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### MRI of the Breast: A Valuable Tool for Accurate Patient Management Decisions

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**Currently, conventional mammography and ultrasound are standard imaging techniques for detection and evaluation of breast disease and are the primary imaging modalities used in screening women at high risk for breast cancer. However, these techniques are associated with limited sensitivity and specificity for the detection and diagnosis of breast lesions, particularly in women with dense breast parenchyma. Clearly, there is increased likelihood of inappropriate patient management if therapeutic decisions are made solely on the basis of mammography and ultrasound findings.**

Numerous studies have confirmed the superior diagnostic performance of breast MRI compared to conventional mammography and ultrasound and the potential of the method for more effective cancer screening in women with high familial risk of breast cancer. The most recent guidelines of the American Cancer Society (ACS) now recommend contrast-enhanced breast MRI for breast screening in women with an approximate 20 - 25% or greater lifetime risk of breast cancer.

Comparatively few studies have compared different MR contrast agents for potential differences in diagnostic yield in patients with suspected breast cancer. In part this is because the R1 relaxivity values of most commercially-available MR contrast agents are similar (approximately 4.3 – 5.0 L•mmol<sup>-1</sup>•sec<sup>-1</sup> at 1.5 Tesla) and thus similar lesion signal intensity enhancement and dynamic contrast behaviour is seen when these agents are administered at equivalent dose. Here, we look at the most recent studies in this field.

Gadobenate dimeglumine (MultiHance®; Bracco Imaging SpA, Milan, Italy) is a contrast agent with increased R1 relaxivity relative to conventional gadolinium agents due to weak, transient interaction of the contrast-effective chelate of this agent (Gd-BOPTA) with serum albumin. Compared with gadopentetate dimeglumine (Magnevist®; Bayer Schering, Berlin, Germany), the R1 relaxivity of gadobenate dimeglumine in blood is roughly two-fold higher at all commercially-available magnetic field strengths, ranging from 10.9 vs. 4.7 L•mmol<sup>-1</sup>•sec<sup>-1</sup> at 0.2 Tesla to 6.3 vs. 3.3 L•mmol<sup>-1</sup>•sec<sup>-1</sup> at 3 Tesla. Numerous studies show that the increased R1 relaxivity of gadobenate dimeglumine translates into greater signal intensity enhancement and thus improved image quality and diagnostic performance compared to comparator contrast agent at equivalent or higher dose.

The possibility to achieve greater contrast enhancement with a standard dose of 0.1 mmol/kg bodyweight relative to that achievable with an equivalent dose of a conventional gadolinium agent may have particular value for imaging applications in the breast in which lesions are often small, poorly-enhancing or otherwise inconspicuous against the surrounding normal breast parenchyma.

Previously, we compared 0.1 mmol/kg bodyweight gadobenate dimeglumine with an equivalent dose of gadopentetate dimeglumine in 25 consecutive women using an intra-individual crossover study, in which all patients received both agents, and demonstrated significant superiority for gadobenate dimeglumine for both the detection and characterisation of breast lesions (Pediconi F. et al, *Radiology*. 2005 Oct;237(1):45-56. Epub 2005 Aug 26).

## Which Contrast Agent Performs Better?

We have since confirmed the findings of this earlier study in a larger population of 47 women, which confirmed that a dose of 0.1 mmol/kg bodyweight gadobenate dimeglumine improves the detection of breast lesions and the performance of the MRI exam regarding the differentiation of benign from malignant breast lesions. In terms of overall diagnostic performance, significant superiority was noted for gadobenate dimeglumine compared to gadopentetate dimeglumine for sensitivity (98.0% vs. 76.0%;  $p=0.0064$ ), accuracy (88.5% vs. 69.2%;  $p=0.0004$ ), PPV (86.0% vs. 76.0%;  $p=0.0321$ ) and NPV (95.2% vs. 57.1%;  $p=0.0003$ ). Specificity was also higher for gadobenate dimeglumine (71.4% vs. 57.1%) although the difference was not significant ( $p=0.1277$ ).

Improved detection and characterisation of breast lesions with gadobenate dimeglumine resulting in a better evaluation of overall tumour extent might also benefit treatment planning for patients with breast cancer. Inappropriate surgical intervention remains a risk of inaccurate pre-operative evaluation of patients with breast cancer.

## Further Specific Applications for Breast MRI

A further specific application of breast MRI is for the evaluation of the contralateral breast in women with malignancy in one breast diagnosed by means of conventional screening mammography or ultrasound.

Several studies have been performed to evaluate the preoperative use of breast MRI as a supplemental examination to clinical examination, mammography and/or ultrasound to assess the extent of disease within the breast. We have shown that MRI of the breast permits the detection of additional malignant foci not seen on mammography and/or ultrasound and that detection of these additional foci results in a change in patient management in 11 – 20% of patients (Pediconi F. et al, *Breast Cancer Res Treat.* 2007 Nov;106(1):65-74. Epub 2007 Jan 3).

## Findings Lead to Change of Diagnosis

Concerning the detection and identification of malignant lesions, breast MRI was markedly superior to mammography/ultrasound (sensitivity for detection: 100% vs. 77.3%, accuracy for malignant lesion identification: 93.4% vs. 72.1%). In large part this can be ascribed to the breast density of the patients concerned: conventional mammography and ultrasound are known to be limited in patients with dense breast parenchyma. In terms of the impact on patient management, our breast MRI findings resulted in a change of diagnosis for 38/164 (23.2%) patients overall and an altered approach to patient management for 32/164 (19.5%) patients.

The altered approach to management involved more extensive surgery in 28/164 (17.1%) patients because of additional lesions or a larger lesion size, and cancellation of a proposed lumpectomy in 4/164 (2.4%) patients (Pediconi F. et al, *Breast Cancer Res Treat.* 2007 Nov;106(1):65-74. Epub 2007 Jan 3.).

In another study (Pediconi F. et al, *Radiology.* 2007 Jun; 243(3): 670-80. Epub 2007 Apr 19) we showed that that 28 (24%) out of 118 patients with malignant breast lesions on conventional xray mammography/ultrasound also had solitary contralateral breast lesions that were detected only on breast MRI. Of these 28 lesions, 22 (18.6% overall) were subsequently confirmed to be malignant after histological evaluation. Previous studies have reported contralateral lesion detection rates for breast MRI ranging from 8.2% (15/182 patients) to 32% (72/223 patients).

## Breast MRI Superior to Mammography and Ultrasound

The sensitivity, specificity, and accuracy of breast MRI for contralateral breasts harbouring malignant or high risk lesions among 118 patients with negative contralateral breasts at mammography/ ultrasound were 100%, 93.8% and 94.9%, respectively. Similarly, the PPV that detected lesions were malignant was 78.6% while the corresponding NPV that the absence of detected lesions was truly indicative of a negative contralateral breast was 100%. This study confirmed that breast MRI is superior to mammography and ultrasound for the depiction of contralateral breast cancer or high risk lesions in patients with a newly diagnosed unilateral breast cancer or high risk lesions depicted with conventional techniques (Pediconi F. et al, *Radiology.* 2007 Jun;243(3):670- 80. Epub 2007 Apr 19).

## Conclusion

Although our results clearly support the view that breast MRI is a valuable imaging modality for accurate patient management decisions, a possible limitation of these studies is that only patients considered suspicious or highly suspicious (BI-RADS IV and V) for breast cancer have been evaluated. Further prospective work in a more diverse group of patients are necessary to ascertain the full additional value of breast MRI..

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