The Impact of Preoperative Breast Magnetic Resonance Imaging on Surgical Management in Symptomatic Patients With Invasive Lobular Carcinoma

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ABSTRACT

OBJECTIVE: Due to an insidious proliferative pattern, invasive lobular breast cancer (ILC) often fails to form a defined radiological or palpable lesion and accurate diagnosis remains challenging. This study aimed to determine the value of preoperative magnetic resonance imaging (MRI) for ILC and its impact on surgical outcomes.

METHODS: Consecutive symptomatic patients diagnosed with ILC in a tertiary centre over a 9-year period were reviewed. The time from diagnosis until surgery, initial type of surgery/index operation (breast-conserving surgery [BCS]/mastectomy) and the rates of reoperation (re-excision/completion mastectomy) were recorded. Patients were grouped into those who received conventional imaging and preoperative MRI (MR+) and those who received conventional imaging alone (MR−).

RESULTS: There were 218 cases of ILC, and 32.1% (n = 70) had preoperative MRI. Time from diagnosis to surgery was longer in the MR+ than the MR− group (32.5 vs 21.1 days, $P < .001$) even when adjusting for age and breast density. Initial BCS was performed on 71.4% (n = 50) of MR+ patients and 72.3% (n = 107) of the MR− group. While the rate of completion mastectomy following initial BCS was higher in the MR+ group (30.0%, n = 15 vs 14.0%, n = 15; $\chi^2 = 5.63$; $P = .018$), this association was not maintained in multivariable analysis. No difference was recorded in overall (initial and completion) mastectomy rate between the MR+ and MR− group (50.0%, n = 35 vs 37.8%, n = 56; $\chi^2 = 2.89$; $P = .089$). Margin re-excision following BCS was comparable between groups (8.0%, n = 4, vs 9.3%, n = 10; $\chi^2 = 0.076$, $P = .783$) despite the selection bias for borderline conservable cases in the MR+ group. The rate of usage of MRI for ILC cases declined over the study period.

CONCLUSION: While MRI was associated with minor delays in treatment and did not reduce overall rates of margin re-excision or completion mastectomy, it altered the choice of surgical procedure in almost a quarter of MR+ cases. The benefit of preoperative breast MRI appears to be confined to select (younger, dense breast, borderline conservable) cases in symptomatic ILC.

KEYWORDS: Breast cancer, invasive lobular cancer, ILC, MRI, surgical outcomes

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Background

Invasive lobular carcinoma (ILC) is the second most common breast malignancy representing between 10% and 15% of all invasive breast cancers.[1] While it accounts for a relatively small percentage of the total cases of breast cancer, it is nonetheless twice as prevalent as cervical cancer and as common as pancreatic cancer and multiple myeloma.[2] In contrast to infiltrating ductal carcinoma (IDC), which tends to be well circumscribed, ILC frequently has a diffuse, irregular growth pattern. Often, no clinically palpable mass lesion is identified, and the breast may have a normal or only slightly firm consistency, representing a diagnostic challenge.[3] Morphologically, malignant cells originating from the lobular epithelium invade the breast tissue adjacent to the mammary ducts in an insidious manner, resulting in minimal fibrous reaction with noncohesive neoplastic cells. As a result, in the absence of a desmoplastic reaction, features such as calcification, necrosis, and haemorrhage are frequently not present.[4] Instead, malignant ILC cells often encase ducts, thus preserving their architecture. While the presentation may be subtle, ILC has a higher propensity for multifocal or multicentric distribution and for bilaterality, with the extent of disease often being underestimated.[3,5]

Accurate local staging is critical to optimise pretreatment planning in the surgical management of breast cancer. It facilitates the appropriate selection of patients for neoadjuvant treatment with chemotherapy and the correct definitive

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Table 1. Inclusion criteria set out for the study.

INCLUSION CRITERIA
1. Female gender
2. Symptomatic presentation
3. Histological subtype of invasive lobular breast cancer
4. No previous surgery to affected breast (biopsy acceptable)
5. Surgical treatment as primary management.

surgical procedure with complete excision of malignant tissue.[6] The discrete insidious proliferation pattern of ILC renders diagnosis with conventional imaging more challenging, which can result in higher false-negative rates than is seen with IDC.[6-8] Preoperative breast magnetic resonance imaging (MRI) has been reported as one potential method to reduce mastectomy rates and decrease positive surgical margins in ILC.[9,10]

The value of preoperative breast MRI in the work-up of ILC remains controversial. Recent randomised trials have demonstrated that preoperative breast MRI may be unnecessary[11] and could even be harmful[12] in the setting of primary ILC. In contrast, other prospective, randomised, data suggest that preoperative breast MRI may provide added benefit in younger patients.[13] Meta-analyses also suggest that preoperative MRI may identify patients with additional disease which may not be discernible on conventional imaging.[14-16] However, this may increase mastectomy rates without necessarily impacting disease recurrence,[17] and the selection bias inherent in the many included observational studies could affect outcomes analyses for preoperative breast MRI.[18]

This study aimed to investigate the real-life experience of preoperative MRI on surgical management and reoperation in symptomatic ILC cases; to determine the influence of preoperative MRI on delays to initial surgical management in symptomatic ILC cases; and to assess trends in the usage of preoperative MRI for symptomatic cases of ILC in a tertiary unit over a 9-year period.

Methods

This study was granted institutional review board approval from the Galway University Hospitals (GUH) Clinical Research Ethics Committee. The inclusion criteria for this study were determined and are detailed in Table 1. A prospectively maintained database was accessed to identify all newly diagnosed female ILC patients, presenting to the GUH Symptomatic Breast Unit (SBU) between January 2009 and December 2017. All cases were initially evaluated by standard triple assessment in a dedicated symptomatic breast clinic and discussed at a weekly multidisciplinary tumour board (MTB) meeting that included specialist breast surgeons, radiologists, pathologists, oncologists, radiation oncologists, and cancer breast care nurses. No screen-detected ILC cases were included. Only female patients with histologically proven, symptomatic ILC with no prior surgery to the affected breast and in whom surgical management was anticipated as the primary management were included in the final analysis. The pathological, oncological, and radiology databases were reviewed for all patients to ensure completeness of data.

Demographics and clinicopathological characteristics

Variables recorded included patient demographic characteristics, age at diagnosis, when diagnosis was established, time until initial surgery from diagnosis, type of initial surgery (breast-conserving surgery [BCS]/mastectomy), and the number and type of repeat operations. Clinicopathological details such as grade, tumour size, lymph node disease status, and the Nottingham Prognostic Index (NPI) were documented. The oestrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor (HER/neu) status of the patients was determined using immunohistochemistry on formalin-fixed, paraffin-embedded sections of resected clinical specimens.

Radiological findings

The radiological database (AGFA IMPAX, Agfa-Gevaert, Mortsel, Belgium) of GUH was assessed and all initial mammography studies reviewed. Breast density was systematically determined from each mammogram by assessing the fibroglandular tissue of each breast employing the fifth edition of the American College of Radiology (ACR) BI-RADS.[19] Density grouping was determined by the density of the breast with ILC. Breast density was categorised as 'low' with Composition A (almost entirely fatty) and B (scattered areas of fibroglandular density), and 'high' with composition C (heterogeneously dense) and D (extremely dense). The tumour size was recorded from mammography and ultrasonography. All ILC patients that had preoperative breast MRI were identified. The indication for preoperative breast MRI referral was recorded, as well as the intervals between pathological diagnosis and MRI, and pathological diagnosis and surgery. Detection methods of collateral and ipsilateral malignant findings were identified. All cases were followed for a minimum 1-year period and surgical outcomes such as reoperation (mastectomy and re-excision of margins) were recorded. Comparisons were drawn between those who had conventional imaging alone, and those who underwent preoperative MRI as an adjunct to conventional imaging.

Breast MRI

Magnetic resonance imaging analyses were performed on a short bore 1.5T magnet (Magnetom Espree 1.5T, Siemens Healthcare, Erlangen, Germany) using 8-channel breast phase array breast coil for signal reception, utilising the following protocol: Sagittal T2 (TR/TE 6570/111, Gap 1 mm, Flip angle

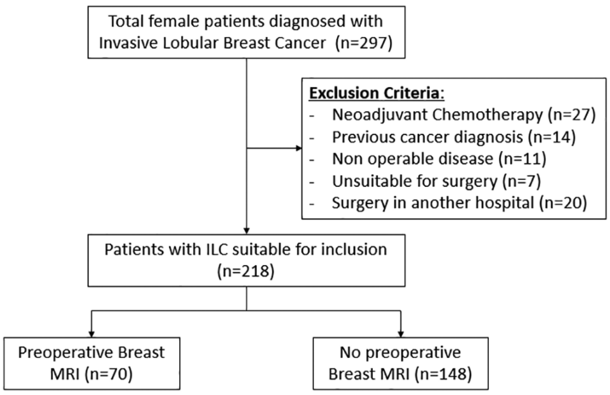

Figure 1. Patient flow chart; of the 297 patients identified with ILC, 218 satisfied the inclusion criteria for the study.
ILC indicates invasive lobular breast cancer.

160°, Matrix 340 × 75), Axial T2 FS fl3d pre contrast (TR/TE 5.15/2.39, Gap 0.6 mm, Flip angle 10°, Matrix 320 × 100), Sagittal T1 fl3d (TR/TE 5.18/1.64, Gap 0.6 mm, Flip angle 10°, Matrix 320 × 100, this sequence is repeated 6 times; 1 precontrast and 5 postcontrast with peak enhancement in the third run), Axial T1 FS fl3d postcontrast. The section thickness was 3 mm for all sequences. The contrast employed was Gadoterate meglumine (Gd-DOTA).

Statistical analysis

Statistical analysis was performed using SPSS, version 20 (IBM Corporation, NY, USA). Continuous variables were summarised using descriptive statistics, including mean, standard deviation, and median. The statistical procedure employed for comparing continuous variables was the unpaired *t*-test or Fisher's exact test where appropriate. The relations between categorical binary variables were studied using χ^2 test. Sensitivity as well as accuracy values were expressed as percentages. Confidence intervals for these measures are 'exact' Clopper and Pearson[20] confidence intervals. Adjustment for confounders was undertaken using multivariable linear or logistic regression for continuous or binary-dependent variables, respectively. For all tests, 2-tailed *P* value of less than .05 indicated statistical significance.

Results

Patient demographics and tumour characteristics

A total of 297 female patients had biopsy-proven ILC diagnosed during the study period. A total of 218 satisfied the inclusion criteria, with a further 79 patients with ILC excluded, having not satisfied the inclusion criteria (Figure 1). Of the 218 patients included, 32.1% (n = 70) underwent a preoperative MRI. The median age at diagnosis was 62.2 (35.6-91.5) years. There was a significant difference in mean age between the MR+ group (56.4 years, standard deviation [SD] 8.05, standard error of mean [SEM] 0.96), and the MR– group (65.6 years, SD 10.97, SEM 0.90), ($P < .001$). The tumour characteristics for both groups were comparable, as detailed in Table 2.

Sensitivity of MRI for ILC

A total of 70 patients underwent preoperative MRI breast. Magnetic resonance imaging sensitivity was 95.7% (95% confidence interval [CI]: 88.0%-99.1%). ILC could not be appreciated in 4.3% (3 of 70), where no mass lesion was conspicuous. All MRI scans were conducted after tissue biopsy and therefore, did not contribute to diagnosis of ILC.

MR characteristics of ILC tumours MRI

There was no significant difference in mean tumour size on MRI (29.4 mm ± SD 16.9, SEM 2.1) and final histology (34.7 mm ± SD 26.9, SEM 3.3, $P = .176$). There was a positive correlation between MRI and final histology ($r = .618$). Findings suspicious for ILC multifocality were identified in 18.6% (13 of 70). Of these, 10 underwent mastectomy, while 3 were successfully managed with BCS alone. Findings suspicious for bilaterality were identified in 10% (7 of 70) of cases. In cases where the BI-RADS lexicon was employed to describe the MRI findings (n = 60), the tumour was described as demonstrating mass enhancement (60%, n = 36), nonmass enhancement (36.7%, n = 22), or described as a focus (3.3%, n = 2).

Tumour size and breast density

Although the average tumour size in the MR– group (40.1 mm ± SD 28.2, SEM 2.3) was larger than the average size in the MR+ group (34.6 mm ± SD 27.7, SEM 3.3), this did not reach statistical significance (Figure 2, $P = .177$). There was a statistically significant difference in the breast density distribution between the 2 groups, with 64.3% of the MR+ group having high density compared with 43.3% in the MR– group ($P = .004$, Table 3).

Preoperative MRI and time to surgery

The median interval from time of pathological diagnosis until undergoing breast MRI was 15 (range 0-29) days. The median interval between MRI and surgery was 10.5 (range 1-64) days. The total surgical waiting time (the time from pathological diagnosis until the date of surgery) was significantly longer in the MR+ group (32.5 days ± SD 16.1, SEM 1.9) than in the MR– group (21.1 days ± SD 12.2, SEM 1.0), (Figure 3, $P < .001$). This significant positive association was maintained, following adjustment for age and breast density ($P < .001$).

Impact of MRI on further investigation and surgical planning

Breast MRI was requested for 90% of cases (63 of 70) to further evaluate biopsy-proven ILC for multifocality/multicentricity and bilaterality, and to assess suitability for BCS. Patients were deemed possible candidates for BCS if MRI findings were in concordance with the conventional imaging showing a small unifocal lesion. A further 7.1% (5 of 70) underwent

Table 2. Tumour characteristics of all female patients diagnosed with ILC during the study period.

TUMOUR CHARACTERISTICS		OVERALL	MRI+	MRI–
		N (%)	N (%)	N (%)
Histological type	Lobular	218 (100)	70 (100)	148 (100)
Epithelial subtype	Luminal A	199 (91.3)	66 (94.3)	133 (89.9)
	Luminal B	11 (5.0)	2 (2.9)	9 (6.1)
	HER2	3 (1.4)	2 (2.9)	1 (0.7)
	Basal	5 (2.3)	0	5 (3.4)
Nodal status	Node positive	78 (35.8)	27 (38.6)	51 (34.5)
	Node negative	140 (64.2)	43 (61.4)	97 (65.5)
Tumour grade	1	5 (2.3)	3 (4.3)	2 (1.4)
	2	190 (87.2)	64 (91.4)	126 (85.1)
	3	23 (10.5)	3 (4.3)	20 (13.5)
Stage (UICC)	I	56 (25.7)	25 (35.7)	31 (20.9)
	II	111 (50.9)	27 (38.6)	84 (56.8)
	III	51 (23.4)	18 (25.7)	33 (22.3)
	IV	0	0	0

Abbreviation: HER2, human epidermal growth factor receptor 2; ILC, invasive lobular breast cancer; UICC, Union for International Cancer Control.

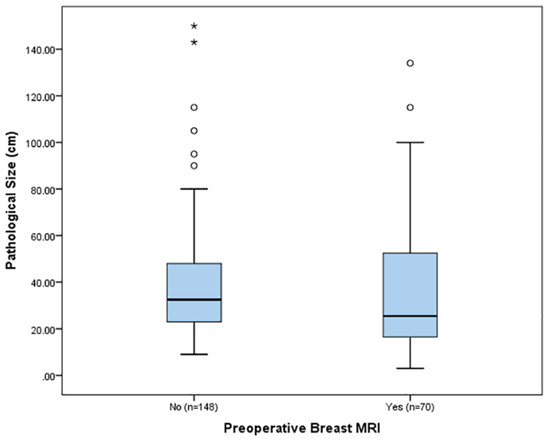

Figure 2. No significant difference was recorded in pathological size between the MR+ group and the MR– group.

breast MRI due to the biopsy-proven ILC lesion being mammographically occult. Finally, 2.8% (2 of 70) underwent breast MRI to further evaluate biopsy-proven ILC found in high-density breasts.

A total 23.2% (16 of 70) had a change in their proposed operation from BCS to mastectomy based on the findings at MRI. This was due to the ILC being larger in size (8 of 70), or the disease being multifocal (8 of 70). Magnetic resonance imaging recommended further imaging or biopsy in 15.7% of cases (11 of 70). The recommendation of additional imaging following MR was associated with a longer median surgical waiting time (35 days ± SD 20.0, N = 11 vs 27 days ± SD 14.5); however, cases requiring additional imaging were too few to draw statistical significance.

Initial surgery

Overall, an initial mastectomy was performed on 28.0% (n = 61) of patients, with the remaining 72.0% (n = 157) undergoing BCS. Mastectomy rates in the MR+ and MR– groups are detailed in Table 4.

Reoperation

Overall, of the 218 patients, 44 (20.2%) patients required breast reoperation (completion mastectomy or margin re-excision) following initial BCS for positive surgical margins. This included 38.0% (n = 19) of patients in the BCS MR+ group, and 23.4% (n = 25) of patients in the BCS MR– group ($\chi^2 = 3.62$, $P = .057$). A total of 30 of 44 underwent a completion mastectomy, with the remaining 14 patients having further surgery to re-excise surgical margins alone for the residual disease (Figure 4). The rate of margin re-excision following BCS was comparable between the MR+ group (8.0%, n = 4) and the MR– group (9.3%, n = 10; $\chi^2 = .076$, $P = .783$). In univariable analysis, the rate of completion mastectomy following BCS

Table 3. The use of preoperative breast MRI was more frequently employed in patients with higher density breasts (Composition C and Composition D).

BREAST DENSITY	OVERALL (%)	MR+ (N = 70) N (%)	MR– (N = 148) N (%)	*P* VALUE
Composition A	17 (7.8)	3 (4.3)	14 (9.5)	.183
Composition B	92 (42.2)	22 (31.4)	70 (47.3)	.027
'Low' density	109 (50.0)	25 (35.7)	84 (56.8)	.004
Composition C	88 (40.4)	29 (41.4)	59 (39.9)	.826
Composition D	21 (9.6)	16 (22.9)	5 (3.4)	.000
'High' density	109 (50.0)	45 (64.3)	64 (43.3)	.004

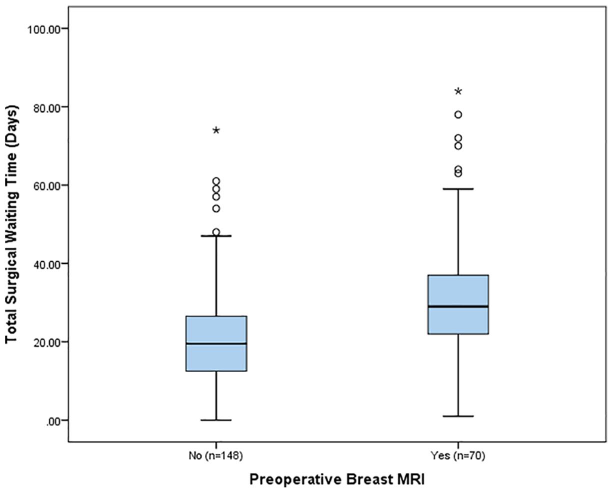

Figure 3. Total surgical waiting time was defined as the time from pathological diagnosis until surgery.

was higher in the MR+ group (30.0%, n = 15) in comparison to the MR– group (14.0%, n = 15). This finding was statistically significant ($\chi^2 = 5.63$, $P = .018$). This association, however, did not maintain statistical significance following adjustment for age ($P = .276$).

Overall mastectomy rate

The overall mastectomy rate (initial and completion mastectomy) was higher in the MR+ group (50%, n = 35) than the MR– group (37.8%, n = 56). However, this finding did not reach statistical significance ($\chi^2 = 2.89$, $P = .089$, Table 4).

Rate of usage of MRI as an adjunct for preoperative staging

Frequency of MRI usage as a staging adjunct was assessed yearly over the study period. A total of 70 patients (32.1%) underwent preoperative MRI, ranging from 51.9% (14 of 27 patients) in 2010 to 5% (1 of 20 patients) in 2016 (Table 5). A staggered decline in usage has been observed with a negative gradient observed when represented schematically ($y = -3.51x + 48.85$, Figure 5).

Discussion

In this observational study of symptomatic ILC patients undergoing resection in a tertiary referral centre, there was a staggered decline in the usage of preoperative breast MRI for this cohort over a 9-year period. Moreover, MRI was associated with statistically significant increased times from diagnosis to surgery and did not reduce overall rates of margin re-excision or completion mastectomy. However, where utilised, MRI altered the choice of surgical procedure in almost a quarter of MR+ cases and margin re-excision following BCS was comparable between groups despite the significant selection bias for borderline conservable cases in the MR+ group. These data suggest that the benefit of preoperative breast MRI appears to be confined to select cases in symptomatic ILC, and this is increasingly recognised at the breast cancer MTB meeting.

The limitations of conventional imaging[21-24] in the work-up of ILC are well known. It was hoped that preoperative breast MRI would enhance surgical staging and primary treatment for this radiologically elusive disease.[9,10] The EUSOMA guidelines in 2010 suggested that MRI would be of value in clinical staging, assessment of the contralateral breast, and surgical planning in ILC cases.[25] Subsequent prospective clinical trials have addressed the value of MRI in staging or in preoperative planning, and in general, are conflicting,[11-13] with no consensus concerning the role of breast MRI in the preoperative setting. The COMICE trial found that it was not beneficial and had inappropriate mastectomy rates.[11] This study is a real-life overview of the impact of MRI in the management of ILC and catalogues the decline in the routine utilisation of this modality for the majority of ILC cases. Over a 9-year period, we have shown that our MTB programme has refined the use of MRI scanning for select ILC cases, in particular younger women, with dense breast tissue and those with borderline conservable tumours.

Table 4. Rates of initial and total mastectomy in the MR+ and MR− groups.

RATES OF MASTECTOMY	INITIAL MASTECTOMY	REOPERATION: MASTECTOMY	TOTAL RATE OF MASTECTOMY
MR+ group (n = 70)	20 (28.6%)	15 (21.4%)	35 (50%)
MR− group (n = 148)	41 (27.7%)	15 (10.1%)	56 (37.8%)
Total (n = 218)	$P = .894$ ($\chi^2 = .018$)	$P = .024$ ($\chi^2 = 5.11$)	$P = .089$ ($\chi^2 = 2.89$)

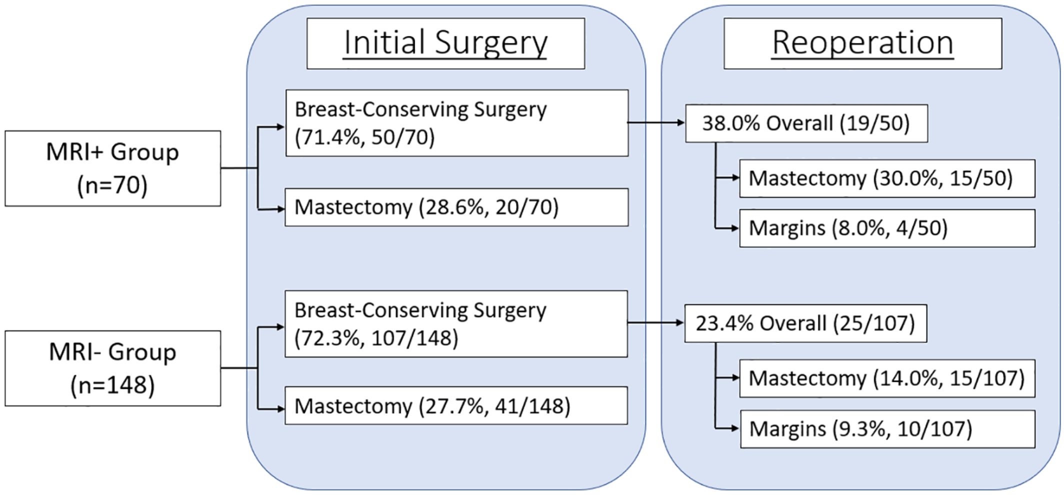

Figure 4. Schematic representation of initial surgical procedures and reoperation for the MR+ and MR− groups.

In this study, the majority of patients in the MR+ group were initially considered for BCS. Breast-conserving surgery for ILC can be challenging. Patients with ILC frequently have higher rates of involved margins, with some reports in excess of 50%,[26,27] and conversion to mastectomy after BCS has been reported as between 16% and 48% of cases.[28-30] This is partly due to the underestimation of tumour size with standard imaging modalities, mainly due to the lack of a desmoplastic reaction for ILC. Preoperative assessment with MRI has been shown to improve size estimation.[31] We observed no difference in mean MRI and postsurgical resection specimen size. Similarly, there was no significant difference seen in rates of BCS and initial mastectomy between the MR+ group (29%) and the MR− group (28%). However, MRI informed an alteration in surgical management, in excess of initial routine imaging, in almost a quarter of cases (23.2%). This finding compares with reports by Mann et al[10] who demonstrated a change in surgical management in 28.3% in a literature review series including 160 ILC patients from 6 studies. While this study is comprehensive in its methods, care must be taken with interpreting the results as most studies included are retrospective cohort studies, each with fewer than 25 patients.

Advocates of MRI hold that its greater sensitivity for the detection of cancer will improve the selection of patients for BCS and increase the likelihood of obtaining negative margins at the first attempt. However, the present MRI+ group had no significant change in rate of conversion to mastectomy following adjustment for age and breast density, and no impact on negative margin rates. This may suggest that MRI could be unnecessary in mammographically occult disease as it does not reliably identify patients that are suitable for BCS. On the contrary, preoperative breast MRI was frequently obtained in borderline breast conservable cases to assess suitability for BCS, and despite this inherent selection bias, the positive margin rate was similar in the MR+ and MRI− groups. This suggests that MRI may aid in the appropriate selection of surgical candidates for successful BCS in these more challenging scenarios. On the other end of this spectrum, recent meta-analyses also suggest that MRI may lead to unnecessary mastectomies and extensive excisions to treat disease that may be adequately controlled with BCS and adjuvant therapies[14,16,17] and there are fears that preoperative MRI may significantly increase mastectomy if used routinely in ILC, without impacting on disease recurrence.[32] However, the rate of initial mastectomy (28.6% vs 27.7%) and overall mastectomy (50% vs 37.8%) were not significantly higher in the MR+ group in comparison to the MR− group in this study.

Guidelines from the NCEC (National Clinical Effectiveness Committee, Ireland), NICE (National Institute for Health and Care Excellence), and NCCN (National Comprehensive Cancer Network) suggest that the addition of MRI can be beneficial in select cases where conventional imaging is inconclusive.[33-35] However, recent publications including randomised data offer conflicting opinions.[11-13] In the COMICE

Table 5. Usage of MRI for preoperative breast MRI staging between 2009 and 2017.

USAGE OF PREOPERATIVE BREAST MRI										
	2009	2010	2011	2012	2013	2014	2015	2016	2017	TOTAL
MR+	13	14	10	8	5	9	6	1	4	70
MR–	22	13	12	17	22	14	19	19	10	148
Total	35	27	22	25	27	23	25	20	14	218
(%)	37.1	51.9	45.5	32.0	18.5	39.1	24.0	5	28.6	32.1

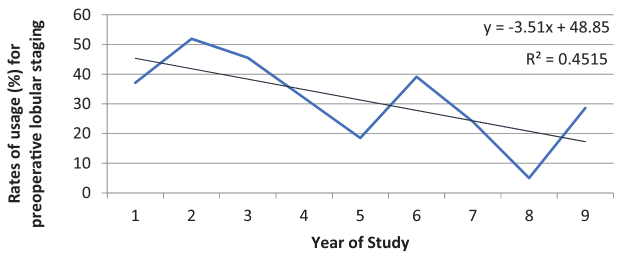

Figure 5. Trends of preoperative MRI usage over the study period.

trial (ISRCTN10841582), a randomised control trial of more than 1600 patients, the addition of MRI to conventional triple assessment was not significantly associated with a reduced reoperation rate.[11] More worryingly, the MONET trial (NCT00302120) demonstrated that the addition of MRI to conventional imaging is associated with an increased re-excision rate in patients with nonpalpable breast cancer.[12] Neither trial, however, analysed ILC cases in isolation. In COMICE, mastectomy was often performed without histological confirmation of MRI-detected additional lesion(s) due to the lack of MRI-guided biopsy availability and women in the trial were already planning on having BCS; therefore, the trial could not address how many patients who had been planning on having a mastectomy converted to BCS after having a reassuring MRI scan. Moreover, there is prospective randomised data to suggest that preoperative breast MRI may be of benefit in select (ie, younger) patients, altering treatment in almost a fifth, with significantly reduced reoperation rates.[13] In this study, no difference in re-excision was identified between the MR– group (9.3%) and the MR+ group (8.0%). However, a nuanced analysis must acknowledge that equivalent positive margin and re-excision rates, given the selection bias for more challenging cases in the MR+ group, may indicate a significant utility for MRI in this cohort.

With increasing emphasis on quality care and development of best-practice guidelines, there has been interest in establishing timeliness of treatment for breast cancer.[36-38] Recommendations put forth by several international organisations propose time to surgical treatment intervals as little as 3 weeks.[37-40] The impact of preoperative breast MRI is controversial, with both no[41] and significant delays[42,43] reported. Further evidence suggests long intervals between surgery and chemotherapy are associated with poorer disease-specific outcomes. This may become a consideration if preoperative MRI increases mastectomy rates and their associated morbidity.[44,45] In this study, undergoing a preoperative MRI delayed surgery by an average of 11.4 days (32.5 days on average for the MR+ group, in comparison to 21.1 days for the MR– group). This thrusts patients in the MR+ group over the 31 day maximum waiting time threshold recommended by the National Institute of Health, although still within the recommended waiting time threshold recommended by the European Society of Breast (6 weeks following initial diagnosis).[39,40] However, the authors acknowledge that comparisons in time delays are difficult to interpret, being significantly impacted by the context of any health care system and the delay in surgical planning because of scarcity of MRI slots in a publicly funded tertiary breast centre must be acknowledged. Moreover, the likely clinical consequences of a minor delay to treatment for slow growing, low grade, ER+ cancers such as 'classical' ILC are likely to be negligible in the context of modern, multimodality therapy.

The EUSOMA working group recommendations highlighted the shortcomings in the literature regarding the use of preoperative breast MRI in ILC patients with dense breasts. In our institution, the MR+ group had a higher proportion of patients with high-density breasts, suggesting a selective approach to preoperative MRI in ILC based on mammographic density.[25] Such an approach has been validated by Wong et al,[46] who demonstrated that higher breast density (BI-RADS density C and D) was a significant predictor (odds ratio 3.19) for additional suspicious lesions detected by MRI in ILC patient. Similarly, Bansal et al[47] demonstrated the value of selectively performing preoperative MRI based solely on high mammographic density. In this study, 25% of MR+ cases (9 of 36) with a high breast density had an appropriate change in surgical treatment. There was also a significantly younger mean age in the MR+ group (56.4 vs 65.6 years) in keeping with randomised evidence.[13] Apart from these cohorts, a steady decline in the use of preoperative MRI has been observed in our institution over the study period (see Figure 5). The implications of this would suggest that in practice, the benefit of preoperative breast MRI appears to be confined to select cases (younger, dense breast, and borderline conservable) in symptomatic ILC and this is increasingly recognised by our experienced and high-volume breast cancer MTB.

This study has a number of limitations. First, we cannot comment on screen detected disease, as this cohort included symptomatic patients only. It is accepted, however, that there is a strong survival advantage of screening compared with symptomatic detection. The majority of this effect is attributable to a shift in prognosticating findings including the size, the number of involved lymph nodes, and the grade of the tumour.[48] With this in mind, it is fair to assume that when assessing a symptomatic cohort in isolation, the disease may often be palpable, reducing the need for further imaging with MRI. In addition, as it is not a prospective randomised trial, a considerable selection bias is acknowledged. The indication for preoperative breast MRI was usually suggested by radiologists at a tertiary breast centre MDM in specific circumstances such as: to accurately assess tumour size and address any discrepancy regarding the extent of disease, if BCS was to be considered, high breast density precluding accurate size assessment and multifocal/multicentric disease. Nonetheless, the final decision was left to the discretion of the surgeon and patient at consultation. In interpreting these results, it is also important to remain cognisant that all cases referred for preoperative MRI posed an initial challenge in surgical planning, frequently with question-marks about density, multifocality, and size. Following discussion at MTB meetings, MRI would have been recommended due to the ambiguity of each case. In this context, the authors accept that these background issues can complicate cases and are not objectively standardised and measurable. These real-life outcomes present an important validation of the reduced value of MRI in preoperative surgical planning for ILC, at a time where other aspects of oncology are becoming increasingly reliant on MRI as a modality.

Conclusions

At a time when the clinical utility of MRI in the preoperative management of ILC remains uncertain, this study demonstrates a real-life overview of its practical application in a large consecutive series of patients. While MRI has a role in the detection of contralateral disease in select cases, this study catalogues the overall decline in the routine utilisation of this modality for most ILC cases. Randomised evidence suggests that routine preoperative MRI is unnecessary in primary ILC because it does not reduce re-excision rates[11,12] and there are good data to suggest that preoperative MRI may also increase mastectomy rates without impacting disease recurrence.[14-17] Current guidelines[33-35] and this study suggest that the addition of MRI can be beneficial in select cases where conventional imaging is inconclusive. Preoperative MRI breast appears to have particular utility in borderline breast conservable younger patients[13] and those with dense breast tissue that are for consideration of BCS.[46,47] A large volume of research both supporting and discouraging the use of MRI in this setting has been published; however, unless a further large RCT demonstrates a significant added benefit of preoperative MRI in ILC, it is prudent to perform preoperative breast MRI in these select cases alone.

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Author Contributions

Conceptualisation was by B.M.M., P.M., É.J.R., R.M.W., and M.K.; data curation was by E.O.B.; formal analysis was by B.M.M., R.M.W., A.M.O.C., R.E., S.W., C.G., A.J.L., P.A.M., and M.J.K.; funding acquisition was by A.J.L. and M.J.K.; investigation was by B.M.M., P.F.M., É.J.R., E.O.B., R.M.W., A.M.O.C., S.W., R.E., C.G., A.J.L., P.A.M., and M.J.K.; resources were by A.M.O.C., S.W., R.E., C.G., and M.J.K.; supervision was by P.A.M. and M.J.K.; writing – original draft was by B.M.M., P.M., É.J.R., and M.K.; writing – review and editing was by B.M.M., A.M.O.C., P.M., É.J.R., R.M.W., A.J.L., P.A.M., and M.J.K.

Consent for Publication

Written informed consent was obtained from each patient.

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Clinical Research Ethics Committee (University College Hospital, Galway). All clinical investigation was performed according to the principles expressed in the Declaration of Helsinki.

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Data Availability

The data that support the findings of this study are available from the corresponding author (B.M.) upon reasonable request.

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