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Editorial Comment

Magnetic resonance imaging in breast cancer: Is seeing always believing?

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It is an indisputable fact that magnetic resonance imaging (MRI) detects foci of carcinoma that cannot be identified by physical examination, mammography, or ultrasound [1,2]. The impact of these additional tumor foci on the selection of local therapy has not been addressed in some studies [1], and has been difficult to evaluate in others due to the heterogeneity of the patients studied and the inclusion of women who either required or desired mastectomy [2,3]. In this issue of the European Journal of Cancer, Deurloo *et al.* [4] report the impact of MRI on surgical therapy in 116 patients (78% with T1 cancers) felt to be candidates for breast conserving surgery after conventional imaging and multidisciplinary clinical assessment. Abnormalities on MRI were present in 41% of patients, and these were further evaluated in 78% of cases. Ultimately, 23% of patients had their therapy changed with conversion to mastectomy in 15%, wider excision in 6%, and contralateral surgery in 2%. These results are remarkably similar to those that have been reported by Berg *et al.* [2] and Bedrosian *et al.* [3]. However, the authors detailed analysis of the additional lesions provides a number of useful insights.

The low specificity of MRI continues to be a clinical concern. MRI guided needle biopsy is a relatively cumbersome procedure which is not widely available. For this reason, after an MRI abnormality is identified a directed ultrasound is usually performed in an attempt to identify the lesion. In the study reported here, only 49% of the MRI detected lesions referred for further workup were ultrasonographically visible. However, lesions which could be visualised by ultrasound were significantly more likely to be malignant than those which could not be visualised. The location of the MR abnormality also influenced the likelihood of malignancy, with abnormalities in the same quadrant as the index cancer more likely to be malignant than those in different quadrants of the breast, and lesions in the contralateral breast having the lowest probability of malignancy. This is entirely consistent with clinical experience. True multicentric carcinoma is seen in fewer than 10% of cases [5,6] and in population based studies contralateral cancer occurs in fewer than 1% of patients per year of follow up [7,8].

As illustrated in this study, the proportion of women with breast cancer undergoing MRI who have additional abnormalities requiring evaluation is unacceptably high, ranging from 24% to 41% [1,2,4]. In this regard, the combination of clinical evaluation and a computerised analysis presented by Deurloo *et al.* [4] is quite promising, with an increase in specificity from 33% for reading alone to 97% for the combined model with no loss of sensitivity. Validation of these results in a larger, independent data set is clearly indicated. When evaluating the extent of further workup, the appearance of the lesion on MRI, its visibility on ultrasound and its location in reference to the primary tumor should be considered. This approach has the potential to avoid costly biopsies and the patient anxiety associated with the identification of multiple "suspicious" abnormalities in a breast known to contain cancer. The latter is not a trivial point. Berg *et al.* [2] reported that 12% of breast cancer patients with MRI findings underwent "unnecessary" mastectomy because of anxiety regarding the need for workup of additional findings. However, efforts to improve the specificity of MRI ignore the essential question about

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the role of this technique in the selection of local therapy: does MRI improve outcome? To some, the answer to this question is obvious. If cancer is present, it is clinically important, so its detection and removal by definition is beneficial to patients. Others, myself among them, would prefer to see clinical trials which provide evidence of improved outcome prior to incorporating MRI into routine practice. After all, serial subgross sectioning of mastectomy specimens in patients with clinically and mammographically localised cancers demonstrates additional foci of carcinoma in 21–63% of patients [9–12]. These studies formed the basis of the argument that treatment of breast cancer with less than a total mastectomy was inappropriate, an argument which seemed logically sound until clinical trials proved it to be incorrect. Current local failure rates for breast conserving therapy of less than 10% at 10 years [13–15] clearly demonstrate that the combination of radiotherapy and systemic therapy controls the majority of these tumor foci, and that mammography and conventional pathologic evaluation identify those patients with a tumor burden too heavy to be controlled with a breast conserving approach. The available data strongly suggests that the cancer found on MRI and the cancer found on serial subgross sectioning is the same disease. Holland *et al.* [12] observed that 95% of the additional foci of carcinoma found on subgross sectioning were located within 4 cm of the primary tumor. In their MRI study, Berg *et al.* [2] noted that 87% of MRI detected tumor foci were within 4 cm of the primary tumor. Sardanelli *et al.* [16] correlated MRI findings with pathology after serial subgross sectioning of mastectomy specimens. The sensitivity of MRI for invasive tumor foci was 89% (140/158), and for *in situ* foci 40% (12/30). However, the positive predictive value of MRI was only 68% and significant differences in sensitivity between mammography and MRI were only seen in women with fibroglandular or dense breasts.

How should clinicians and patients regard the seemingly contradictory facts that breast conserving therapy results in long term local control for the overwhelming majority of patients, yet MRI demonstrates lots of cancer which in the past has been undetected and untreated surgically? Deurloo *et al.* [4] make the obvious, but often overlooked, point that treatment should not be changed without histologic proof of malignancy. But, will we ever know what, if any, are the appropriate modifications of treatment when additional foci of tumor are found? The traditional response is usually mastectomy. But, could MRI be a method of identifying patients who will benefit from a boost dose of radiation, or perhaps those who are candidates for partial breast radiotherapy? A trial to assess the benefit of MRI in the entire population of breast cancer patients would have to be enormous and is unlikely to show more than a 2–3% reduction in local failure, making the expense of the study difficult to justify. An alternative approach is to study a population such as young women, or those with infiltrating lobular carcinoma, where a clinical problem exists and the benefits of MRI are said to be greatest. Without appropriate clinical trials, the debate between the breast imaging community, who see malignant foci on MRI and believe in their importance, and the clinical community, who have seen the long term outcomes of breast conserving therapy without MRI and know them to be favorable, is unlikely to be resolved.

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