



## Editorial

## Pre-operative breast MRI in women with recently diagnosed breast cancer – Where to next?

The appropriate application of breast MRI in the pre-operative evaluation of women with a new diagnosis of breast cancer is currently one of the most debated and controversial issues in breast cancer management.<sup>1–5</sup> While it initially seemed clear to many that MRI's superior detection capability relative to conventional breast imaging<sup>1,3,4,6</sup> for both the affected breast, and the contralateral breast, would result in improved patient outcomes, an increasing body of evidence based on clinical experience suggests that this may not be the case.<sup>7–10</sup> This issue of the journal presents some of the varying perspectives on this topic in three commentaries reflecting the views of physicians specializing in breast imaging and the local therapy of breast cancer, and decision-making experts.<sup>11–13</sup>

Sardanelli provides an overview on pre-operative MRI and makes recommendations to help guide the use of MRI in this setting. A counter-view from Solin presents an evidence-driven discussion on pre-operative MRI, emphasizing that existing evidence has not shown any clinical benefit. McCaffery & Jansen provide insights into the complex process of decision-making for both clinicians and patients, and outline methods to potentially improve decision-making around pre-operative MRI in breast cancer. All three commentaries raise the need for prospective clinical trials.

For clinicians working in breast diagnosis, it is difficult to ignore the detection capability of MRI, and equally difficult to comprehend (or even accept) that finding additional disease (that would have remained occult on conventional imaging) in either the affected or contralateral breast<sup>6,8</sup> does not necessarily translate into improved clinical outcomes. There is no question about the ability of MRI to detect additional occult cancer in women newly affected by breast cancer: this has been shown in numerous studies and confirmed in pooled analyses.<sup>1,8</sup> Yet the one consistent finding in studies of pre-operative MRI is that its detection capability results in more extensive surgery (frequently a change to mastectomy)<sup>8,9,14,15</sup> than what would have been done based on routine care – without associated evidence that this leads to improved short-term outcomes such as a decreased need for re-excision for involved margins or a decrease in the number of unplanned mastectomies.<sup>1,9</sup> It is also not clear that long-term clinical endpoints such as the incidence of local recurrence in the conserved breast are improved when MRI is used for patient selection.<sup>1,2,7</sup> While more extensive surgery due to false positive MRI results should be avoidable with the use of MRI-guided biopsy to confirm malignancy prior to changes in the surgical plan, the real debate is

centered upon the need for changes in treatment in women with additional cancer detected by MRI, when the rate of detection of additional disease is 2–3 fold higher than the rate of local recurrence in women selected for breast conserving surgery without MRI.<sup>1,2</sup>

It is unlikely that consensus can be reached on the role of pre-operative MRI in the near future despite anticipated evidence from 2 randomized trials. The only available evidence from a randomized trial on the impact of MRI on surgical planning comes from COMICE (Comparative Effectiveness of MRI in Breast Cancer trial),<sup>16</sup> an RCT of 1625 women thought to be candidates for BCS based on conventional imaging and clinical evaluation. The study was designed to measure the effect of MRI on re-excision rates as a primary endpoint, and no reduction in re-excision rates was reported in the initial presentation of the data.<sup>16</sup> After 3 years of follow-up, no differences in disease-free survival have been observed between the two arms, but long-term results are clearly needed to address this endpoint. The second RCT, implemented in Europe, MONET (MR mammography of non-palpable breast tumors)<sup>17</sup> will examine whether MRI in addition to mammography and/or ultrasound, in patients with suspicious breast lesions, improves management (specifically, whether it reduces the number of surgical procedures or core needle biopsies). It aims to recruit 500 subjects and will also examine local recurrence as an outcome. Unfortunately, the study population will include a mix of patients with and without breast cancer, and the study is not adequately powered to address the important clinical endpoint of the effect of MRI on local recurrence, leaving the COMICE trial as the only source of prospective, randomized data for this endpoint.

At present, it is important that we remain clear on what we know based on evidence, and what we still do not know because we are lacking data from adequately designed trials, and that we acknowledge the divergent perspectives on this issue. It is likely that the only way forward is to direct our efforts towards planning and implementing well-designed prospective trials. It is debatable whether a trial designed to address the impact of MRI on local recurrence in the general breast cancer population is feasible or a reasonable use of resources. Such a trial would need to be adequately powered,<sup>1</sup> and given the generally low background prevalence of local recurrence in the context of current standards of care, would be costly and time-consuming. Given that local recurrence occurs in about 6–8% of patients over 10 years, it is also worth asking whether a 1–2% reduction in local recurrence

(although a 13–33% *relative* benefit), is actually clinically meaningful. More importantly, a continued focus on tumor burden as the key factor in local recurrence in the modern era may be inappropriate. Clinical experience has demonstrated that local recurrence is least common after breast conservation therapy or mastectomy in the presence of effective targeted therapy.<sup>18,19</sup> If even mastectomy does not eliminate the problem of local failure, because some local recurrences are a first site of metastasis, then is it reasonable to believe that an improved imaging modality will? Rather than focus on the problems of patient selection for breast conserving surgery and local recurrence due to excessive tumor burden, which in large part have been solved, it makes far more sense to ask in which clinical problem area the improved cancer visualization provided by MRI is likely to have the greatest impact, and design a trial addressing this issue.

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