

MRI for breast cancer: who benefits, who is harmed?

→ Emma Mason

When a woman is diagnosed with breast cancer, and a technique exists that could identify additional lesions in the same or the opposite breast, what possible reason could there be for not using it? Unnecessary delays and unnecessary mastectomies to name but two, say the opponents of routine MRI. The debate continues.

At the European Breast Cancer Conference in Barcelona this year, one of the closing debates is entitled: "This house believes that MRI for breast cancer is standard of care" – thus tapping into a controversy that has been the subject of much research and discussion in recent months and years.

For many it is not at all clear that magnetic resonance imaging (MRI) should be used routinely in the diagnosing, staging and treatment of breast cancer. In fact, a number of influential voices have been asking whether MRI does more harm than good, particularly before surgery in women with uncomplicated early breast cancer.

Speaking against the motion at EBCC7 in Barcelona will be Lawrence Solin, chairman of the Department of Radiation Oncology at the Albert Einstein Medical Center, in Philadelphia, USA.

In a recent article for *The Breast* (in press) Solin argues that a medical test or treatment should be of benefit to patients if it is to be used in routine clinical practice, and that, for the typical patient with early-stage breast cancer, "no such benefit has been shown to date for the routine use of preoperative breast MRI beyond the benefit already conferred by conventional breast imaging (i.e. mammography with correlation ultrasound as indicated)." Thus, he concludes, the routine use of preoperative breast MRI for early-stage breast cancer patients is unwarranted.

Others go further, pointing to a potential link between increased use of MRI and a rise in the rate of mastectomies, many of which may be unnecessary. In an editorial for the *Journal of Clinical Oncology* last September, Monica Morrow, head of the Breast Surgery Service at

New York's Memorial Sloan-Kettering Cancer Center, argues that the assumption that using MRI to select patients for breast-conserving therapy would reduce the need for re-excision, reduce local recurrence, and even improve long-term survival does not seem to have been borne out in practice. "At present, no studies have provided support for any of these improved clinical outcomes," she writes. "However, breast MRI has been shown to result in additional biopsies and costs, increased patient anxiety, and delays in the start of definitive treatment." She points out that while accepted practice is for MRI-detected abnormalities to be biopsied before altering surgical treatment plans, some patients choose to forgo these biopsies or additional work-ups and opt to go straight for mastectomy, "because of concerns about delaying definitive therapy."



GETTY IMAGES

“The detection capability of this technique is such that it would be wrong to wait for conclusive evidence”

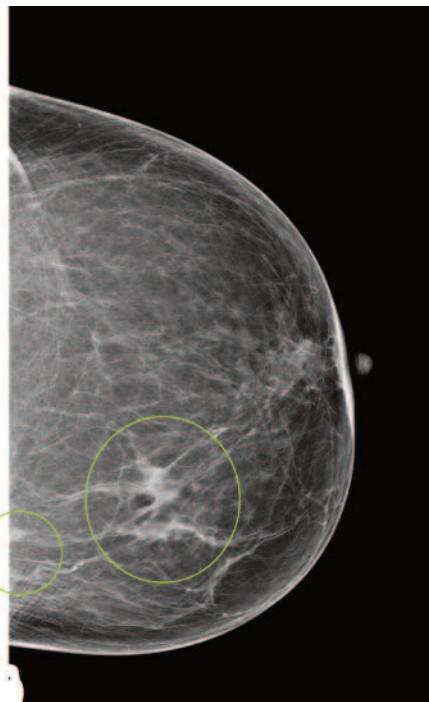
A VERY GOOD TECHNIQUE

At the heart of this debate is the undisputed fact that MRI is an extremely good imaging technique. It can detect tumours that are missed by more conventional techniques such as mammography and ultrasound, it is better at correctly assessing tumour size and detecting additional foci of disease (multi-focal or multi-centric cancers, or both), and it is better at detecting abnormalities in the dense breasts typically seen in younger women.

Francesco Sardanelli, professor of radiology at the University of Milan School of Medicine and head of the Radiology Unit at the IRCCS Policlinico San Donato in Milan, Italy, pioneered the use of MRI in breast cancer in Europe. Writing in *The Breast* (in press), he argues that the detection capability of this imaging technique is such that it would be wrong to wait for conclusive evidence for or against preoperative MRI. “To deny this examination to all women newly diagnosed with breast cancer is a questionable decision because the evidence is ‘uncertain’ rather than against a benefit from preoperative MRI.”

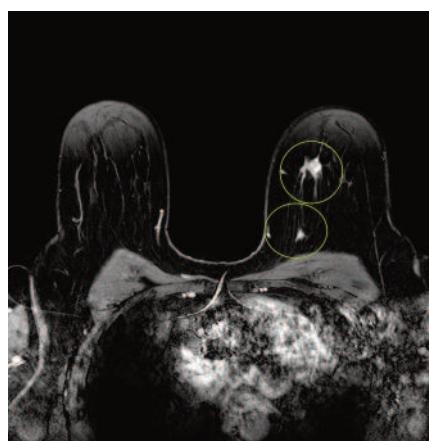
Morrow disagrees. “It seems very obvious that something that shows the cancer clearly must be a good thing for patients,” she told *Cancer World*, “but there is an increasing body of data that shows that, so far, this doesn’t seem to be true.”

Indeed, the success with which MRI picks up even the most minor abnormalities is exactly where the problem lies, she says, as many of these will be false-positives – benign abnormalities or cancers so tiny that they would be dealt with effectively by radiotherapy during or after surgery, or by



This multifocal lobular breast cancer was picked up using normal mammography (upper), but MRI was instrumental in clarifying the real extent of the disease (lower)

By permission of Elena Cauzza



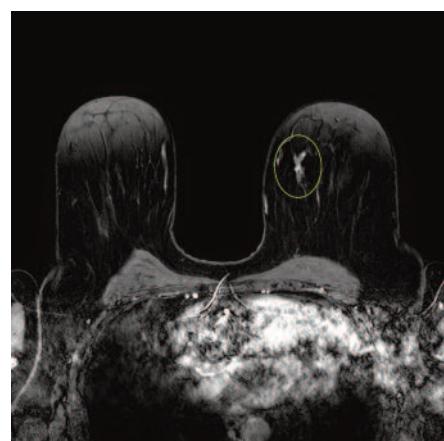
systemic therapies such as endocrine or chemotherapy.

“There’s fairly convincing evidence that says that MRI shows a lot of small-volume disease that’s always been there and that’s successfully treated with radiotherapy, but when we see it we feel obliged to do something about it, and that something is usually mastectomy,” she said.

“So far what we know about MRI is that it doesn’t increase your likelihood of getting negative margins with a single lumpectomy. It does not decrease the risk of unexpected conversion from lumpectomy to mastectomy, and although the data with longer-term follow-up are still very limited, what there are show that it doesn’t decrease the risk of local recurrence in the breast.

“So, of any of the potential benefits to patients, none of them have been proven. What we do know is that it can delay treatment, it results in more biopsies, and it increases cost.”

In a review of preoperative MRI, published in *CA: A Cancer Journal for*



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Clinicians last September, Nehmat Houssami and Daniel Hayes make a similar case. “Evidence consistently shows that MRI *changes* surgical management, usually from breast conservation to more radical surgery; however, there is no evidence that it *improves* surgical care or prognosis.” Like Morrow, they argue that the emerging data indicate that MRI does not reduce re-excision rates and that it causes false-positives in terms of detection and unnecessary surgery.

The authors also point out that, while local recurrence rates are between 5% and 10% for breast conserving surgery combined with radiotherapy, a meta-analysis has found that MRI detected additional small cancers in the same breast in 16% of cases on average. “That’s more than twice as many as the number of women who ever develop evidence of a recurrence,” says Morrow, commenting on these findings, “and I think this is evidence that this type of disease does not need to be treated surgically.”

From the patient’s point of view, MRI gives more information, but can increase the complexities of the decision-making process, for both her and her physician.

If an MRI shows up suspicious tissue elsewhere in the affected breast, or the contralateral breast, then international guidelines recommend that an MRI-

CLAIMS AND COUNTERCLAIMS

Supporters of routine use of MRI argue that it offers a number of benefits:

- by visualising the size and extent of the disease, it can enable surgeons to excise the correct amount of tissue, removing the tumour entirely, while not removing unnecessarily large quantities of healthy tissue;
- this, in turn, reduces the likelihood of re-excision to remove remaining tissue that turns out to be cancerous;
- it can reduce rates of the tumour recurring in the same breast;
- it detects other tumours in the same breast (ipsilateral cancer) or the other breast (contralateral cancer), enabling surgeons, in theory, to remove all tumours in one go;
- it can visualise whether preoperative treatment, such as radio-, chemo- or hormonal therapy, is having an effect in shrinking a tumour before surgery, possibly enabling a lumpectomy to be performed rather than a mastectomy;
- it can visualise whether the same treatments are mopping up small cancerous deposits after surgery;
- it provides better images of dense breasts;
- it is better at detecting certain cancers, such as invasive lobular breast – a particularly aggressive cancer;
- all of the above could lead to an improvement in recurrence and overall survival rates.

Opponents counter that, while many of the benefits listed above were expected when MRI was first introduced for breast cancer, they have not been borne out in reality.

They argue that, on the basis of the evidence so far, MRI:

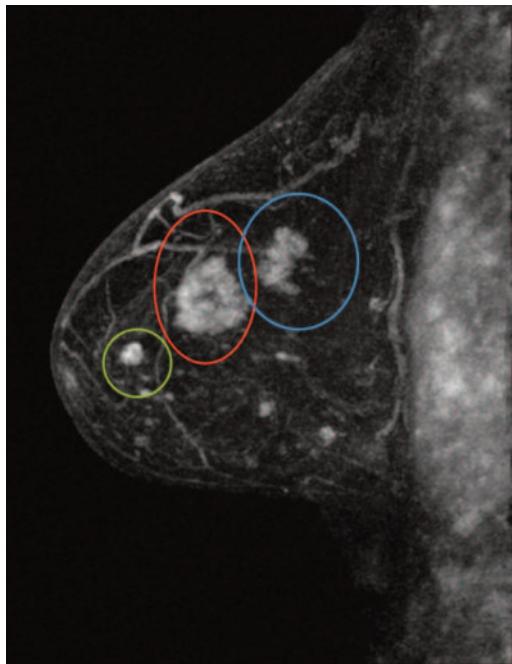
- does not increase your likelihood of getting negative margins with a single lumpectomy;
- does not decrease the risk of unexpected conversion from lumpectomy to mastectomy ;
- does not decrease the risk of local recurrence in the breast.

It does, however, lead to:

- additional biopsies and costs;
- increased patient anxiety, and
- delays in the start of definitive treatment.

“MRI *changes* surgical management, however, there is no evidence that it *improves* surgical care or prognosis”

“Some people want to diagnose every little patch and are not aware of what really threatens the patient’s life”



MRI scans have a high false-positive rate. On this scan, the area circled in blue showed a highly significant signal, yet nothing was found on pathological investigation. The area circled in red was found to be an invasive cancer, and the area in green a fibroadenoma

By permission of Elena Cauza

LOSS OF FOCUS

The radiologist, physician and patient also have to focus on what is the main threat to the patient’s life. Sylvia Heywang-Köbrunner, director of the Referenzzentrum Mammographie München, a mammography reference centre in Munich, Germany, told *Cancer World*, “In my experience, when you do an MRI and find something that is enhanced, that does

delay surgery. We all try very hard to schedule the biopsy quickly, but this can be difficult and you may also need to consider the woman’s menstrual cycle, so that you pick the right time of the month.”

Delaying treatment of a large, grade III tumour on the grounds that MRI has indicated there may be an additional small lesion could make things worse, she argues. “For me, the big question is: do I help the patient by finding a small, 3- to 5-mm lesion elsewhere in the breast or in the contralateral side, if the patient’s life is really threatened by the first, large tumour?

“Sometimes people want to diagnose every little patch and are not aware of what really threatens the patient’s life. One should really consider which patients can we help with MRI and which patients might we delay the diagnosis and cause

more problems than we solve.

“I think we should be very careful not to over-read and overtreat. We still need to prove whether, by finding additional tiny foci, that’s helpful for the patient, because we cause harm by converting from breast reconstruction to mastectomy if the patient has no better survival.”

WHO NEEDS MRI?

So when should MRIs be performed and when not? Most commentators seem to agree about when they can be useful, but there is less agreement about when MRI should be avoided, with some proponents of the technique arguing that it should always be used because of the extra information it provides.

Morrow and Heywang-Köbrunner both argue against using MRI in uncomplicated early breast cancer where other imaging techniques suffice.

“I definitely would not recommend MRI in breasts that are adequately analysed by mammography and ultrasound, or by a combination,” says Heywang-Köbrunner. “This combination has an acceptable sensitivity [proportion of true-positives correctly identified], especially for the lesions that are larger than 5 mm; the false-positive rate is much lower than MRI and, importantly, it’s very easy to clarify something that I see. For instance, if I see something on mammography or ultrasound, a mammographically-guided procedure or ultrasound-guided procedure can be done very fast, it’s reliable and you have the people available who can do it and this is solved very easily.”

She does, however, recommend an MRI in dense breasts and where lobular

guided biopsy should investigate the tissue. This delays the diagnosis and the start of treatment, and introduces yet another procedure to undergo. Already anxious and stressed by the initial diagnosis of breast cancer, many women decide that they can’t face the added delay and uncertainty involved in having a biopsy, and opt to go straight to a mastectomy in the hope that this will deal with all the cancer in one go.

Other factors may also play a role in the decision to opt for mastectomy, such as the availability of MRI-guided biopsies, how they are funded (does it require extra permission from the health insurers, hence further delay), cultural differences, the medical-legal climate of a country and the availability of plastic surgery.

When MRI throws up false-positives

MRI tends to throw up more false-positives than either mammography or ultrasound, and great care must be taken when using preoperative MRI to guide decisions on surgery.

The most frequent causes of false-positives include adenosis (a benign condition affecting the lobes in the breast) and benign tumours such as fibroadenomas or papillomas. Less frequently, inflammatory changes, granulomas or lipo-filling may cause confusion.

Lipo-filling is a new technique in plastic surgery which involves aspirating fat tissue from another part of the patient's body and then re-injecting it into the areas of the breast that are not completely filled, making it possible to shape the breast

better. But breast surgeon Alberto Costa warns that on MRI it can be mistaken for an area of cellular growth. "This happened to me, when the radiologist saw this and rang me to say that there were multiple recurrences and we needed to do an immediate mastectomy," says Costa. "Luckily we worked out what the problem was."

Even when the MRI shows real cellular growth, he adds, while it may be cancer, it may also be general growth, such as a scar. "So if you do magnetic resonance too soon after surgery, it's biased because it will flag up areas of cellular growth that are simply the process of scarring after surgery. So you never do MRI after surgery earlier than at least a month or six weeks."

breast cancer has been diagnosed, "because we know that mammography and ultrasound is weak in these situations and might not detect quite large tumours that could threaten the patient's life, or would make a change of therapy necessary."

MRI may also be beneficial, she adds, in women who are at high risk of inherited breast cancer, in young women with dense breasts, in cases where there is a big discrepancy in the size of the tumour when measured by mammography and ultrasound and possibly also to help a surgeon who is uncertain about whether mastectomy or breast reconstruction is the best way forward.

Heywang-Köbrunner would like to see research to find out whether MRI can offer early evidence if a certain treatment, such as chemotherapy, is not working. "If we can find this out early on, we can suggest a change of chemotherapy so that the patient does not lose time on a treatment that is not going to work."

THE RIGHT QUESTIONS

Morrow agrees that more research is needed to establish where the information provided by MRI might help. "For example, one such clinical problem is women who received chemotherapy prior to surgery to shrink their cancers to allow a lumpectomy; it's very difficult to evaluate how much cancer is actually present. And that's a place where MRI appears to be better than other tools that we have."

What we don't need, she says, is yet another general study of MRI for all breast cancer patients, "because I think that question 'can it find more cancer?' has been asked and we know the answer is yes, but that doesn't say that it benefits patients." Questions about whether MRI can identify a subset of patients who don't benefit from radiotherapy or a subset who are appropriate for radiating only part of the breast, would, however, be useful to investi-

gate, says Morrow. "There's room for more of these trials that ask about the benefit to patients."

One thing that most people agree on is the need for expertise in the use and interpretation of MRI. Alberto Costa, director of ESO (the European School of Oncology), and coordinator of both the Breast Surgery Unit at the Maugeri Foundation in Pavia, Italy, and the Canton Ticino Breast Unit in Lugano, Switzerland, summed it up: "You need to have a radiologist who is specialised in magnetic resonance imaging and then sub-specialised in breast cancer. Otherwise, MRI can create incredible disasters. It's a very good technique, a new technology, which could be of great help in genetically predisposed women, in preoperative medical treatment and in a number of other situations, but which, in not very expert hands, could create damage because it can overestimate the diagnosis."

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