Chapter 4
MRI and Preoperative Staging in Women Newly Diagnosed with Breast Cancer

Su-Ju Lee and Mary C. Mahoney

Abstract Breast magnetic resonance imaging (MRI) is well established as the most sensitive and accurate imaging modality for local-regional staging of breast cancer. It is superior to clinical examination, mammography and ultrasound, alone or combined, in delineation of size and extent of tumor, additional sites of disease, pectoralis muscle and chest wall invasion, nipple and skin involvement, as well as lymph node metastasis. However, the use of MRI for staging of newly diagnosed breast cancer has been a subject of intense debate, because the expected clinical benefits of improved staging by MRI have been called into question. The clinical outcome literature on the benefits of preoperative MRI shows conflicting results regarding re-excision rates and local recurrence rates, and the data do not support a benefit on long-term survival. There are also concerns that preoperative MRI causes delayed definitive therapy and increased mastectomy rates. This chapter details the advantages of MRI staging of newly diagnosed breast cancer, discusses the benefit of MRI staging for a subset of patients and certain clinical scenarios, and reviews the current literature with respect to the pros and cons of MRI staging.

Keywords Breast MRI • Breast cancer staging • MRI staging • Benefits of preoperative breast MRI • Size and extent of disease • Multifocal/multicentric disease • Contralateral disease • Regional lymph node staging • Surgical planning • Re-excision rate • Mastectomy rate • Utility in clinical scenarios

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Abbreviations

ADC	Apparent diffusion coefficient
AJCC	American Joint Committee on Cancer
ALND	Axillary lymph node dissection
BCT	Breast conservation therapy
BPE	Background parenchymal enhancement
DCIS	Ductal carcinoma in situ
EIC	Extensive intraductal component
ER	Estrogen receptor
Her2	Human epidermal growth factor receptor 2
IBC	Inflammatory breast cancer
ILC	Invasive lobular cancer
IM	Internal mammary
MIP	Maximal-intensity projection
MLO	Mediolateral oblique
MRI	Magnetic resonance imaging
NAC	Nipple-areolar complex
NME	Nonmass enhancement
NSM	Nipple sparing mastectomy
PBI	Partial breast irradiation
PR	Progesterone receptor
SLNB	Sentinel lymph noe biopsy

4.1 Introduction

The TNM system developed by American Joint Committee on Cancer (AJCC) is routinely used for determination of prognosis and treatment options for breast cancer (see Tables 4.1, 4.2, 4.3, and 4.4) [1]. The TNM system categorizes the stage of disease based on data from the primary tumor (T), regional lymph nodes (N), and distant metastases (M). Prior to the advent of breast magnetic resonance imaging (MRI), clinical staging and treatment planning for newly diagnosed breast cancer were based on clinical examination, mammography, and ultrasound. This is then replaced by pathologic staging after resection of the primary tumor and lymph node sampling. Breast cancer biologic markers, including estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) also play a role in treatment planning.

Breast MRI is the most sensitive and accurate imaging modality for local-regional staging of breast cancer [2–7]. It is superior to clinical examination,

Table 4.1 The American Joint Committee on Cancer staging system: breast primary tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
Tis (Paget's)	Paget's disease of the nipple not associated with invasive carcinoma or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma
T1	Tumor ≤20 mm in greatest dimension
T1mi	Tumor ≤1 mm in greatest dimension
T1a	Tumor >1 mm but ≤5 mm in greatest dimension
T1b	Tumor >5 mm but ≤10 mm in greatest dimension
T1c	Tumor >10 mm but ≤20 mm in greatest dimension
T2	Tumor >20 mm but ≤50 mm in greatest dimension
T3	Tumor >50 mm in greatest dimension
T4	Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules) Note: Invasion of the dermis alone does not qualify as T4
T4a	Extension to the chest wall, not including only pectoralis muscle adherence/invasion
T4b	Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma
T4c	Both T4a and T4b
T4d	Inflammatory carcinoma

Source: Edge et al. [1] (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois)

mammography and ultrasound, alone or combined, in delineation of the size and extent of tumor, additional sites of disease, pectoralis muscle and chest wall invasion, nipple and skin involvement, as well as lymph node metastasis. The ability of MRI to assess the size and extent of the index tumor and to identify additional, otherwise occult disease of the index and contralateral breasts has added sensitivity and complexity to clinical staging and surgical planning.

4.2 Size and Extent of Index Tumor

All published studies show that breast MRI is the most accurate imaging tool for evaluation of the size and extent of breast tumor [2–7]. Lesion size as determined by MRI correlates best with the pathologic size assessment among all imaging modalities (Fig. 4.1), although overestimation and underestimation do occur. MRI may

Table 4.2 The American Joint Committee on Cancer staging system: breast regional lymph nodes (N)

Clinical	
NX	Regional lymph nodes cannot be assessed (e.g. previously removed)
N0	No regional lymph node metastases
N1	Metastases to movable ipsilateral level I, II axillary lymph node(s)
N2	Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detected[a] ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases
N2a	Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures
N2b	Metastases only in clinically detected[a] ipsilateral internal mammary nodes and in the absence of clinically evident level I, II axillary lymph node metastases
N3	Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; Or in clinically detected[a] ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; Or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
N3a	Metastases in ipsilateral infraclavicular lymph node(s)
N3b	Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
N3c	Metastases in ipsilateral supraclavicular lymph node(s)

Source: Edge et al. [1] (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois)

[a]*Clinically detected* is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration biopsy with cytologic examination

Table 4.3 The American Joint Committee on Cancer staging system: breast distant metastases (M)

Mo	No clinical or radiographic evidence of distant metastases
cM0(i+)	No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells in circulating blood, bone marrow, or other nonregional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastases
M1	Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm

Source: Edge et al. [1] (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois)

overestimate tumor size (by greater than 5 mm) in up to 35 % of cases and underestimate size in 13 % of cases [5, 6]. The causes of over- or under-estimation have yet to be defined. Some studies suggest that MRI tumor size correlates better with pathologic measurement with high-grade invasive tumor and high-grade ductal carcinoma in-situ (DCIS), and tends to underestimate size in low-grade tumors [8, 9]. However, a recent report showed high-grade tumor and DCIS to be the strongest negative factors resulting in overestimation of tumor size on MRI [10]. There is a greater tendency for tumor size overestimation when tumors are larger than 2 cm in

Table 4.4 The American Joint Committee on Cancer staging system: breast anatomic stage/prognostic groups

Stage	Tumor	Node	Metastasis
0	Tis	N0	M0
IA	T1[a]	N0	M0
IB	T0	N1mi	M0
	T1[a]	N1mi	M0
IIA	T0	N1[b]	M0
	T1[a]	N1[b]	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1[a]	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

Source: Edge et al. [1] (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois)

[a]T1 includes T1mi

[b]T0 and T1 tumors with nodal micrometastases only are excluded from Stage IIA and are classified as Stage IB disease

size [6, 10]. The MRI sequence on which the tumors are measured may also be a factor. A recent report suggests that index tumor size is best measured on T2 weighted images, whereas the whole extent of disease is best estimated on early-subtracted dynamic contrast enhanced T1 weighted images [11].

MRI is more accurate than mammography or ultrasound for detection of an intraductal component of an invasive cancer (Figs 4.2 and 4.3). However, it may overestimate this finding in 11–28 % and underestimate it in 17–28 % of cases [12–14]. Overestimation may be due to enhancement of normal glandular tissue, other coexisting benign entities, or lymphovascular invasion [15]. Since extensive intraductal component (EIC) is a contributing factor for positive surgical margins at breast conserving surgery, preoperative delineation of the extent of EIC is essential.

Contrary to early reports, MRI has been shown to be more sensitive in detection of DCIS than mammography and ultrasound (Fig. 4.4). This is largely attributable to a greater emphasis on high spatial resolution over high temporal resolution in MRI technique [16]. Reported MRI sensitivity for DCIS in the more recent literature is 79–97 %, compared with only 52–56 % by mammography. The sensitivity reaches 98 % in high-grade or comedo type DCIS [16, 17]. Several recent studies investigated the utility of MRI in the detection of invasive component in DCIS diag-

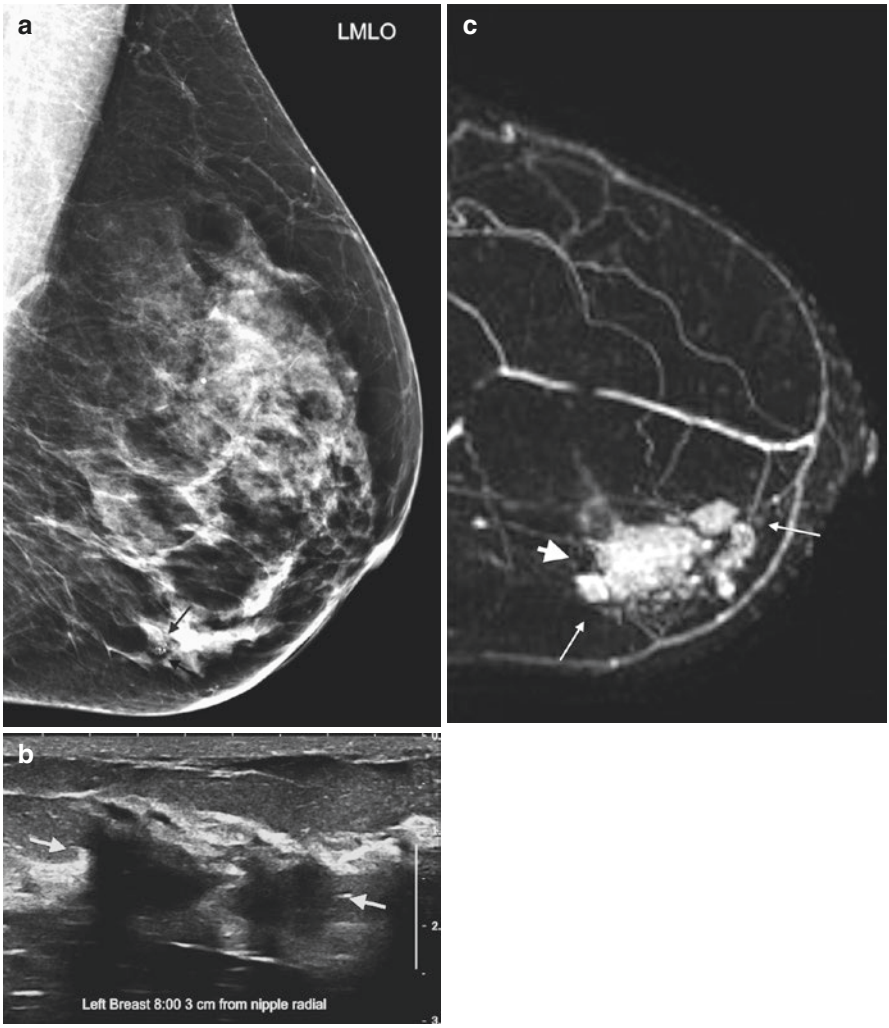

Fig. 4.1 Clinical stage IIA, T2N0M0 tumor in a 52-year-old with a palpable mass in the left breast and discordant tumor size between breast examination, mammography, and ultrasound. (**a**) Left mediolateral oblique view (MLO) mammogram reveals a small group of microcalcifications (*black arrow*). Biopsy revealed invasive lobular carcinoma. (**b**) Ultrasound of the left breast at the biopsy site shows two adjacent irregular hypoechoic masses, measuring 2.7 × 1.5 cm in aggregate. (**c**) Sagittal post contrast T1-weighted maximal-intensity projection (MIP) MR image reveals an irregular enhancing mass, 3.7 × 2.5 × 2.0 cm in size (between *arrows*). *Arrowhead* denotes focal susceptibility artifact caused by a tissue marker at the site of microcalcifications. Histopathology confirmed the large tumor size

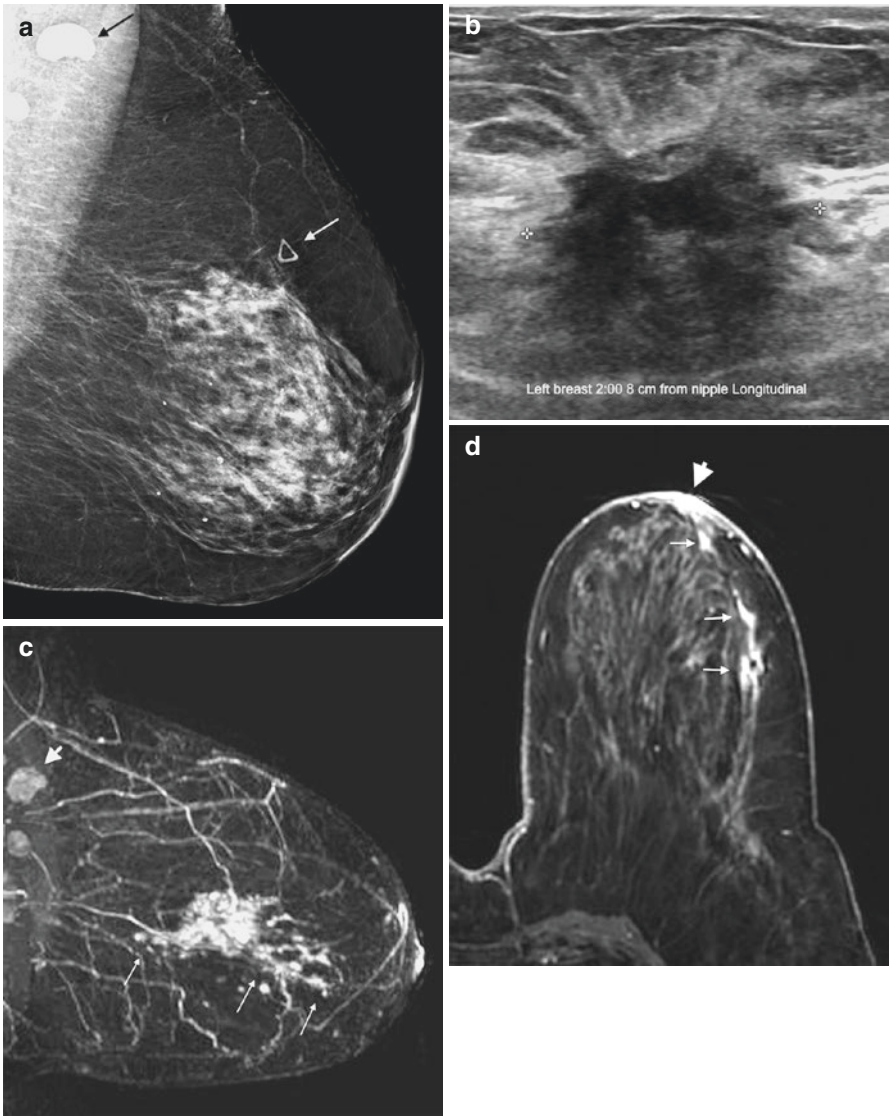

Fig. 4.2 Clinical stage IIIA, T3N1M0 tumor in a 72-year-old with extensive intraductal component (EIC) and unsuspected nipple involvement. (**a**) Left MLO view mammogram shows heterogeneously dense breast tissue with a triangular marker (*white arrow*) indicating a palpable mass. The mass is not visible on mammography. An abnormal high-density axillary lymph node is visible (*black arrow*). (**b**) Ultrasound of the palpable mass reveals a 2.7 cm irregular mass. Ultrasound guided biopsy confirmed invasive ductal carcinoma. Fine needle aspiration of the suspicious lymph node was positive for metastasis. (**c**) Sagittal post contrast T1 MIP MR image demonstrates an irregular enhancing mass corresponding to the known invasive cancer, with nonmass enhancement (*long arrows*) extending from the mass both anteriorly and posteriorly, consistent with EIC. The maximal anteroposterior extent of the tumor is 12 cm. Note the metastatic node with loss of fatty hilum (*arrowhead*). (**d**) Axial post contrast fat-saturated T1 MR image reveals nonmass enhancement in a ductal distribution (*short arrows*) extending to the nipple, with enhancement of the nipple-areolar complex (NAC) (*arrowhead*) consistent with tumor invasion

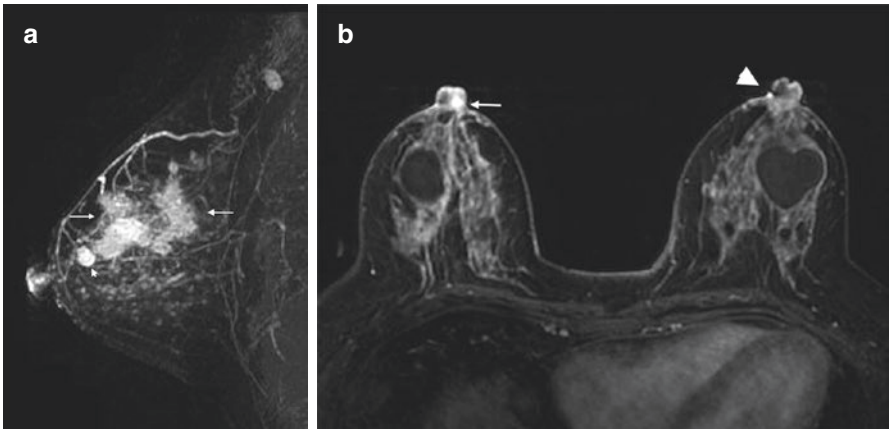

Fig. 4.3 Clinical stage IIIA, T3N1M0 tumor in a 42-year-old woman with multicentric right breast cancer, EIC, and nipple involvement. (**a**) Sagittal post contrast subtraction T1 MIP MR image of the right breast shows a small known invasive tumor (*arrowhead*) and extensive nonmass enhancement consistent with EIC, involving the upper outer and upper inner quadrants (between *arrows*). There is a metastatic lymph node in the axilla. (**b**) Bilateral axial post contrast fat-saturated T1 MR image demonstrates nodular enhancement in the right nipple (*arrow*), compared to non-enhancement of the left nipple. The focal signal abnormality in the left nipple (*arrowhead*) is an artifact

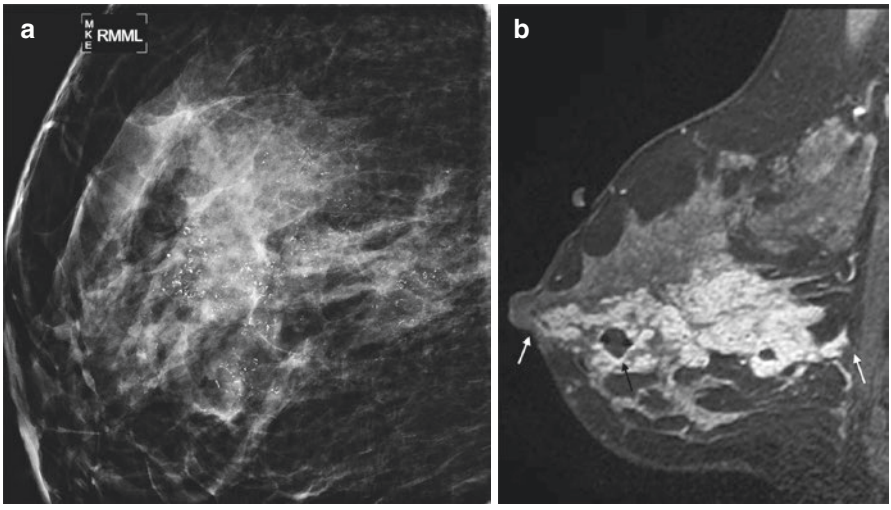

Fig. 4.4 Clinical stage 0, TisN0M0 tumor in a 39-year-old woman with extensive DCIS. (**a**) Spot magnification mediolateral view mammogram of the right breast demonstrates dense breast tissue with extensive pleomorphic microcalcifications that did not extend to the nipple. Biopsy confirmed high grade DCIS. (**b**) Sagittal post contrast fat-saturated T1 MR image shows extensive clumped nonmass enhancement. The tumor extends to within 2 mm of the nipple anteriorly and 3 mm of the pectoral muscle posteriorly (*white arrows*). A small hematoma from biopsy is present (*black arrow*). The patient is not an appropriate candidate for nipple-sparing mastectomy because the close proximity of tumor to the nipple suggests occult nipple invasion

nosed on needle biopsies. The presence of a mass, rapid initial enhancement, washout kinetics, larger lesion size, higher lesion to background signal intensity ratios, higher number of tissue cores involved by tumor nests, and lower apparent diffusion coefficient (ADC) values have been linked to the presence of occult invasion [18–20].

4.3 Additional Sites of Disease

Multifocal disease is defined as two or more tumor foci in the same quadrant of the breast (Fig. 4.5). Multicentric disease is a condition with two or more tumor foci in different quadrants of the breast (Fig. 4.6). Although TNM staging system does not

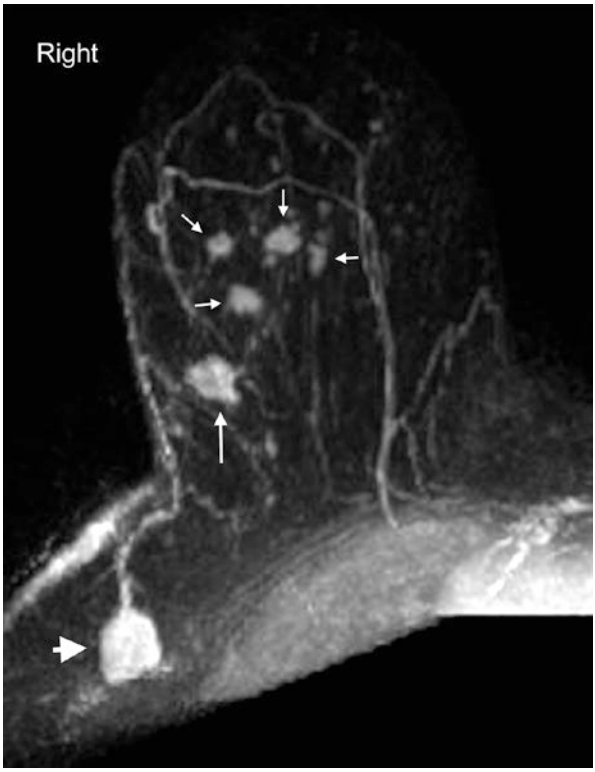

Fig. 4.5 Clinical stage IIA, T1N1M0 tumor in a 52-year-old woman with multifocal carcinoma. Axial post contrast subtraction T1 MIP MR image of the right breast demonstrates multiple enhancing masses in the central and lateral aspects of right upper breast. The largest, 1.2 cm mass is a known invasive carcinoma (*long arrow*). Four additional tumors (*short arrows*) are seen anterior to it. An enlarged level I right axillary lymph node with loss of reniform shape and fatty hilum (*arrowhead*) was positive for metastatic disease on fine needle aspiration

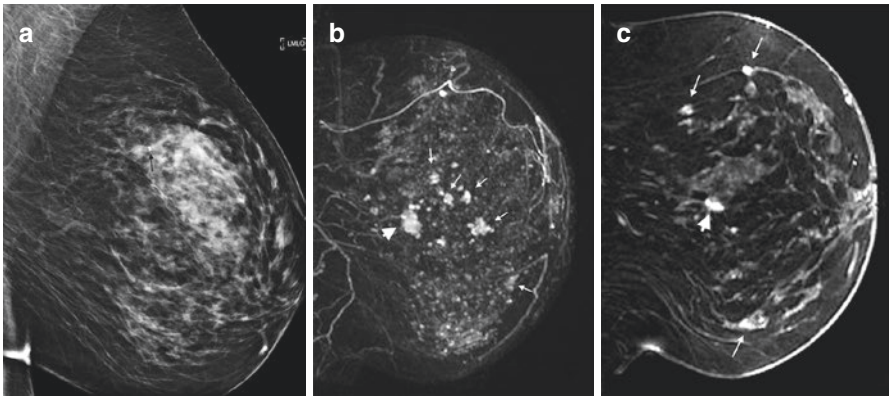

Fig. 4.6 Clinical stage IIA, T1N0M0 tumor in a 48-year-old woman with multicentric tumors. An architectural distortion on her screening mammogram led to the ultrasound biopsy of a 1.2 cm mass, which revealed invasive lobular carcinoma. (**a**) Left MLO view mammogram shows heterogeneously dense breast with a biopsy marker at the site of the index tumor (*black arrow*). No other suspicious abnormality is visible. (**b**) Sagittal post contrast T1 MIP MR image demonstrates the lobulated index mass (*arrowhead*) and multiple additional small irregular enhancing masses (*small arrows*). (**c**) Sagittal post contrast fat-saturated T1 MR image shows part of the known index tumor (*arrowhead*). Multiple tumors in different quadrants (*long arrows*) are better appreciated. Biopsies of two additional masses confirmed multicentric invasive lobular cancers

take these into consideration, the detection of additional sites of disease greatly impacts surgical management. While multifocal disease may be amenable to breast conservation, multicentric disease is usually treated with mastectomy. MRI is superior to conventional imaging for identifying additional cancer foci in the same breast as the index tumor, and in the opposite breast [21–26]. The preoperative identification of these additional tumor foci may alter surgical and radiation therapy. In a recent meta-analysis of 50 studies, Plana and associates found that preoperative MRI detected additional, otherwise occult, cancers in the ipsilateral breast in 20 % of cases, with a summary positive predictive value (PPV) of 67 % and accuracy of 93 %. The PPV increased to 75 % when MR scanner ≥1.5 T was used [23]. These results are similar to the findings of an earlier meta-analysis of 19 studies, showing detection of additional disease in 16 % of cases with a summary PPV of 66 % and accuracy of 86 % [24]. In this and another meta-analysis, MRI found additional cancer in the contralateral breast in 4.1–5.5 % of patients (Fig. 4.7) at the time of diagnosis [23, 25]. This is similar to the 3.1 % rate reported by the ACRIN 6667 multicenter prospective trial [26].

Many studies have examined the surgical impact of finding additional sites of disease. Plana's meta-analysis of 26 studies found an appropriate change in surgical management in 12.8 % of patients with confirmed additional malignancy, with 8.3 % of patients converted from breast conservation therapy (BCT) to mastectomy and 4.5 % receiving more extensive excision [23]. However, false positive cases resulted in inappropriate alteration in surgical treatment in 6.3 % of cases, including

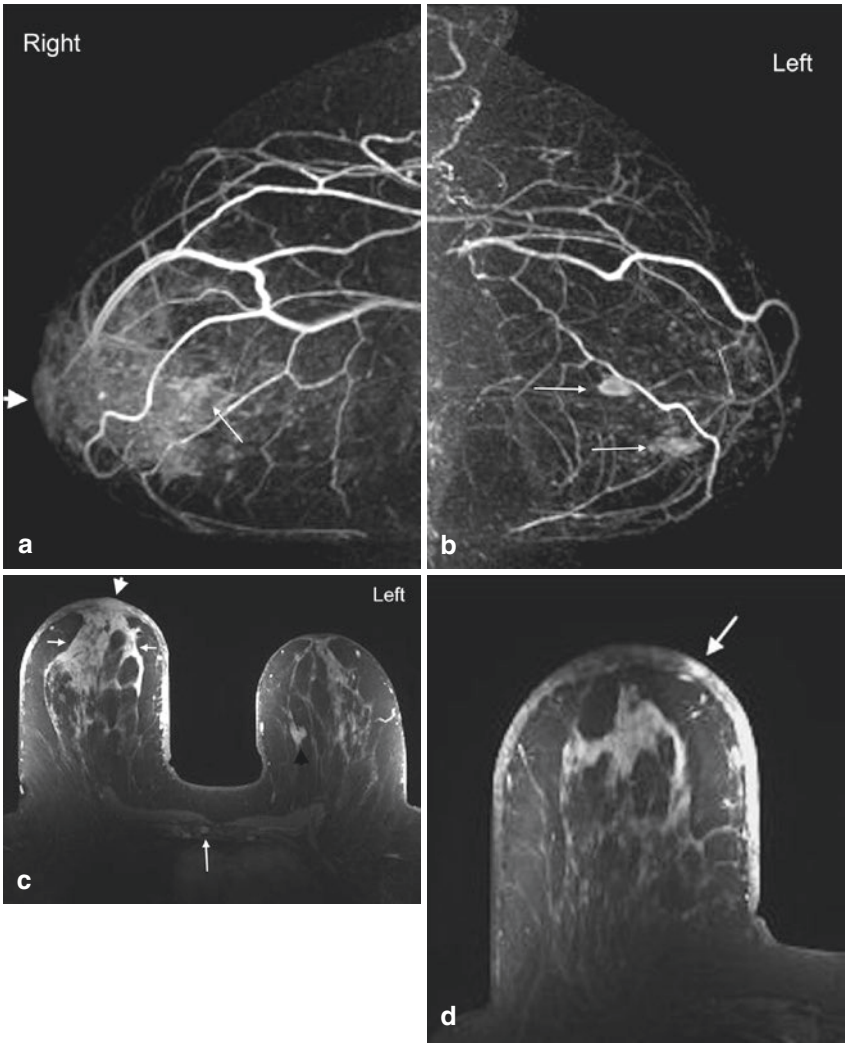

Fig. 4.7 Clinical stage IV, T4dN1M1 tumor in a 63-year-old woman with diffuse erythema of the right breast. Skin punch biopsy confirmed inflammatory breast cancer (IBC). Staging MRI showed contralateral left breast cancers and positive right axillary level I, II nodes. (**a**) Sagittal T1 MIP MR image of the right breast reveals extensive nonmass enhancement (between *arrow* and *arrowhead*) and enhancement of the nipple consistent with invasion (*arrowhead*). A partially obscured irregular mass is seen more posteriorly (*long arrow*). (**b**) Sagittal T1 MIP MR image of the left breast shows two masses with heterogeneous enhancement. Biopsy confirmed both to be invasive ductal carcinoma. (**c**) Bilateral axial post contrast fat-saturated T1 MR image demonstrates asymmetric enlargement of the right breast with diffuse thickening and heterogeneous enhancement of the skin. Nipple invasion (*white arrowhead*) and extensive subareolar nonmass enhancement (between *short arrows*) are obvious. An enhancing mass is seen in the left breast (*black arrowhead*). An enhancing focus in the right sternum (*long white arrow*) was positive on PET/CT scan, consistent with distant metastasis. (**d**) Axial post contrast fat-saturated T1 MR image of the right breast demonstrates enhancing nodule in the skin (*arrow*) caused by dermal lymphatic embolus (the "punched out" lesion). Diffuse thickening and heterogeneous enhancement of the skin are evident

1.7 % undergoing mastectomy and 4.6 % receiving more extensive excision [23]. These results parallel the findings of another meta-analysis, which showed a 1.1 % conversion rate to mastectomy and a 5.5 % rate of more extensive surgery due to false positive MRI [24]. The false positive cases illustrate the importance of histologic confirmation of suspicious MRI findings before performing more extensive surgery.

Occasionally, additional tumor may be present, but not detected by MRI. These false negative cases may be caused by non-enhancing tumor or obscuration by moderate to marked background parenchymal enhancement (BPE) of normal tissue [2, 27, 28]. BPE is mediated by hormonal activity, and is not correlated with mammographic density [28]. Attempts should be made to schedule breast MRI during the second week of the menstrual cycle or discontinuing exogenous hormone therapy for several months before MRI to reduce BPE. However, to avoid delay in therapy, this is not possible in patients newly diagnosed with breast cancer.

4.4 Pectoral Muscle and Chest Wall Involvement

Knowledge of pectoral or chest wall invasion by breast cancer prior to surgery is important, because of its impact on tumor staging, surgical planning and overall therapeutic approach. Chest wall invasion is defined as tumor infiltration of ribs, intercostal muscles and/or serratus anterior muscle [29]. Breast tumor with chest wall invasion is considered locally advanced disease with a tumor classification of T4a and a minimum TNM stage of IIIB with a 5-year survival rate of 23 % [30, 31]. Breast tumor with chest wall invasion may require neoadjuvant chemotherapy, with or without chest wall radiation, followed by more extensive surgery including chest wall resection [30, 31]. A tumor that invades only the pectoral muscle may require partial excision of the muscle if the invasion is superficial, or radical mastectomy with resection of the entire muscle if full thickness of the muscle is involved (Fig. 4.8) [30].

Evaluation of the pectoral muscle and chest wall underlying a posteriorly located breast tumor is usually limited on physical examination, mammography and ultrasound [30–32]. Far posterior tumors are difficult to include in the field of view on mammography. On sonography, the strong acoustic shadowing by breast cancer often obscures the underlying pectoral muscle. By contrast, the pectoral muscle and chest wall are well demonstrated on MRI (Fig. 4.9) [32]. Previous studies showed that contrast enhancement of the pectoral muscle or chest wall structures, either infiltrative or mass-like (Figs. 4.8 and 4.10a), are the only reliable MRI finding to predict invasion [32, 33]. Proximity of the tumor or violations of the fat plane alone are not sufficient evidence of muscle invasion (Fig. 4.11a) [32, 33]. Pectoral muscle enhancement caused by recent biopsy of nearby primary tumor is a known cause of false positive interpretation [33].

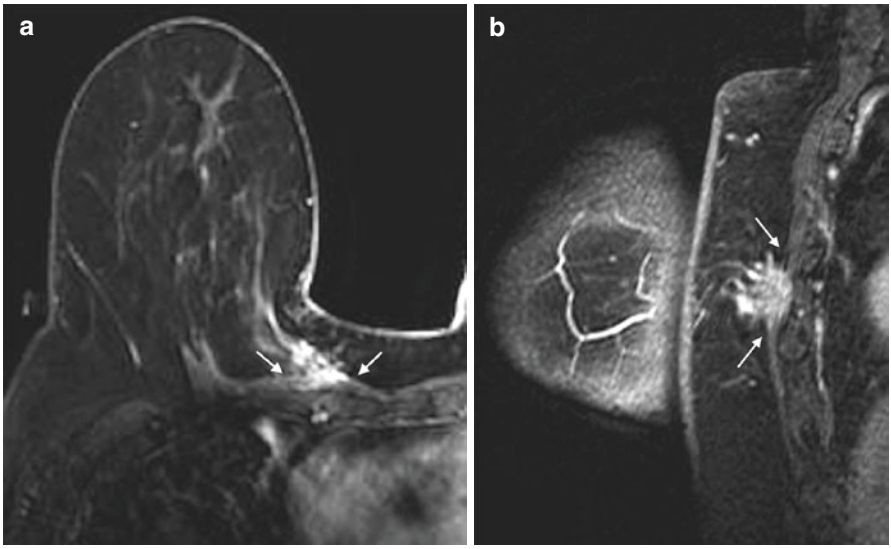

Fig. 4.8 Clinical stage IIA, T2N0M0 tumor in a 70-year-old woman with invasive ductal carcinoma of the right breast. (**a**) Axial post contrast fat-saturated T1 MR image demonstrates a posteriorly located tumor in the right breast with full thickness involvement of the pectoral muscle (between *arrows*). The tumor has a maximum dimension of 2.2 cm. (**b**) Sagittal post contrast fat-saturated T1 MR image shows the irregular mass invading the pectoral muscle (between *arrows*) without affecting the underlying intercostal muscles

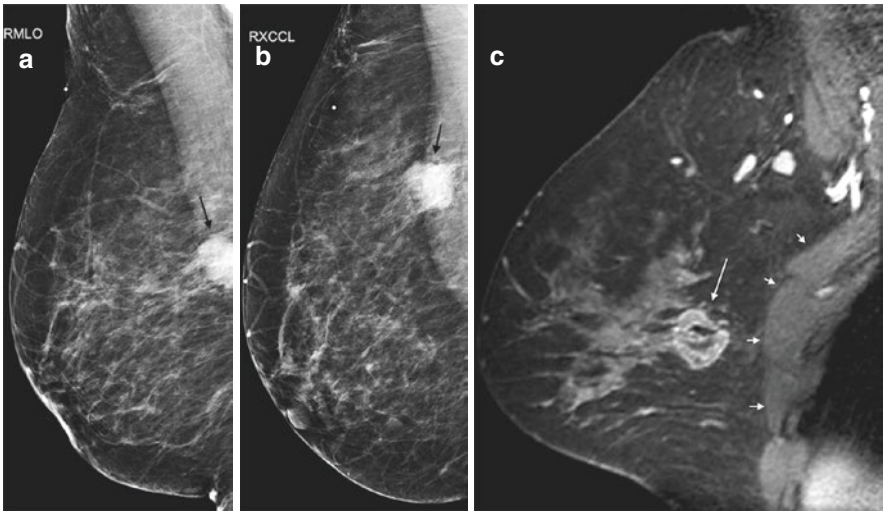

Fig. 4.9 Clinical stage IIA, T2N0M0 tumor in a 44-year-old woman with a posteriorly located invasive ductal carcinoma of the right breast. (**a**) Right MLO view mammogram demonstrates a 2.5 cm mass (*black arrow*) in the posterior breast, incompletely imaged and inseparable from pectoral muscle. A BB on the breast skin denotes a palpable mass. (**b**) On the laterally exaggerated CC view, the tumor again overlaps with the pectoral muscle. (**c**) Sagittal post contrast fat-saturated T1 MR image shows the mass (*long arrow*) not in close proximity or invading the pectoral muscle (*four small arrows*)

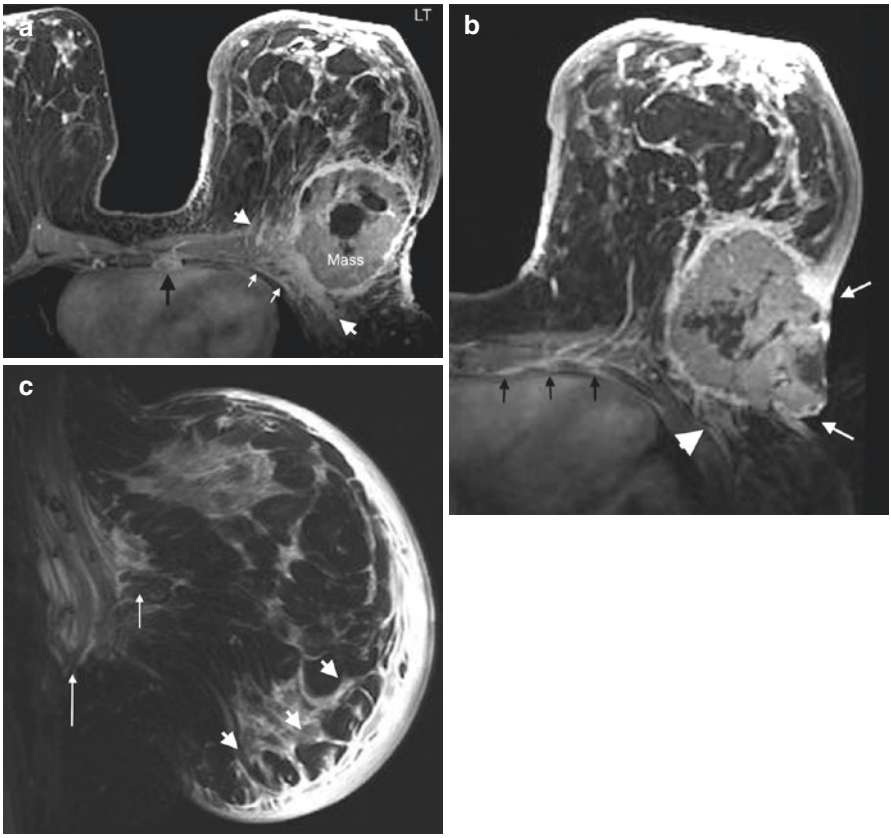

Fig. 4.10 Clinical stage IIIC, T4dN3Mx tumor in a 41-year-old woman with triple-negative invasive ductal carcinoma, and clinical evidence of inflammatory carcinoma of the left breast. (**a**) Axial post contrast fat-saturated T1 MR image demonstrates a 10 cm left breast mass with enhancement of the pectoral muscle, indicating invasion (between *arrowheads*). Enhancement of intercostal muscles and pleura (*small white arrows*) indicates chest wall invasion. An enlarged left internal mammary lymph node (*black arrow*) and palpable left axillary nodes constitute N3 nodal status. Diffuse thickening and enhancements of the skin and Cooper ligaments are consistent with inflammatory carcinoma. (**b**) Axial post contrast fat-saturated T1 MR image shows the locally advanced tumor invading the skin with ulceration (between *small white arrows*), the pectoral muscle (*arrowhead*) and the intercostal muscle (*black arrows*). (**c**) Sagittal fat-saturated T2 image demonstrates diffuse cutaneous and subcutaneous edema (*arrowheads*), prepectoral edema (*short arrow*), and intramuscular edema (*long arrow*). These are differential features in favor of IBC

4.5 Skin and Nipple Involvement

According to AJCC TNM system for clinical staging of breast cancer, ulceration and/or satellite nodules and/or edema (including peau d'orange) of the skin which do not meet the criteria for inflammatory carcinoma, are classified as T4b tumor, resulting in at least stage IIIB disease (Tables 4.1 and 4.4). Invasion of the dermis

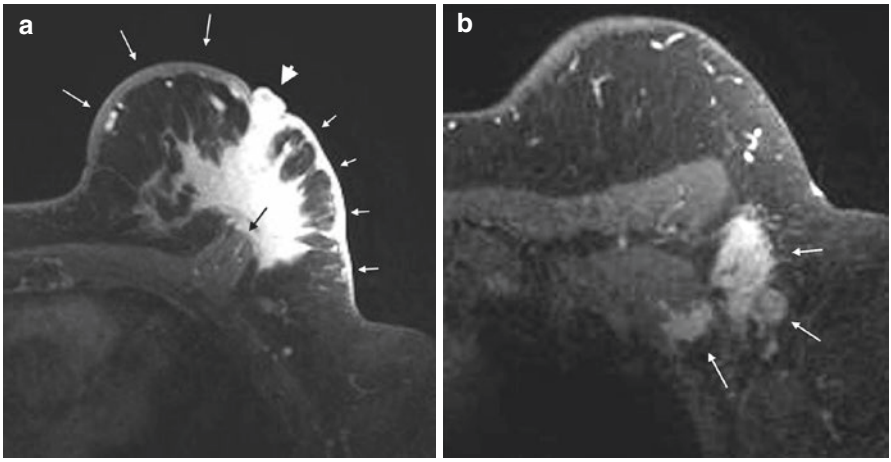

Fig. 4.11 Clinical stage IIIA, T3N2M0 tumor in a 54-year-old woman with a left breast mass and left nipple retraction. (**a**) Axial post contrast fat-saturated T1 MR image of the left breast reveals a large (7.1 cm) spiculated enhancing mass abutting the pectoral muscle (*black arrow*). Obliteration of the muscle fascia and tenting of the muscle are present, but there is no muscle enhancement to indicate invasion. Enhancement and retraction of the nipple (*arrowhead*) indicates nipple invasion. Diffuse thickening and enhancement of the skin in the lateral aspect of the breast (*four short arrows*) signal skin invasion by local extension. Skin thickening without enhancement in the medial breast (*three long arrows*) reflects lymph edema without invasion. (**b**) Axial post contrast fat-saturated T1 MR image more superiorly reveals three abnormal level I axillary nodes lying lateral to the pectoralis muscles. The two lateral nodes are matted to each other, while the medial node adheres to the pectoralis minor muscle. Note the loss of hilar fat in the nodes. Spiculated margins of the nodes suggest extracapsular tumor extension, which was confirmed by core biopsy

alone, without the above mentioned skin changes, does not meet the criteria of a T4 tumor (Table 4.1). On MRI, direct invasion of the skin appears as localized skin thickening and enhancement, which is contiguous with an underlying malignancy, with or without skin retraction (Fig. 4.11a). Skin edema, seen as areas of non-enhancing skin thickening (>3 mm) on MRI, may occur as a result of lymphatic obstruction, with or without malignant involvement (Fig. 4.11a). In later stages, enhancing skin nodules, masses, and ulceration are well demonstrated on MRI (Fig. 4.10b). When skin involvement by a locally advanced tumor is extensive, differentiating it from inflammatory carcinoma on clinical examination and MRI is difficult without a skin punch biopsy [34].

Preoperative evaluation of the nipple-areolar complex (NAC) is important for surgical planning because involvement of the NAC by tumor requires resection of the NAC and precludes patient from nipple-sparing mastectomy. Assessment of the NAC for tumor involvement on MRI may be difficult, because normal nipples may show various patterns of enhancement or no enhancement at all [28]. Sakamoto and colleagues found unilateral nipple enhancement continuous with the underlying index tumor to be highly suggestive of tumor involvement (Figs. 4.2, 4.3, 4.7 and 4.11) [35]. Characteristics of the nipple enhancement include diffuse enhancement, periareolar

skin enhancement, and rim or periductal enhancement within the nipple [35]. Nodular enhancement in the involved nipple is occasionally seen (Fig. 4.3b). Tumor size >2 cm and distance from the tumor edge to the NAC < 2 cm on MRI are statistically significant indicators for NAC involvement [36]. However, the tumor to NAC distance indicative of nipple involvement has been reported as <5 mm or <10 mm in other studies (Fig. 4.4) [37, 38]. Moon and associates found enhancement of the NAC itself to have higher predictive value for NAC invasion than short tumor to nipple distance [39].

4.6 Staging of Regional Lymph Nodes

Identification of regional nodal metastases is critical for staging, prognosis and treatment planning in patients with newly diagnosed breast cancer (Table 4.2). Regional lymph nodes include ipsilateral intramammary, axillary, internal mammary, and supraclavicular nodes.

The axilla is divided into 3 levels by the pectoralis minor muscle. Level I nodes are low axillary nodes lateral to pectoralis minor muscle, including the intramammary nodes (Fig. 4.12a). Level II nodes are mid-axillary nodes between the medial and lateral borders of the pectoralis minor muscle, including the Rotter nodes between the pectoralis major and minor muscles (Figs. 4.12b and 4.13a). Level III nodes are apical axillary nodes medial to the pectoralis minor muscle, i.e. the infraclavicular nodes (Fig. 4.12c). The internal mammary nodal chain runs along the margins of the sternum following the course of internal mammary artery and vein (Fig. 4.13b and 4.13c). The internal mammary (IM) nodes are found in the first through sixth intercostal spaces [40]. The supraclavicular nodes are located in the supraclavicular fossa.

The current 7th edition of the AJCC TNM staging system includes clinical and pathologic node staging schemes [1, 41]. The “clinical” scheme classifies “clinically detected” nodes, which are defined as nodes detected by clinical examination and imaging studies. The “pathologic” scheme classifies nodes identified with sentinel node biopsy or axillary node dissection. In the clinical scheme (Table 4.2), ipsilateral level I and II axillary nodes are N1 disease if movable, but become N2 disease when fixed to each other or adjacent structures (i.e. matted), which raises the stage to at least IIIA (Table 4.4). Metastases in the ipsilateral IM nodes in the absence of axillary node metastases are classified as N2 disease, but become N3 disease if the axillary nodes are also involved. Metastasis to the ipsilateral level III axillary (infraclavicular) or supraclavicular nodes indicates N3 disease, which raises the stage to at least IIIC. Metastases to cervical, contralateral internal mammary and contralateral axillary lymph nodes are considered distant metastases (M1 disease) and indicate stage IV disease (Table 4.4) [30]. Metastases to the IM nodes usually occur after a tumor has metastasized to the axilla (N3 disease). Isolated metastasis to the IM nodes is rare, occurring in only 1–5 % of breast cancers, usually from deep or medial lesions [41, 42]. Metastatic involvement of the IM nodes, without or with

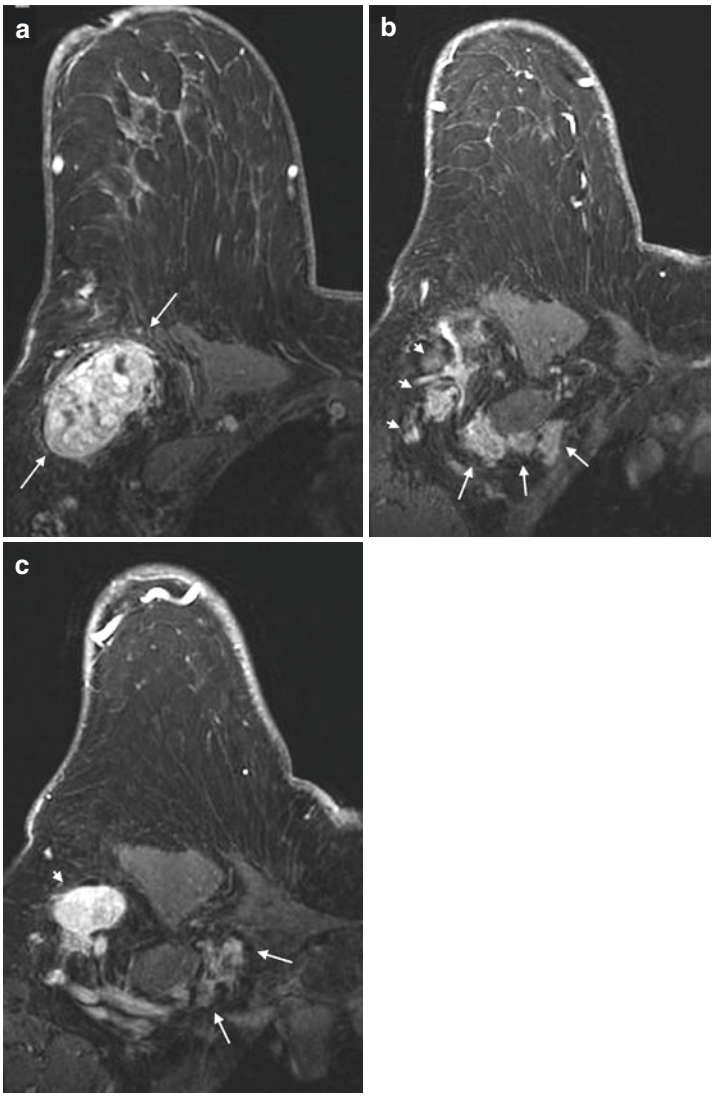

Fig. 4.12 Clinical stage IIIC, TxN3M0 tumor in a 75-year-old woman with right axillary lymphadenopathy and no apparent primary tumor on mammography and ultrasound. (**a**) Axial post contrast T1 fat-saturated MR image shows a large right axillary level I lymph node with heterogeneous enhancement, complete absence of hilar fat and perinodal stranding which may be due to recent biopsy or lymph edema. Biopsy of this node revealed poorly differentiated mammary carcinoma. (**b**) Axial image at a higher level reveals multiple level II nodes posterior to the pectoralis minor muscle (*long arrows*). Some level I nodes lying lateral to the pectoralis minor muscle are seen (*arrowheads*). All nodes show ill-defined margins suspicious for extranodal tumor extension. (**c**) Axial image at the level of infraclavicular fossa demonstrates matted level III lymph nodes medial to the pectoralis minor muscle (between *arrows*). An abnormal level I node is seen (*arrowhead*). No primary tumor is identified in either breast

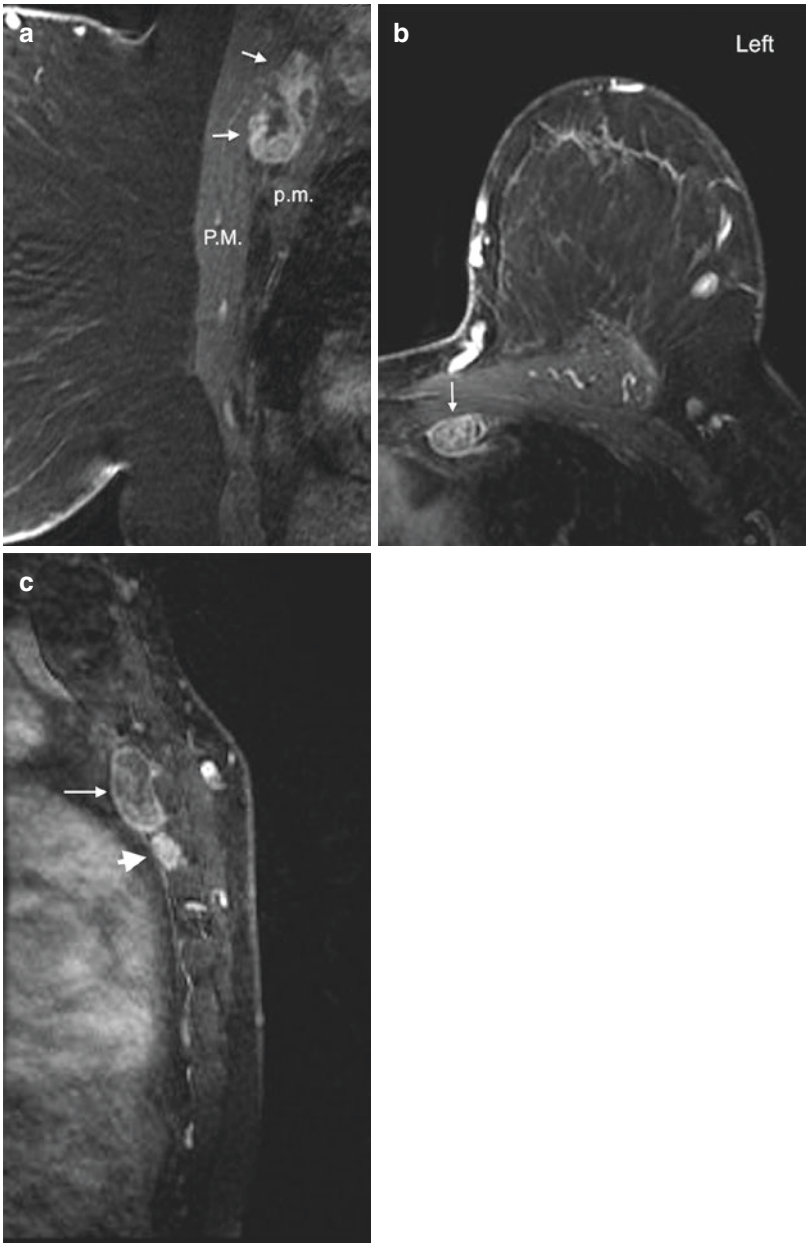

Fig. 4.13 Interpectoral node and internal mammary (IM) nodes. (**a**) Sagittal post contrast fat-saturated T1 image shows an enlarged lymph node (*arrows*) with heterogeneous enhancement between the pectoralis major (P.M.) and pectoralis minor (p.m.) muscles. The interpectoral node is also known as a Rotter node. (**b**) Axial post contrast fat-saturated T1 image of left breast in a different patient demonstrates an enlarged left IM node (*arrow*). (**c**) Sagittal post contrast T1 image of the same patient as in image (**b**) shows the IM node (*arrow*) along the sternal border. A second abnormal IM node is seen inferior to it (*arrowhead*)

axillary disease, carries a small but definite risk of local recurrence and reduced long-term survival [42]. Due to the morbidity involved, dissection of the internal mammary nodes is usually not performed. However, radiation treatment can be utilized to treat these nodes [41, 42].

In most institutions, ultrasound is the primary imaging modality for evaluation of axillary nodes, with moderate sensitivity and high specificity for detection of metastases, especially when morphologic criteria rather than size, are used for diagnosis [41, 43, 44]. However, the results are operator dependent and the evaluation of infraclavicular, supraclavicular and internal mammary nodes is not routinely performed. By contrast, regional lymph nodes, except for supraclavicular nodes, are included in the field of view on most routine breast MRI protocols. The ability of MRI to predict axillary nodal metastases is similar to ultrasound, with reported sensitivity of 36–88 % and specificity of 73–100 % [45–50]. MRI is less operator-dependent than ultrasound and provides a global view of both axillae and internal mammary chains. This may enhance the detection of potentially abnormal nodes and allows comparison with the contralateral axilla [41]. Occasionally, pulsation artifacts through the axilla may limit evaluation of the axillary nodes [41].

On non-contrast MRI, normal lymph nodes are reniform, circumscribed, with low signal intensity on T1-weighted and high signal intensity on T2-weighted sequences. Hilar fat is best seen on a T1-weighted non-contrast sequence without fat saturation, a sequence that should be included in the breast MRI protocol. Upon contrast injection, the normal lymph nodes enhance rapidly and homogeneously with a type III wash out delayed kinetics. Hence, the enhancement kinetics are not useful in differentiating benign and metastatic lymph nodes. Like ultrasound, nodal size alone is not useful for identifying metastatic nodes on MRI [41]. Morphologic features on MRI that suggest a nodal metastasis include: round shape or a long axis to short axis ratio of less than two, loss of the fatty hilum, increased cortical thickness (>3 mm), eccentric or focal cortical thickening, irregular or spiculated margins, edema surrounding the nodes, and asymmetry of morphology of the nodes compared with the contralateral axilla [41, 50–53]. One study described “perifocal edema” (edema surrounding the lymph nodes) and “rim enhancement” (higher signal intensity in the periphery of the nodes) 11 min after contrast injection as the two features with 100 % positive predictive value for the detection of metastases [53]. IM nodes are more likely to contain a metastasis when 5 mm or larger in size [54]. Normal IM nodes are usually not visible on MRI. When visualized, they should be regarded as suspicious and reported [30].

Traditionally, preoperative identification of axillary nodal metastases will spare patients with invasive breast cancer an unnecessary sentinel lymph node biopsy (SLNB) and allow them to proceed directly to axillary lymph node dissection (ALND). In 2011, Giuliano and associates published the results of the American College of Surgeons Oncology Group (ACOSOG) Z0011 randomized trial [55]. This trial suggested that patients with T1 or T2 invasive breast cancer, no palpable nodes, and one or two positive sentinel nodes, who underwent lumpectomy with

negative margins, tangential whole-breast radiation, and systemic therapy, might not benefit from ALND [55]. While this finding is potentially practice changing, controversies exist about the relatively short median follow-up interval of 6.3 years and the number of patients enrolled. In light of the Z0011 results, some have questioned the role of imaging for preoperative axillary staging, expressing concerns that preoperative detection of axillary metastasis would prompt ALND for disease that could otherwise have been treated according to Z0011 protocol [56]. Many authors believe that imaging still plays an important role in the axillary staging, especially in identifying patients with N2 and N3 disease. Since nodal disease beyond levels I and II are not routinely included in an axillary dissection, identification of nodes in these higher N categories by imaging may affect initial staging and treatment planning. Two recent studies showed that MRI can predict metastatic disease in more than two sentinel nodes, thereby identifying patients who require further local-regional therapy beyond SLND [57, 58]. In the future, patients may undergo imaging for the purpose of excluding N2 or N3 disease, rather than for diagnosing axillary metastases [41].

4.7 Subsets of Newly Diagnosed Breast Cancer Patients Likely to Benefit from MRI Staging

Because of the ability of MRI to identify lesions that are occult on conventional imaging and to better define extent of disease, it is intuitive that MRI staging is particularly beneficial for a subset of patients with newly diagnosed breast cancer.

Patients with Invasive Lobular Cancer (ILC) ILC tends to present with multiple and bilateral tumor sites and is better detected with MRI than mammography. The reported sensitivity of MRI for detection of ILC, ranging from 93 % to 96 %, is significantly higher than the sensitivity of mammography, which is in the range of 34–81 % [2, 22, 59]. Further more, MRI is more accurate in assessing the extent of ILC than mammography, leading to lower re-excision rates for positive surgical margins [60, 61].

Patients at High-Risk for Developing Breast Cancer A study has shown that patients with genetic alterations (BRCA 1 and BRCA2 mutations) or a history of mantle chest radiation are also at high risk for multiple and bilateral breast cancers [62]. Patients with a family history of breast cancer may also benefit [22].

Patients with Dense Breast Tissue MRI is useful in women with mammographically dense breast, in which an additional cancer tends to be obscured [63]. However, some studies have found MRI staging to be equally beneficial in patients with non-dense breasts [21, 22, 64].

Patients with Posterior Breast Cancer As previously illustrated, MRI is very useful in the detection of pectoral muscle and chest wall invasion, which will impact surgical planning.

Patients with High Grade DCIS or Invasive Cancer with EIC As previously demonstrated, MRI has a higher sensitivity for detection of high grade DCIS, or EIC in an invasive cancer, compared to conventional imaging. Hence the extent of disease in these patients can be better defined with MRI.

Patients with Plans for Partial Breast Irradiation (PBI) PBI is increasingly used for treatment of early stage breast cancers. However, patients with multiple tumors are not fully treated with PBI and are not appropriate candidates. Several studies have demonstrated the benefit of preoperative MRI for appropriate selection of patients to undergo such therapy [65–68].

Patients with Plans for Nipple-Sparing Mastectomy (NSM) NSM is a skin-sparing mastectomy with preservation of the nipple-areolar complex to provide a good cosmetic outcome. Due to the increased cancer recurrence risk, patients with tumors invading the NAC or in close proximity to the NAC on MRI are not appropriate candidates for NSM. Conversely, a negative MRI showing no NAC involvement has a high negative predictive value, as only 2.2 % of these patients were found to have NAC involvement at surgery [69]. MRI is useful in patient selection for this procedure.

4.8 The Utility of MRI in Special Clinical Scenarios

4.8.1 Inflammatory Breast Cancer

Inflammatory breast cancer (IBC) is a rare, aggressive form of breast cancer, accounting for 1–4 % of all breast cancers [34]. As defined by AJCC, the diagnostic criteria for IBC include rapid onset of breast edema; and/or peau d'orange skin changes; and/or erythema of the breast; with or without an underlying palpable mass; duration of the symptoms no more than 6 months; skin edema occupying at least one third of the breast; and pathologic confirmation of invasive carcinoma [70]. The pathologic hallmark of IBC is tumor emboli obstructing the dermal lymphatics of the breast, although this is not a requisite for diagnosis [71].

IBC is classified as a T4d tumor regardless of the primary tumor size (Tables 4.1). The prognosis is poor, with an average survival of 12–36 months [17]. At the time of diagnosis, 55–85 % of patients have regional nodal metastases and 20 % have distant metastases [17]. The treatment for IBC is neoadjuvant chemotherapy, followed by mastectomy and chest wall radiation [71]. The role of breast imaging in IBC is to identify an underlying malignancy, guide biopsy, stage locoregional disease and monitor response to neoadjuvant chemotherapy [72].

MRI has shown superior sensitivity, in the range of 94–98 % for detection of a primary breast tumor in IBC, compared to sensitivities of 43–68 % for mammography and 94–95 % for ultrasound [73, 74]. One study reported the most frequent MRI features of IBC to be: an underlying primary breast lesion (98 %), global skin thickening (93 %), heterogeneous skin enhancement with or without nodular or irregular skin foci (84 %), breast and chest wall edema (78 %), and breast enlargement (68 %). The primary lesion may be a single mass, diffuse nonmass enhancement, or multiple masses that are confluent or interconnected by nonmass enhancement. Multicentric or multifocal disease is more common than a unifocal mass. The majority of the masses exhibited malignant features such as irregular margins, heterogeneous internal enhancement pattern, and delayed washout kinetics. In 79 % of the cases, the enhancing skin lesion showed persistent kinetics [74]. Two examples of these features are shown in Figs. 4.7 and 4.10. The most common histologic type involved in IBC is invasive ductal carcinoma (84 %), although poorly differentiated carcinoma (6 %) and invasive lobular carcinoma (5 %) are also found [74].

It is important to differentiate IBC from locally advanced breast cancer, because the treatments are different. While IBC is treated with mastectomy, patients with locally advanced breast cancer may be candidates for breast conservation after neoadjuvant chemotherapy [17]. IBC and locally advanced breast cancer have many overlapping features on MRI [34]. Some potential differentiating features in favor of IBC include: edema of the breast tissue, skin thickening, thickening and pathologic enhancement of Cooper ligaments, and the "punched-out sign" defined as initially strong focal enhancement of dermal or subcutaneous tissue, followed by slow-continuous enhancement of the surrounding skin (Figs. 4.7 and 4.10) [34].

A difficult clinical and imaging differential diagnosis of IBC is acute mastitis. Differentiation of these two entities with MRI remains challenging due to the significant overlap of morphology and enhancement kinetics [28]. Potential differentiating features in favor of IBC are: masses with a greater average size, T2 hypo intensity of masses, blooming phenomenon (decreasing sharpness of lesion borders on delayed images), infiltration or pathological enhancement of the pectoralis major muscle, perifocal edema, prepectoral and intramuscular pectoral edema, central and dorsal location of the malignant mass vs. the usual subareolar location of an abscess (Fig. 4.10) [75]. A histological punch skin biopsy is needed in cases of diagnostic uncertainty if clinical symptoms fail to improve after a trial of antibiotic therapy.

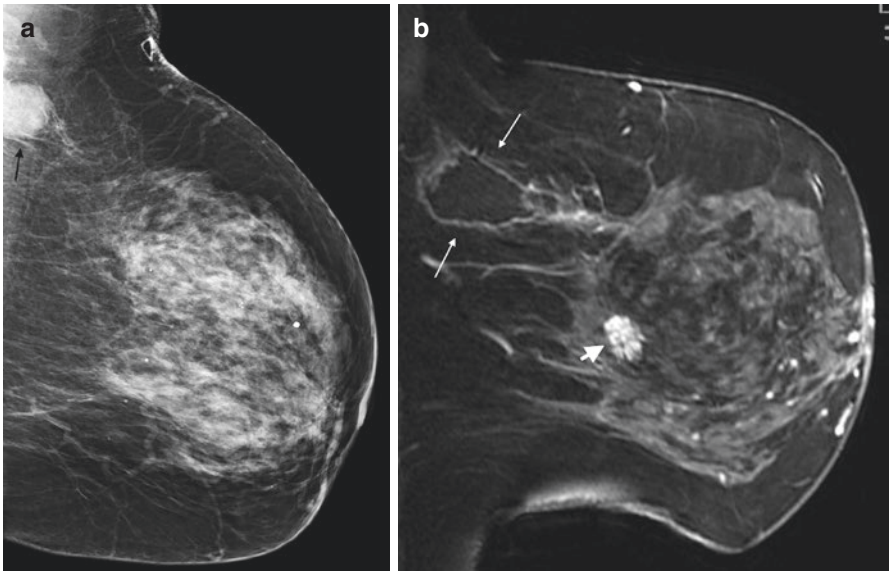

Fig. 4.14 Clinical stage IIA, T1N1M0 tumor in a 68-year-old woman with excisional biopsy of an enlarged left axillary lymph node, yielding metastatic carcinoma suggestive of a breast primary. (**a**) Left MLO view mammogram shows heterogeneously dense breast tissue with a partially visualized large high-density left axillary node (*black arrow*). No visible abnormality is identified in the breast. (**b**) Sagittal post contrast fat-saturated T1 image of left breast demonstrates a seroma at the site of lymph node excision (between *white arrows*). A 1.7 cm enhancing mass (*arrowhead*) is visualized in the central breast. Ultrasound guided biopsy revealed an invasive ductal carcinoma

4.8.2 Metastatic Axillary Lymphadenopathy of Unknown Primary Malignancy

Rarely, breast cancer may present as metastatic axillary lymphadenopathy without a known primary tumor (stage TXN1-2 M0). When a patient presents with unilateral axillary adenopathy, ultrasound guided lymph node sampling is indicated. In the event of nondiagnostic lymph node sampling, a surgical lymph node biopsy should be considered. If a malignant diagnosis suggestive of a breast primary is made, and no primary breast tumor is identified with clinical examination, mammography or ultrasound, breast MRI should be performed. The ability of MRI to identify occult primary breast cancer ranges from 62 to 86 %, with the primary tumor often less than 2 cm in size [76, 77]. The identification of the primary tumor by MRI offers patients the benefit of histologic diagnosis and biomarker evaluation (Fig. 4.14). This will provide information to guide targeted chemotherapy, hormonal treatment, and breast conservation surgery [30]. Otherwise, patients are treated with

mastectomy and axillary node dissection if the primary malignancy remains unknown. In one third of cases, a primary tumor may not be identified in the mastectomy specimen (Fig. 4.12). If treated with axillary dissection alone, a high percentage of these patients will develop ipsilateral breast cancer [78]. Recently, some patients are being treated with axillary dissection and whole breast radiation, without mastectomy. The data on the efficacy of this approach are limited, with two small studies showing a 5-year local recurrence rate of 15—16 % and 5-year survival rate of 72—75 %, compared to the rates of 13 and 79 %, respectively, in the mastectomy group [78, 79].

4.8.3 Paget's Disease of the Nipple with Negative Conventional Breast Imaging

Paget's disease of the breast is an uncommon form of breast cancer accounting for 1–3 % of all breast cancers [80, 81]. It is characterized by infiltration of the nipple epidermis by large malignant adenocarcinoma cells (Paget's cells) that contains abundant cytoplasm with large pleomorphic and hyperchromatic nuclei. Patients typically present with symptoms related to the nipple and areola characterized by eczema, scaling, crust formation, erosion or ulceration, without or with a palpable mass [80]. An underlying invasive carcinoma or ductal carcinoma in situ is identified in 82–94 % of cases [81, 82]. The diagnosis is usually suspected on clinical findings, and confirmed by full thickness surgical biopsy of the nipple and areola. Imaging is required to identify an underlying malignancy and assess the extent of disease. However, imaging is normal in 22–50 % of cases with mammography alone and in 13 % of cases when both mammography and ultrasound are performed [30]. Mammography may underestimate the extent of disease in up to 43 % of cases [83]. Breast MRI is both sensitive in detecting the underlying malignancy and accurate in assessing the extent of disease, especially when mammography and ultrasound are negative [82, 83].

The MRI finding of Paget's disease is asymmetric enhancement of the nipple-areolar complex, seen in 100 % of patients with clinically proven Paget's disease in one report [39]. The underlying malignancy may appear as an enhancing mass in the case of invasive cancer or nonmass enhancement, typical of DCIS. Traditionally, Paget's disease is treated with mastectomy. Since the underlying tumors are confined to the central breast in two thirds of patients, central lumpectomy combined with resection of the NAC and radiation therapy has been adopted recently, with similar survival rates [30]. MRI can delineate the location and extent of the underlying malignancy. It can also identify the presence of multifocal or multicentric disease. This is very important, especially for patients planning breast conservation surgery [84]. A negative MRI, however, does not exclude an underlying malignancy [82].

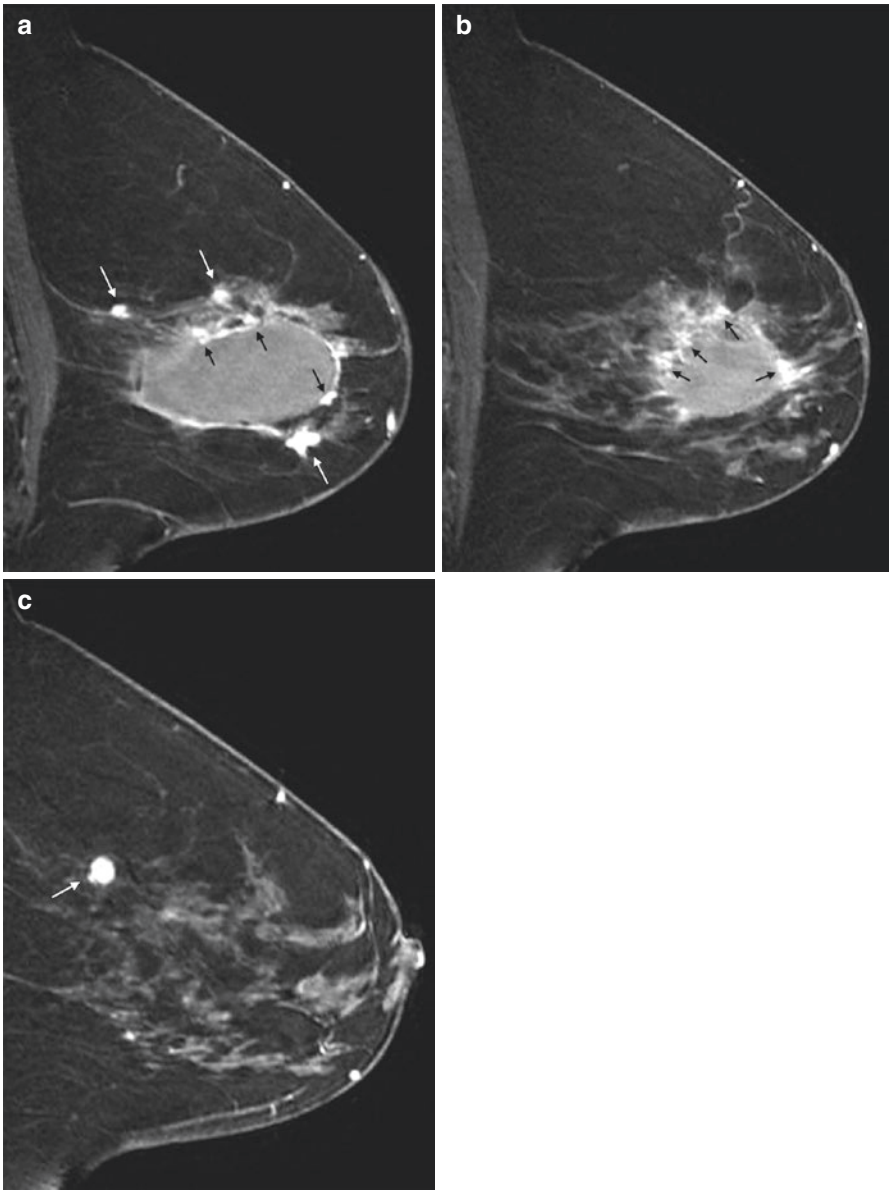

Fig. 4.15 Clinical stage II or higher, TxN1M0 tumor in a 62-year-old woman. The patient underwent a surgical biopsy at another institution for architectural distortion. Pathology yielded ILC and lobular carcinoma in situ with positive resection margins that persisted upon re-excision. Sentinel node biopsy yielded three positive metastatic nodes. (**a**) Sagittal post contrast fat-saturated T1 MR image reveals a large seroma with areas of lumpy enhancement (*black arrows*) at its margins suggestive of residual tumor. Three small enhancing masses (*white arrows*) away from the surgical cavity are concerning for multicentric tumors. (**b**) A more lateral sagittal image shows additional lumpy enhancement at the superior, posterior and anterior margins of the seroma (*black arrows*), suggestive of residual tumor. (**c**) A more medial sagittal image reveals an additional tumor focus (*arrow*)

4.8.4 Positive Surgical Margins After Initial Lumpectomy

Positive surgical margins denote the situation in which malignancy is found at the margins of the lumpectomy specimen after breast conservation surgery for breast cancer. This indicates potential residual malignancy in the breast. Patients are typically treated with repeat excision of the involved margins and may eventually require mastectomy if clear margins cannot be achieved after repeated surgery. Breast MRI has a reported sensitivity of 61–86 % for detection of residual malignancy [85–87]. It is useful in identifying bulky residual tumor at the lumpectomy site or multifocal/multicentric disease elsewhere in the breast (Fig. 4.15). This will guide the repeat excision or identify patients with extensive residual disease that would ultimately require mastectomy.

4.8.5 Known Multifocal, Multicentric or Bilateral Disease

Patients with known multifocal, multicentric or bilateral breast cancers on conventional breast imaging can benefit from MRI staging to determine the true extent of disease. This guides appropriate decision-making regarding breast conservation surgery vs. mastectomy.

4.8.6 Discordant Findings Between Clinical Examination and Imaging or Between Imaging Modalities

When the tumor size on clinical examination differs significant from the size on mammography or ultrasound, the extent of disease is uncertain. A discrepancy in tumor size between mammography and ultrasound greater than 1 cm also raises question about the true size of the tumor [14]. With its superior accuracy in determining tumor size and extent of disease, MRI should be considered in these scenarios (Fig. 4.1).

4.8.7 Planned Neoadjuvant Chemotherapy

Adjuvant chemotherapy is used to decrease the risk of recurrence and improve survival from invasive breast cancer. Neoadjuvant chemotherapy prior to surgery and radiation for local regional control has become widely adopted. It is found to be as effective as adjuvant chemotherapy, but has the added benefit of predicting patient outcome based on tumor response, and helping more patients achieve breast conservation [30]. This will be discussed in detail in the next chapter entitled "*MRI and neoadjuvant chemotherapy*".

4.9 Controversies on MRI Staging of Newly Diagnosed Breast Cancer

Improved staging with breast MRI should lead to decreased positive margins/re-excision rates, and better stratification of patients between breast conserving surgery and mastectomy due to improved surgical planning. There should be decreased local recurrence rates by identification and resection of otherwise occult multifocal or multicentric tumors. The metachronous contralateral cancer rates should also decrease, due to the simultaneous detection and treatment of contralateral tumors. However, the literature regarding the benefit of MRI staging is showing conflicting results. Therefore, the use of preoperative MRI to evaluate breast cancer remains controversial. The recent debates over the use of MRI staging are focused on the issues of *delay in definitive therapy, conflicting data on re-excision rates, increased mastectomy rates, and lack of long- term survival impact.*

4.9.1 Delay in Definitive Therapy

Two retrospective studies reported a mean treatment delay of 12.2–22.4 days in the group of patients undergoing preoperative breast MRI [88, 89]. However, Hollingsworth and associates, who routinely use preoperative MRI, asserted that all of their patients completed MRI workup within 2 weeks of diagnosis, before the surgeon's first available clinic date to see the patient. Hence, there is no delay in treatment among their patients [90]. The detection of additional lesions by MRI, necessitating additional imaging and biopsy is the downside of preoperative MRI and a potential source of delay. While unlikely to affect long-term outcome, it may contribute to patient anxiety and cost. To minimize delay, the facilities that offer breast MRI should have the capability and commitment to complete ultrasound- or MRI- guided biopsy of MRI-detected lesions promptly, or they should at least have an established referral arrangement with an experienced breast center to provide these services in a timely fashion.

4.9.2 Conflicting Data on Re-excision Rates

There are conflicting data on the impact of MRI staging on re-excision rates [60, 61, 89–98]. A meta-analysis of nine studies published between 2009 and 2012, including two randomized controlled trials and seven comparative studies (n = 3112) showed that preoperative MRI staging had no effect on re-excision rates, 11.6 % for the MRI group and 11.4 % for the non-MRI group [99]. The two prospective trials in the meta-analysis were the COMICE (Comparative Effectiveness of MRI in Breast Cancer) and MONET (MR Mammography of Nonpalpable Breast Tumors)

Table 4.5 The impact of preoperative staging MRI on re-excision rates

Lead author	Year published	Type of study	Number of patients	MRI group	No MRI group	P value
Grady	2012	Retrospective	184	11 %	26 %	0.04
Obdeijn	2013	Retrospective	123	18.9 %	37.4 %	<0.01
Sung	2014	Retrospective	174	29 %	45 %	0.02
Gonzalez	2014	Prospective	440	5 %	15 %	<0.001

Sources: Refs. [93, 100–102]

trials [97, 98]. The COMICE trial conducted in UK found no difference in re-excision rates between patients with or without MRI, both at 19 % [97]. However, because UK national health policy mandates reduction of reoperation rate for positive margins to under 10 %, surgeons routinely performed very wide excisions which could have negated the benefit of MRI. The MONET trial found a paradoxical increase in re-excision rates in patients with MRI (34 %) vs. patients without MRI (12 %). The critics of this study noted that the volume of the excised tissue in the MRI group (69.1 cm^3) was much smaller than the volume in the no MRI group (90.2 cm^3). It was even smaller in patients with DCIS and negative MRI (40.3 cm^3). Such bias in surgical approach resulted in the paradoxically higher rate of positive margins and re-excision rate in the MRI group [98].

The recent data on re-excision rates are more promising. Table 4.5 summarizes recently published studies demonstrating decreased rates of re-excision by the use of MRI staging [93, 100–102]. The data regarding ILC are particularly compelling. Although the meta-analysis by Houssami et al. showed only weak evidence that MRI reduced re-excision rate in patients with ILC, numerous studies have found significantly lower re-operation rates with the use of preoperative MRI in these patients [60, 61, 103, 104]. A recent population based study by Fortune-Greeley found a 40 % reduction in re-operation rate by MRI staging in patients with ILC (n = 1928), without increasing mastectomy [104].

4.9.3 Increased Mastectomy Rates

There has been a dramatic increase in the use of MRI staging among patients newly diagnosed with breast cancer, with a concurrent rise in the number of unilateral and bilateral mastectomies [105–107]. Many studies identified preoperative MRI as a predictor of mastectomy [88, 91, 99, 108, 109]. However, it is not clear whether the relationship is one of cause and effect [106]. A meta-analysis of 26 studies on the surgical impact of MRI staging found pathologically justified conversion from BCT to mastectomy in 8.3 % of cases [23]. This 8.3 % conversion rate roughly equals the 10-year local recurrence rate for breast cancer. It is probable that MRI identifies the patients with otherwise occult additional tumor burden and high likelihood for recurrence and converts their treatment to mastectomy at initial surgery. On the

other hand, false positive MRI findings caused inappropriate conversion to mastectomy in only 1.7 % of cases [23]. These inappropriate mastectomies should decrease by the confirmation of more extensive disease with MRI-guided biopsy before changing the surgical plan, which was not done in all of the prior studies.

Several studies evaluated the rates of mastectomy before and after the widespread use of preoperative MRI. One study found that the mastectomy rate in the United States increased from 29 to 41 % between 2004 and 2006, predominantly among patients without MRI [105]. Another study compared the mastectomy rate before and after installation of MRI scanner at the authors' institution and found the mastectomy rate decreased from 29.9 to 24.5 %, despite sharply increased use of preoperative MRI in breast cancer patients from 17.2 to 78.7 % [107]. Hollingsworth and associates reported increased BCT rate from 48 to 60 % with the use of preoperative MRI, due to its high negative predictive value [110]. Killelea and colleagues also found that the highest BCT rate (66 %) of any group in their study was among patients with a normal MRI, even greater than in those patients without MRI [106].

A study by McGuire et al. showed three strong predictors of mastectomy to be age <40 years, large tumor size, and lymphovascular invasion. Fear of recurrence and fear of radiation are additional factors, while MRI had no impact on mastectomy rates [111]. There are several reports on the increasing rates of contralateral prophylactic mastectomy, especially among younger, highly educated patients, those with a lower stage of breast cancer, and those with a positive family history [106, 107, 112, 113]. One author observed that the rise in contralateral mastectomy is independent of increased MRI use [107].

It is clear that MRI is not the sole cause of rising ipsilateral and contralateral preventive mastectomy rates nationwide. The trend is likely multi-factorial and driven by patients [111–113]. The availability of skin and nipple sparing mastectomy and breast reconstruction surgery with good cosmetic results, the ability to identify women at high risk for in-breast recurrence, the clearer understanding of the late effects of breast irradiation, and patients' increasing knowledge about their disease and options are all contributing factors to this trend [113].

4.9.4 No Demonstrated Long-Term Survival Impact

The impact of MRI staging on long-term survival after BCT is uncertain due to the lack of long-term outcome data. Since long-term survival is directly linked to local control, study of local recurrence rates may provide some clues. However, few reports are available. A meta-analysis of four studies showed no significant effect of MRI on local or distant recurrence-free survival [114]. This analysis did not include a study by Fischer et al. that demonstrated benefits of MRI in reducing local recurrence rates (1.2 % with MRI, 6.8 % without MRI) and contralateral breast cancer rates (1.7 % with MRI, 4 % without MRI) [115]. However, the authors asserted that inclusion of Fischer's data would not have changed their conclusion [114]. A recent study by Yi et al. showed that preoperative bilateral breast MRI was associated with

a reduced risk of contralateral breast recurrence [116]. Another study by Bae et al. showed the absence of preoperative MRI to be associated with an increased risk of recurrence in patients with triple-negative breast cancer [117]. This provides indirect evidence of the benefit of MRI in reducing local recurrence rates.

Given the current low rates of local recurrence after BCT and whole breast radiation (4.8–10.1 % over 10 years) and the low rate of contralateral breast cancer (4.1–5.5 %), the opponents of preoperative MRI question the benefit of finding additional cancer foci, since these foci are likely effectively treated with whole breast radiation and systemic therapy and are clinically insignificant [118, 119]. However, this may not be the case for patients undergoing partial breast irradiation. Furthermore, the International Breast MRI Consortium (IBMC) 6883 study showed that cancers detected only on MRI were similar in size and histology to cancers detected on mammography, but had a higher likelihood of being higher grade [21]. Hence, there is no basis to assume that the additional MRI-detected cancers are biologically inert or clinically irrelevant.

4.10 Conclusion

Breast MRI demonstrates superior accuracy for assessment of breast tumor size and extent of disease. Identification of multifocal/multicentric and contralateral tumors helps guide surgical planning and adjuvant therapy. While there is no consensus on the routine use of MRI in staging of all newly diagnosed breast cancers, it is proven to be beneficial in certain subsets of women. There is emerging evidence of decreases in re-excision or re-operation rates with MRI staging. No survival benefit has been demonstrated so far. A well-designed prospective randomized controlled trial on the short- and long- term benefits and cost analysis of preoperative MRI staging is needed. This is currently under development by the American College of Radiology Imaging Network (ACRIN) [120].

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