

# Role of Breast MRI in Patients with Newly Diagnosed Breast Cancer

Marissa L. Albert<sup>1</sup> · Yiming Gao<sup>1</sup> · Linda Moy<sup>1</sup>

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**Abstract** The role of breast MRI in patients with newly diagnosed breast cancer is controversial. Preoperative MRI is highly sensitive and accurate in assessing tumor size, extensive intraductal component (EIC), and in detection of additional sites of disease. It also has utility in assessing chest wall, nipple-areolar complex, and nodal involvement. Yet there are conflicting results in whether the use of preoperative MRI improves re-excision rate, local recurrence rate, and ultimately, survival. MRI has also been associated with overestimation of disease and increased mastectomy rates, and may contribute to treatment delay. Nevertheless, certain subgroups of patients may benefit more from preoperative MRI than others, including those with invasive lobular cancer (ILC), dense breasts, and those at elevated risk for breast cancer.

**Keywords** Breast MRI · Preoperative breast MRI · Preoperative breast imaging · Breast cancer · Disease extent · Multifocal · Multicentric · Re-excision · Recurrence · Mastectomy rate · Locoregional staging

## Introduction

Magnetic resonance imaging (MRI) is highly sensitive and accurate for diagnosis of breast cancer. Although breast MRI has become widely utilized in locoregional staging of newly diagnosed breast cancer [1, 2], its clinical benefits are unclear.

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✉ Linda Moy  
linda.moy@nyumc.org

<sup>1</sup> NYU Langone Medical Center, New York, NY 10016, USA

Despite superior diagnostic accuracy of breast MR over mammography and ultrasound in characterizing disease burden [3–21], there are conflicting results in whether the use of preoperative breast MR improves re-excision rate, local recurrence rate, and ultimately, survival. Concerns of overestimation of disease [3, 22–24] and increased mastectomy rate [22, 25, 26] have also been raised. This is reflected in the paucity of standardized recommendations regarding the use of preoperative breast MRI from diagnostic imaging and surgical societies [27–30]. In this article, we will review strengths of breast MR in locoregional staging, discuss controversies surrounding its use, and review relevant current literature. We will also highlight subgroups of patients who may benefit most from a preoperative breast MR and clinical scenarios where breast MR is the most helpful.

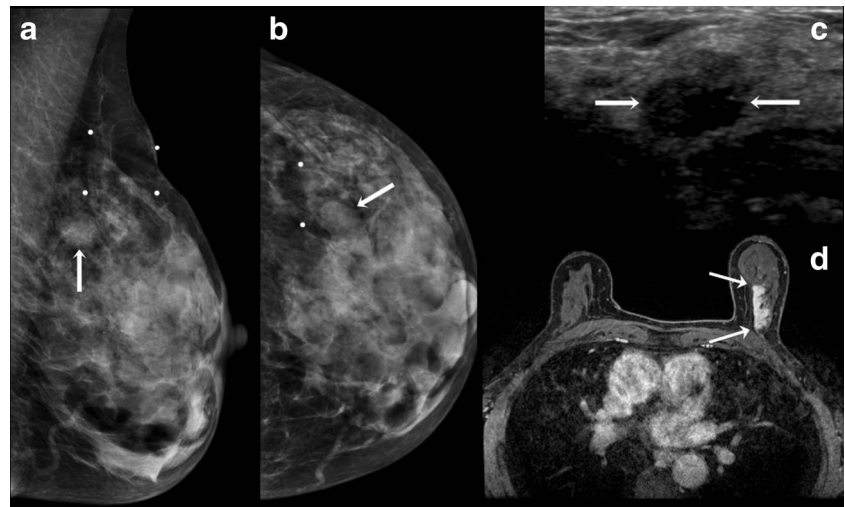
## Strengths of Breast MR in Locoregional Disease Staging

### Size and Extent of Known Tumor

#### *Index Tumor*

When compared to the diagnostic performance of 2D mammography, digital breast tomosynthesis (DBT), and ultrasound, MRI has been shown to have improved sensitivity and superior accuracy in estimating tumor size [3–14, 31] (Fig. 1). In a study by Berg et al., MRI outperformed mammography in detecting all histologic tumor types and had higher sensitivity than ultrasound for the detection of ductal carcinoma in situ (DCIS) [3]. Though overestimation does occur, improved correlation of MRI with pathologic index lesion size has been consistently demonstrated in multiple

**Fig. 1** Sixty-two-year old female presented with palpable abnormality in the upper outer quadrant of left breast, found to have a mass measuring approximately 1 cm on the mammogram in MLO (a) and CC (b) views (arrows), and on ultrasound (c) (arrows). Contrast-enhanced MRI (d) showed much more extensive disease measuring at least 3–4 cm in the largest dimension (arrows)



studies [4–7]. Even higher correlation with final pathology lesion size has been demonstrated with 3 T magnets over 1.5 T [32].

#### *Extensive Intraductal Component*

Accurate estimation of size and extent of disease depends on the ability to adequately assess the degree of surrounding extensive intraductal component (EIC) associated with the primary tumor [33]. The entire extent of disease including the index tumor and its surrounding EIC determines candidacy for breast conservation therapy (BCT) and defines the margins of excision. Improved accuracy of MRI over mammography in estimating the size of surrounding EIC has been consistently reported [3, 12–14]. The overall sensitivity of MRI for EIC varies between studies. A meta-analysis by Schouten van der Velden in 2009 found a wide range of sensitivities from 33 to 100 % in 11 studies [34], with lower sensitivities associated with low-grade tumors, presumably due to lower levels of enhancement reflecting weaker angiogenesis.

#### *DCIS*

With improved technique and higher spatial resolution, MRI has become increasingly sensitive for detecting both calcified and noncalcified DCIS [35–38]. Detection is particularly improved in intermediate- to high-grade tumors [22, 37, 39]. Given the challenge of diagnosing DCIS and high rates of re-excision, accurate assessment of extent of disease is vital in these patients. Although more accurate size estimation of DCIS by MRI over mammography and ultrasound has not been consistently established in the literature [3, 22–24, 39, 40], there is evidence that MRI improves lesion size assessment over mammography, particularly in high-grade DCIS.

Patients with DCIS may benefit from preoperative MRI for the detection of an invasive tumor component not

demonstrated at the time of biopsy, which has important staging, treatment, and prognostic implications. In several studies, MRI outperformed mammography in the detection of occult invasive component in DCIS [40–43], with greater sensitivities associated with larger lesion size and the presence of a mass [41, 44]. On the other hand, the absence of occult invasion on breast MRI has a high negative predictive value and helps confirm preoperative staging in a patient with DCIS.

#### **Detection of Additional Disease**

Preoperative MRI has consistently demonstrated high diagnostic accuracy in visualizing otherwise occult sites of disease, including multifocal, multicentric, and contralateral involvement [16–19]. In a meta-analysis including 2610 patients, MRI detected additional tumors in 16 % of patients, resulting in a change in surgical management in 11 % [16]. A larger meta-analysis by Plana et al. included 10,811 patients from 50 studies, found even higher rates of additional disease detection in 20 % of patients [17]. The detection of additional contralateral breast cancer was also reported in an average 5.5 % of patients [17]. The diagnosis of additional suspicious findings on MRI usually require tissue sampling to confirm disease extent, which in turn, dictate the ultimate surgical and medical treatment planning.

#### **Assessment of Chest Wall, Nipple, and Skin Involvement**

##### *Posterior*

MRI is an excellent modality in assessing chest wall involvement by a posterior tumor. This is possible given superior anatomic detail and contrast enhancement of the posterior breast to the level of the chest wall encompassed in the field of view. Invasion is indicated by infiltration and abnormal enhancement of underlying musculature and not simply by

violation of the fat planes, a distinction readily made by MRI [45]. Pectoralis muscle invasion, while it does not change the tumor staging by TNM classification, affects surgical approach. Chest wall invasion, defined as involvement of the ribs or chest wall musculature (serratus anterior and intercostal muscles), does alter staging, prognosis, and treatment.

### *Anterior*

MRI is helpful in assessing disease involvement of the nipple-areolar complex (NAC) for similar reasons previously stated. While involvement of the NAC on MRI does not necessarily change tumor staging, it alters surgical planning and precludes the patient from nipple-sparing mastectomy. MRI has been shown to be useful in determining NAC involvement in multiple studies [46–49]. The involvement of the NAC on MRI manifests in asymmetric nipple enhancement contiguous with enhancement from index tumor [47], or in proximity of index tumor to the NAC (within 2 cm, range 5 mm–2 cm) without direct nipple enhancement [48, 49]. Similarly, MRI is helpful in detecting skin involvement (in non-inflammatory cancers), which appears as localized skin thickening and enhancement contiguous to the index tumor. This however requires clinical correlation of local skin ulceration or nodule on physical exam, and diagnosis requires skin punch biopsy. Direct skin invasion upgrades disease to at least stage IIIB and portends poor prognosis.

### **Nodal Evaluation**

The detection of lymph node involvement affects staging, treatment, and prognosis in breast cancer patients. The ability to accurately exclude axillary nodal disease preoperatively helps spare patients from the morbidity associated with axillary lymph node dissection (ALND). While ultrasound is traditionally the mainstay for evaluating axillary nodal involvement, it is operator dependent and unable to consistently assess higher axillary nodal levels II and III, supraclavicular and internal mammary lymph nodes, which are better visualized and more consistently assessed by MRI given its wider field of view. Adding MRI to ultrasound has been found to reduce false negative rate, and increase negative predictive value (98 %) in evaluating level III axillary nodes (infraclavicular nodes), supraclavicular nodes, and internal mammary nodes [50].

MRI allows for the assessment of morphologic, signal intensity, and enhancement characteristics, which can help differentiate benign from metastatic lymph nodes. Features of pathologic lymph nodes on MRI include irregular nodal contour, high T2-weighted signal intensity, marked gadolinium enhancement, round fatty hila, and abnormal cortices [51]. A prospective study of 65 patients with invasive breast cancer found that early contrast enhancement, as defined by an

increase in signal intensity of >100 % on the first post contrast image obtained at 57 s after injection, was found to be both sensitive (83 %) and specific (90 %) for the detection of metastatic nodal involvement [52]. Quantitative features such as diffusion-weighted imaging (DWI) and dynamic contrast enhancement (DCE) are of questionable additional value in distinguishing benign from malignant lymph nodes [53, 54]. Fine needle aspiration and ultimately sentinel lymph node dissection (SLND) help further assess nodal involvement.

The traditional preoperative determination of axillary nodal involvement prompting axillary lymph node dissection (ALND) has been called into question by the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial [55], which found no benefit in performing ALND in patients with early stage T1/T2 invasive cancers and one or two positive sentinel lymph nodes treated with chemoradiation therapy, as compared to SLND. The implications of these results have been debated, and the short study follow-up (median 6.3 years) and small sample size have been criticized. Despite this controversy, because ALND does not routinely include higher axillary level II/III nodes, or internal mammary and supraclavicular nodes, MRI remains an important diagnostic tool in preoperative staging. Involvement of internal mammary and supraclavicular lymph nodes may not change surgical planning, but will alter radiation treatment parameters.

### **Controversies of Breast MR in Locoregional Disease Staging**

While superior sensitivity and diagnostic accuracy of MR are well established, improvement in clinical outcomes associated with preoperative MR is less clear.

### **Positive Margins and Re-excision Rates**

Surgical margins positive for tumor indicate failure of initial surgical excision to include the entire extent of disease, necessitating re-excision. The primary aim of a preoperative MRI is to improve disease extent assessment, allowing for better initial surgical success, thus minimizing re-excision. While preoperative MRI has been shown to alter surgical management [3, 56–58], there are mixed results on its impact on re-excision rates (Table 1). Multiple prior studies including two prospective trials (MONET and COMICE) showed preoperative MRI did not reduce re-excision rate. The MONET (MR mammography of non-palpable breast tumors) trial from the Netherlands included 418 patients with nonpalpable breast cancers diagnosed on mammography and ultrasound. This study showed an unexpectedly increased re-excision rate in patients with MRI (34 %) vs those without MRI (12 %) [64]. However, surgical bias in this study (wider surgical excision in

**Table 1** Impact of preoperative MRI on surgical outcomes based on index lesion histology

Study	Type of study	No. of MRI patients/total	Re-excision with MRI	Re-excision without MRI	P value	Initial mastectomy with MRI	Initial mastectomy without MRI	P value	Conversion to mastectomy with MRI	Conversion to mastectomy without MRI	P value	Summary	
Invasive lobular cancer	Retro	70/178	4.2 %	9.2 %	0.2	31.9 %	23.9 %	0.23	2.8 %	7.3 %	0.189	Decreased re-excision rates; no significant effect on mastectomy rates	
	Retro	99/267	5.0 %	14.9 %	0.01	45 %	46 %	0.753	7 %	23 %	0.013		
	Retro	92/178	11.3 %	9.0 %	0.32	37.7 %	30.3 %	0.12	8 %	9 %	0.401		
	Meta	417/766	10.9 %	18.0 %	0.031	31.1 %	24.9 %	0.056	12.4 %	16.4 %	0.22		
	Retro	396/1928	25.3 %	29.1 %	0.21	33.1 %	35.5 %	0.37	–	–	–		
All histologies	Retro	130/577	–	–	–	27.7 %	19.9 %	0.024	9.8 %	5.9 %	0.35	Equivocal impact on re-excision rates; increased initial mastectomy rates	
	RCT	816/1623	18.8 %	19.3 %	0.769	–	–	–	–	–	–		
	(COMICE)												
	Peters 2011 [64] (MONET)	RCT	207/418	34 %	12 %	0.008	–	–	–	14 %	0.49		
	Houssami 2013 [25]	Meta	1802/3112	11.6 %	11.4 %	0.71	16.4 %	8.1 %	<0.001	6.0 %	7.3 %		0.23
	Gonzalez 2014 [65 <sup>a</sup> ]	RCT	220/440	5 %	15 %	<0.001	–	–	–	20 %	10 %		0.024
	Chandwani 2014 [66]	Retro	304/609	18.1 %	20.3 %	0.484	38.2 %	33.1 %	0.194	–	–		–
	Patel 2015 [67]	Retro	96/250	7.1 %	25.0 %	<0.001	51.3 %	40.6 %	0.1	–	–		–
	Fancellu 2015 <sup>a</sup> [68]	Meta	1077/3252	41.6 %	40.1 %	0.759	27.6 %	18.2 %	0.012	13.9 %	11.5 %		0.340

Retro retrospective study, Meta meta-analysis, RCT randomized control trial

<sup>a</sup> Meta-analysis including only patients with DCIS

patients without MRI compared to those with MRI) may have masked any benefit from MRI, and could potentially account for the paradoxically increased re-excision rate. The COMICE (Comparative Effectiveness of MRI in Breast Cancer) trial, a multicenter study that included 1623 patients from the UK, also demonstrated no reduction in re-excision rate with preoperative MRI [63]. This study was performed before MRI-guided localization and biopsy were routinely available, and not all suspicious findings were biopsied prior to excision, therefore likely overdiagnosing the need for additional surgery [33]. Moreover, very wide surgical excisions routinely implemented in the UK as a result of national benchmark for low re-excision rates (mandated to fall below 10 %) likely masked any potential benefit of preoperative MRI.

Recent studies have shown more favorable results, demonstrating decreased re-excision rates with preoperative MRI [65, 67, 69–71], while other studies continue to show the contrary [62, 68]. The inconsistencies in the data are confounded by surgical bias, which is a major challenge in breast imaging research, highlighting the need for standardization and collaboration across specialties.

### Mastectomy Rates

Preoperative MRI has been shown to be correlated with an increased rate of mastectomy in multiple studies [17, 25, 26, 62, 65, 66], including in a meta-analysis of 3112 patients with all histologic types of breast cancer which showed increased initial and overall mastectomy rate in those who underwent preoperative MRI [25] (Table 1). The upward trend of mastectomy in patients diagnosed with breast cancer, however, is not attributed to preoperative MRI alone. There is evidence that multiple other factors such as improved ability to identify high-risk women, better understanding of post radiation changes, further advancement in oncoplastic techniques allowing superior cosmetic results, and patient empowerment and choice, all contribute to the decision to choose mastectomy [72]. In addition, there is evidence that in the setting of preoperative MRI diagnosing additional foci of disease, the majority of surgical conversion from BCT to mastectomy is appropriate (8.3 %) [17] versus inappropriate based on false-positive findings (1.1–1.7 %) [16, 17].

### Overestimation of Disease

Although the majority of the existing literature supports high accuracy of MRI in tumor size estimation, several studies have demonstrated a tendency of MRI to overestimate disease [3, 4, 6, 22–24]. Berg et al. found that the addition of MRI to preoperative planning resulted in overestimation of extend of disease in 21 % of cases, compared to 3.1 % cases with clinical breast exam (CBE) and mammography, and 12 % with CBE, mammography, and ultrasound [3]. This is not entirely

unexpected, given high sensitivity but moderate specificity of MRI. Overestimation may be due to enhancement of a number of benign structures such as normal surrounding fibroglandular tissue, fibrocystic disease, or fat necrosis [73]. Tumor size overestimation has been shown to be more common in larger tumors (size >2 cm) [4, 6], and less common in high-grade tumors [13, 37, 39, 74]. The possibility of disease overestimation on MRI underscores the importance of tissue sampling for confirmation. Although additional potentially unnecessary biopsies are associated with unintended negative psychosocial stigma, MRI remains highly effective in excluding significant disease (high negative predictive value).

### Recurrence and Disease-Free Survival

Actual implications of having a preoperative MRI on breast cancer patient prognosis and long-term survival are much less clear. The effect of preoperative MRI on recurrence rates and overall disease-free survival has not been well established in the literature due to a lack of long-term outcome data (Table 2). A recent meta-analysis by Houssami et al. showed that preoperative MRI did not affect local or distant recurrence rates [76]. Other recent retrospective studies [71, 75, 77, 78] yielded similar results. A study of 2321 women with DCIS found that the use of MRI afforded no benefit in long-term locoregional recurrence or in the development of contralateral cancer at 8 years [77]. The lack of demonstrable survival benefits may in part reflect the fact that small volume additional disease detected on MRI may be adequately treated by whole-breast radiation therapy (WBRT) following BCT with or without MRI.

Other more recent studies have suggested that preoperative MRI provided a benefit in recurrence rate and disease-free survival, including a study of 398 patients with early-stage triple-negative breast cancers, which found that the absence of preoperative MRI was associated with an increased risk of recurrence [79, 80]. In particular, there is evidence that contralateral breast cancer recurrence is reduced with MRI [78, 80].

### Treatment Delay

Performing preoperative MRI may delay definitive treatment. Studies reported significant treatment delay of 12.2 to 22.4 days due to additional workup prompted by preoperative MRI [57, 62, 66]. On the other hand, a smaller retrospective study of 147 patients out of Ontario found no significant delay in treatment as a result of preoperative MRI [57]. The authors contributed the lack of delay to prompt performance of the MRI and post MRI workup in accordance with maximum wait time benchmarks set by the Ministry of Health. Similarly, prompt workup should be the goal of any facility offering

preoperative MRI to minimize harm, reduce patient anxiety, reduce cost, and optimize care.

## Subgroups Most Likely to Benefit From a Preoperative Breast MR

### Invasive Lobular Cancer

Invasive lobular cancer (ILC) is relatively occult on mammography due to its lepidic growth pattern, and associated with increased incidence of multifocal and contralateral disease [58, 59, 81–84]. MRI has shown improved sensitivity and superior tumor size estimation over clinical breast exam, mammography, and ultrasound for ILC. MRI is particularly beneficial in the ILC group in detecting additional foci of disease, both in the ipsilateral and in the contralateral breast [18, 83–85]. In turn, changes in surgical management based on preoperative MRI findings have been greater in ILC than in other histologic subtypes [56, 58, 83, 84]. Overall surgical outcomes in ILC are improved by performing a preoperative MRI. Whereas data on re-excision rates are equivocal for all histologic types, multiple studies have shown lower re-excision rates in ILC following BCT [25, 59, 61, 86]. However, the detection of more foci of disease by MRI seems to be associated with a higher rates of initial mastectomy as more patients are found not to be candidates for BCT [25, 60]. Although the data for diagnostic accuracy and clinical outcomes are still not unanimous, overall findings suggest preoperative MRI to be of benefit in the setting of ILC.

### Occult Primary Breast Cancer

In the rare instance that axillary nodal metastasis presents without clinical or imaging evidence of primary tumor, patients may ultimately undergo axillary lymph node dissection with mastectomy or whole-breast radiation (WBRT). MRI has an important role in diagnostic workup in these patients, as the identification of a primary tumor may allow for conversion to BCT. A meta-analysis by de Bresser, et al. reviewed 8 studies including 220 women with occult breast cancer [87]. Overall, MRI was able to identify a suspicious lesion in an average of 72 % of patients, yielding an overall sensitivity of 90 %. However, as in other clinical settings, specificity of MRI was considerably lower at 31 %, highlighting the utility of MRI as a negative predictive study [87]. The successful identification of an otherwise occult primary cancer allowed for the conversion to BCT in an average of 35 % of women.

### Elevated Risk Patients

Patients at elevated risks for breast cancer, including those with genetic mutations, personal and family history of breast cancer, and childhood chest radiation, may benefit from a

**Table 2** Impact of preoperative MRI on locoregional recurrence and disease-free survival

Study	Type of study	No MRI/total	Path of index lesion	Length of follow-up (years)	LRR with MRI	LRR without MRI	P value	Disease-free survival benefit of MRI (P value) <sup>b</sup>	Summary
Ko 2013 [75]	Retro	229/615	Invasive or in situ	5.7	6.1 %	6.3 %	1.0	–	Equivocal impact on locoregional recurrence and disease free survival
Houssami 2014 [76•]	Meta	1347/3169	Invasive or in situ	2.9	1.8 %	2.2 %	0.88	0.87	
Sung 2014 [71]	Retro	174/348	Invasive or in situ	8	12 %	17 %	0.33	0.73	
Pilewskie 2014 [77]	Retro	596/2321	DCIS	4.9	8.5 %	7.2 %	0.52	–	
Yi 2015 [78]	Retro	97/194 <sup>a</sup>	Invasive or in situ	6.1	3.1 %	4.1 %	0.18	<0.001**	
Bae 2015 [79]	Retro	345/398	Invasive	6.1	13.6 %	30.1 %	0.006	<0.001	

Retro retrospective study, Meta meta-analysis, LRR locoregional recurrence

<sup>a</sup> Data presented from bilateral MRI imaging period

<sup>b</sup> Based on Kaplan- Meier survival analysis

\*\*Disease-free survival benefit due to reduction in contralateral disease recurrence

preoperative MRI, as they have a higher rate of synchronous ipsilateral and contralateral disease [18, 19, 88]. A prospective study by Lehman et al. of 171 elevated risk women who underwent screening mammography, US and MRI found that MRI had a higher diagnostic yield than mammography and US (3.5 % versus 1.2 % and 0.6 %, respectively), but also prompted a higher biopsy rate [89]. Additional studies confirmed the added sensitivity of MRI over other modalities in high/moderate risk surveillance [31, 90, 91]. While these studies included asymptomatic women in a screening setting, they highlighted the increased sensitivity of MRI in this group of patients. Importantly, there is no current evidence to show that the improved diagnostic performance of MRI in this setting results in a survival benefit.

### Dense Breasts

Mammographic breast density has been established as an independent marker for breast cancer risk [92, 93]. As in other groups of elevated risk patients as previously discussed, much of the data on MRI is derived from screening data such as the ACRIN (American College of Radiology Imaging Network) 6666 trial [94]. This multicenter study included 2809 high risk patients with dense breasts and found that the additional of MRI to screening mammogram and ultrasound provided a supplemental cancer yield of 14.7 cancers per 1000 screened, but also resulted in a higher false-positive rate. As a result of such screening data, dense breast legislation enacted in several states recommends the addition of screening ultrasound or MRI for women with dense breasts. Similarly, in studies of patients with previously diagnosed breast cancer, MRI provides increased detection sensitivity and identification of additional foci of disease over mammography in patients with dense breast tissue [3, 7, 95].

### Partial Breast Irradiation Candidacy

Standard protocol for BCT includes whole-breast radiation (WBRT) following lumpectomy. In select patients, partial breast irradiation (PBI) may be offered as an alternative regimen. The American Society for Radiation Oncology defines a “suitable” candidate for PBI as a patient with a small unifocal unicentric tumor (<2 cm) [96]. PBI offers the benefit of limiting nontarget radiation to adjacent organs such as the heart and lung and minimizes the time course of treatment to 5 days as compared to the standard 5–6 weeks required for WBRT. Since PBI only treats a portion of the breast tissue at the site of the primary tumor, lack of additional disease must be established to ensure adequate treatment. Given high sensitivity and high negative predictive value, MRI is the perfect test to confirm unifocal disease in a PBI candidate. A prospective study by Dorn et al. of 521 patients found preoperative MRI changed eligibility in 13 % of patients screened for PBI,

suggesting MRI to be an important step in preoperative assessment to establish PBI candidacy [97].

## Conclusions

Breast MRI is superior in assessing tumor size and extent, optimizing treatment planning. Although the role of MRI in routine preoperative assessment of newly diagnosed breast cancer is not entirely clear, it has been shown to be of benefit in certain subgroups of women. While current data on preoperative MRI do not show a benefit in decreasing repeat surgery or increasing survival, more positive results have emerged in recent studies, and further data is needed. Meanwhile, the decision of whether or not to pursue a preoperative MRI continues to be one made on a patient by patient basis.

## Compliance with Ethical Standards

**Conflict of Interest** Marissa Albert, Yiming Gao, and Linda Moy declare that they have no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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