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Research Article
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Tumor Size and Nodal Status of Invasive Breast Carcinomas in Women with Dense Breasts Depending on Previous Breast MRI

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Abstract

Purpose: The study evaluates the influence of prior breast MRI on the size of invasive breast carcinomas and their nodal status at the time of diagnosis in women with density type ACR C and D.

Material and Methods: The evaluation included 444 patients with histologically verified invasive breast cancer after percutaneous or open biopsy to clear findings categorized as MR-BIRADS 4 or 5. All patients had high tissue density type ACR C or D. The study differentiated two groups: Patients, who had a breast MRI with unsuspicious result in the last 5 years (group A), and patients who had no MRI of the breast before (group B). Moreover, the significance of the time interval between previous MRI and MRI was also evaluated.

Results: In the period from 2014 to 2020, 15,673 breast MRIs were performed during breast consultations for different indications. 2,170 findings were categorized as MR-BIRADS 4 or 5. At least, 444 cases with invasive breast cancer (319 NOS, 94 ILC, 18 TUB, 8 MUC, 5 other) were included in the analysis after elimination of cases with exclusion criteria. Patient in group A (n=113) had an average tumor size of 11.1 mm at the time of diagnosis, compared to patients in group B (n=331) with 21.9 mm. Regarding only women in a screening constellation (n=145), the average tumor size was 9.8 mm (previous MRT within last 2 years), 10.2 mm (previous MRI last 2-3 years), and 15.6 mm without previous MRI. The average tumor size was also higher for all other indications: Unclear cutaneous or palpable findings (19.0 mm; n=16 *vs*. 24.0 mm; n=82), unclear mammography (17.5 mm; n=21) or ultrasound findings (18.4 mm; n=39), CUP syndrome (11.0 mm; n=3) and local MR staging with BIRADS 5 or 6 (24.3 mm; n=138). The rate of nodal-positive carcinomas was 6.2% (7/113) with previous MRI and 28.4% (94/331) without MRI within the last 5 years.

Conclusion: If women with density type ACR C and D, who had a previous normal breast MRI within the last 5 years, get an invasive breast cancer, the tumor size will be around half of the size compared to women without previous MRI. The rate of nodal-positive carcinomas in invasive breast cancer is reduced by 75% with previous MRI.

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Abbreviations

ACR: American College of Radiology; ACR A: Mostly Fatty Dense Breast Tissue; ACR B: Fibroglandular Breast Tissue; ACR C: Inhomogeneous Dense Breast Tissue; ACR D: Extremely Dense Breast Tissue; BCT: Breast Conserving Therapy; CEBCT: Contrast-Enhanced Breast Computer Tomography; CEM: Contrast-Enhanced Mammography; CEMRI: Contrast-Enhanced Magnetic Resonance Imaging; CM: Contrast Material; CUP: Carcinoma of Unknown Primary; DCIS: Ductal Carcinoma in situ; Gd: Gadolinium; EUSOBI: European Society of Breast Imaging; IDC: Invasive Ductal Carcinoma, NOS; ILC: Invasive Lobular Carcinoma; IR: Inversion Recovery; ME: Mastectomy; m: Months; mm: Millimeter; MUC: Mucinous carcinoma; MX: Mammography; NOS: Not Otherwise Specified invasive breast cancer, IDC; pre-MRI: Previously performed breast MRI; TUB: Tubular carcinoma; US: Ultrasound

Introduction

Contrast-Enhanced Breast MRI (CEMRI) has proven to be superior to all other examination methods in the early detection of breast cancer. This applies especially to women with a high tissue density ACR C and ACR D, as mammography and tomosynthesis are limited in these cases [1-

3]. For this reason, EUSOBI recommended the primary use of breast MRI in women with extremely dense breasts type D [4]. If MRI shows no suspicious lesion and the image quality is high, CEMRI may be regarded as a stand-alone technique. The aim of this study was to evaluate, if a previous Breast MRI within the last 5 years has an effect on the tumor size of invasive carcinomas and their nodal status at the time of diagnosis.

Material and Methods

Over a period of seven years, all breast MRI examinations performed at the Diagnostic Breast Center Göttingen were consecutively evaluated in this retrospective study. From this collective, all patients who had a high tissue density (ACR C or ACR D), who had findings categorized as MR BIRADS 4 or 5, and who had a histologically verified invasive breast carcinoma after percutaneous or open biopsy were included in this study. This MRI is named "current MRI".

Exclusion criteria applied to all women and patients with

- Density type ACR A or ACR B
- Benign findings or DCIS
- MR examinations during or after chemotherapy as part of a neoadjuvant treatment concept
- Inflammatory breast cancer
- Incomplete data

In a next step, it was checked, if the included patients had a Breast MRI at our institute categorized as MR BIRADS 1, 2 or 3 within the last 5 years before current MRI. Depending on this aspect, the patients were divided in two groups: Group A enclosed patients who had a breast MRI within the last 5 years before current MRI. Patients in group B had no previous Breast MRI outside or at our institute.

All MRI-examinations were performed at our institute on different systems: (a) 1.5 Tesla whole-body scanner Signa HDX (Fa. GE Healthcare, Milwaukee, WI, USA) by using a dedicated open 4-channel-breast surface coil (Fa. MRI Device, Knaresborough, NY, USA). (b) 1.5 Tesla whole-body scanner Altea (Fa. Siemens, Erlangen, Germany) by using a dedicated open 7-channel-breast surface coil (Fa. Noras, Hoechberg, Germany), and (c) 3.0 Tesla whole-body scanner Lumina (Fa. Siemens, Erlangen, Germany) by using a dedicated open 7-channel-breast surface coil (Fa. Noras, Hoechberg, Germany). All systems had an integrated device for the fixation of both breasts in cranio-caudal orientation (Noras, Hoechberg, Germany). The MRI examination included a fat-saturated T2 weighted IR-sequence. Subsequently, a 3D T1 weighted gradient-echo-sequence was performed repetitively once before and 2 times after administration of contrast material Gd-DTPA (Gadovist, Bayer company, Leverkusen, Germany) [5].

Postprocessing included the subtraction of the pre-contrast image from the first and second measurements after contrast administration on a pixel-to-pixel base, and the presentation of these subtraction images and the T2-images as Maximum-Intensity-Projections (MIP).

Breast MRI findings were categorized into 5 categories (MR-BIRADS 1,2,3,4,5) based on the guidelines of the American College of Radiology [6]. All findings in the MR-BIRADS 4 or 5 category were clarified histologically by percutaneous biopsy or primary open biopsy. Depending on the findings, the interventional procedures were stereotactic or tomosynthesis-guided as well as US- or MR-guided [5].

The following data were included in the evaluation:

- Age of the patient
- Indication for contrast-enhanced breast MRI
  - Early detection of breast cancer
  - Unclear inspection findings
  - Unclear palpation findings
  - Unclear mammography findings
  - Unclear sonographic findings
  - Local pre-therapeutic staging
- Risk profile
  - Not increased
  - Moderately increased
  - Status after BET or ME
  - High-risk profile
- Histology
  - IDC
  - ILC
  - TUB
  - MUC
  - Other
- Tumor size
- Tumor stage
  - pT1a
  - pT1b
  - pT1c
  - pT2
  - pT3 and higher
- Luminal status
  - Luminal A
  - Luminal B
  - Non-Luminal
  - Triple negative
- Ki67 proliferation index
- Nodal status
  - N0
  - N+

The size of the invasive carcinomas at the time of detection was evaluated depending on the presence or absence of a previous MRI and – in case of previous MRI - on the time interval between previous and current MRI. Moreover, the dependence of tumor size and nodal

status on the indication for MRI and the histological entity of the invasive carcinoma was evaluated.

Results

In the period from 2014 to 2020, 15,406 breast MRI examinations were carried out for various indications as part of the local breast consultation. Common indications were screening in asymptomatic women, assessment of unclear clinical, mammographic and/or sonographic findings, follow up after breast cancer, and preoperative staging in patients with lesions categorized as BIRADS 5 or 6. This resulted in 2,014 findings in the MR-BIRADS 4 or 5 category. After elimination of the patients who fulfilled exclusion criteria, 444 cases with invasive breast cancer (319 NOS, 94 ILC, 18 TUB, 8 MUC, 5 other) were included in the study.

Regarding all indications for MRI, the average tumor size for patients with previous MRI within 5 years before current MRI (group A, n=113) was 11.1 mm, compared to patients without previous MRI (group B, n=331) with 21.9 mm. If the previous MRI was performed within the last 2 years, the average tumor size in group A varied between 10 mm to 11 mm. With longer time intervals, the tumor size increased slowly (Figure 1).

For the different indications for current MRI, the average tumor size (size/number) was as follows (excluding screening in asymptomatic women):

Screening	(n=145)
Unclear cutaneous findings	19.0 mm (n=16),
Unclear palpable findings	24.0 mm (n=82),
Unclear mammography findings	17.5 mm (n=21),
Unclear ultrasound findings	18.4 mm (n=39),
Primary tumor search for CUP syndrome	11.0 mm (n=3),
Local MR staging for BIRADS 5 or 6	24.3 mm (n=138).

In women with previous MRI, non-luminal carcinomas were only slightly larger than luminal carcinomas (9.8 mm) at an average of 11.3 mm. Without previous MRI, these values were 21.4 mm and 24.6 mm respectively. Patients with a high-risk profile and previous MRI had an average size of 11.7 mm, patients without previous MRI 15.7 mm. However, this group comprised a total of only 35 patients.

For the various tumor entities, the tumor size was halved on average at the time of diagnosis if a previous MRI was performed. As expected, ILCs showed the largest tumor size due to their non-mass-like character, which results in a larger metric size than IDCs with a predominantly mass-like character (Figure 2).

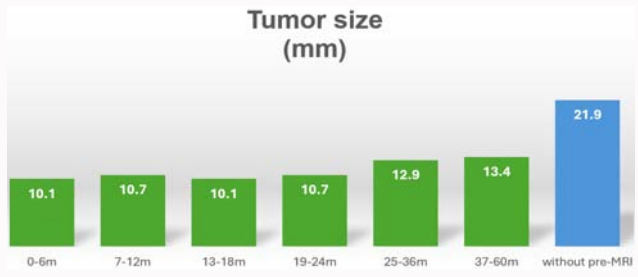

Figure 1: Tumor size at the time of diagnosis depending on the interval between previous MRI and current MRI (green, group A, n=113), and in patients without previous MRI (blue, group B, n=331) for all indications.

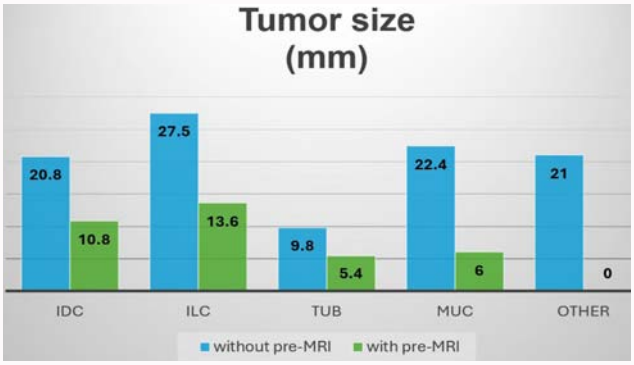

Figure 2: Average tumor size in mm according to histology without (blue) and with previous MRI (green) for all indications (319 IDC, 94 ILC, 18 TUB, 8 MUC, 5 other). Pre-MRI = Previous MRI

Table 1: Comparison of various parameters of the groups without and with previous MRI.

	Group B without previous MRI, n=331		Group A with previous MRI, n=113	
AGE	**56.8**		**61.9**	
Age MIN-MAX	28-91		36-83	
RISK PROFILE				
Normal	199	60.1%	39	34.5%
Moderately increased	90	27.2%	29	25.7%
BET	20	6.0%	32	28.3%
High risk	22	6.7%	13	11.5%
DENSITY C and D*)	3.60		3.63	
pT-STADIUM				
pT1a	14	4.2%	22	19.4%
pT1b	48	14.5%	42	37.3%
pT1c	132	39.9%	39	34.5%
pT2	113	34.1%	10	8.8%
pT3 and higher	24	7.3%	0	0.0%
Luminal state				
Luminal A	88	26.6%	42	37.1%
Luminal B	190	57.4%	54	47.8%
Non-Luminal	13	3.9%	3	2.7%
Triple negative	40	12.1%	14	12.4%
Ki 67, average	27.8%		23.5%	

*Average value, if the density levels ACR C and D are equated with ACR 3 and 4

For 145 asymptomatic women undergoing screening, an interval of 1 to 2 years to the current MRI resulted in an average size of 9.8 mm; an interval of 2 to 3 years resulted in 10.2 mm, while the mean carcinoma size in patients without previous MRI was 15.6 mm.

The rate of nodal-positive carcinomas was 6.2% (7/113) in patients with previous MRI compared to 28.4% (94/331) without previous Breast MRI within the last 5 years.

To determine the comparability of both groups, the average age, the risk profile, the density type, the pT stage and luminal status were compared. Table 1 shows that there is a good comparability between the two groups.

Discussion

In breast diagnostics, mammography shows clear limitations

for the detection of breast cancer in women with high or very high tissue density [2,7]. This limitation cannot be significantly improved by tomosynthesis [3]. Sonography can also only compensate the limitation of mammography to a limited extent [2,7]. The combination of mammography and sonography ultimately leads to unsatisfactory results compared to the results of contrast-enhanced techniques. It was demonstrated, that a high sensitivity for the detection of breast cancer in women with high or very high tissue density can only be achieved if contrast-enhanced examination methods are used, as these methods allow the visualization of tumor neoangiogenesis. In principle, these methods include CE MRI, Contrast-Enhanced Mammography (CEM) and Contrast-Enhanced Breast Computer Tomography (CEBCT), which is actually only available to a very limited number of institutes [6,8-10].

Depending on the examination technique, mammography achieves a sensitivity of between 33% to 50% for the detection of breast cancer in women with density type ACR C and D [2,7]. Additional ultrasound enables an increase of 10% to 15% [2,7]. Ultimately, this results in a rate of non-detected breast carcinomas in the order of 50% and more. The limitations of mammography in women with dense and very dense breasts is relevant insofar as around 50% of women in a breast cancer-relevant age groups have a density type C or D. These women are underdiagnosed with mammography alone.

Regarding the sensitivity to depict breast cancer, CEMRI in high quality is superior to all other imaging modalities. This applies to both, intraductal tumors and invasive carcinomas. With adequate examination technique, CE Breast MRI achieves a sensitivity for the detection of breast cancer of over 95% [7]. The specificity is equivalent to other examination procedures [7].

In this retrospective study, a representative collective of women and patients in a diagnostic breast consultation is analyzed. Several findings emerge from the presented results:

In view of the usual tumor doubling times of invasive breast cancer in the order of 100 to 300 days, the use of breast MRI in women with dense breasts type ACR C and D allows the diagnosis of invasive breast cancer at least around one year earlier. In these women, breast cancer is often diagnosed at an excellent prognostic stage when breast MRI is used regularly as part of early detection. The proportion of small breast carcinomas in stages pT1a and pT1b is over 50%. In national screening programs, this rate is between 30 and 35%, depending on the initial and follow-up examinations [11]. This excellent rate applies to both, luminal and non-luminal breast carcinomas. In patients with previous MRI, the rate of nodal-positive carcinomas at the time of diagnosis of invasive carcinoma is around 6% compared to mammography screening with 24% [11]. The presented results suggest, that those patients with an average size of invasive carcinoma of less than 10 mm and node-negative lymph node status have an excellent prognosis with a mortality rate of less than 5%.

Concordant to the results of other working groups, breast MRI plays in the millimeter league if it is performed with high technical and methodological quality [12]. This will increasingly lead to modifications in treatment in the future. The spectrum here ranges from increased breast-conserving surgery to modifications according to chemotherapy or radiotherapy [13,14].

Looking at the group of women and patients without a previous MRI, the number of large tumors in the order of 2 cm to 3 cm and more is alarmingly high. Obviously, there is a need for even more consistent and targeted information, especially for women with high breast density. In principle, they should be advised to undergo contrast-enhanced imaging at an age relevant to breast cancer. Such techniques (CEM, CEMRI) allow an examination in a time of less than 10 min [15,16]. In summary it is recommended to integrate especially MRI as an additionally or primary examination method in the current screening concept for around 50% of clients with density type. In this context, MRI is preferred to CEM due to the lack of irradiation dosage. However, critical aspects concern to aspects like costs, imaging respectively reader quality, and an adequate number of MR systems.

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