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The value of "constant sharpness" as a diagnostic sign in MR-Mammography

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ABSTRACT

Purpose: To examine "constant lesion sharpness" as a morphological diagnostic sign in the differential diagnosis between benign and malignant lesions.
Material and methods: This prospective study had institutional review board approval and was HIPAA compliant. In total 1014 consecutive patients were examined (mean age 55 years ± 13 years) and evaluated in our University hospital towards the morphological shape of the lesion borders. The "Constant sharpness Sign" was defined as a lesion remaining continuously sharp for the duration of the dynamic scan. Inclusion criteria were unclear findings (e.g. BIRADS III/IV), Preoperative staging (BRIDAS IV/V), and referred patients from local clinic of gynecology. Exclusion criteria were MRM-examination ≤1 year before, status after surgery and/or biopsy, chemotherapy and/or radiation therapy. Reference Standard was histological verification. Images were diagnosed by two experienced radiologists in consensus, blinded to the standard of reference.
Results: 1014 patients with 1084 lesions (436 benign, 648 malignant lesions) were included into the study.

41.5% of benign lesions and 6.8% (181/436) of malignant lesions displayed a constant sharpness as an accompanying morphological sign ($P < 0.001$). This resulted in a sensitivity of 41.5%, specificity of 93.2%, a positive likelihood ratio of 6.1%, a negative likelihood ratio of 0.63 and an odd's ratio of 9,7%.
Summary and conclusion: The constant sharpness sign seems to be an accurate predictor of benign breast lesions, which may help to increase the accuracy of MRM as a morphological sign.

1. Introduction

The current guidelines of the American College of Radiology (ACR) list among the specific indications for breast MR (MR-Mammography: MRM) mainly patients after operation or radiation, preoperative staging, cancer of unknown primary (CUP Syndrome) and genetic disposition (BRCA 1 or 2, etc.) [1]. Although MRM is internationally accepted to be the most accurate imaging tool in the detection of breast cancer, there is still a broad discussion about a general use of MRM for all women, i.e. screening especially since specificity and cost are much disputed [2,3].

Through the introduction of additional diagnostic signs, defining a lesion and its differential diagnoses such as the Blooming sign [4], perifocal edema sign [5], the darkness in T2 Sign [6], etc. the general specificity of MRM could be raised to levels above 95% [3], suggesting that reader experience, and technical standards are prerequisites for "high-quality"- MRM [2].

During clinical routine the "Constant sharpness sign" (CS) as the opposing feature of the Blooming Sign was discovered to be a strong hint towards benign lesions. It is defined as a lesion obtaining a sharp contour all through the duration of the dynamic scan (Figs. 1 and 2).

While the commonly known "blooming sign" is a strong indicator for malignant lesions [4], the diagnostic value of the CS has not

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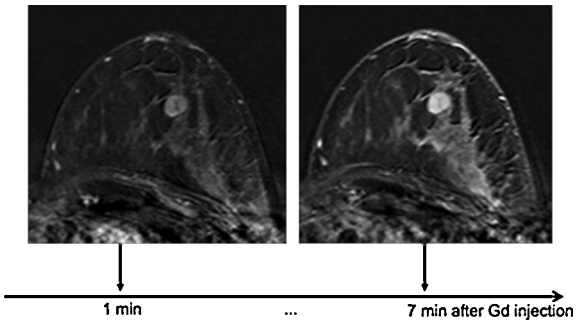

Fig. 1. Subtraction 1 and 7 min of the left breast after the injection of 0,1 mmol Gd-DTPA per kg body weight within 10 s, followed by the injection of 30 ml saline via an automatic injector (Medrad, Spectris, Pittsburgh) with 3 ml/s. The lesion in the medial aspect obtains its smooth margins throughout the duration of the dynamic scan.

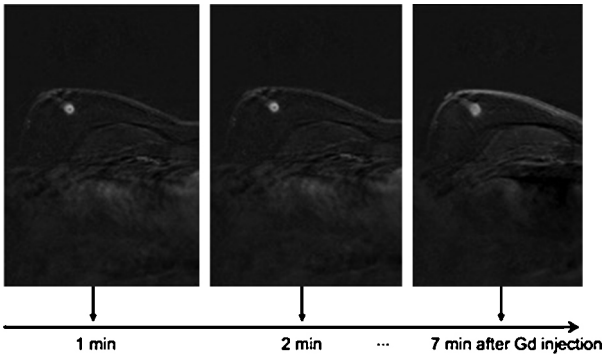

Fig. 2. Subtraction 1, 2 and 7 min of the right breast after the injection of 0,1 mmol Gd-DTPA per kg body weight within 10 s, followed by the injection of 30 ml saline via an automatic injector (Medrad, Spectris, Pittsburgh) with 3 ml/s. The lesion margins in the medial aspect blooms and becomes unsharp throughout the duration of the dynamic scan.

been evaluated yet. In an effort to complete this task we wanted to answer the question as to whether CS is a reliable indicator for benign lesions.

2. Material and methods

All patients gave their written informed consent for the examination in this IRB approved prospective study. CS was defined as a lesion obtaining continuously sharp margins for the duration of the dynamic scan, while the shape of the lesion was not relevant, i.e. absence of the "Blooming-Sign".

2.1. Patient collective

The study involved a consecutive number of series of 1014 patients (mean patient age e 55.5 years ± 13.0 years). In total there were 1084 lesions (436 benign lesions, 648 malignant lesions.

Inclusion criteria were unclear findings (e.g. BIRADS III), preoperative staging (BRIDAS IV/V), referred from local clinic of gynecology. Exclusion criteria were surgery and/or biopsy, as well as chemotherapy and/or radiation therapy less than 1 year ago. Histological verification served as reference standard.

2.2. Preparation

Before a planned MRM examination an extensive patient education about risks, the examination itself and contraindications was conducted, including patient anamnesis (i.e. day of the menstrual cycle, breastfeeding-, tumor-, hormone- and family history). Patients under HRT (hormone replacement therapy) were asked to stop HRT 4 weeks prior the MRM examination. Directly before being put into the scanner, the patients were asked to minimize motion in order to prevent artifacts.

2.3. Image acquisition and interpretation

All MRM exams were performed with a 1.5 T-MR Scanner (Siemens Symphony and Avanto) using the following protocol, as also described in detail in other publications (Table 1) [7].

The MRM examinations were performed and diagnosed by two experienced radiologist in consensus (>29 years of experience in MRM and >10 years of experience in MRM), blinded to the standard of reference.

2.4. Statistical methods

Diagnostic parameters were calculated using the following formulas:

Sensitivity: TP/(TP + FN); Specificity: TN/(TN + FP); Positive predictive value: TP/(TP + FP); Negative predictive value: TN/(TN + FN); Accuracy: (TP + TN)/(TP + FP + FN + TN); Positive likelihood ratio: Sens./1-Spec.; Negative likelihood ratio: 1-Sens./Spec.

3. Results

1014 patients with 1084 lesions (436 benign, 648 malignant lesions) were included into the study.

41.5% of benign lesions (Table 2) and 6.8% (181/436) of malignant lesions (Table 3) displayed constant sharpness as an accompanying morphological sign (P < 0.001). There was no significant difference in grading of malignant lesions, i.e. invasive cancers (Table 4). This resulted in a sensitivity of 41.5%, specificity of 93.2%,

Table 1
Examination protocol.

Sequence (Nr.)	1. Nat cor	2. Dynamic* tra	3. CM cor	4. T2-TSE	5. STIR
Weighting	T1	T1	T1	T2	T2 (T1, 150 ms)
Puls sequence	FLASH	FLASH	FLASH	TSE	TSE
Orientation	cor	transv	cor	transv	transv
TR (ms)	113	113	113	8900	8420
TE (ms)	4,6	4,6	4,6	207	70
Flip angle (°)	80	80	80	191	180
Slice thickness (mm)	3	3	3	3	3
Gap (mm)	0	0	0	0	0
Field of view (mm)	350	350	350	350	350
Nr. of slices	44	44	44	44	44
Matrix (Pixels)	230 × 256	307 × 384	230 × 256	435 × 512	326 × 384

* Connotation: dynamic study before and after the i.v. application of 0,1 mmol Gd-DTPA per kg body weight within 10 s, followed by the injection of 30 ml saline via an automatic injector (Medrad, Spectris, Pittsburgh) with 3 ml/s.

Table 2
Benign lesions showing the Constant sharpness sign (CS).

Diagnosis	CS positive [%]	95% Confidence Interval
Fibroadenoma	63.1 (65/103)	53.5–71.8
Phylloid tumor	90.0 (9/10)	59.6–98.2
Papilloma	45.8 (38/83)	35.5–56.5
Inflammation	15.0 (3/20)	5.2–36.4
Fibrocystic changes	30.0 (66/220)	24.3–36.4
Total	41.5 (181/436)	37.0–46.2

Table 3
Malignant lesions showing the Constant sharpness sign (CS).

Cancer Type	CS positive (%)	95% Confidence Interval
Ductal invasive	4,3 (15/347)	3,7–4,6
Lobular invasive	7,4 (8/108)	3,8–13,9
Ductal and lobular inv.	4,2 (1/24)	0,7–20,2
Tubular	3,7 (1/27)	0,07–18,3
Mucinous	16,7 (1/6)	3,0–56,4
Papillary	50 (1/2)	9,5–90,6
Other	14 (7/47)	7,0–26,2
Total	6,8 (44/648)	5,1–9,0

Table 4
Grading of invasive tumors in relation to the constant sharpness Sign (CS).

Grading	CS positive (%)	95% Confidence Interval
G1 - invasive	9,7 (6/62)	4,5–19,6
G2 - Invasive	5,1 (13/253)	3,0–8,6
G3 - Invasive	5,1 (11/217)	2,9–8,9

Table 5
Sensitivity, Specificity, NPV, PPV and Odds Ratio of CS.

Parameter	Value	95% Confidence Interval
Sensitivity	41.5%	37.0–46.2
Specificity	93.2%	91.0–94.9
Positive likelyhood ratio	6.1%	4.51–8.31
Negative likelyhood ratio	0.63%	0.58–0.68
Diagnostic odds ratio	9.7%	6.8–14.0

a positive likelihood ratio of 6.1%, a negative likelihood ratio of 0.63 and an odd's ratio of 9,7% (Table 5).

4. Discussion

According to our study "constant sharpness" (CS) represents a valuable morphological sign in MR-Mammography (MRM). CS may be considered the counterpart of the "Blooming-Sign" [4] and presenting as an accurate predictor of benignity. Blooming is merely caused by arterioveneous shunts, known to be responsible for the kinetic wash-in and -out effect. Aside from vessel density, also cellular density and changes in the extracellular matrix as well as in hydrostatic pressure seem to affecting the formation of the "Blooming-Sign" as well as CS.

A sensitivity of 41% of CS stretches the fact, that this morphological sign may not be seen in all cases. However, a specificity of 93.2% and an odds ratio of 9,7% underline its diagnostic power in the case of its presence. As the differential diagnosis of fibroadenoma and papilloma may be considered quite difficult in MRM, our study revealed constant sharpness to be a rather typical attribute of fibroadenoma with 63,5% of CS positive cases vs. papilloma with 45% CS positive cases, in line with the data of Fischer et al. [4].

In hypothesis papilloma have a higher stromal vessel density, which may lead to extravasation of contrast medium, which in turn may be deported more slowly within the space between insterstitium and the intracellular space. Additionally papilloma tend to be more associated with dissociated fibrosis (pseudoinfiltrations) and sclerosis, leading to the presence of blooming [8].

Along with other predicting morphological and kinetic signs of papilloma, constant sharpness may contribute to an improved differential diagnosis as well as improve the accuracy of MR-mammography all together.

On a different note however, there were some malignant lesions, displaying CS as well. Especially 16.7% CS positive mucinous cancers and 50% CS positive papillary cancers (Table 3) emphasize the fact that the dynamically constant sharpness of a lesion may not be considered a pure sign of benignity. Papillary cancers are usually rich in parenchyma, lacking stroma, hypothetically making an interstitial accumulation (blooming) of contrast medium almost impossible [8].

These morphological and kinetic exceptions hint towards the necessity for the implementation of as many possible diagnostic signs, when forming a diagnosis and differential diagnosis in MR-Mammography and points towards the ongoing need for the scientific evaluation of additional morphological and kinetic signs in order to optimize MRM in its accuracy. It also indicates, that the common MR-BIRADS descriptors of lesions may need to be updated, as many known diagnostic signs [9] known in MR-Mammography are still not yet scientifically evaluated.

4.1. Study limitations

Our results were obtained within a single center study and therefore should be confirmed in a multicenter setting. Also there is a need to test on constant sharpness with other techniques, using commonly used 3D techniques with/without fat suppression in order to evaluate technical differences.

5. Conclusion

The constant sharpness sign (CS) was a strong predictor of benignity. It seems to be a more typical morphological sign of fibroadenoma than papilloma.

Conflicts of interest

There are no conflicts of interest.

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