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ORIGINAL ARTICLE **CME**

Role of Breast Magnetic Resonance Imaging in the Preoperative Assessment and Its Impact on Surgical Management of Patients with Newly Diagnosed Breast Cancer

KCH Lau, CY Lui, LMF Tee, YHA Tsang, KKT Pak, M Ying, CM Chan, HS Lam

Department of Radiology, Kwong Wah Hospital, 25 Waterloo Road, Kowloon, Hong Kong

ABSTRACT

Objective: *To determine the role of breast magnetic resonance imaging in the preoperative assessment of patients with newly diagnosed breast cancer and its impact on surgical management.*

Methods: *In all, 22 patients with recently diagnosed breast cancer underwent preoperative magnetic resonance imaging and subsequent surgery or biopsy between 1 January 2010 and 30 June 2011. Patients with a change from initial planned surgical treatment to final surgical treatment based on additional mammographically occult magnetic resonance imaging findings were identified.*

Results: *Additional magnetic resonance imaging findings were found in 10 (45%) of the 22 patients; in eight there were additional suspicious lesions, and in two more extensive local disease became evident. In seven (32%) of the patients, there was a change in the initial planned surgical management owing to additional ipsilateral magnetic resonance imaging findings. One (5%) of the patients had contralateral surgery due to detection of synchronous contralateral cancer, and in five others additional suspicious lesions were only noted on magnetic resonance imaging that were confirmed to be malignant, giving a positive predictive value of 63%. In two (9%) of the 22 patients, the index tumours appeared significantly larger on magnetic resonance imaging than in mammograms, which changed the initial planned surgical management from breast conservation to mastectomy; there being less than one month between mammography and magnetic resonance imaging. For these two patients, calculated average tumour size underestimation on mammograms was 15.9 cm^3 (range, 11.9 - 19.9 cm^3). Another 23% (5/22) had additional mammographically occult cancers diagnosed by magnetic resonance imaging, with 18% having additional site(s) of ipsilateral cancer and 5% having unsuspected contralateral cancer.*

Conclusion: *Breast magnetic resonance imaging is a valuable tool in determining surgical management and detecting additional mammographically occult cancers in newly diagnosed breast cancer patients.*

Key Words: *Breast neoplasms; Carcinoma; Diagnosis; Incidental findings; Magnetic resonance imaging; Prognosis*

中文摘要

乳腺磁共振（MRI）對於新診斷乳癌在術前評估中的角色及對其手術治療的影響

劉仲恒、呂振英、鄭文輝、曾彥豪、白錦姿、英偉亮、陳志梅、林漢城

目的：探討乳腺MRI對於新診斷乳癌在術前評估中的角色及其對手術治療的影響。

Correspondence: *Dr Kevin CH Lau, Department of Radiology, 1/F, Kwong Wah Hospital, 25 Waterloo Road, Kowloon, Hong Kong.*
Tel: (852) 3517 8220 ; Fax: (852) 3517 5454 ; Email: kevin@lau.net

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方法：2010年1月1日至2011年6月30日期間，22名新診斷乳腺癌患者進行術前MRI及其後的手術或活檢，在其中找出因MRI檢查而額外發現隱性乳癌，並因此改變手術治療模式的病例。

結果：22位新診斷乳癌患者中，10例（46%）MRI檢查有額外結果，其中8例為新發現的可疑病灶，另2例的局部病灶變得更明顯。7例（32%）由於有額外的同側MRI結果而改變最初的手術治療模式。1例（5%）因發現有對側乳癌而要進行對側手術。另5例在MRI上發現額外的可疑病灶，後證實為腫瘤，陽性預測值為63%。22位患者中，2例（9%）在乳腺鉬靶檢查後不足一個月進行MRI，發現腫瘤在MRI上明顯地比乳腺鉬靶所顯示的大，因此治療模式由最初的保乳治療改為乳房切除。在這兩名患者中，乳腺鉬靶得出的腫瘤大小比真實的平均少了15.9 cm^3（介乎11.9至19.9 cm^3）。另5例（23%）的MRI結果發現有隱性乳癌，其中18%有額外同側癌，5%有新發現對側癌。

結論：乳腺MRI對於新診斷乳癌患者在決定手術治理模式以及檢測額外隱性乳癌方面都很重要。

INTRODUCTION

During the past decades, remarkable progress has been made regarding the early diagnosis of symptomatic and screen-detected breast cancers which has led to an increasing number of breast cancers amenable to surgery. Studies have shown that screening for and early detection of cancers at an early stage is associated with a reduction in mortality.[1]

The impressive evolution of early breast cancer surgery from the radical mastectomy pioneered by William Halsted to cosmetically appealing breast conservation has been welcomed by women and surgeons. Six randomised clinical trials have reported that for women with stage I or stage II breast cancer, survival is comparable regardless of whether patients undergo mastectomy or breast conservation.[2-7]

This led to a consensus statement by the National Institute of Health Consensus Development Panel in 1990[8] that breast conservation is the preferred method of primary surgical therapy for women with early stage breast cancer. After this consensus statement in the US, the percentage of women undergoing breast conservation increased from 35% to 60% for stage I and 19% to 29% for stage II breast cancer from 1989 to 1995. In the European Union, similar trends are seen with 80% of early breast cancer patients treated by breast conservation.[9,10] Despite not having a difference in survival with breast conservation, it is however associated with subsequent radiotherapy, regular surveillance, additional procedures and operations.

Studies have shown that occult, synchronous ipsilateral or contralateral breast cancers are not infrequently undetected by mammography or ultrasound. The rate of multifocality (i.e. additional breast cancer in the same quadrant as the index cancer) and multicentricity (i.e. additional breast cancer in a different quadrant than the index cancer) varies from 11% to 57%.[11-14] The rate of contralateral additional breast cancer was detected in up to 10%.[15-18] If these additional foci can be identified preoperatively, the planned surgical management can be altered and optimised. Unfortunately, mammograms and ultrasounds are not sensitive enough to detect some of these synchronous lesions.

The aim of preoperative imaging assessment is to accurately delineate the local disease extent, to identify contraindications to breast conservation, and to assess synchronous tumour foci in the contralateral breast. All published studies have consistently shown that breast magnetic resonance imaging (MRI) is superior to conventional imaging (mammography and ultrasound) in identifying multifocal, multicentric or contralateral breast cancer foci.[19-42] The lesion size detected on MRI also correlates best with pathological size.[29,32] Moreover, MRI is more accurate in delineating contraindications to breast conservation such as larger-than-clinically-detected lesion size, inadequate lesion-to-breast size ratio, as well as nipple or chest wall invasion.[19-42] In women with newly diagnosed breast cancers, MRI demonstrates additional, otherwise undetected tumour foci in 27% to 37% of patients.[19-42]

Therefore, MRI has the potential to detect synchronous multifocal, multicentric and contralateral cancers that would have developed into future aggressive cancers. These mammographically and sonographically occult lesions could lead to future additional procedures and

operations. Such imaging also has a very high negative predictive value (99.6%) in predicting absence of breast cancer in the same or contralateral breast. This could be used to help optimise treatment with a more targeted approach (e.g. partial breast irradiation) and help avoid prophylactic contralateral mastectomy.

The aim of this study was to ascertain the impact of a preoperative breast MRI on the surgical management of newly diagnosed breast cancer patients.

METHODS

Patients

A retrospective study was performed to assess the impact of preoperative MRI on the management of patients with newly diagnosed breast cancer. Patients were included if they had pathology-proven newly diagnosed breast cancer and with initial planned surgical treatment by a multidisciplinary team of breast cancer specialists. Preoperative breast MRI examinations were then performed to look for synchronous tumour foci. Consecutive breast MRI examinations between 1 January 2010 and 30 June 2011 yielding breast cancer were reviewed. A total of 25 patients with recently diagnosed breast cancer who underwent preoperative MRI with subsequent surgery or biopsy were reviewed. Three patients were excluded as they defaulted treatment. All patients underwent mammography before MRI examination. Patients were also excluded if they had undergone previous surgery for breast cancer or had begun neoadjuvant chemotherapy.

Approval has been obtained from the Kowloon West Cluster Research Ethics Committee.

Magnetic Resonance Imaging Technique

All participants underwent contrast-enhanced dynamic breast MRI of both breasts, performed in a prone position with a 1.5 T system (Achieva XR; Philips Medical Systems) using a dedicated breast surface coil. The following axial images were obtained: T1- and T2-weighted sequences with turbo spin echo (TSE), T2-weighted sequences with spectral attenuated inversion recovery TSE and apparent diffusion coefficient using a b value of 1000. T1-weighted images were obtained before and after contrast injection at one, two, three, four, and five minutes. Spatial resolution with voxels smaller than 1 mm in the frequency-encoding direction, phase-encoding direction and slice direction were used.

Data Collection

The MRIs were interpreted by one of five trained breast imaging specialists. Examinations were reviewed with the clinical history and other breast imaging modalities (e.g. mammography and ultrasound) when available. The morphology of the lesion, kinetic features, assessments and recommendations were made with reference to the American College of Radiology Breast Imaging Reporting and Data System.[43]

Biopsy was recommended for all additional suspicious lesions seen only on MRI examinations.

Additional Findings

Additional findings were classified as follows: (a) more extensive local disease on MRI as depicted by the area of enhancement of the local tumour when compared to conventional imaging, and (b) additional enhancing lesions as seen on MRI separate from the index lesion. At histology, however, these could be connected by areas of ductal carcinoma in situ.

Statistical Analysis

The positive predictive value and overall cancer yield in detecting an otherwise occult cancer on MRI in the ipsilateral and contralateral breast were calculated. The positive predictive value was defined as the percentage of positive examinations that resulted in histological diagnosis of cancer (i.e. on biopsy or pathological examination of the surgical specimen) within three months. Overall cancer yield was defined as the number of patients with additional cancer detected, divided by the total number of patients who had preoperative breast MRI performed.

A change in management was defined as a change in planned surgical treatment before and after the patients had breast MRI examinations.

RESULTS

During the study period from 1 January 2010 to 30 June 2011, 25 eligible patients with recently diagnosed breast cancer who underwent preoperative MRI were identified. Of the 25 patients, three defaulted follow-up and were excluded from the study. Of the remaining 22 patients who met the inclusion criteria, significant additional MRI findings were found in 10 (45%) of the patients, in which eight (36%) patients showed additional suspicious lesions that were mammographically occult, while two (9%) patients showed more extensive disease with significantly larger

lesion sizes.

In five of the eight patients who had additional suspicious lesions that were mammographically occult, they were subsequently confirmed to be malignant, giving a positive predictive value of 63%.

In five of the 10 patients with additional MRI findings, a change in the surgical treatment from breast conservation to mastectomy was made, though the relevant lesions were mammographically occult. In four of these five patients, pathological examination of the surgical specimens confirmed additional malignant foci as detected by the preoperative MRI. In another two (20%) of the patients, preoperative MRI showed a significantly larger lesion size compared to that detected on the mammogram, which had also led to a change from breast conservation to mastectomy. In three (30%) of the 10 patients, no change in surgical plan was made after the MRI, in which one patient had malignant pathological findings upon biopsy but mastectomy was already planned prior to MRI. Moreover, the two patients had benign pathological findings upon biopsy with subsequent breast conservation treatment.

The overall cancer yield and the MRI-detected mammographically occult cancers are shown in Table 1.

In the eight patients who had additional MRI-detected mammographically occult lesions, four had one additional lesion; four patients had 2 additional lesions, as illustrated in Table 2. All additional ipsilateral lesions were multicentric.

A detailed summary of the management of additional lesions detected initially only on MRI and its subsequent histological diagnosis is shown in Table 3.

In two of the 22 study patients, preoperative MRI revealed a significantly larger lesion size compared to that perceived on the mammogram (with no greater time difference than 1 month between examinations). For these two patients, the calculated mean underestimate of tumour size by mammography was 15.9 cm^3 (range, 11.9 - 19.9 cm^3). This had necessitated a change from breast conservation to mastectomy in both patients.

These additional MRI findings (additional or larger lesions) detected preoperatively led to a change in surgical treatment before and after the preoperative MRI. In seven (32%) of the 22 patients, a conversion from breast conservation to mastectomy ensued. In one of the 22 patients, additional contralateral surgery

Table 1. Patients with incidental cancers found during magnetic resonance imaging examination for the extent of disease.

Extent of disease	Overall No. (%) of cancer yield (n = 22)	No. (%) of cancers found (n = 5)
Contralateral cancer	1 (5)	1 (20)
Ipsilateral cancer	4 (18)	4 (80)
Single lesion	2 (9)	2 (40)
Multiple lesions	3 (14)	3 (60)

Table 2. Number of additional lesions per patient, their localisation and type compared to the index lesion.

Additional lesions	Localisation	No. of patients		
		Benign	Malignant	Total
One additional lesion	Ipsilateral	0	2	2
	Contralateral	2	0	2
Two additional lesions	Ipsilateral	1	2	3
	Bilateral	0	1	1
Total		3	5	8

Table 3. Management and histological diagnosis of additional magnetic resonance imaging (MRI) lesions.

Patient age (years)	Management of additional MRI lesions	Histological diagnosis of additional MRI lesions
53	Subsequent mastectomy	Benign
42	MRI biopsy	Benign
44	Second-look ultrasound with biopsy	DCIS
48	Second-look ultrasound with biopsy	Benign
35	Second-look ultrasound with biopsy	High-grade comedo
58	MRI biopsy	DCIS
48	Subsequent mastectomy	Invasive ductal carcinoma
63	Subsequent mastectomy	Invasive ductal carcinoma

Abbreviation: DCIS = ductal carcinoma in situ.

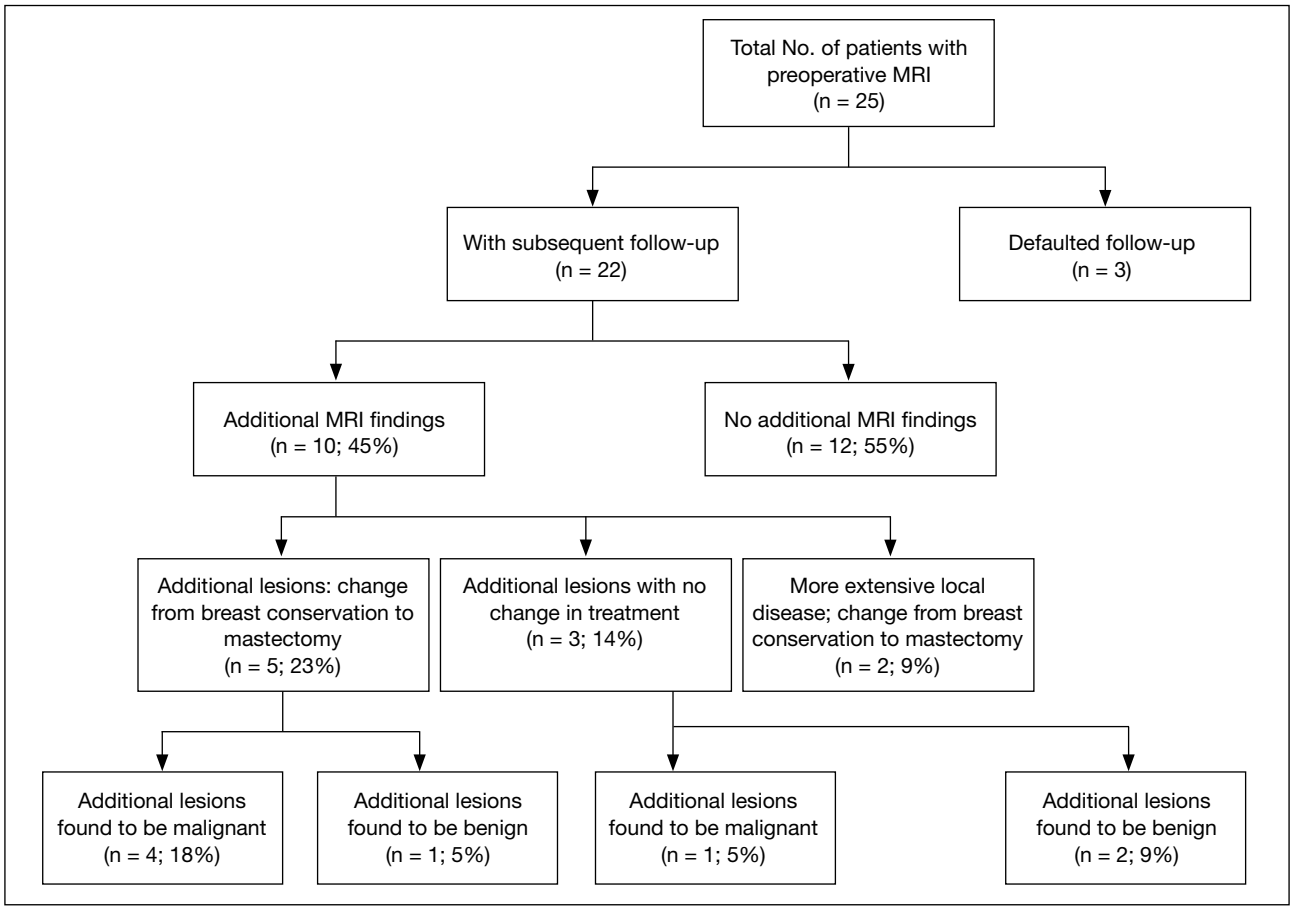

Figure 1. Flowchart showing the distribution of patients with and without additional magnetic resonance imaging (MRI) findings, subsequent management, and histological results.

was performed due to detection of a synchronous contralateral cancer.

Overall, 23% (5/22) of the patients had additional MRI-detected biopsy-proven malignant lesions that were clinically and mammographically occult, of which 18% had additional site(s) of ipsilateral cancer and 5% had unsuspected contralateral cancers.

Figure 1 summarises the findings in this study. Figures 2 and 3 are illustrations of bilateral synchronous cancers and more extensive local disease detected on MRI than mammography and ultrasound, respectively.

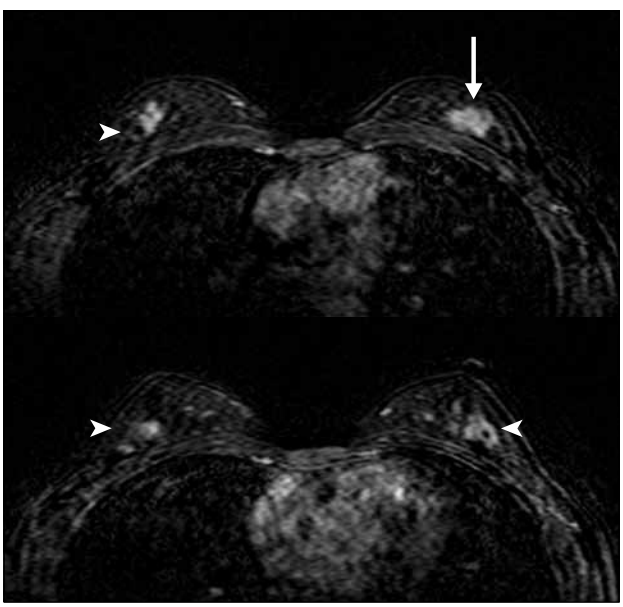

Figure 2. Synchronous bilateral breast cancers: contrast-enhanced subtracted axial magnetic resonance imaging shows an enhancing index lesion (arrow), with synchronous additional bilateral lesions (arrowheads) that are occult on mammogram and ultrasound. Subsequent resection confirmed bilateral ductal carcinoma in-situ.

DISCUSSION

Diagnostic Accuracy of Preoperative Breast Magnetic Resonance Imaging

Our study supplements the current growing data showing preoperative breast MRI to be useful in detecting additional conventional imaging occult disease among women with newly diagnosed breast cancer.[19-42] Meta-analysis of 19 observational studies of

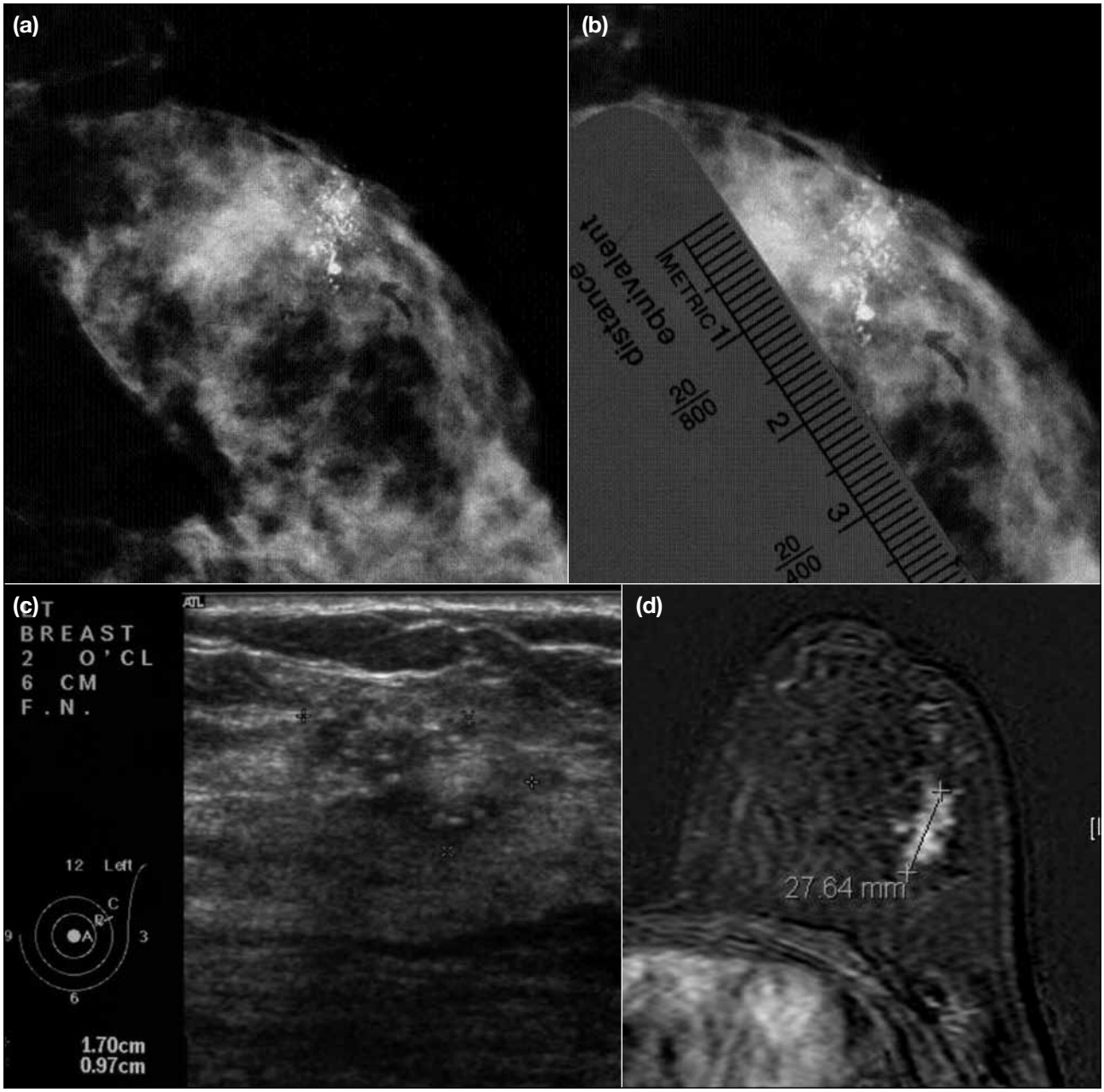

Figure 3. More extensive local disease detected on magnetic resonance imaging (MRI) than mammogram and ultrasound. (a, b) Mammograms (localised cranio-caudal view) show pleomorphic microcalcifications. (c) Ultrasound shows ill-defined heterogeneous mass with microcalcifications. (d) Contrast-enhanced subtracted axial MRI shows ill-defined enhancing lesion, which is larger than that detected in mammogram and ultrasound.

preoperative MRI by Houssami et al[44] showed that the median prevalence for the detection of additional foci of cancer within the affected breast is 16% (interquartile range, 11-24%) based on a total of 2,610 patients. They also reported a positive predictive value of 66%. In our study, we showed that prevalence of additional foci of cancer within the affected breast is 18% and the positive predictive value was 63%. This shows that our results were similar and concordant with those from other international centres (Table 4[29,32,33,45-53]). Moreover, despite differences in the incidence of breast cancers in the western and Asian populations, similar diagnostic accuracy was observed for preoperative breast MRI in Asian population.

The overall added cancer yield for otherwise occult cancers identified by breast MRI was 23%. This was significantly higher than the 12% reported previously by

Table 4. Incremental magnetic resonance imaging (MRI) detection in women with newly diagnosed breast cancer based on studies reporting MRI-only detection and specifying the quadrant of additional disease foci (relative to the index cancer in the affected breast).

Study	Study population	No. of subjects (% with DCIS-only index cancer included)	No. (%) with additional MRI-only detection	Estimated PPV of MRI-only detection (%)
Godinez et al[45]	Candidates for BCS and eligible for PBI	79 (15%)	30/70 (42.9)	57.0
Zhang et al[46]	Fine-needle cytology diagnosis of breast cancer, confined to 1 quadrant, candidates for BCS	54 (22%)	14/49 (28.6)	73.4
Liberman et al[47]	Core needle biopsy–proven breast cancer, confined to 1 quadrant, and candidates for BCS	70	19/70 (27.1)	52.8
Drew et al[48]	Women with breast cancer who had MRI	178	41/178 (23.0)	69.5
Orel et al[49]	Women with breast cancer who had MRI	64	13/64 (20.3)	72.2
Sardanelli et al[32]	Candidates for mastectomy (whole-breast sectioning as reference standard to define MRI accuracy)	90	13/80 (16.3)	41.9
Fischer et al[33]	Women with breast cancer who had MRI	336 (with MRI data from 463)	54/336 (16.1)	98.2
Boetes et al[29]	Candidates for mastectomy (whole-breast sectioning as reference standard)	60	8/60 (13.3)	72.7
Mumtaz et al[50]	Women with breast cancer confined to 1 quadrant and candidates for BCS	90 (7.6%)	10/85 (11.8)	71.4
Deurloo et al[51]	Women with breast cancer confined to 1 quadrant and candidates for BCS	116	13/116 (11.2)	50.0
Bilimoria et al[52]	Women with breast cancer who were eligible for BCS and had MRI	155 (21%)	13/155 (8.4)	19.1
Al-Hallaq et al[53]	Candidates for BCS who would have been eligible for PBI based on NSABP trial B-39 criteria	110	9/110 (8.2)	56.5 to 72.2
Present study	Women with breast cancer who had MRI	22	10/22 (45.5)	62.5

Abbreviations: BCS = breast conservation surgery; DCIS = ductal carcinoma in situ; NSABP = National Surgical Adjuvant Breast and Bowel Project; PBI = partial breast irradiation; PPV = positive predictive value.

Table 5. Studies on the incidence of additional findings in breast cancer patients by magnetic resonance imaging (MRI).

Study	No. of included lesions	Inclusion criteria	No. of patients with additional findings	Ipsilateral	Contralateral	No. of patients with additional malignant lesion	Total change in management
Drew et al[48]	178	All	59 (33%)	59	NST	50 (28%)	0
Fischer et al[33]	336	All	69 (21%)	54	15	69 (21%)	-
Esserman et al[65]	57	All + AE*	10 (18%)	NSP	NSP	9 (16%)	1 (2%)
Tan et al[66]	83	All + AE	13 (16%)	NSP	NSP	5 (6%)	8 (10%)
Bedrosian et al[67]	231	All	31 (13%)	NSP	NSP	19 (8%)	12 (5%)
Tillman et al[31]	207	All + AE	43 (21%)	NSP	NSP	30 (14%)	13 (6%)
Bedrosian et al[21]	267	All + AE	69 (26%)	NSP	NSP	49 (18%)	20 (7%)
Liberman et al[47]	70	BCT	36 (51%)	36	NST	19 (27%)	16 (23%)
Liberman et al[36]	223	All	72 (32%)	NST	72	12 (5%)	49 (22%)
Lee et al[42]	182	All	15 (8%)	NST	15	7 (4%)	8 (4%)
Deurloo et al[51]	116	BCT	48 (41%)	37	11	26 (22%)	1 (1%)
Present study	22	All	10 (45%)	9	1	5 (23%)	8 (36%)

Abbreviations: BCT = breast conservation therapy; NSP = not specified; NST = not studied.
* AE = after excision: patients who underwent MRI after excision of breast cancer.

Gutierrez et al[54] and the added cancer yield of up to 7% for MRI screening in high-risk patients.[55-62]

The difference in the overall added cancer yield can in part be challenged by the limited sample size in our study. However, with the advent of standardised MRI image interpretation criteria and quality assurance programmes for MRI,[42] more recent studies are showing improved sensitivity for cancer detection and overall specificity.[63,64] As such, our study conforms to this trend with an improved overall added cancer yield with MRI.

Impact of Preoperative Magnetic Resonance Imaging on Surgical Treatment and Planning

Several studies have reported the clinical impact of a preoperative breast MRI in relation to additional breast findings (Table 5[21,31,33,36,42,47,48,51,65-67]). Our study showed that 45% of the patients had additional MRI findings,

23% had biopsy-proven malignant lesions, and a change of surgical management followed in 36%, breast conservation being converted to mastectomy in 32% and 5% having additional contralateral surgery. The percentage in whom surgical management changed was slightly higher than in previously published studies from elsewhere. This was expected, as in our study there was a higher positive predictive value with breast MRI. Given that similar figures are observed, this suggests that results from previous studies were reproducible in our centre, and similar advantages and benefits were likely to accrue at our centre in the future.

Arguably, the advent of breast MRI has led to a possible increase in mastectomy rates and is more cosmetically impairing.[68] However, the most important advantage was the ability to accurately image local disease and therefore allow more patients to have a single operation that achieved clear margins. Less optimal imaging of local disease leads to more local recurrences and more positive margins (with breast conservation), requiring repeated if not repetitive investigations and surgeries, and possibly even salvage mastectomy. Such consequences would very likely incur a greater psychological burden and a less satisfactory cosmetic result. Achieving the best oncologic and cosmetic treatment therefore seems to depend on the most accurate method for imaging local disease prior to surgery, namely, breast MRI.

Impact of Preoperative Magnetic Resonance Imaging on Long-term Outcomes

Critics of breast MRI argue that currently breast conservation and radiotherapy yields excellent and comparable survival benefits to mastectomy. However, long-term follow-up of patients after breast conservation reveals that local recurrence rates are up to 19% (above 10% for most studies).[5,69-71] Based on previous studies, it was believed that higher local recurrences with breast conservation did not incur a survival difference compared to mastectomy. It is, however, associated with subsequent radiotherapy, regular surveillance, higher numbers of subsequent investigations and operations (e.g. wider excisions, salvage mastectomy). Recent studies also show that local recurrences have an impact on disease-free as well as overall survival.[16,69,72-79] As such, more precise assessment of local staging leads to improved local treatment of breast cancers and lower local recurrence rates.

Fischer et al[38] showed that a three-year recurrence rate of 1.2% in patients who underwent breast MRI for staging, as compared to 6.8% in patients having conventional breast imaging for that purpose. The retrospective design can be criticised, though the results are impressive due to a more than 5-fold reduction in breast cancer recurrence rates. Solin et al[80] reported that MRI staging of patients was not associated with an improvement in local control after breast conservation. However, one of that study's limitations admitted by the authors was a significantly lower age in women in the MRI group, making differences in local recurrence difficult to identify. The authors highlighted that the eight-year rate of local recurrence in 4% for patients not having breast MRI was sufficiently low, and that a very large number of patients would need to be recruited to show statistical significance.

Limitations in Advocating Preoperative Magnetic Resonance Imaging

Critics argue that randomised studies are needed before we modify standards of care in breast cancer. This is true for therapeutic or preventive interventions, but not for diagnostic modalities. Current Oxford evidence-based guidelines emphasise that if several prospective studies show that a particular diagnostic modality has superior accuracy, this translates into Oxford level 1a of evidence for diagnostic studies, resulting in grade A recommendation.[81]

There is a valid and justified fear that preoperative breast MRI leads to overtreatment. However, current guidelines for mastectomy were devised when only ultrasound and mammography were used for diagnosis and staging.[82] Previous recommendation of mastectomy for multicentric tumours noted on mammograms and ultrasound might not be necessary for all additional small tumour foci detected on MRI. This is not because these additional tumour foci are unimportant, rather because they might be adequately treated with radiotherapy. Therefore an update of the current guidelines for mastectomy taking breast MRI into account as a diagnostic imaging modality is urgently required.

As with any imaging modality, imaging diagnoses must be proven by biopsy before a change of medical or surgical treatment can be advocated. If a centre does not have the necessary expertise and equipment to perform MRI-guided biopsy, this could hinder it preoperatively.

Arguably, breast MRI for routine staging of all patients

with newly diagnosed breast cancers could lead to increased health care costs. However, studies have shown that breast MRI is a valuable cost-saving tool for preoperative planning and by facilitating a single surgery for breast cancers.[65]

CONCLUSION

We have highlighted that current guidelines of mastectomy are based on the detection of multicentric tumours using conventional breast imaging (i.e. mammograms and ultrasound). With the increased detection of additional tumour foci with breast MRI, however, we anticipate current guidelines need reviewing to take into account of such findings.

Despite differences in the incidence of breast cancer in Asian and western population, our study demonstrated that the diagnostic accuracy of preoperative breast MRI and its impact on surgical management is similar to that in published western studies. As such, we would anticipate benefits and advantages, particularly on long-term outcomes of breast cancer to be enjoyed in Asian populations. Further studies are required to assess the impact of preoperative breast MRI on long-term outcomes in Asian populations.

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