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A Prospective Study of the Utility of Magnetic Resonance Imaging in Determining Candidacy for Partial Breast Irradiation

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Abstract

Purpose—Retrospective data have demonstrated that breast magnetic resonance imaging (MRI) may change a patient's eligibility for partial breast irradiation (PBI) by identifying multicentric, multifocal, or contralateral disease. The objective of the current study was to prospectively determine the frequency with which MRI identifies occult disease and to establish clinical factors associated with a higher likelihood of MRI prompting changes in PBI eligibility.

Methods and Materials—At The University of Chicago, women with breast cancer uniformly undergo MRI in addition to mammography and ultrasonography. From June 2009 through May 2011, all patients were screened prospectively in a multidisciplinary conference for PBI eligibility based on standard imaging, and the impact of MRI on PBI eligibility according to National Surgical Adjuvant Breast and Bowel Project protocol B-39/Radiation Therapy Oncology Group protocol 0413 entry criteria was recorded. Univariable analysis was performed using clinical characteristics in both the prospective cohort and in a separate cohort of retrospectively identified patients. Pooled analysis was used to derive a scoring index predictive of the risk that MRI would identify additional disease.

Results—A total of 521 patients were screened for PBI eligibility, and 124 (23.8%) patients were deemed eligible for PBI based on standard imaging. MRI findings changed PBI eligibility in 12.9% of patients. In the pooled univariable analysis, tumor size ≥ 2 cm on mammography or ultrasonography ($P=.02$), age <50 years ($P=.01$), invasive lobular histology ($P=.01$), and HER-2/neu amplification ($P=.01$) were associated with a higher likelihood of MRI changing PBI eligibility. A predictive score was generated by summing the number of significant risk factors. Patients with a score of 0, 1, 2, and 3 had changes to eligibility based on MRI findings in 2.8%, 13.2%, 38.1%, and 100%, respectively ($P<.0001$).

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Preliminary versions of this study were presented at the 52nd and 53rd Annual Meetings of the American Society of Radiation Oncology in San Diego, CA, October 31–November 4, 2010, and in Miami Beach, FL, (ASTRO) October 2–6, 2011, respectively.

Conflict of interest: Dr Chmura is a consultant for the American College of Radiology Imaging Network for clinical trial development regarding breast MRI.

Conclusions—MRI identified additional disease in a significant number of patients eligible for PBI, based on standard imaging. Clinical characteristics may be useful in directing implementation of MRI in the staging of PBI candidates.

Introduction

The standard of care after breast-conserving surgery is whole-breast radiation therapy (WBRT) delivered over 5-6 weeks. Accelerated partial breast irradiation (PBI) administered over 5 treatment days is emerging as an alternative to WBRT in select patients with early stage disease. PBI is attractive to both patients and practitioners due to the convenience of a shortened course of therapy and the potential to reduce radiation toxicity to adjacent organs. Accordingly, the use of PBI has markedly increased over the past decade (1). Early results from prospective studies investigating PBI show promising results. However, mature data from randomized trials will not be available for many years.

As evidence supporting the safety and efficacy of PBI continues to accumulate, appropriate patient selection remains controversial. After breast-conserving surgery, WBRT addresses the remainder of the intact breast with doses capable of eradicating occult microscopic foci of disease. In contrast, undetected disease elsewhere in the breast may not be included in PBI treatment volumes, theoretically increasing the risk for a subsequent in-breast recurrence. Attempts to stratify PBI candidates by risk of occult disease by using known clinical prognostic factors such as age, tumor size, and histology have not reliably correlated with the observed local failure rates in patients treated with PBI reported in the literature (2-4).

The ongoing randomized trial comparing PBI to WBRT (National Surgical Adjuvant Breast and Bowel Project protocol B-39/Radiation Therapy Oncology Group protocol 0413 [NSABP B-39/RTOG 0413]) requires pretreatment evaluation of the breast with mammography and physical examination. Magnetic resonance imaging (MRI) is not required for enrollment, and its use is not recorded for patients entering the trial. The extent to which MRI is implemented in the work-up of potential PBI candidates within and outside of the framework of clinical trials is unknown; however, practice guidelines typically do not recommend its routine use (4, 5).

Retrospective data demonstrate that MRI detects additional multicentric, multifocal, or contralateral disease in 5%-10% of early stage patients who would be considered candidates for PBI based on findings of standard imaging (6-8). Previous reports are limited by retrospective design and nonuniform use of MRI for staging. We initiated a prospective study to determine the utility of MRI in the detection of clinically occult disease not identified by mammography, ultrasonography, or physical examination from a cohort of consecutively identified PBI candidates uniformly undergoing MRI for pretreatment evaluation. We used our prospective cohort, in addition to a separate retrospectively identified cohort, to identify clinical features correlated with an increased risk of MRI identifying additional disease. Using a pooled analysis of both cohorts, we generated a scoring index to predict the likelihood of MRI rendering a patient ineligible for PBI.

Methods and Materials

All patients with newly diagnosed breast cancer at The University of Chicago undergo staging workup that includes physical examination and mammography with or without ultrasonography. Since 2005, all patients have undergone staging breast MRI. Currently, exceptions to the uniform implementation of MRI include contraindications to MRI or contrast agents, patient refusal, patient size, or clinically inoperable disease. All cases are reviewed in a multidisciplinary breast oncology conference with specialist representatives from surgical oncology, medical oncology, radiation oncology, radiology, and pathology. Patients undergoing initial workup at outside institutions are required to have all images submitted and officially interpreted by The University of Chicago radiologists.

Institutional review board (IRB) approval was obtained to prospectively examine the effects of MRI on PBI eligibility (Protocol 09-025-A). A waiver of consent was granted to screen all patients presented in multidisciplinary conference for PBI eligibility and to examine the impact of MRI on eligibility. From June 2009 to May 2011, all patients presented in multidisciplinary conference were screened by a physician or research assistant for PBI eligibility according to the original NSABP B-39/RTOG 0413 inclusion criteria, using mammography, ultrasonography, and surgical pathology data. These criteria can be summarized as (1) an invasive or intraductal lesion no greater than 3 cm in size; (2) negative pathologic margins; (3) 3 positive lymph nodes; (4) no extracapsular extension; and (5) full axillary staging. Multifocal disease was permissible as long as all disease was encompassed within a 3-cm area.

The impact of MRI findings on PBI eligibility was subsequently recorded. MRI-identified secondary lesions were sampled by biopsy to confirm pathology. Invasive lesions and ductal carcinoma in situ (DCIS) were identified and designated by location: within the same quadrant (multifocal), in a different quadrant or >4 cm away from the index lesion (multicentric), or in the contralateral breast.

Our analysis focused on secondary lesions identified by MRI that were pathologically proven invasive carcinoma or DCIS and would have rendered the patient ineligible for PBI. Secondary lesions of interest were those not identified by diagnostic mammography, ultrasonography, or examination. Data regarding the following tumor characteristics were gathered: tumor palpability, tumor size, grade, excision margin, and lymph node status, estrogen receptor status, HER-2/neu status, lymphovascular invasion, extensive intraductal component, and American Society for Radiation Oncology (ASTRO) consensus group criteria.

Patients who did not go on to excision with clear margins and complete axillary staging were excluded. Patients with synchronous bilateral cancer or a history of breast cancer were excluded according to RTOG 0413 protocol guidelines. In an attempt to eliminate incidental lesions that would have been identified pathologically, only secondary DCIS or invasive lesions found by MRI 1 cm away from the primary lesion site were considered to have changed PBI candidacy.

A second cohort of patients was identified retrospectively, using the aforementioned inclusion and exclusion criteria. This group consisted of 82 consecutive PBI candidates undergoing MRI nonselectively in the 15 months prior to initiation of the prospective study. Analysis of the impact of MRI on eligibility was assessed in the same manner as for the prospective cohort.

MRI technique

MRI was performed using Achieva scanners (Philips Medical Systems, Best, The Netherlands) with either 1.5- or 3-Tesla magnets. Both scanners were equipped with dedicated, bilateral, 16-channel breast coils that provide high signal-to-noise ratios. Imaging protocol consists of axial T2-weighted fast spin-echo images and axial fat-saturated T1-weighted 3-dimensional gradient echo images following a localizer sequence. Fat-saturated T1-weighted images consisted of 1-precontrast and 6-postcontrast image series with a bolus injection of 0.01 mmol/kg gadodiamide (Omniscan; Amersham Biosciences Corp., Piscataway, NJ), followed by a 20-mL saline flush, using a power injector at a rate of 2 mL/sec. Scan delay time was 20 sec after the start of the contrast injection. Image resolution was 0.7-0.8 mm in each dimension, with 1-mm slice thickness without a gap for both T2- and T1-weighted images; temporal resolution for kinetic analysis was 60-75 sec. All enhanced images were processed by subtracting the corresponding precontrast scan images. Contrast uptake kinetic curves including color-coding maps were analyzed for each suspicious lesion with the aid of CADStream (Confirmix Inc) or DynaCAD (*Invivo*) software using the second and fifth contrast image series as the early and delayed phases, respectively (9).

MR images were interpreted by 1 of 4 dedicated breast radiologists (4-7 years of experience), with history and conventional images available for comparison. All lesions were reported according to the Breast Imaging Reporting and Data System (BI-RADS) BI-RADS lexicon for MRI. When the lesion was assessed as benign (BI-RADS 2), no further work-up was performed. When the lesion was assessed as probably benign (BI-RADS 3), short-interval (6-month) follow-up with MRI was performed. When the lesion was assessed as either a suspicious abnormality (BI-RADS 4), highly suggestive of malignancy (BI-RADS 5) or incomplete (BI-RADS 0), second-look ultrasound (US)-guided biopsy and/or US/MR-guided biopsy was performed.

Statistical analysis

The normal approximation of the binomial distribution was used to calculate 95% confidence intervals (CI). Univariate analysis was performed using the chi-squared test. Multivariate analysis could not be performed due to the small number of events. A pooled univariate analysis using both the prospective and the retrospective cohorts was performed to identify clinical factors that were associated with changes in PBI eligibility ($P < .05$). Significant variables were used to create a scoring index. The Cochran-Armitage test for trend was used to assess the significance of rising scores.

Results

Between June 2009 and May 2011, 718 patient cases were reviewed in multidisciplinary conference. Among them, 137 (19.1%) patients were excluded due to recurrent or metastatic disease ($n = 39$), second opinion only ($n = 27$), benign or non-breast histology ($n = 53$), locally advanced or inflammatory breast cancer ($n = 10$), or male sex ($n = 8$). Of the remaining 581 patients, 60 (10.3%) patients did not undergo breast MRI prior to definitive therapy primarily due to medical contraindications or patient refusal (Table 1). Of the 521 patients who underwent MRI, a total of 124 (23.8%) were deemed eligible for PBI based on NSABP B-39 entry criteria. Most patients were estrogen receptor-positive (68.5%), older than 50 years (76.6%), and node negative (73.4%). The retrospective cohort included patients with similar clinical characteristics (Table 2).

Among 124 PBI-eligible patients, 41 (33.1%) had additional findings on MRI that were not seen on mammography or ultrasonography. Of these 41 patients, 29 went on to second-look ultrasonography and/or mammography. Second-look imaging revealed findings in 6 patients that appeared benign, were no longer present, or were recommended for 6-month follow-up MRI. The remaining 35 patients underwent a biopsy. Of the 124 PBI-eligible patients, 16 (12.9%; 95% CI, 7.6%-20.1%) were found to have multicentric, multifocal, or contralateral disease not identified by mammography or ultrasonography which rendered the patient ineligible for PBI (Fig. 1). In addition, 2 of the 35 patients had biopsy result-proven multifocal disease with no change in PBI eligibility as the total span of the multifocal disease was 3 cm. Overall, the positive predictive value of MRI was 51.4% (18 of 35 patients; 95% CI, 34.0%-68.6%).

Of the 16 patients for whom PBI eligibility was altered, 2 patients (1.6%; 95% CI, 0.2%-5.7%) were found to have contralateral disease, 3 patients (2.4%; 95% CI, 0.5%-6.9%) were found to have multicentric disease, and 11 patients (8.9%; 95% CI, 4.5%-15.3%) were found to have multifocal disease 1 cm away from the index lesion (Fig. 2). The mean distance between the index lesion and the multifocal or multicentric lesion was 2.2 cm (range, 1.0-5.5 cm). All multifocal lesions were 4 cm from the index lesion.

MRI analysis prompted a negative biopsy in 18 of 124 patients, and therefore, the proportion of patients with a false-positive MRI was 14.5% (95% CI, 8.8%-22.0%). Of the 18 patients with false-positive MRIs, 3 patients had 2 separate lesions biopsied which were both negative. Based on MRI findings, 1 patient was found to have both a benign lesion and a multifocal site of invasive carcinoma in the ipsilateral breast upon biopsy.

Univariable analysis was performed to assess factors associated with the higher likelihood of MRI identifying additional disease (Table 3). In patients younger than 50, MRI identified additional disease in 24.1% compared to 9.5% in older patients ($P=.04$). Patients with a clinical tumor size on standard imaging of 2 cm were found to have additional disease in 29.6% of cases compared to 9.1% in patients with smaller tumors ($P=.01$). Of 10 patients with invasive lobular primaries, 3 patients (30%) were found to have additional disease by MRI compared to 12 of 86 (14.0%) patients with invasive ductal carcinoma and 1 of 28 (3.6%) patients with DCIS ($P=.09$). HER-2/neu-amplified tumors were associated with

changes in PBI eligibility prompted by MRI results in 42.9% of patients compared to 14.1% in patients with nonamplified primaries ($P=.05$).

Univariable analysis was repeated in the retrospective cohort of 82 consecutively identified patients (Table 3). Pooled analysis of 206 patients in both cohorts revealed 4 clinical variables routinely available before definitive surgery that were significantly associated with an increased risk of MRI identifying additional disease: age <50, clinical tumor size ≥ 2 cm, HER-2/neu amplification, and invasive lobular histology. These clinical features were used to generate a scoring index with 1 point assigned for each risk factor. Increasing scores were associated with an increased likelihood that MRI would change PBI eligibility (Cochran-Armitage test, $P<.0001$) (Table 4).

Discussion

This is the first series to prospectively evaluate the impact of MRI in a cohort of PBI candidates uniformly undergoing MRI in addition to mammography and ultrasonography. We found that MRI detected clinically occult foci of disease in 12.9% of patients who would have been appropriate PBI candidates according to standard imaging. This finding coincides with our previously reported retrospective data in which PBI candidates were found to have additional disease detected by MRI in 10% of cases and with data from other investigators who found rates that ranged from 5.8% and 16% (6-8, 10-12).

The role of MRI in preoperative staging of breast cancer patients has been extensively studied; in a systematic review, Houssami et al (13) found that MRI identified multifocal or multicentric disease in a median of 16% of patients (range, 6%-34%). Retrospective data have evaluated the impact of preoperative MRI on disease control, revealing that initial MRI does not improve outcomes in the setting of adjuvant WBRT (14). In patients without MRI staging, it is hypothesized that undetected microscopic disease is eradicated with adjuvant radiation, thus reducing the observed rates of local recurrence to only a fraction of the expected incidence of multicentricity or multifocality (15). However, studies of MRI in the setting of standard breast conservation therapy cannot be applied to the PBI population, in which patients may have different disease characteristics and would have additional foci of disease left intact and untreated in the absence of adjuvant WBRT.

We identified several clinical features associated with an increased risk of MRI identifying additional disease. Patients with clinical tumor size ≥ 2 cm, invasive lobular histology, HER-2/neu amplification, and age <50 were more likely to have biopsy-proven disease detected only by MRI. The adverse features identified in this cohort have been previously shown to correlate with mammographically occult disease, multifocality/multicentricity, and more aggressive disease (16-18). In a similar cohort of PBI candidates undergoing MRI, Tendulkar et al (8) noted that 18% of patients with invasive lobular lesions were found to have additional disease by MRI compared to 3%-4% of patients with other histologies. In addition, there was a significant association between size and MRI findings as 13% of patients with pT2 disease compared to only 3% of patients with smaller lesions had MRI findings positive for separate foci of malignancy.

Although younger patients, those with invasive lobular histology or those with tumors ≥ 2 cm, make up only a small percentage of patients enrolled in PBI trials, early results from retrospective studies reveal that PBI in select women with high-risk features can provide excellent control. Shah et al (19) reported no difference in local control outcomes between a group of PBI patients with invasive lobular disease and a group with invasive ductal cancer (19). Subset analysis of patients enrolled in the MammoSite registry trial reveals no difference in local control between ASTRO consensus “unsuitable” patients and those in other risk categories (3). Whether MRI was used in the selection of these patients is not stated. We strongly recommend the use of staging MRI in patients with 1 or more of the identified risk factors in order to rule out disease that would not be encompassed in surgical margins or limited radiation fields.

In the absence of randomized trials, clinical decision making regarding staging MRI requires weighing the risks and benefits of the test based on available data. In the current cohort, the risks were minimal, with a false-positive rate of 14.5% and no reported biopsy sample-related complications. Conversion to mastectomy based on MRI findings was planned only after confirmation of disease by image-guided biopsy. On the other hand, potential benefits of MRI include identification of additional disease in a significant percentage of patients and minimization of the risk of a subsequent local recurrence.

One limitation of our study is that the fate of multifocal lesions that are undetected preoperatively is unknown. Most lesions identified were multifocal, with a mean distance from the primary of 2.2 cm. While MRI lesions were considered significant only when ≥ 1 cm from the index lesion, it is possible that these lesions could have been encompassed within surgical margins or PBI treatment volumes. We are unable to predict whether they would be adequately treated or whether they could give rise to subsequent local failures in the absence of WBRT. In addition, although this is the largest reported prospective study of MRI in the staging of PBI candidates, our analysis is limited by the relatively low number of events. The findings derived from our pooled analysis require validation in external cohorts.

Conclusions

MRI identifies additional disease in a significant number of patients eligible for PBI, based on standard imaging. Implementing MRI in select PBI candidates may reduce the likelihood of clinically occult foci in the breast receiving noncytotoxic doses of RT. In addition, confirming unifocal disease by MRI may allow physicians to comfortably offer PBI to patients with features typically considered to portend a worse prognosis.

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Summary

Retrospective data suggest that breast MRI may change eligibility for partial breast irradiation (PBI) by identifying occult disease. This study prospectively evaluated the impact of MRI on PBI eligibility in a cohort of patients uniformly undergoing MRI, mammography, and ultrasonography. Our results show that MRI identified multicentric, multifocal, or contralateral disease in 12.9% of patients. MRI should be strongly considered in staging PBI candidates.

Fig. 1. Outcomes of the imaging and pathologic work-up of patients eligible for PBI based on standard imaging.

Fig. 2.

Representative images of a 78 year old female with a 1.3 cm invasive ductal carcinoma of the left breast initially detected mammographically. Images show a mediolateral (a) and craniocaudal (b) mammogram of the breast with a clip at the site of the index lesion. A postcontrast T1-weighted fat suppressed MRI (c) and a maximum-intensity projection, sagittal MRI (d) show a retroareolar lesion 5.5 cm away from the index mass which was consistent with DCIS spanning 2.1 cm.

Table 1
Reasons why MRI was not performed in patients screened during the multidisciplinary breast conference

Reason why MRI was not performed	No. of patients
Chronic renal insufficiency or pacemaker	20
Patient refusal/intolerance to examination	14
Patient size exceeded machine capacity	10
No surgery planned (comorbidities, age, patient refusal)	7
Patient refused breast conservation	6
Unknown	2
Pregnancy	1
Total no. without MRI/total (% of total)	60/581 (10.3)

Abbreviation: MRI = magnetic resonance imaging.

Table 2
Patient and disease characteristics

Characteristic	No. of patients (%) in the prospective cohort	No. of patients (%) in the retrospective cohort	P value
Age (y)			
Median	57.0	56.0	NS
Range	26-86	36-85	
<50	29 (23.3%)	24 (29.7%)	
50-59	44 (35.5%)	21 (25.6%)	
60	51 (41.1%)	37 (45.1%)	
Histology			
Ductal carcinoma in situ	28 (22.6%)	17 (20.7%)	NS
Invasive ductal	85 (68.5%)	54 (65.9%)	
Mixed ductal/lobular carcinoma	1 (0.8%)	3 (3.7%)	
Invasive lobular carcinoma	10 (8.1%)	8 (9.8%)	
Clinical size (mammogram or ultrasonogram)			
<2 cm	88 (71.0%)	62 (75.6%)	NS
2 cm	27 (21.8%)	15 (18.3%)	
Unknown	9 (7.3%)	5 (6.1%)	
Pathologic T stage [†]			
Tis	28 (22.6%)	17 (20.7%)	NS
T1	76 (61.3.2%)	54 (65.9%)	
T2	20 (16.1%)	11 (13.4%)	
N stage			
N×	24 (19.4%)	14 (17.1%)	NS
N0 or N0 (i+)	91 (73.4%)	59 (72.0%)	
N1 (mic)	4 (3.2%)	4 (4.9%)	
N1	5 (4.0%)	5 (6.1%)	
Palpable			
Yes	39 (31.5%)	28 (34.1%)	NS
No	84 (67.7%)	52 (63.4%)	
Unknown	1 (0.8%)	2 (2.4%)	
Hormone receptor status			
ER positive (>10%)	85 (68.5%)	58 (70.7%)	NS
ER negative	16 (12.9%)	7 (8.5%)	
Not assessed/unknown	23 (18.5%)	17 (20.7%)	
HER-2/neu status			
Amplified (FISH >2.0)	7 (5.6%)	2 (2.4%)	NS
Not amplified	85 (68.5%)	62 (75.7%)	
Not assessed/unknown	32 (25.8%)	18 (22.0%)	
Neoadjuvant chemotherapy			
Yes [*]	6 (4.8%)	0 (0%)	.04

Characteristic	No. of patients (%) in the prospective cohort	No. of patients (%) in the retrospective cohort	P value
No	118 (95.2%)	82 (100%)	
ASTRO consensus group			
Suitable	14 (11.3%)	18 (22.0%)	<.01
Cautionary	73 (58.9%)	31 (37.8%)	
Unsuitable	37 (29.8%)	33 (40.2%)	
TOTAL	124	82	

Abbreviations: ASTRO = American Society for Radiation Oncology; ER = estrogen receptor; FISH = fluorescent in situ hybridization; i+ = immunohistochemistry; mic = microscopic; NS = not significant.

* Neoadjuvant chemotherapy was administered based on MRI findings of multifocal/multicentric disease (n = 6).

[†] If neoadjuvant chemotherapy was administered, clinical T stage was used.

Table 3
Univariable analysis of factors associated with MRI-identified additional disease that would render the patient ineligible for PBI

Patient/disease characteristics	Prospective cohort		Retrospective cohort		Pooled cohort	
	No. of patients in whom MRI identified additional disease/total (%)	P value	No. of patients in whom MRI identified additional disease/total (%)	P value	No. of patients in whom MRI identified additional disease/total (%)	P value
Age [‡]						
<50	7/29 (24.1%)	.04	4/24 (16.7%)	.04	11/53 (20.8%)	.01
50	9/95 (9.5%)		2/58 (3.4%)		11/153 (7.7%)	
Histology [‡]						
Invasive ductal	12/86 (14.0%)	.09	4/57 (7.0%)	.08	16/143 (11.2%)	.01
Invasive lobular	3/10 (30.0%)		2/8 (25.0%)		5/18 (27.7%)	
DCIS	1/28 (3.6%)		0/17 (0.0%)		1/45 (2.2%)	
Clinical size ^{*,‡}						
<2 cm	8/88 (9.1%)	.01	5/62 (8.1%)	.86	13/150 (8.7%)	.02
2 cm	8/27 (29.6%)		1/15 (6.8%)		9/42 (21.4%)	
Pathologic T stage						
Tis	1/28 (3.6%)	<.01	0/17 (0.0%)	<.01	1/45 (2.2%)	<.01
T1	7/76 (9.2%)		2/54 (3.7%)		9/130 (6.9%)	
T2 (up to 3 cm)	8/20 (40.0%)		4/11 (36.4%)		12/31 (38.7%)	
N stage [‡]						
N1	2/5 (40.0%)	.17	1/5 (20.0%)	.55	3/10 (30%)	.12
N1 (mic)	0/4 (0%)		0/4 (0.0%)		0/8 (0%)	
N0 or N0 (i+)	12/91 (13.2%)		5/60 (8.3%)		17/151 (11.3%)	
Palpable Tumor						
Yes	8/39 (20.5%)	.09	3/28 (10.7%)	.43	11/67 (16.4%)	.07
No	8/84 (9.5%)		3/52 (5.8%)		11/136 (8.1%)	
Hormone receptor status [‡]						
ER positive	2/16 (12.5%)	.69	6/58 (10.3%)	.19	8/74 (10.8%)	.41
ER negative	14/85 (16.5%)		0/7 (0.0%)		14/92 (15.2%)	
HER-2/neu Status ^{†,‡}						

Patient/disease characteristics	Prospective cohort		Retrospective cohort		Pooled cohort	
	No. of patients in whom MRI identified additional disease/total (%)	P value	No. of patients in whom MRI identified additional disease/total (%)	P value	No. of patients in whom MRI identified additional disease/total (%)	P value
Amplified	3/7 (42.9%)	.05	1/2 (50.0%)	.04	4/9 (44.4%)	.01
Not amplified	12/85 (14.1%)		5/63 (7.9%)		17/148 (11.5%)	
Lymphovascular invasion						
Yes	2/16 (12.5%)	.89	1/7 (14.3%)	.46	3/23 (13.0%)	.58
No	12/106 (11.6%)		5/75 (6.7%)		17/181 (9.4%)	
Extensive intraductal component [†]						
Yes	1/19 (5.3%)	.42	0/4 (0%)	.53	1/23 (4.3%)	.37
No	8/69 (11.3%)		6/67 (9.0%)		14/136 (10.3%)	
ASTRO consensus group						
Suitable	2/14 (14.3%)	.38	1/18 (5.6%)	.37	3/32 (9.4%)	.24
Cautionary	7/73 (9.6%)		1/31 (3.2%)		8/104 (7.7%)	
Unsuitable	7/37 (18.9%)		4/33 (12.1%)		11/70 (15.7%)	

Abbreviations: ASTRO = American Society for Radiation Oncology; ER = estrogen receptor; i+ = Immunohistochemistry; mic = microscopic; MRI = magnetic resonance imaging; PBI = partial breast irradiation.

* Largest size of the index lesion on a mammogram or ultrasonogram (MRI size was not included).

[†] Ductal carcinoma in situ (DCIS) patients do not undergo routine ER status or HER-2/neu testing or pathologic evaluation of nodes. Extensive intraductal component was not applicable to DCIS patients; lymphovascular invasion was considered negative for all DCIS patients.

[‡] Clinical variables were available preoperatively that were significant in pooled univariable analysis. These variables were used to create a predictive index.

Table 4
Predictive scoring index for the likelihood of MRI identifying additional disease in patients otherwise eligible for PBI

Score*	% of cases in which MRI identified additional disease % [†]	No. of patients/total
0	2.8	(3/108)
1	13.2	(10/76)
2	38.1	(8/21)
3	100.0	(1/1)
4	NA	

Abbreviations: MRI = magnetic resonance imaging; NA = not available; PBI = partial breast irradiation.

Cochran-Armitage test $P < 0.0001$ indicating that increasing scores are associated with significantly increased risk of MRI, prompting changes in PBI eligibility.