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Breast cancer size estimation with MRI in BRCA mutation carriers and other high risk patients

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ABSTRACT

Objective: To assess the value of breast MRI in size assessment of breast cancers in high risk patients, including those with a BRCA 1 or 2 mutation. Guidelines recommend invariably breast MRI screening for these patients and therapy is thus based on these findings. However, the accuracy of breast MRI for staging purposes is only tested in sporadic cancers.
Methods: We assessed concordance of radiologic staging using MRI with histopathology in 49 tumors in 46 high risk patients (23 BRCA1, 12 BRCA2 and 11 Non-BRCA patients). The size of the total tumor area (TTA) was compared to pathology. In invasive carcinomas ($n = 45$) the size of the largest focus (LF) was also addressed.
Results: Correlation of MRI measurements with pathology was 0.862 for TTA and 0.793 for LF. TTA was underestimated in 8(16%), overestimated in 5(10%), and correctly measured in 36(73%) cases. LF was underestimated in 4(9%), overestimated in 5(11%), and correctly measured in 36(80%) cases. Impact of BRCA 1 or 2 mutations on the quality of size estimation was not observed.
Conclusions: Tumor size estimation using breast MRI in high risk patients is comparable to its performance in sporadic cancers. Therefore, breast MRI can safely be used for treatment planning.

1. Introduction

Breast MRI has been accepted as screening modality for women with a very high risk for the development of breast cancer [1,2]. Women at high risk either have a BRCA 1, BRCA 2, or other recognized high risk gene, are untested relatives of women with these genes, or have been tested negative but remain at very high risk due to their family history. For these women the lifetime risk to develop breast cancer is 30% or more.

Although breast MRI is usually still combined with mammography for the detection of microcalcifications, treatment decisions are nowadays largely based on MRI findings. This seems deservedly so, as studies have repeatedly shown that tumor size estimation with MRI is much better than with mammography [3–7]. This holds especially true in women with dense breasts and those developing invasive lobular carcinomas [8,9]. Moreover, breast MRI tends to detect carcinomas in an earlier stage than mammography and many carcinomas are not even visible on mammography [10].

Nevertheless, it has been shown that tumors of BRCA carriers, especially those with a BRCA 1 mutation, differ in their features from sporadic cancers. In general they have more benign features, often with a round or oval shape and sharp borders [11,12], and also more commonly show a high signal on T2 weighted images [13]. Moreover, compared to BRCA 2 carriers and other women at high risk tumor size at diagnosis in BRCA 1 carriers is larger and the fraction of pure ductal carcinoma in situ (DCIS) lesions is lower [14]. This leads to the assumption that, if anything, cancers in high risk women are easier to measure than sporadic cancers. Nevertheless, at the same time in prophylactic mastectomy specimen malignant and pre-malignant lesions are found even after negative MRI studies [15,16], which leads to the conclusion that at least some of the

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lesions in high risk patients are not easily recognized as potential malignancies. Therefore, it is not certain that tumor size measurements using MRI in these patients are as accurate as in other breast cancer patients, nor has it ever been tested.

Accurate size estimation is of clinical relevance for treatment planning. Several sizes are important. For patients that receive surgery as their primary treatment, the size of the total tumor area is the most important, including the dominant invasive lesion, eventual other invasive tumor foci, and surrounding DCIS [17]. However, all guidelines for administration of chemotherapy are based on the pathologic T-score that only takes the largest invasive focus into account [18]. In the neoadjuvant setting this score is not available. Guidelines recommend the use of the clinical T-score, but this is notably inaccurate. Consequently, treatment decisions are often based on a radiologic surrogate for the T-score. The largest enhancing mass or confluent area, hereafter referred to as "largest focus", is the surrogate score that is most commonly used [6].

In literature it is often unclear which size is actually measured and specific data for women with a gene mutation or familial predisposition are lacking altogether. Consequently, the aims of our study are:

1. To assess the quality of tumor size estimation using MRI in high risk patients.
a. For the whole tumor area (including invasive carcinoma and DCIS).
b. For the largest focus (in the subset of patients with invasive carcinomas).
2. To assess whether differences in the quality of size estimation between BRCA1, BRCA2, and non-BRCA carrier patients are present.

2. Materials and methods

2.1. Patients

We retrospectively reviewed the prospective databases of the departments of Human Genetics and Pathology for all high risk women (based on presence of BRCA mutation or family history) who presented with breast cancer at our hospital between June 2002 and January 2011. Patient characteristics such as age at diagnosis and presence of a BRCA mutation were extracted from the patient files. Subsequently, this list was cross-referenced with the archive of the radiology department to obtain all women who underwent a contrast enhanced breast MRI within 3 months prior to surgery. Institutional review board (IRB) approval is waived by law for such observational studies.

2.2. Imaging

All patients were scanned in the prone position using a 1.5T or 3T MRI machine (Avanto or TRIO Tim, Siemens, Erlangen, Germany), with a 4, 7 or 16 Channel bilateral breast coil. Contrast was administered in the cubital vein trough an intravenous canula inserted just before the procedure at a dose of 0.1–0.2 mmol/kg (Gd-DOTA, Guerbet, France) using a power injector at a speed of 2.5 ml/s.

The scan protocol has been adapted over the years to keep up with the state-of-the-art, however all scans contained a 3D T1 weighted non-fatsat spoiled gradient echo sequence, that was performed prior to and at least four times after contrast administration. The spatial resolution of this sequence ranged from 0.9 to 1.3 mm isotropic. Our breast MRI protocol before June 2002 did not meet these standards, therefore patients scanned earlier are excluded. All mammograms were obtained with a full field digital mammography machine (Senograph2000/SenographDS, GE, USA).

2.3. Image evaluation

All MRI studies were independently evaluated by two experienced readers (R.M., J.V.) at a dedicated breast MRI workstation (DynaCAD, Invivo/Philips, Eindhoven, The Netherlands). This workstation provides subtraction of precontrast and postcontrast acquisitions, image registration to correct for motion artifacts, multi plane reconstructions in any plane, maximum intensity projections, and instant dynamic analysis tools including color overlays of enhancement characteristics such as wash-out of contrast.

Both readers were aware of the breast in which the tumor was located but had no further patient information nor information on tumor histology. All tumors were evaluated according to the BI-RADS lexicon [19]. Furthermore, the maximum diameter of the total tumor area in any plane as well as the maximum size of the largest focus were recorded (Fig. 1). Incidentally, measurement of the total tumor area was difficult due to strong background enhancement or other enhancement that could or could not be part of the tumor. In case of strong doubt, readers were asked to provide two measurements. The best corresponding measurement was then selected after review of pathology. This reflects clinical practice, as such findings would have led to biopsy to observe the nature of the abnormal surrounding enhancement. Both readers were instructed to measure the largest focus as a surrogate for the T-score. Consequently, areas that they interpreted as surrounding DCIS needed to be excluded. Since this does not often influence therapy, it is generally no indication for biopsy. Therefore, only one size was allowed.

All mammograms were evaluated by only one reader (R.M.) using a normal PACS system with a 5 MP breast certified monitor (Barco N.V., Kortrijk, Belgium)

2.4. Pathology

Specimen processing in our hospital is performed according to protocol. The handling of the simple mastectomy specimens was based on the correlated radiographic and pathology technique developed by Egan [20], which has been routinely performed in our pathology department for many years [21], and is described in detail elsewhere [22]. In summary, the specimens were cooled and sliced in serial sections with approximately 5 mm intervals. Radiographs were made from these tissue slices. Suspicious lesions and randomly selected areas from each quadrant and the nipple were sampled for histopathologic evaluation. Lumpectomy specimens were, after inking of the resection margins, sliced in approximately 5 mm intervals usually perpendicular to the longest axis of the specimen. Radiographs were made from these tissue slices. Small lumpectomies were totally embedded and large specimen were extensively sampled for histopathologic evaluation. Size measurements were performed on the specimen X-rays after microscopic examination of tissue samples.

All pathology data were extracted from the pathology reports by a dedicated breast pathologist (P.B.). In any case of lack of clarity in the pathology report, the histologic slides and specimen radiographs were reviewed (P.B.).

2.5. Statistics

Interreader variability in the evaluation of the MRI images was first explored using a scatter plot. Subsequently we calculated intraclass correlation coefficients (ICC) for the whole tumor area in all tumors and for the largest focus in invasive carcinomas.

All MRI measurements were averaged between the two readers. Relevant under- or overestimation of tumor size on MRI compared to pathology was defined as a size difference of more than 1 cm, corresponding to the usual margin our surgeons use. Correlations

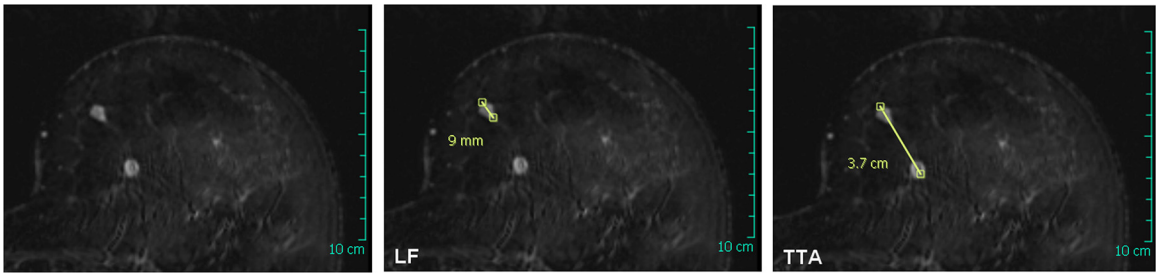

Fig. 1. Subtraction images of a bifocal breast tumor in the left breast. Both masses measure 9 mm in diameter (LF). The total tumor area (TTA) is 37 mm.

of MRI and mammographic measurements (both for total tumor area and largest focus) with pathologic size were explored with scatter plots and Pearson's correlation coefficients (PCC). This was performed for the whole dataset, as well as for specific subsets containing all BRCA 1 carriers, all non-BRCA 1 carriers, all BRCA 2 carriers, and all non-BRCA 2 carriers. Differences in correlation were evaluated using Fisher's r-to-z transformation. Differences in tumor size estimations were further explored using the independent samples *T*-test.

To test whether it is feasible to determine the T stadium from MRI images, we created a crosstab of radiologic T-stages (defined as size (cm) of the largest focus: rT1a $\leq$ 0.5, rT1b > 0.5- $\leq$ 1.0, rT1c > 1.0- $\leq$ 2.0, rT2 > 2.0- $\leq$ 5.0, and rT3 > 5.0) and pathologic T-stages and calculated a linear weighted kappa. Larger tumors may be eligible for neoadjuvant systemic therapy. A tumor size of 3 cm or more is an often used arbitrary cut-off size. Therefore, we performed an ROC analysis to evaluate the accuracy of MRI to determine whether the size of the largest focus is actually 3 cm or more.

Finally, differences between BRCA 1 carriers, BRCA 2 carriers, and non-BRCA high risk patients were explored using one-way ANOVA analysis for continuous data, and a Chi-square test or Fisher exact test whenever appropriate for categorical data.

2.6. Results

Seventy-six high risk patients presented between June 2002 and January 2011 at our hospital with breast cancer. Fifty-one and had an MRI within 3 months prior to surgery. Twenty-five women were excluded because no MRI was available within this timeslot. Three patients underwent neoadjuvant chemotherapy, one was treated with radiofrequency ablation, and in one no pathologic size could be determined due to fragmentation of the specimen. Consequently, these 5 patients were excluded. Of the remaining 46 patients, two presented with synchronous bilateral breast cancer, while 1 other presented with a metachronous tumor in the other breast 9 years after detection of the first malignancy. In total 49 tumors were thus included in our analysis, 45 invasive carcinomas and 4 cases of pure DCIS. Characteristics of patients, MRI findings, and histopathology are depicted in Table 1. Mammograms were available for 47 of these tumors. However, in 5 cases the mammograms were obtained more than 6 months prior to the MRI and were therefore excluded.

At MRI all tumors were visible, although in 1 case only after reviewing the mammogram to observe the location of mammographically detected microcalcifications. At mammography, abnormalities were only seen in 28 cases, and 14 tumors were even retrospectively occult.

2.7. Interreader variability

Both readers agreed well in their tumor size estimation on MRI. The ICC for size estimation of the total tumor area was 0.981 ($p < 0.001$), while the size estimation of the largest tumor focus was only slightly less robust (0.921, $p < 0.001$). Fig. 2 provides a scatter plot of the respective measurements.

2.8. Correlation of findings with pathology

Overall correlation of MRI measurements with pathology was good. The PCC for assessment of the total tumor area was 0.862 ($p < 0.001$), while the PCC for the largest focus was 0.793 ($p < 0.001$) for the subset of invasive carcinomas ($n = 45$), as depicted in Fig. 3. The mean size of the total tumor area on MRI was 2.3 mm smaller than at pathology, whereas the size of the largest focus was overestimated by a mean of 0.9 mm. Mammographic size estimates were substantially poorer. PCC for total tumor area and largest focus were 0.563 ($p < 0.01$) and 0.567 ($p = 0.08$), respectively.

We observed a moderate agreement between MRI determined T stage and pathologic determined T stage, with a linear weighted kappa value of 0.496. However, the overall accuracy in classifying tumors as larger or smaller than 3 cm is excellent with an area under the curve of 0.951.

2.8.1. BRCA 1 Carriers

Twenty-six of all 49 tumors occurred in BRCA 1 carriers. Two of these tumors were pure DCIS, all others were invasive. Assessment of the total tumor area was slightly poorer in BRCA 1 carriers, compared to all others, although this was not statistically significant (PCC 0.759 vs. 0.868 ($p = 0.28$)).

Evaluation of the size of the largest focus was however significantly worse than in other types of tumor (PCC 0.583 vs. 0.894 ($p = 0.02$)) (Fig. 4).

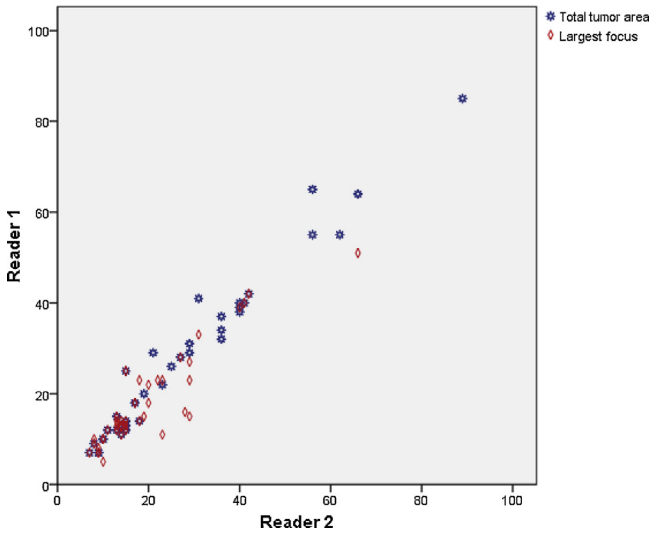

Fig. 2. Scatter plot of interreader variability (*x*- and *y*-axis: size in mm).

Table 1
Characteristics of patients, MRI findings, and histopathology.

	Total	BRCA 1	BRCA 2	NON-BRCA	
Tumors (*n*)	49	26	12	11	
Age at diagnosis (years)	46 (11)	44 (10)	52 (12)	45 (10)	$P=0.118$
MRI lesion type (*n*)	Mass: 40 NMLE: 9	Mass: 22 NMLE: 4	Mass: 10 NMLE: 2	Mass: 8 NMLE: 3	$P=0.714$
Average MRI size total tumor area (mm)	27 (22)	22 (11)	20 (16)	49 (33)	$P=0.000$
Average MRI size largest focus (mm)	18 (11)	18 (9)	13 (7)	25 (15)	$P=0.025$
Average pathologic size total tumor area (mm)	30 (29)	23 (15)	16 (11)	61 (42)	$P=0.000$
Average pathologic size largest focus (mm)	17 (16)	16 (10)	8 (3)	32 (27)	$P=0.002$
Histological type (*n*)	IDC: 38 ILC: 4 TC: 1 SecCa: 1 DCIS: 5	IDC: 22 ILC: 1 SecCa: 1 DCIS: 2	IDC: 9 ILC: 1 TC: 1 DCIS: 1	IDC: 7 ILC: 2 DCIS: 2	$P=0.384$
Histological grade invasive tumors (*n*)	I: 4 II: 15 III: 25	I: 1 II: 6 III: 17	I: 1 II: 5 III: 5	I: 2 II: 4 III: 3	$P=0.233$

Numbers between parenthesis represent standard deviations. NMLE = non-mass like enhancement. IDC = invasive ductal carcinoma. ILC = invasive lobular carcinoma. TC = tubular carcinoma. SecCa = secretory carcinoma.

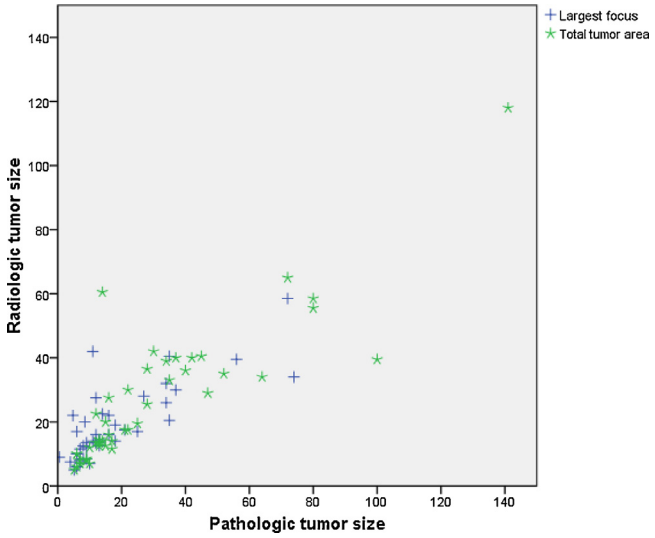

Fig. 3. Scatter plot of radiologic versus pathologic tumor size (*x*- and *y*-axis: size in mm).

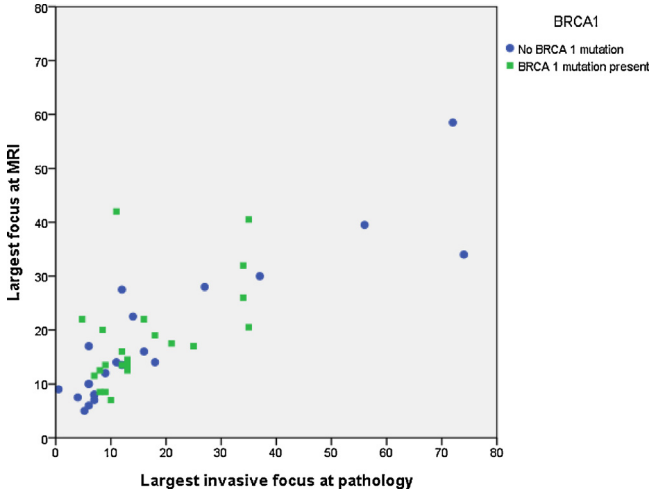

Fig. 4. Correlation of largest radiologic focus with largest invasive tumor at pathology (*x*- and *y*-axis: size in mm).

The largest invasive focus was on average overestimated on MRI by a mean of 2.2 mm in BRCA 1 carriers, whereas it was underestimated by 0.7 mm in all other patients (ns).

2.8.2. BRCA 2 carriers

Twelve tumors occurred in BRCA 2 carriers, 11 invasive carcinomas and 1 pure DCIS. While in BRCA 2 carriers the quality of tumor size estimation of the largest focus was highly comparable to its quality in all other patients (PCC 0.746 vs. 0.793 ($p=0.77$)), the quality of estimation of the total tumor area was worse (PCC 0.406 vs. 0.904 ($p<0.01$)) (Fig. 5). On average the total tumor area was overestimated in BRCA 2 carriers by 3.9 mm, whereas it was underestimated in all others by a mean of 4.3 mm (ns).

2.9. Overestimated and underestimated lesions with more than 1 cm

2.9.1. Total tumor area

Underestimation of the total tumor size with more than 1 cm occurred in 8 cases (16%; 1.7, 1.8, 1.9, 2.2, 2.3, 2.5, 3.0, and 6.0 cm, respectively), whereas 5 cases were overestimated with more than 1 cm (10%; 1.1, 1.2, 1.2, 2.3, and 4.3 cm respectively). This is strongly related to tumor size, larger lesions (≥T2) were more often underestimated whereas in smaller lesions

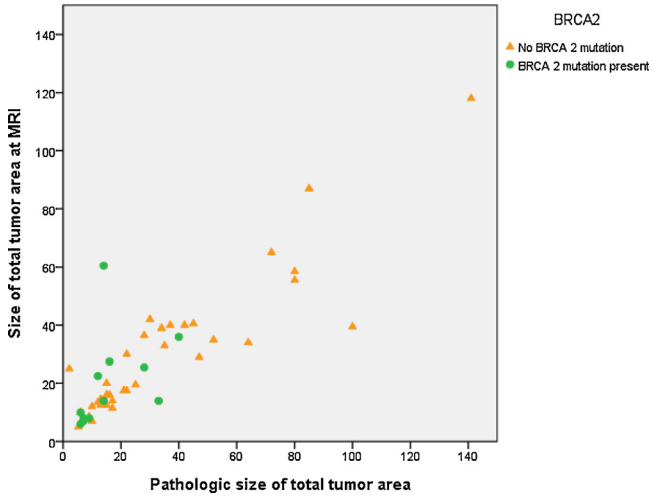

Fig. 5. Correlation of total tumor area at MRI with total tumor size at pathology (*x*- and *y*-axis: size in mm).

Table 2
Number of cases in which the total tumor size on MRI was under- and overestimated in relation to pathologic tumor size.

pT-stage	Underestimated (>1 cm)	MRI measurements within 1 cm from pathologic size	Overestimated (>1 cm)
pTis	1 (25)	2 (50)	1 (25)
pT1a	2 (67)	1 (33)	0 (0)
pT1b	0 (0)	14 (93)	1 (7)
pT1c	1 (7)	11 (73)	3 (20)
pT2	2 (22)	7 (78)	0 (0)
pT3	2 (66)	1 (33)	0 (0)
Total	8 (16)	36 (73)	5 (10)

Numbers between parentheses represent percentages.

underestimation and overestimation were equally likely (Table 2) ($p = 0.02$). Furthermore, mass like lesions were more accurately measured than non-mass like lesions, both underestimation (22 vs. 15%) and overestimation of lesion size (33 vs. 5%) were more frequent in non-mass like lesions ($p = 0.02$). It also appears that tumors with an extensive DCIS component outside the tumor are more likely to be underestimated. Four of 8 cases were underestimated, only once the lesion was overestimated ($p = 0.06$).

Proportions of underestimation and overestimation with more than 1 cm were similar in the BRCA 1 carriers (2 overestimated and 3 underestimated lesions) and BRCA 2 carriers (3 overestimated and 1 underestimated). The total tumor area was underestimated in 4 of 11 non BRCA carriers, whereas in these patients no overestimation occurred. However, this did not reach statistical significance ($p = 0.13$). We did not observe a relation between under- or overestimation of the total tumor area with patient age, mammographic density, tumor histology, or tumor grade.

2.9.2. Largest focus

The largest focus was underestimated with more than 1 cm in 4 cases (9%; 1.4, 1.5, 1.7, and 4.0 cm, respectively) and overestimated in 5 cases (11%; 1.1, 1.2, 1.6, 1.7, and 3.1 cm, respectively). Also here, pathologic tumor size was most strongly related to the risk of under- or overestimation. Whereas larger tumors (≥T2) tend to be underestimated, smaller tumors are overestimated (Table 3) ($p < 0.01$). Tumors presenting as non-mass like enhancement are less adequately measured ($p < 0.01$). The amount of DCIS in and around the tumor is not of influence ($p = 0.32$), nor did we detect a relation with patient age, mammographic density, tumor histology, or tumor grade.

Both in BRCA 1 carriers (3 vs. 1) and BRCA 2 carriers (2 vs. 0) the largest focus was more often overestimated than underestimated, whereas in patients without a known BRCA mutation underestimation was more frequent. However, this was not statistically significant ($p = 0.12$).

3. Discussion

In this study we show that there is reasonable agreement of MRI determined tumor sizes with histopathologic findings in high risk patients. MRI strongly outperforms mammography, both in sensitivity and in tumor size estimation. The presence or absence of a BRCA 1 or BRCA 2 mutation does not appear to be strongly related to failures of tumor size estimation, nor are BRCA related tumors better measured than sporadic tumors. The poor correlation of the radiologically assessed total tumor area with pathologic size in BRCA 2 carriers is a striking exception, but must be interpreted with caution due to the low number of BRCA2 carriers in our study.

The most influential factor for failure of adequate tumor size estimation is the pathologic T-score. We observed a clear risk of tumor size underestimation in larger cancers. This also implies that tumors with a lot of surrounding DCIS are less accurately measured than tumors with only a limited DCIS fraction. Moreover, the quality of tumor size estimation is dependent on the appearance of a tumor at MRI, and is worse in non-mass like enhancing lesions than in clear masses.

Our results are in line with reported MRI-pathology correlations in women without specific high risk profile that are usually calculated by correspondence of the largest focus with the largest invasive tumor at pathology although this is often not specifically mentioned. Reported correlation coefficients range from 0.75 to 0.98 [3–7] and are within the same range for tumors with an extensive intraductal component (0.87), invasive lobular carcinoma (0.89), and DCIS (0.65–0.83) [8,23–26]. However, in the largest prospective trial to preoperative staging with MRI, reported correlations are much lower. Turnbull et al. reported a correlation of only 0.4 for patients with invasive lobular carcinoma and 0.53 for patients with other tumors, which is probably largely explained by lack of experience of the participating radiologists within this trial, but may also imply that accurate tumor size estimation is more difficult in a prospective setting [27].

Surprisingly little is reported in the literature on the causes of under- and overestimation of tumor size on MRI compared to pathology, even though many papers on the correlation of size have appeared. In our study the allowed delay of up to 3 months between MRI and surgery may explain some under-estimation, especially since tumors in high risk patients tend to grow faster than in the general population. However, most MRI's were performed within a week from surgery and consequently the effect is, if present, small. One of the major contributors may be the large difference in the shape of the breast at both examinations. Whereas on MRI the

Table 3
Number of cases in which the largest focus on MRI was under- and overestimated compared to pathologic tumor size in the subset of invasive carcinomas.

pT-stage	Underestimated (>1 cm)	MRI measurements within 1 cm from pathologic size	Overestimated (>1 cm)
pT1a	NA	2 (67)	1 (33)
pT1b	NA	13 (87)	2 (13)
pT1c	0 (0)	13 (87)	2 (13)
pT2	1 (11)	8 (89)	0 (0)
pT3	3 (100)	0 (0)	0 (0)
Total	4 (9)	36 (80)	5 (11)

Numbers between parentheses represent percentages. NA = not applicable.

breast hangs freely within the loops of the breast coil, at pathology the simple mastectomy specimen or lumpectomy specimen are flat on the table. Consequently, the left-to right and cranial-to-caudal diameter of the breast at pathology is larger than at MRI, while the anterior–posterior diameter decreases [28]. Especially diffuse growing tumors may stretch with the normal fibroglandular tissue and hence change in shape and size. Moreover, pathologic specimen handling results in fixation and dehydration of the tissue, which leads to shrinkage of the tissue, which may also cause some shrinkage of the tumor. An average shrinkage of 4.5% was reported [29]. However, in our study this was of no concern, as size assessment was estimated on the specimen radiographs, which were made of the fresh non-fixed specimen slices, after microscopic examination.

Furthermore, MRI features of the breasts may affect the quality of size estimation. Especially in women with moderate to marked background enhancement the quality of tumor size estimation is relatively poor [30].

Occurrence of overestimation of tumor size may further be related to the occurrence of neovascularisation just outside of the pathologic tumor area, which has been documented especially for DCIS [31], and is probably due to diffusion of vascular growth factors produced by the tumor. Moreover, some precursor lesions such as atypical ductal hyperplasia and lobular carcinoma in situ may enhance, but are not included within the pathologic total tumor area [32,33].

Underestimation of tumor size on the other hand is most likely due to small satellite foci that do not show enhancement. After meticulous pathologic evaluation Schmitz et al. reported the occurrence of MR invisible satellite foci beyond 10 mm from the largest invasive focus in 52% of patients and even beyond 20 mm in 25% of patients [6]. In our study breast specimens were also examined in a more than standard way with specimen radiographs and extensive tissue sampling. However, we observed underestimation of the total tumor area with more than 1 cm in only 10% of cases. Consequently, many of these occult foci occur apparently within the MRI visible total tumor area and will therefore be correctly treated when the treatment plan is based on the MRI.

It is likely that at least some tumor foci may escape detection on both MRI and in standard pathologic analysis. The importance of these occult satellite foci for surgery is, however, questionable. It is well known that lumpectomy is often debulking rather than curative in itself. Earlier studies by Holland et al. showed that residual disease within the breast more than 2 cm from the known cancer is present in up to 43% of patients [21]. However, as long as lumpectomies are followed by radiotherapy local recurrence rates are under 10% and overall survival is not affected. This holds also true for high risk patients, including BRCA 1 and 2 carriers [34].

Therefore, despite the less than perfect concordance of MRI with pathologic findings,we conclude that treatment decisions in high risk patients can safely be made on the basis of MRI findings. Obviously, it remains essential to inform patients about the risks of tumor size under- and overestimation that nevertheless exist.

Conflicts of interest

None declared.

References

[1] Mann RM, Kuhl CK, Kinkel K, Boetes C. Breast MRI: guidelines from the European Society of Breast Imaging. European Radiology 2008;18:1307–18.

[2] Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. CA: A Cancer Journal for Clinicians 2007;57:75–89.

[3] Amano G, Ohuchi N, Ishibashi T, Ishida T, Amari M, Satomi S. Correlation of three-dimensional magnetic resonance imaging with precise histopathological map concerning carcinoma extension in the breast. Breast Cancer Research and Treatment 2000;60:43–55.

[4] Davis PL, Staiger MJ, Harris KB, et al. Breast cancer measurements with magnetic resonance imaging, ultrasonography, and mammography. Breast Cancer Research and Treatment 1996;37:1–9.

[5] Ramirez SI, Scholle M, Buckmaster J, Paley RH, Kowdley GC. Breast cancer tumor size assessment with mammography, ultrasonography, and magnetic resonance imaging at a community based multidisciplinary breast center. American Surgeon 2012;78:440–6.

[6] Schmitz AC, van den Bosch MA, Loo CE, et al. Precise correlation between MRI and histopathology – exploring treatment margins for MRI-guided localized breast cancer therapy. Radiotherapy and Oncology 2010;97:225–32.

[7] Yang WT, Lam WW, Cheung H, Suen M, King WW, Metreweli C. Sonographic, magnetic resonance imaging, and mammographic assessments of preoperative size of breast cancer. Journal of Ultrasound in Medicine 1997;16:791–7.

[8] Mann RM. The effectiveness of MR imaging in the assessment of invasive lobular carcinoma of the breast. Magnetic Resonance Imaging Clinics of North America 2010;18, 259-76, ix.

[9] Sardanelli F. Overview of the role of pre-operative breast MRI in the absence of evidence on patient outcomes. Breast 2010;19:3–6.

[10] Warner E, Hill K, Causer P, et al. Prospective study of breast cancer incidence in women with a BRCA1 or BRCA2 mutation under surveillance with and without magnetic resonance imaging. Journal of Clinical Oncology 2011;29:1664–9.

[11] Schrading S, Kuhl CK. Mammographic, US, and MR imaging phenotypes of familial breast cancer. Radiology 2008;246:58–70.

[12] Veltman J, Mann R, Kok T, et al. Breast tumor characteristics of BRCA1 and BRCA2 gene mutation carriers on MRI. European Radiology 2008;18: 931–8.

[13] Trecate G, Manoukian S, Suman L, et al. Is there a specific magnetic resonance phenotype characteristic of hereditary breast cancer? Tumori 2010;96: 363–84.

[14] Rijnsburger AJ, Obdeijn IM, Kaas R, et al. BRCA1-associated breast cancers present differently from BRCA2-associated and familial cases: long-term follow-up of the Dutch MRISC screening study. Journal of Clinical Oncology 2010;28:5265–73.

[15] McLaughlin SA, Stempel M, Morris EA, Liberman L, King TA. Can magnetic resonance imaging be used to select patients for sentinel lymph node biopsy in prophylactic mastectomy? Cancer 2008;112(6):1214–21.

[16] Hoogerbrugge N, Kamm YJ, Bult P, et al. The impact of a false-positive MRI on the choice for mastectomy in BRCA mutation carriers is limited. Annals of Oncology 2008;19(4):655–9.

[17] Lim HI, Choi JH, Yang JH, et al. Does pre-operative breast magnetic resonance imaging in addition to mammography and breast ultrasonography change the operative management of breast carcinoma? Breast Cancer Research and Treatment 2010;119:163–7.

[18] Kaufmann M, von Minckwitz G, Mamounas EP, et al. Recommendations from an international consensus conference on the current status and future of neoadjuvant systemic therapy in primary breast cancer. Annals of Surgical Oncology 2012;19:1508–16.

[19] Molleran V, Mahoney MC. The BI-RADS breast magnetic resonance imaging lexicon. Magnetic Resonance Imaging Clinics of North America 2010;18, 171-85, vii.

[20] Egan RL. Multicentric breast carcinomas: clinical-radiographic-pathologic whole organ studies and 10-year survival. Cancer 1982;49:1123–30.

[21] Holland R, Veling SH, Mravunac M, Hendriks JH. Histologic multifocality of Tis, T1-2 breast carcinomas. Implications for clinical trials of breast-conserving surgery. Cancer 1985;56:979–90.

[22] Bult P, Hoogerbrugge N. Familial breast cancer: detection of prevalent high-risk epithelial lesions. In: Hayat MA, editor. Methods of Cancer Diagnosis, Therapy and Prognosis, Volume 1: Breast Carcinoma. 1 ed. London: Springer; 2008. p. 61–71.

[23] Kim do Y, Moon WK, Cho N, et al. MRI of the breast for the detection and assessment of the size of ductal carcinoma in situ. Korean Journal of Radiology 2007;8:32–9.

[24] Marcotte-Bloch C, Balu-Maestro C, Chamorey E, et al. MRI for the size assessment of pure ductal carcinoma in situ (DCIS): a prospective study of 33 patients. European Journal of Radiology 2011;77:462–7.

[25] Schouten-van der Velden AP, Boetes C, Bult P, Wobbes T. The value of magnetic resonance imaging in diagnosis and size assessment of in situ and small invasive breast carcinoma. American Journal of Surgery 2006;192:172–8.

[26] Van Goethem M, Schelfout K, Kersschot E, et al. MR mammography is useful in the preoperative locoregional staging of breast carcinomas with extensive intraductal component. European Journal of Radiology 2007;62: 273–82.

[27] Turnbull LW, Brown SR, Olivier C, et al. Multicentre randomised controlled trial examining the cost-effectiveness of contrast-enhanced high field magnetic resonance imaging in women with primary breast cancer scheduled for wide local excision (COMICE). Health Technology Assessment 2010;14: 1–182.

[28] Docquier PL, Paul L, Cartiaux O, et al. Formalin fixation could interfere with the clinical assessment of the tumor-free margin in tumor surgery: magnetic resonance imaging-based study. Oncology 2010;78:115–24.

[29] Yeap BH, Muniandy S, Lee SK, Sabaratnam S, Singh M. Specimen shrinkage and its influence on margin assessment in breast cancer. Asian Journal of Surgery 2010;30:183–7.

[30] Uematsu T, Kasami M, Watanabe J. Does the degree of background enhancement in breast MRI affect the detection and staging of breast cancer? European Radiology 2011;21:2261–7.

[31] Guidi AJ, Schnitt SJ, Fischer L, et al. Vascular permeability factor (vascular endothelial growth factor) expression and angiogenesis in patients with ductal carcinoma in situ of the breast. Cancer 1997;80:1945–53.
[32] Mann RM, Veltman J, Barentsz JO, Wobbes T, Blickman JG, Boetes C. The value of MRI compared to mammography in the assessment of tumour extent in invasive lobular carcinoma of the breast. European Journal of Surgical Oncology 2008;34:135–42.
[33] Perlet C, Heinig A, Prat X, et al. Multicenter study for the evaluation of a dedicated biopsy device for MR-guided vacuum biopsy of the breast. European Radiology 2002;12:1463–70.
[34] Pierce LJ, Levin AM, Rebbeck TR, et al. Ten-year multi-institutional results of breast-conserving surgery and radiotherapy in BRCA1/2-associated stage I/II breast cancer. Journal of Clinical Oncology 2006;24:2437–43.