



Original article

Role of magnetic resonance imaging in managing selected women with newly diagnosed breast cancer

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ABSTRACT

The purpose of this study is evaluation of therapeutic impact of magnetic resonance imaging (MRI) in breast cancer patients that cannot be imaged adequately with traditional radiology: dense breasts, microcalcifications suspicious for carcinoma in situ or discordance between mammography and ultrasound. A review was performed of 493 patients' records: determination of breast MRI effect on clinical management was made for the selected 70 cases by analysing pre-MRI and post-MRI therapeutic plans. Analysis of final pathology was useful to determine if the change in surgical plan prompted by MRI was appropriate. Breast MRI added clinical information in 52.9% of patients that resulted in 44.3% of management changes that were judged as appropriate in 83.9% of cases. Breast MRI provides additional useful information, but causes more extensive surgery (40%) with no proven prognostic benefit. MRI should be considered optional in the clinical staging of breast cancer and performed in selected cases.

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Introduction

Surgical treatment of early breast cancer is often breast conserving surgery (BCS). To optimize the results of BCS and to define optimal local treatment, clinical workup prior to surgery requires accurate assessment of tumor extent.^{1,2} MRI, thanks to his ability to image precise delineation of soft tissue and thanks to his high sensitivity rate (95–100%)^{1–5} provides a very accurate evaluation of breast. On the other hand, false positive findings of breast MRI are common^{2,6–8} and MRI staging causes significant changes in breast cancer patient management with possibly unnecessary extensive surgery^{9–11}. International guidelines¹² consider optional the use of MRI as a staging procedure for breast cancer women: according to this idea we performed MRI in a selected group of patients. The aim of the study is to evaluate the influence of pre-surgical breast MRI on the clinical management of a selected cohort of patients.

Patients and methods

Patients selection

An analysis was conducted on the records of 493 patients with breast carcinoma who underwent a surgical procedure from March 2002 to November 2008 at Department of General Surgery of Trieste University. Our study population is the result of a selection of 67 consecutive breast cancer patients who underwent pre-surgical breast MRI (13.6%). Data and clinical information were recorded from patient charts, radiology and pathology reports.

The study group was collected according to the following criteria:

1. breast carcinoma suspected at fine needle aspiration (FNA) or diagnosed with core biopsy (CB) or VAB-Mammotome[®] either in situ or invasive;
2. American Joint Committee on Cancer (AJCC) clinical stage 0, I or II disease at presentation;
3. breast radiological and pathological studies available;
4. preoperative breast MRI performed at the Hospital of Trieste University;
5. initial management plan based on history, physical exam and conventional imaging information: mammography (MMG) and ultrasound (US) classified as recommended from American

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College of Radiology Practice Guidelines (BiRADS®-revised 2008)¹³ by a Radiologist experienced in breast studies and attending the Regional Breast Cancer Screening Study Group;

6. re-evaluation of therapeutic plan based on MRI findings;
7. definitive surgical treatment (BCS or mastectomy) performed at the Department of General Surgery of Trieste University;
8. pathological analysis of surgical samples performed at the Department of Pathology of Trieste University.

We excluded from the study patients with:

1. breast MRI after neo-adjuvant therapy;
2. local recurrence after BCS.

Patients underwent breast MRI for the characterization of breast disease according to NCCN and ACR guidelines with the following indications:

1. high breast density (BiRADS® 3–4);
2. pathological pre-surgical diagnosis of DCIS or presence of suspicious microcalcification-patterns at MMG (patterns 3, 4 and 5 according to Le Gal Classification);
3. MMG reports suggesting multifocality or multicentricity;
4. discordance in MMG and US findings: US negative with MMG positive and vice versa. Tumor extent was measured at conventional imaging: we considered the largest diameter of lesion at MMG and US. We considered as discordant each case with a difference in magnitude of size of more than 10 mm.¹⁴

Breast MRI technique

We performed breast MRI after diagnosis of breast carcinoma obtained at FNA, CB or VAB. In the whole study population we performed bilateral breast MRI, read by an expert breast imaging team working with the multidisciplinary treatment team. In the selected cohort of patients, both surgeon and radiologist agreed, after clinical examination and conventional imaging, in performing breast MRI. Each case was discussed: pre-MRI surgical plan based on conventional imaging was defined and recorded by the surgeon and, at the same time, the surgeon himself asked the radiologist to perform MRI. After analysis of MRI findings the surgeon defined the final surgical plan.

According to ACR equipment specifications, MRI was performed with PHILIPS GYROSCAN 1.5 T, 7 RF coil channels. We always performed T2 weighted sequences and six contrast sequences (3D GE FFE spoiled T1w, TR 8.8 ms, TE 4.4 ms. Flip angle 25°, FOV 360 mm RL, 163 mm FH, 150 mm AP. Voxel size 0.7 mm RL, 1.01 mm FH, 2.5 mm AP. Voxel in-plane resolution of 6.7 × 1 mm, voxel reconstruction 0.68 × 0.69 × 2.5 mm). Gd-DTPA contrast was administered with power injector as a bolus with a standard dose of 0.1 mmol/kg followed by a saline flush of at least 20 ml. We obtained a pre-contrast scan and five contrast scans after bolus injection.

Analysis of MRI findings was conducted on:

1. morphology and estimated size of primary tumor;
2. enhancement distribution;
3. kinetic information;
4. description of additional suspicious lesions separate from the primary tumor (multifocality, multicentricity, bilaterality);
5. muscular or skin involvement.

All MRI findings were discussed by breast cancer multidisciplinary board and compared with information obtained thanks to

MMG, US or physical investigation in order to classify any unexpected report as additional finding. Tumor extent was measured at conventional imaging and at MRI. Tumor extent at conventional imaging was defined as the largest diameter of a tumor at US or at MMG when the diameter of the tumor, including suspicious microcalcifications, exceeded that at US. We defined underestimation and overestimation as a difference of tumor extent at conventional imaging and at MRI of less or more than 10 mm. In some patients, according to our Radiologist's indication, we performed "Second-look-US" and/or additional pathological analysis (FNA), in order to better evaluate unexpected intramammary additional enhancement foci. When MRI simply confirmed information obtained by traditional radiology, MRI was judged to have had no effect on clinical management.

We also analysed pre-surgical evaluation time as the time between pathological diagnosis of breast carcinoma and date of surgery in order to identify any treatment delay due to preoperative MRI.

Assessment of change in surgical plan

In order to assess the impact of MRI on surgical decision making, we analysed differences between surgical therapy planned thanks to traditional radiology and definitive surgical plan prompted by MRI. Both pre-MRI and post-MRI surgical plans were defined by the surgeon according to radiologist's and pathologist's comments.

We considered as significant changes in breast cancer patient management:

1. more extensive surgery instead of BCS;
2. mastectomy instead of BCS;
3. neo-adjuvant therapy instead of mastectomy.

All patients treated with BCS (quadrantectomy) were submitted to postoperative radiation therapy.

We evaluated the correlation between MRI findings and final pathology in order to determine if change in breast cancer patient management due to MRI was appropriate. Surgical samples were analysed by pathologists experienced in breast evaluation for the following aspects:

1. largest diameter of any malignancy, either invasive and in situ;
2. histological type and grade;
3. growth pattern of lesion;
4. presence of nodal metastasis.

In order to verify if there is any trend for a different impact of pre-surgical breast MRI in subgroups of patients, we divided our selected population according to the following criteria and performed statistical analysis (Chi-Square Test, *F*-Fisher Test) with software R (R Project for Statistical Computing):

1. indication for breast MRI;
2. histological type;
3. patients' inclusion in Regional Screening Group.

Results

Out of 67 patients eligible to pre-surgical breast MRI, 20 cancers (29.9%) were diagnosed by screening MMG thanks to Regional Screening Program, while 47 cases (70.1%) were diagnosed otherwise (three patients had bilateral lesions). The median age was 62 years (range 35–75) and the mean breast density was BiRADS® 3. In the screening group we diagnosed three DCIS and 17 T1 lesions. Six patients (8.6%) were symptomatic. In the other group

(50 breasts) we diagnosed seven DCIS, 26 T1 carcinoma, 15 T2 and two T3. Thirty-three patients (47.1%) were symptomatic.

In the subgroup of patients not submitted to breast MRI ($n = 426$), the mean breast density was BiRADS[®] 2, 4.5% of patients had pure DCIS ($n = 19$), 40.4% had T1 tumors ($n = 172$), 35.4% T2 ($n = 151$), 3.5% T3 ($n = 15$) and 69 patients had T4 lesions (16.2%).

In the cohort of patients selected for MRI, MMG showed 31 solid lesions, 20 clusters of microcalcifications, four associations of both reports and four mammary distortions. Eleven MMG BiRADS[®] 4 were negative: six patients were completely asymptomatic (three patients from the screening group and three from the other one), while the other five had palpable lesions.

According to the above mentioned criteria, we found discordance in traditional radiology findings in 46 cases (65.7%): MMG was negative in 11 cases of positive US (six E3 and five E4), US was negative in eight cases of positive MMG (one R3, five R4 and two R5) and traditional radiology showed differences in tumor extent in 27 cases. For the rest of patients ($n = 24$, 34.3%), MMG and US were concordant and we decided for pre-surgical breast MRI according to other selection criteria: in 12 cases MMG demonstrated microcalcifications and in 12 cases we had a very high breast density. Table 1 summarizes indication for breast MRI.

Any report obtained thanks to MMG and US was evaluated by FNA, CB and/or VAB (we performed biopsy under stereotactical guidance for the eight patients with US negative and microcalcification at MMG): we obtained 80 malignancy in 70 breasts.

MRI confirmed traditional radiology in 33 cases (47.1%), it was able to detect additional findings (additional foci and/or larger extension of a single lesion) in 30 cases (42.8%) and described seven lesions (10%) smaller than expected thanks to MMG or US.

In the group of patients with additional foci (19 cases), we considered five lesions (7.1%) as malignant, according to MRI enhancement features: as requested by patients themselves, we decided to directly go to more extensive surgery. In the other 14 cases we performed Second-look-US with confirmation of additional lesion in 11 cases. In three cases we discovered no lesions. We performed six US-guided FNA and obtained four benign lesions (adenosis, typical ductal hyperplasia) and two carcinoma. MRI false positive rate at pre-surgical workup was 10% (seven patients): three additional foci not showed by Second-look-US and four lesions identified as benign ones at FNA.

For 25 non-palpable lesion we provided pre-surgical imaging guided localization with charcoal-marker placed under US guidance. Intraoperative mammographic control of surgical specimen was performed for each patient with microcalcifications selected for BCS ($n = 11$).

Thanks to MRI we changed our previous established therapeutic plan in 31 patients (44.3%). We performed 15 (21.4%) mastectomy and 13 wider excisions (18.6%) instead of primarily planned BCS. One patient (1.4%) with previous diagnosis of T1 and MRI larger lesion size was selected for neo-adjuvant therapy and two patients (2.8%) with MRI demonstration of smaller tumor had their surgical plan changed for BCS instead of mastectomy (Table 2).

In order to verify each management change, we correlated MRI and final pathology: we considered as discordant each case with a difference in magnitude of size of more than 10 mm.

Table 1
Indication for Breast MRI.

	No of cases ($n = 70$) (%)
High breast density	39 (55.7)
Microcalcifications suggesting DCIS	20 (28.6)
Discordance in traditional radiology findings	11 (15.7)
Suspicious multifocal/multicentric disease	0 (0)

Table 2
Management changes due to MRI additional findings.

Management changes	Total (%)
Mastectomy instead of BCS	15 (21.4)
Wider excision instead of BCS	13 (18.6)
Neo-adjuvant chemotherapy instead of immediate surgery	1 (1.4)
BCS instead of mastectomy	2 (2.9)
Total	31 (44.3)

If we exclude from the analysis MRI false positive cases detected at pre-surgical workup (seven patients, 10%), MRI false positive rate is 7.1%. The cumulative false positive rate of MRI was 17.1% (12 patients) (Table 3).

We considered appropriate 26 management change out of 31 (83.9%) planned on MRI findings and confirmed at final pathology (Table 4).

We found no different impact of pre-surgical breast MRI in management changes in different subgroups of patients (Table 5).

We performed four re-resection in the selected series (5.7%) and 20 (7.4%) in the group of patients eligible to BCS that did not undergo MRI ($n = 271$). In this group 1 patient had recurrence after 5 years from the first surgical procedure (0.4%). The median follow-up was 36 months.

Concerning pre-surgical evaluation time, in the group of patients that did not undergo breast MRI we were able to perform surgical procedure in 43 days (range 2–132), in the present series we performed surgery after 44 (10–155) days from pathological diagnosis of carcinoma.

Discussion

The safety and benefits of breast conservation for early stage breast cancer patients have extensive been confirmed through randomized trials and long-term results: local excision and radiotherapy provide excellent local control with a low, long-term risk of local recurrence, typically 0.7–1% per year and with substantial equivalence of survival outcome with mastectomy.¹⁵

Appropriate evaluation of disease extent improves patients selection for BCS.^{2,4,9,16,17} MRI is demonstrated to be much more accurate than MMG in identifying disease extent (98 versus 54%),¹⁸ additional foci^{6–8,11,16} and intraductal components.^{19,20}

A meta-analysis published by Houssami,²¹ based on evidence from 19 studies on 2610 patients, showed that the prevalence of detection of additional foci ranged from 6 to 34% across studies with a median of 16%. In our series, MRI detection rate of additional foci is 27.1%.

The improved sensitivity of MRI has great impact on clinical management. A systematic review^{12,21} documented breast MRI staging to alter surgical treatment in 7.8–33.3% of women. Houssami et al.²¹ showed an incidence of conversion from BCS to mastectomy or wider local excision in respectively 8.1 and 11.3% of patients. Another study⁹ gives a percentage of 44.4% as overall rate of management changes in a non-selected cohort of patients and

Table 3
Performance of MRI in detecting breast lesions: comparison between MRI findings and final pathology.

	Suspicious (%)	True (%)	False (%)
Additional foci	19 (27.1)	12 (17.1)	7 (10)
Larger extent of single tumor	11 (15.7)	6 (8.6)	5 (7.1)
Smaller extent of single tumor	7 (10)	4 (5.7)	3 (4.3)
Confirmation of conventional imaging lesion extent	33 (47.1)	30 (42.9)	3 (4.3)

Table 4
Impact of MRI on clinical management.

	Total	Appropriate effect of MRI	Non-appropriate effect of MRI
Mastectomy instead of BCS	15	13	2
More extensive surgery instead of BCS	13	10	3
Neo-adjuvant chemotherapy instead of immediate surgery	1	1	–
BCS instead of mastectomy	2	2	–
Total	31 (100%)	26 (83.9%)	5 (16.1%)

other reports demonstrated change in management ranging from 12.5 to 24%.^{1,11}

Study design and patients selection vary widely across published investigations, but the great majority of studies includes a broad range of patients who had their MRI as a standard procedure of staging.

In our series of selected patients we observed 44.3% of therapeutic changes, 83.9% of them judged appropriate after histological verification. Breast MRI caused more extensive surgery in 32.8% of patients and led to overtreatment in 7.1% of cases.

One reason for overtreatment is MRI associated false positive findings. Houssami review²¹ indicates that 66% of MRI additional findings are confirmed as malignant at histology: false positive rate of MRI is nearly 33%. False positive rate calculated on final pathology is significantly lower (6.6%), probably thanks to preoperative additional tissue sampling of each MRI additional finding: MRI practice sites should have the ability to perform MRI-guided biopsy or needle localization and surgical management decisions should be based on confirmed histology, and not solely on the suspicious appearance of lesions on breast MRI.^{12,13}

In our series, during pre-surgical workup we identified 10% MRI false positive additional foci and after surgery we recognized other 7.1% false positive cases: our cumulative false positive rate is 17.1%, which is lower than preoperative false positive rate published by Houssami (33%), probably thanks to patients selection. Increasing pre-surgical verification of any MRI additional finding by performing MRI-guided biopsy, not already feasible at our hospital, would increase pre-surgical false positive rate and decrease overtreatment.

Re-resection rate in our selected population is 5.7%, similar to re-resection rate of our patients eligible for BCS that underwent no pre-surgical MRI (7.4%) as demonstrated by the COMICE study, which is the first prospective randomized trial that investigated the role of the addition of MRI to routine techniques for loco-regional staging of primary breast cancer.^{22,23} The study indicated no

Table 5
Impact of pre-surgical MRI on different subgroups of breast cancer patients.

	Management change (%)	<i>p</i>	Appropriate management change (%)	<i>p</i>
<i>Diagnosis</i>		<i>p</i> = 0.64		<i>p</i> = 0.61
Screening	8/20 (40)		7/8 (87.5)	
No-screening	23/50 (46)		19/23 (82.6)	
<i>MRI indication</i>		<i>p</i> = 0.39		<i>p</i> = 0.31
Microcalcifications	10/20 (50)		9/10 (90)	
High breast density	15/39 (38.5)		13/15 (86.7)	
Discordance in traditional radiology	6/11 (54.5)		4/6 (66.7)	
<i>Histology</i>		<i>p</i> = 0.44		<i>p</i> = 0.25
Invasive carcinoma	24/51 (47)		18/24 (75)	
Carcinoma in situ	7/19 (36.8)		7/7 (100)	

significant benefit in terms of reduction of re-resection rates by the addition of MRI to conventional assessment (18.8 versus 19.3%).

In our selected cohort of patients, we experienced no recurrence at a median follow-up of 36 months and we performed 32.8% of appropriate more radical surgical procedures prompted by MRI. If we consider the whole series of patients eligible for BCS ($n = 341$) and recurrence rate observed in the population not selected for MRI (0.4%), we will obtain a total hypothetical recurrence rate of 7%, which is much more than expected from the known recurrence rates after BCS (0.7–1% per year). Overall, more extensive surgery was recommended at MRI in about one third of cases planned for BCS based on conventional staging. One might assume that all these cases would have developed a breast recurrence if treated with BCS, but this assumption is questionable. Even considering the expected recurrence rate after BCS and re-excision rate prompted by resection for margin positivity, this would hardly reach 20%. Thus a substantial fraction of subjects undergoing more extensive surgery prompted by MRI staging was not bound to develop breast recurrence (indolent carcinoma, therapeutic effect of postoperative radiotherapy or adjuvant treatment). In our opinion, this fraction of management changes due to MRI correct staging probably would be considered as overtreatment: there are many evidences that show that radiation therapy provides effectively reduction in local recurrence. Probably more extensive surgery is not always necessary, because adjuvant treatment would be able to optimally control small tumor foci not showed at traditional radiology but showed at MRI.¹⁵

The impact of preoperative breast MRI on long-term outcomes was investigated by two retrospective studies in order to verify if more radical surgery would potentially reduce recurrence rates. Fischer et al.²⁴ reported that women who had preoperative MRI were significantly less likely to experience recurrence (1.2%) than those who did not (6.8%), but treatment and control groups were not matched, and those who had undergone preoperative MRI had tumors that were less advanced than those who did not. More recently one retrospective non-randomized analysis²⁵ reported no difference in recurrence rates among women who underwent preoperative MRI (3 versus 4% at 8 years).

In conclusion MRI is well documented to provide improved cancer detection, it allows more radical surgery that adds no proven benefit from the prognostic perspective: detection and removal of previously unrecognized malignancy wouldn't always lead to prognosis improvement, because additional foci would be effectively treated by adjuvant therapy. Despite this, pre-surgical breast MRI is a useful tool in delineating tumor extent in all cases of unclear findings at conventional imaging, such as microcalcifications, high breast density or discordant findings at MMG and US. It must be considered that breast MRI may cause additional procedures, longer time of waiting before surgery^{26,27} and more additional costs. Our analysis confirms MRI utility in pre-surgical workup of selected breast cancer patients: careful application of MRI restricted to appropriate patients is urged until well-designed randomized controlled trials will establish the clinical, psychosocial and long-term effect of MRI.

Conflict of interest statement

The authors indicated no potential conflicts of interest.

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