breast Cancer (multifocal, multicentric, bilateral), study of dense breast and additional assessment of probably benign nodules or densities. However, it hasn't yet been studied in the assessment of breast lesions that appear in mammography as clusters of microcalcifications(1).

The MRI technique has changed greatly along recent years. At present, new dedicated breast MRI coils have been developed which, thanks to their multiple channels in phase, can collect a higher MR signal in this area and therefore can obtain thinner cuts (less than 3 mm.), increasing spatial resolution. Also new faster sequences have been developed which can get images with fat saturation without increasing scan time, as well as new computer software programs that make easier and more reliable the analysis of contrast enhancement curves. These have all significantly improved the studies quality, so that we can now best locate, identify and catalog MRI breast lesions. On the other hand, better education and experience of the whole human staff involved in this diagnostic method has also been a qualitative jump in breast MRI (2-4).

The aim of this study is to analyze what role breast MRI might play in the assessment and monitoring of underlying breast lesions that appear as mammographic clusters of microcalcifications, particularly those which are part of BI-RADS category 3 (probably benign) and BI-RADS 4a (low suspicion of malignancy), using scan optimized protocols.

Methods and Materials

Population-
We have selected retrospectively all patients who have attended a Radiological Center specializing in Magnetic Resonance Imaging (MRI) to perform diagnostic MRI, in whom groups of microcalcifications (BI-RADS category 3 or 4a) not associated with other mammographic findings (i.e., associated nodule or density with pathological aspect) were detected in a recent mammography. In most cases, the detection of these clusters of microcalcifications was the main reason for the performance of MRI in order to assess associated injuries. In a few cases, these microcalcifications were not the main reason, but a secondary element important for the diagnosis (i.e. patients diagnosed or treated for breast cancer who show microcalcifications in the contralateral breast).

The vast majority of patients included in the study (68.3%) had not performed recently breast ultrasound or no pathological findings were detected associated with the groups of microcalcifications studied. Only in almost one of five patients (19.5%) breast ultrasound in addition to mammography revealed pathological alterations in appearance, and MRI study was requested to confirm the diagnosis. No-one had made prior cytology or histology with regard to the groups of microcalcifications in study.

Patients were classified according to the BI-RADS category specified in its mammographic report. If this categorization did not appear, they were classified by consensus between two expert radiologists in mammography, others than who interpreted the MRI scan. All cases were confirmed by pathological examination of the lesion or mammographic follow-up for at least two years.

**Technique and interpretation**

Scans were performed in an MRI machine of main magnetic field 1.5 Tesla (Signa Excite, General Electric, Milwaukee, Wisconsin, USA), using a four-channel dedicated coil (four breast array coil).

Imaging protocol consisted of the acquisition of basic sequences with normal resolution in both breasts:

- Axial T1 fast Spin Echo (FSE) (TR/TE: 460/9; Matrix: 320/256, Field of view:300 mm, slice thickness / spacing: 5 mm/1 mm)
- Sagittal T2 fast spin echo (FRFSE) (TR/TE: 4000/100, Matrix 224/224, Field of view:200 mm, slice thickness / spacing: 5mm/1 mm)
- Coronal Short Time Inversion Recovery (STIR) (Fat suppression. TR/TE: 5000/50, TI: 150, Matrix: 256/192, Field of view:300 mm, slice thickness spacing /: 5 mm/1 mm)
In all cases was performed a dynamic sequence of high resolution images VIBRANT (Volume Imaged Breast Assessment) with fat saturation, 3D, without spacing between cuts with maximum slice thickness of 3 mm. (1.5-3 mm) (TR / TE: 5.4/2.1, TI: 7, Matrix: 256/160, Field of view:200 mm), with a first basal package of images without contrast. A dose of 0.2 mmol / kg of gadolinium contrast was injected intravenously (Gadodiamide hydrate, Omniscan, General Electric), followed by 30 ml of saline, using a dual-head infusion pump compatible with the magnetic field and five packages of images was obtained with the same protocol as the baseline sequence. This sequence was used for dynamic and morphological analysis of the lesions by subtraction with basal package, subsequent 3D MIP reconstruction and analysis of the enhancement curves in the suspicious lesions with a specific program (Functool 2/SER, General Electric).

The imaging findings were classified by contrast enhancement shape:

- **Nodular**
  1. Smooth (convex margins)
  2. Irregular (spiculated margins)
  3. Focal (small rounded nodules with smooth edges less 5 mm in diameter)
- **Non nodular:**
  1. Diffused
  2. Regional
  3. Linear
  4. Ductal (branched with tendency to converge to the nipple)

The lesions also were classified according to the contrast enhancement curve:

- **C-1:** Discrete slow and progressive enhancement until late in acquisition.
- **C-2:** Rapid enhancement in the first two minutes, with subsequent plateau.
- **C-3:** Early rapid and intense enhancement with late flushing.

Suspicious lesions were defined as following characteristics:

- Spiculated or irregular nodules with C-2 and C-3 curves.
- Regional enhancement with C-3 curve.
- Ductal enhancement with C-2 and C-3 curve.

**Results**
From November 2005 to September 2009, 68 patients with clustered microcalcifications BI-RADS 3 or 4a in a recent mammogram were studied by MRI. 27 were excluded because not complying the conditions of the study, being lost the follow-up or not completing 2 years. The remaining 41 patients had 42 lesions, resulting in 20 True Positives (TP), 16 True Negatives (TN), 6 False Positives (FP) and 0 False Negatives (FN), with a Sensitivity: 1'00 (100%), Specificity: 0'73 (73%), Positive Predictive Value (PPV) 0'77 (77%) and Negative Predictive Value (NPV): 1'00 (100%).

Analyzing this data, we can observe that most VP have microcalcifications BI-RADS category 4a (85%), while the VN and FP dominate category 3 (68.75% and 66.67% respectively).

Regarding the MRI lesion morphology, it is noteworthy that in all positive lesions (both true and false positives) there was a predominate of spiculated lesions, which account for 80% in the VP group and 50% of all that we can find in the FP, while the predominant situation in the VN is that the area of suspicious mammogram microcalcifications shows no pathological enhancement (68.75%).

As to morphology of the contrast uptake curve, the VP in our study are presented mostly with clearly pathological C3 curves (75%), and C2 curves predominate in the FP (66.67%). It is significant that no VN presented curves C3 and no VP showed curves C1.

Note that in most of the VP additional ultrasound has been done before or after MRI (60%) with no evidence of pathological findings in half of the cases, although most of them were performed prior to MRI (75%).

Despite the low number of false positives it is noted that the majority of them (66.67%) have performed a complementary ultrasound study and suspicious findings were found in the three performed prior to MRI (75%). A half of FP showed an MR speculated lesion, although in most cases, had a C2 plateau enhancement. Regarding to histology, 55% of the VP corresponded to infiltrating ductal carcinoma, 35% to ductal carcinoma in situ and 10% infiltrating lobular carcinoma.

Images for this section:
Fig. 1: Table
Fig. 2: Two groups of microcalcifications in the same breast (upper outer quadrant and upper aspect of Right Breast), both classified as BI-RADS 4a.
Fig. 3: Image enlarged upper outer quadrant microcalcifications
**Fig. 4:** Image of microcalcifications in upper aspect of same breast also enlarged.
**Fig. 5:** 3D MIP reconstruction of substracted postcontrast MRI acquisition, we can see that only the UCS injury presents a regional enhancement poorly defined. TN and TP (ductal carcinoma in situ), both confirmed by biopsy.
Conclusion

The diagnostic management of breast lesions that manifested in the mammography as clusters of microcalcifications has always been a challenge that even standardization of terminology and diagnostic categories in breast disease (BI-RADS) could not overcome. The subjectivity inherent in this system makes categories such as BI-RADS3 in practice become a "catch-all" wherein doubtful injuries or with obscure features are grouped. There is also an inter and intraobserver variability inherent in this type of standardization, not only when categorizing breast lesions, but also in terms of handling. Normally, the recommendation is to follow these lesions in a short term, but various factors can influence in deciding what to do in the sight of a group of microcalcifications (5). On the other hand, the practical utility of the division of BI-RADS category4 in4a (low suspicion), 4b (moderate) or 4C (high suspicion of malignancy) is unclear, when in all cases the recommendation is always biopsy.

The utility of breast MRI in the evaluation of lesions associated with mammographic microcalcifications has always been hotly debated, and traditionally this indication was not considered (6,7), however, many recent studies point to the possibility that breast MRI may play a role in the management of this type of injury (8,9). Especially if we consider the clinical context in which are some conflicting cases such as multiple groups of microcalcifications difficult to evaluate in isolation, microcalcifications in patients previously operated upon, in patients with personal or family history of breast cancer and previous mammograms not available or comparables or microcalcifications BIRADS 4 and previously submitted to biopsy with benign outcome.

Several breast lesions may appear as groups of microcalcifications, many of them benign. Among the malignant tumors with this type of presentation, the most common is ductal carcinoma (10), which becomes especially relevant in situ because it is often the only mammographic sign of this type of lesions clinically occult (11). Recent studies seem to show that breast MRI can identify ductal carcinoma in situ reliably (12) due to diffusion to the intraductal space of gadolinium contrast demonstrated in this type of tumors (13) - especially in high-grade which often progress to invasive ductal carcinoma (14) - and it can reliably determine the actual ductal tumor extent (15,16).

The results of our study suggest that breast MRI can detect malignant lesions presenting as mammographic finds of breast microcalcifications with high reliability. Moreover, as suggested in other items (17) normal MRI study makes it unlikely that there is an underlying breast carcinoma. Hence, high Sensitivity and high Negative Predictive Value should be noted (all of the 20 breast carcinomas have been detected in our series by MRI).
Even taking into account differences in the approach of the recent publications in this field, which leads to a relative disparity in outcomes, the results obtained in our study were similar to other researches, but better in the case of the Sensitivity and NPV (8, 9, 14, 18). This fact can be justified by one of the limitations of our work: the majority of cases in which MRI was positive, biopsy was performed, so that a definitive diagnosis was immediate, while frequently, when MRI was normal, there will be a follow-up imaging for at least two years, which delayed diagnosis. So there is a bias toward positive results while others take time to appear, especially the false negative cases, none was recorded so far. For this reason also occurs a relatively high rate of carcinomas in our series.

New researches would be needed in a larger population to confirm these results, especially if they are prospective observational studies. Although ours is a prospective study, the number of cases is still short and not carried out breast MRI systematically on all BI-RADS 3 or 4a microcalcifications. The decision to undertake this exploration has depended more on random factors such as the presence of other lesions in the breast or patient and referring physician's preferences.

We must clarify that we do not intend in this paper to evaluate the role of MRI breast systematic management of microcalcifications BI-RADS 3 and 4, but determine whether MRI can locate and evaluate breast lesions detected as microcalcifications in mammography, and thus serve to support or guidance on individual and conflicting cases or particularly difficult situations, as suggested for other types of mammographic findings (19).

CONCLUSION.-

Breast MRI can help in the management of breast lesions associated with microcalcifications BI-RADS type 3 or 4a in individual or particularly conflicting cases.

Images for this section:
Fig. 6: Group of BI-RADS 3 microcalcifications in external aspect of right breast

Fig. 7: Enlarged image of clusters of microcalcifications Bi-RADS 3.
Fig. 8: This group of BI-RADS 3 microcalcifications in external aspect of right breast, has presented in RM as a nodular irregular lesion...
Fig. 9: ...showing a C3 shape curve in the same area. False Positive on biopsy (non-proliferative mastopathy).
References

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