



Original research

Can we predict lesion detection rates in second-look ultrasound of MRI-detected breast lesions? A systematic analysis



Alexander Bumberger, Paola Clauser, Michael Kolta, Panagiotis Kapetas, Maria Bernathova, Thomas H. Helbich, Katja Pinker, Pascal A. Baltzer*

Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Austria

ARTICLE INFO

Keywords:

Breast
Breast neoplasms
Ultrasonography
Mammary
Clinical decision making
Magnetic resonance imaging

ABSTRACT

Purpose: To predict detection rates (DR) in second-look ultrasound of MRI-detected breast lesions by systematically combining clinical and anthropomorphic features.

Methods: A total of 104 suspicious breast-lesions, that were initially detected on breast MRI and underwent subsequent SLU from January 2013 through December 2013, were evaluated in this retrospective analysis. All images were reviewed by an experienced radiologist for this study. Both anthropomorphic, spatial and BI-RADS lesion features were recorded. Uni- and multivariate Classification and Regression Trees (CRT) statistics were used to predict SLU DR by these features.

Results: Among 104 MRI-detected lesions, 58 (55.8%) showed a correlate on SLU. In univariate analysis, homogeneous fatty or dense fibro-glandular-tissue-composition (FGT) as assessed by ultrasound, segmental non-mass-distribution pattern and small breast size as assessed by MRI were significantly associated with higher DR on SLU. The remaining BI-RADS features did not significantly affect SLU DR according to our data. The predictive model could stratify the likelihood of SLU correlates as high, intermediate and low according to FGT, lesion type, size and position.

Conclusions: By systematically combining the features FGT, lesion type, size and position, we could predict SLU DR of MRI-detected breast lesions. This may help to decide the preferable method for lesion biopsy or follow-up in clinical practice.

1. Introduction

Magnetic Resonance Imaging (MRI) of the breast is considered the most sensitive imaging method for detection of malignant breast lesions in a variety of indications and settings [1–6]. Consequently, MRI of the breast is increasingly utilized in clinical practice [7,8]. High sensitivity however results in a significant number of incidental findings ranging between 5.3 [9] and 32% [10] that need to be further assessed. Second-look ultrasound (SLU) is considered a fast, less expensive and more easily accessible method for further patient workup of suspicious MRI findings [11]. While SLU can be considered a useful tool to further assess incidental MRI findings, evidence suggests that SLU detection rates depend on lesion type (mass vs non-mass and benign vs malignant) and lesion size [12–19]. A systematic review identified higher SLU detection rates in mass (66 vs 29%) and malignant (79 vs 52%) lesions but reported a lack of data regarding further factors which could predict whether an MRI-detected lesion would be identified by SLU

[20]. This however would be of help to optimize the clinical workflow within assessment centers: while lesions with a high likelihood to be visible on SLU should generally be scheduled for this examination, lesions with a lower likelihood to be detected by SLU could either be directly scheduled for MRI follow-up or biopsy or undergo SLU performed by experts only.

Hence, this study aims to predict detection rates (DR) in second-look ultrasound of MRI-detected breast lesions by systematically combining clinical and anthropomorphic features.

2. Methods

Eligible for this retrospective analysis were 1522 patients with 1692 MRI examinations that were assessed between January 2013 and December 2013 at the Department of Radiology at the Medical University of Vienna, a tertiary care university screening and assessment center. MRI-detected BI-RADS category 4 or 5 lesions with SLU

* Corresponding author at: Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna/Vienna General Hospital, Waehringer Guertel 18-20, 1090 Vienna, Austria.

E-mail address: pascal.baltzer@meduniwien.ac.at (P.A. Baltzer).

<https://doi.org/10.1016/j.ejrad.2019.02.008>

Received 21 July 2018; Received in revised form 22 January 2019; Accepted 9 February 2019

0720-048X/© 2019 Elsevier B.V. All rights reserved.

List of abbreviations		EUSOMA	European Society of Mastology
BI-RADS	Breast Imaging Reporting And Data System	FGT	Fibroglandular Tissue
CRT	Classification and Regression Tree	MRI	Magnetic Resonance Imaging
DR	Detection Rates	SLU	Second-look ultrasound (or targeted ultrasound)
EUSOBI	European Society Of Breast Imaging	STIR	Short Tau Inversion Recovery
		T1w/T2w	T1-weighted/T2-weighted

within 6 weeks after MRI and subsequent biopsy or follow-up for at least 12 months, were included in this study. Of the 1522 patients, 103 patients (mean age 51 ± 12 years, range 26–78 years) with 104 lesions in 103 exams fulfilled the inclusion criteria and were identified based on a standardized retrospective review of our electronic hospital database. All other cases were excluded as they did either not fulfill the inclusion criteria or retrospective database review could not establish whether a lesion was first identified by MRI or not.

At the reviewed time frame, there was no predefined protocol as to whether patients should undergo SLU or not, thus it was recommended at the discretion of the respective radiologist.

MRI images were acquired on different scanners both in house and at multiple (n > 10) referring imaging centers. All examination protocols included a T2w and or STIR sequence as well as T1-weighted contrast-enhanced dynamic images before and after single dose Gd-based contrast media injection at 1.5 or 3 T, all in line with EUSOBI and EUSOMA recommendations [21,22]. SLU was performed by one out of five radiologists with at least 5 years of experience in breast imaging, using a high frequency transducer for B-mode imaging (Acuson S3000 Siemens Germany).

All MRI and ultrasound images were retrospectively reviewed by a specialized breast radiologist (P.C.) with over 5 years of experience in breast imaging. Imaging review included breast size (estimated in an empirical 4-step manner as small (A) – medium (B) – large (C) – very large (D) as established elsewhere [23]), amount (MRI) and composition (US) of fibro-glandular tissue and lesion position, type and morphological criteria according to the MRI BI-RADS lexicon [24]. Lesion position is defined as retroareolar if in proximity to the nipple and prepectoral if in the immediate vicinity of the thoracic wall. All other lesion locations, comprising about 70% of the breast are defined as

central. In addition, the following information was collected: patient age, biopsy method, histopathological results and follow-up information.

Histopathologic results were obtained for 92 lesions. 50 lesions were biopsied under ultrasound-guidance (16 G), 35 under MR-guidance (9 G vacuum-assisted biopsy), one under stereotactic guidance (9 G vacuum-assisted biopsy) and six were primarily surgically excised. The remaining twelve lesions were classified BI-RADS 3 and followed up for 24 months by MRI, US or MG as deemed appropriate.

2.1. Statistics

Univariate analysis was performed using cross-tabulations of recorded criteria against SLU detection status (detected versus not detected) and chi-square or Fisher’s exact testing as appropriate. The multivariate classification and regression tree (CRT) algorithm was used to calculate a predictive model for SLU detection rates. The CRT-model utilizes dichotomized parameters to create a decision tree, aiming to distinguish lesions which are likely to exhibit an SLU-correlate from those that are not. The splitting method used was the Gini-index, the minimum size of parent and child nodes set to 10 and 5. Automated Bonferroni-correction was performed to avoid accumulation of alpha-errors in multiple testing, and the decision tree was tenfold cross-validated. ROC-Analysis was performed to assess the accuracy of the resulting predictive model.

The alpha error to define presence of statistical significance for this exploratory study was set to 10% for all statistical analyses. Consequently, tests yielding P-values ≤ 0.1 were interpreted as representing statistically significant results.

Table 1
Detection Rates by Lesion Features and BI-RADS category assignment.

Feature	SLU correlate in No. (%) of lesions		Total (%)	P-Value	
	absent	present			
Lesion type	mass	20 (35.1)	37 (64.9)	57 (100)	0.116
	non-mass	22 (55.0)	18 (45.0)		
MRI mass shape	focus	4 (57.1)	3 (42.9)	7 (100)	0.512
	oval	8 (33.3)	16 (66.7)	24 (100)	
	round	7 (46.7)	8 (53.3)	15 (100)	
	irregular	5 (26.3)	13 (73.7)	18 (100)	
Mass margins	circumscribed	5 (27.8)	13 (72.2)	18 (100)	0.478
	irregular	14 (41.2)	20 (58.8)	34 (100)	
	spiculated	1 (20.0)	4 (80.0)	5 (100)	
Mass internal enhancement	homogeneous	9 (42.9)	12 (57.1)	21 (100)	0.626
	heterogeneous	11 (32.4)	23 (67.6)	34 (100)	
	rim	0 (0.0)	1 (100.0)	1 (100)	
	dark septations	0 (0.0)	1 (100.0)	1 (100)	
Non-mass distribution	focal	6 (50.0)	6 (50.0)	12 (100)	0.027
	linear	9 (90.0)	1 (10.0)	10 (100)	
	segmental	0 (0.0)	3 (100.0)	3 (100)	
	regional	7 (46.7)	8 (53.3)	15 (100)	
Non-mass internal enhancement	homogeneous	5 (71.4)	2 (28.6)	7 (100)	0.383
	heterogeneous	15 (53.6)	13 (46.4)	28 (100)	
	clumped	1 (25.0)	3 (75.0)	4 (100)	
	clustered ring	1 (100.0)	0 (0)	1 (100)	
MRI BI-RADS category	BI-RADS 3	4 (44.4)	5 (55.6)	9 (100)	0.568
	BI-RADS 4	36 (42.4)	49 (57.6)	85 (100)	
	BI-RADS 5	6 (60)	4 (40)	10 (100)	

3. Results

A total of 104 lesions (32 malignant, 72 benign) matched the inclusion criteria of this study and were considered for statistical analysis that focused on the association of recorded clinical and imaging lesion-features with SLU DR. Among 104 MR-detected lesions, 58 (55.8%, 18 of them malignant) were seen on SLU.

Table 1 gives an overview of all lesion features stratified by their SLU detection status. Though not significant on univariate testing ($P = 0.116$), masses showed the highest SLU DR (64.9%), whereas SLU DR in non-masses was lower (45.0%). Foci and mass lesions with associated non-mass enhancements had a 42.9% chance to be detected on SLU.

In non-mass lesions, the distribution pattern was significantly associated with SLU DR ($P = 0.027$): while segmental non-mass distribution pattern was predictive of lesion identification on SLU (3 out of 3, 100% SLU DR), linear non-mass distribution pattern was not (1 out of 10, 10% SLU DR). Focal or regional distribution were unspecific and associated with intermediate SLU DR (Table 1).

Lesions in breasts composed of homogeneous fatty or dense fibroglandular tissue (FGT) as assessed by ultrasound were associated with SLU correlates in 69.4% (25/36) of the cases. This number dropped to 47.8% (32/67) in case of heterogeneous FGT. This difference was statistically significant ($P = 0.040$). MRI amount of FGT was not associated with SLU DR ($P = 0.183$, see Table 2).

Breast size was significantly associated with different SLU DR ($P = 0.063$): it was 100% (5/5) in case of small breasts (A) and implants, decreased to 55.8% (48/86) in medium sized breasts (B, C) and further to 38.5% (5/13) in large breasts (D).

MR lesion size was dichotomized at a cut-off of 10 mm. 50% (23/46) of the lesions ≤ 10 mm were detected on SLU, while an ultrasound correlate was found in 60.3% (35/58) among lesions > 10 mm ($P = 0.352$) (Table 2).

In addition, lesion position ($P = 0.332$), MRI mass shape ($P = 0.512$), mass margins ($P = 0.478$), mass internal enhancement ($P = 0.626$) and non-mass internal enhancement ($P = 0.383$) were not predictive of SLU DR upon univariate analysis (Table 1).

Supplementary Figure 1 represents the decision-tree as calculated by multivariate CRT analysis. All recorded lesion features were considered for this analysis. Feature selection is done by automated repetitive calculations, selecting significant features by hierarchical ordering after statistical testing. The first database split thus presents the most significant criterion, in this case FGT-breast-composition as assessed by ultrasound. Subsequent features leading to a significant improvement in stratifying lesions by their SLU DR included: lesion size

and type, lesion position and US FGT composition. As listed in Table 3, lesions ≤ 10 mm, centrally located within breast with heterogeneous US FGT composition had a low likelihood of detection by SLU while masses in case of homogeneous US FGT or masses > 10 mm in case of heterogeneous FGT had high SLU detection rates. All other feature combinations demonstrated intermediate SLU detection rates (see Table 3).

4. Discussion

As a fast, easily accessible and relatively inexpensive test, SLU is an important method to guide biopsies or perform follow-up examinations when it comes to clinical management of MR-detected breast-lesions that haven't been found on mammography or ultrasound. This is why SLU has been recommended as the method of choice to primarily investigate unclear or suspicious lesions detected by MRI [20]. However, though a fast and inexpensive examination, SLU can accumulate to substantial personnel costs if generally performed in all MRI-detected lesions. It was therefore the purpose of this study to investigate predictors of SLU DR to assist the clinical decision whether to do SLU or not. We identified simple and clinically available criteria that can be used to check the probability of a lesion to show a correlate on SLU. By systematically combining the features FGT, lesion type, size and position, we could predict SLU DR of MRI-detected breast lesions. Mass lesions in case of homogeneous US FGT and mass lesions > 10 mm in size in case of heterogeneous FGT demonstrated a high likelihood of success while lesion detection failed in most (80%) cases of lesions ≤ 10 mm that were centrally located in breast parenchyma with heterogeneous presentation upon US. Therefore, while it would be most helpful to identify lesions that should not undergo SLU due to very low identification rates, such simple conclusions cannot be drawn from our data: as the lowest lesion detection rate was 20% in our population, our findings rather suggest that SLU could always be tried.

This applies particularly in BI-RADS ≥ 4 lesions: even avoiding only one out of five expensive MRI-guided breast biopsies indicated in these cases would likely prove cost-effective [25,26]. In addition, a recent survey on the use of MR imaging in Europe has identified a significant shortage in the availability of MRI-guided biopsy resources, further stressing the need for alternative procedures to resolve suspicious breast lesions such as SLU [27]. On the other hand, MRI follow-up may be the method of choice in BI-RADS 3 lesions with a low likelihood of detection by SLU. This is of importance as the results can be directly transferred to clinical practice, thereby helping to focus personnel and equipment according to their availability. Of note, it is still unclear how many follow-up examinations are necessary to resolve BI-RADS 3 lesions as suggested in [28]. While we did not investigate a connection

Table 2
SLU detection Rates by anthropomorphic features and lesion position and size.

Feature		SLU correlate in No. (%) of lesions		Total (%)	P-Value
		absent	present		
breast size (MRI)	Small (A), implants	0 (0.0)	5 (100.0)	5 (100)	0.063
	Medium-large (B, C)	38 (44.2)	48 (55.8)	86 (100)	
	Very large (D)	8 (61.5)	5 (38.5)	13 (100)	
Amount of FGT (MRI)	ACR a	4 (25)	12 (75)	16 (100)	0.183
	ACR b	15 (53.6)	13 (46.7)	28 (100)	
	ACR c	20 (51.3)	19 (48.7)	39 (100)	
	ACR d	7 (35)	13 (65)	20 (100)	
FGT composition (US)	homogeneous fatty or dense	11 (30.6)	25 (69.4)	36 (100)	0.040
	heterogeneous	35 (52.2)	32 (47.8)	67 (100)	
Lesion position (MRI)	retro-areolar	8 (32.0)	17 (68.0)	25 (100)	0.332
	central	28 (46.7)	32 (53.3)	60 (100)	
	posterior	10 (52.6)	9 (47.4)	19 (100)	
Lesion size (MRI)	≤ 10 mm	23 (50.0)	23 (50.0)	46 (100)	0.325
	> 10 mm	23 (39.7)	35 (60.3)	58 (100)	

Table 3

Predictive model feature combinations hierarchically ordered by SLU detection rates marked by white (low likelihood of SLU correlate), bright grey (intermediate likelihood of SLU correlate) and grey (high likelihood of SLU correlate).

Feature combination	SLU correlate in No. (%) of lesions		Total (%)
	absent	present	
Heterogeneous FGT & lesion size ≤10mm & central lesion position	12 (80.0)	3 (20.0)	15 (100)
Heterogeneous FGT & lesion size >10mm & non-mass lesion type & central lesion position	9 (60.0)	6 (40.0)	15 (100)
Heterogeneous FGT & non-mass or focus lesion type	7 (50.0)	7 (50.0)	14 (100)
Heterogeneous FGT & lesion size ≤10mm & retroareolar or posterior lesion position	7 (46.7)	8 (53.3)	15 (100)
Heterogeneous FGT & lesion size >10mm & non-mass lesion type & retroareolar or posterior lesion position	4 (44.4)	5 (55.6)	9 (100)
Heterogeneous FGT & lesion size >10mm & mass lesion type	3 (23.1)	10 (76.9)	13 (100)
Homogeneous FGT & mass lesion type	4 (17.4)	19 (82.6)	23 (100)

between the sonographer's experience in SLU and SLU success, it may be suggested that the more challenging cases should generally be second-read by an experienced radiologists to increase lesion yield. In addition, this approach would increase the experience of less experienced sonographers.

While prior studies mainly sought to investigate the performance of SLU in specific clinical settings and lesion types, the current study focused on systematically identifying subgroups of MR-detected lesions that are likely or not likely to present with a correlate on SLU. Previous studies have stressed the necessity to address this topic to improve clinical decisions whether to do or not to do an SLU examination [12,20].

We identified several anthropomorphic features that were helpful to predict whether SLU would yield a correlate or not. Our data suggests, that the composition of fibro-glandular-tissue (FGT) as assessed by ultrasound ranges among the features that are most likely to predict SLU DR and should therefore be considered in pre-SLU assessment. This does not astonish: homogeneous FGT is more easily assessed on ultrasound as compared to heterogeneous FGT. In addition, smaller breast size was significantly associated with a higher SLU DR in our study. While this might not be a surprising result, it is an important factor influencing SLU-DR that has not been demonstrated previously.

Lesion type (mass/non-mass) counts among the features that have been most frequently observed to be a significant predictor for SLU DR, showing masses to be significantly more often associated with an ultrasound-correlate [12,20,29]. In our study, SLU DR for masses was 64.9% and 45.0% for non-masses, which is roughly consistent with the reported pooled rates of 66% and 29%, respectively [20]. However, this difference in DR was not statistically significant in our univariate analysis, an observation also made by Aracava et al., in a prospective trial concerning this topic [30]. One further important parameter to predict SLU detection rates was non-mass enhancement distribution pattern. Previous studies have mainly investigated the predictive value of non-mass features regarding malignancy rates [31–34]. However, our analysis showed that focal and segmental non-mass lesions are better depicted by SLU than linear or regional ones.

MR lesion size- although not being significantly associated with SLU-DR in univariate analysis - was a significant predictor of SLU-DR in the multivariate CRT-model. This might in a sense account for the controversial data that have been published, regarding the predictive value of MR-lesion-size, with some studies pointing towards a significant predictive value [12,13], and some suggesting that there is none [13,14,29,30,35]. However, as Spick and Baltzer pointed out in their meta-analysis, a test that is not stratified by lesion type disregards the fact that masses are regularly smaller than non-masses, and could

therefore incorrectly suggest that lesion size is not associated with SLU detection rates [20,31]. According to the subgroup analysis by Wir- atkapun et al., increasing lesion size resulted in a significantly higher ultrasound conspicuity among masses only [13], whereas Meissnitzer et al. found this to be true for both masses and non-masses [12]. Considering the generally lower SLU DR in non-mass lesions, an adequate number of non-mass lesions is crucial to identify significant differences of SLU-DR regarding lesion size. This might partially account for the insignificant predictive value of lesion size among non-masses as compared to masses, e.g. in [13].

This study has several limitations, foremost the retrospective design and a limited number of cases. Most important, there was no predefined protocol as to whether SLU should be performed in a specific case or not. Thus, SLU was performed at the discretion of the attending radiologist, potentially limiting generalizability of the reported findings. As the results were obtained in a large assessment center, we deem them to quite accurately reflect clinical practice. While we did not identify criteria to suggest not to do SLU, they encourage further research in this direction. The proposed categories of high, intermediate and low likelihood of SLU correlates warrant prospective validation and further refinement, e.g. by considering the examiner's experience and further imaging findings such as mammography. It should be noted that stereotactical biopsy could be another alternative to MRI-guided biopsy in case of a negative SLU examination. The potential value of second-look tomosynthesis has been suggested in [36].

5. Conclusion

We identified criteria based on breast size, tissue composition assessed by ultrasound and lesion features including type, size and position that predict SLU detection rates and could define specific feature combinations associated with low, intermediate and high probability of MRI-detected lesions to be detected by SLU. While our reported SLU detection rates of ≥ 20% suggest that SLU can always be tried, some suggestions could be given: in BI-RADS ≥ 4 lesions, SLU should always be used due to the high costs and low availability of MRI-guided biopsies. In BI-RADS 3 lesions with a low likelihood to be detected by SLU, MRI follow-up may be the preferable decision. Lesions with a high likelihood of detection by SLU could be examined by less experienced readers while challenging cases should be second-read by an experienced reader. These findings could help to guide daily clinical decisions depending on the available resources in personnel and equipment.

Conflict of interest

Manuscript: Can we predict lesion detection rates in second-look ultrasound of MRI-detected breast lesions? A systematic analysis.

The authors (Alexander Bumberger, Paola Clauser, Michael Kolta, Panagiotis Kapetas, Maria Bernathova, Thomas H. Helbich, Katja Pinker and Pascal Baltzer) have no conflicts of interest to declare. No funding was used for this scientific work.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ejrad.2019.02.008>.

References

- [1] E. Warner, H. Messersmith, P. Causer, A. Eisen, R. Shumak, D. Plewes, Systematic review: using magnetic resonance imaging to screen women at high risk for breast cancer, *Ann. Intern. Med.* 148 (2008) 671–679.
- [2] C.C. Riedl, N. Luft, C. Bernhart, M. Weber, M. Bernathova, M.-K.M. Tea, M. Rudas, C.F. Singer, T.H. Helbich, Triple-modality screening trial for familial breast cancer underlines the importance of magnetic resonance imaging and questions the role of mammography and ultrasound regardless of patient mutation status, age, and breast density, *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* (2015), <https://doi.org/10.1200/JCO.2014.56.8626>.
- [3] N. Houssami, S. Giatto, P. Macaskill, S.J. Lord, R.M. Warren, J.M. Dixon, L. Irwig, Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer, *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* 26 (2008) 3248–3258, <https://doi.org/10.1200/JCO.2007.15.2108>.
- [4] B. Bennani-Baiti, N. Bennani-Baiti, P.A. Baltzer, Diagnostic performance of breast magnetic resonance imaging in non-calcified equivocal breast findings: results from a systematic review and meta-analysis, *PLoS One* 11 (2016) e0160346, <https://doi.org/10.1371/journal.pone.0160346>.
- [5] B. Bennani-Baiti, P.A. Baltzer, MR imaging for diagnosis of malignancy in mammographic microcalcifications: a systematic review and meta-analysis, *Radiology*. (2016) 161106, <https://doi.org/10.1148/radiol.2016161106>.
- [6] N. Berger, A. Luparia, G. Di Leo, L.A. Carbonaro, R.M. Trimboli, F. Ambrogi, F. Sardanelli, Diagnostic performance of MRI versus galactography in women with pathologic nipple discharge: a systematic review and meta-analysis, *AJR Am. J. Roentgenol.* (2017) 1–7, <https://doi.org/10.2214/AJR.16.16682>.
- [7] D.A. Hill, J.S. Haas, R. Wellman, R.A. Hubbard, C.I. Lee, J. Alford-Teaster, K.J. Wernli, L.M. Henderson, N.K. Stout, A.N.A. Tosteson, K. Kerlikowske, T. Onega, Utilization of breast cancer screening with magnetic resonance imaging in community practice, *J. Gen. Intern. Med.* (2017), <https://doi.org/10.1007/s11606-017-4224-6>.
- [8] B.K. Killelea, J.B. Long, A.B. Chagpar, X. Ma, P.R. Soulos, J.S. Ross, C.P. Gross, Trends and clinical implications of preoperative breast MRI in medicare beneficiaries with breast cancer, *Breast Cancer Res. Treat.* 141 (2013) 155–163, <https://doi.org/10.1007/s10549-013-2656-1>.
- [9] C. Spick, D.H.M. Szolar, K.W. Preidler, P. Reittner, K. Rauch, P. Brader, M. Tillich, P.A. Baltzer, 3 Tesla breast MR imaging as a problem-solving tool: diagnostic performance and incidental lesions, *PLoS One* 13 (2018) e0190287, <https://doi.org/10.1371/journal.pone.0190287>.
- [10] R.M. Mann, Y.L. Hoogveen, J.G. Blickman, C. Boetes, MRI compared to conventional diagnostic work-up in the detection and evaluation of invasive lobular carcinoma of the breast: a review of existing literature, *Breast Cancer Res. Treat.* 107 (2008) 1–14, <https://doi.org/10.1007/s10549-007-9528-5>.
- [11] R.M. Mann, C. Balleyguier, P.A. Baltzer, U. Bick, C. Colin, E. Cornford, A. Evans, E. Fallenberg, G. Forrai, M.H. Fuchsjäger, F.J. Gilbert, T.H. Helbich, S.H. Heywang-Köbrunner, J. Camps-Herrero, C.K. Kuhl, L. Martincich, F. Pediconi, P. Panizza, L.J. Pina, R.M. Pijnappel, K. Pinker-Domenig, P. Skaane, F. Sardanelli, European Society of Breast Imaging (EUSOBI), with language review by Europa Donna—the European breast Cancer coalition, breast MRI: EUSOBI recommendations for women's information, *Eur. Radiol.* 25 (2015) 3669–3678, <https://doi.org/10.1007/s00330-015-3807-z>.
- [12] M. Meissnitzer, D.D. Dershaw, C.H. Lee, E.A. Morris, Targeted ultrasound of the breast in women with abnormal MRI findings for whom biopsy has been recommended, *AJR Am. J. Roentgenol.* 193 (2009) 1025–1029, <https://doi.org/10.2214/AJR.09.2480>.
- [13] C. Wiratkapun, D. Duke, A.S. Nordmann, P. Lertsithichai, V. Narra, P.T. Barton, C.F. Hildebolt, K.T. Bae, Indeterminate or suspicious breast lesions detected initially with MR imaging: value of MRI-directed breast ultrasound, *Acad. Radiol.* 15 (2008) 618–625, <https://doi.org/10.1016/j.acrad.2007.10.016>.
- [14] W.B. Demartini, P.R. Eby, S. Peacock, C.D. Lehman, Utility of targeted sonography for breast lesions that were suspicious on MRI, *AJR Am. J. Roentgenol.* 192 (2009) 1128–1134, <https://doi.org/10.2214/AJR.07.3987>.
- [15] H. Abe, R.A. Schmidt, R.N. Shah, A. Shimauchi, K. Kulkarni, C.A. Sennett, G.M. Newstead, MR-directed (“Second-Look”) ultrasound examination for breast lesions detected initially on MRI: MR and sonographic findings, *AJR Am. J. Roentgenol.* 194 (2010) 370–377, <https://doi.org/10.2214/AJR.09.2707>.
- [16] G. Carbognin, V. Girardi, C. Calciolari, A. Brandalise, F. Bonetti, A. Russo, R. Pozzi Mucelli, Utility of second-look ultrasound in the management of incidental enhancing lesions detected by breast MR imaging, *Radiol. Med.* 115 (2010) 1234–1245, <https://doi.org/10.1007/s11547-010-0561-9>.
- [17] R. Candelaria, B.D. Fornage, Second-look US examination of MR-detected breast lesions, *J. Clin. Ultrasound JCU.* 39 (2011) 115–121, <https://doi.org/10.1002/jcu.20784>.
- [18] M.L. Luciani, F. Pediconi, M. Telesca, F. Vasselli, V. Casali, E. Miglio, R. Passariello, C. Catalano, Incidental enhancing lesions found on preoperative breast MRI: management and role of second-look ultrasound, *Radiol. Med.* 116 (2011) 886–904, <https://doi.org/10.1007/s11547-011-0630-8>.
- [19] A.P. Lourenco, M.T.M. Chung, M.B. Mainiero, Utility of targeted sonography in management of probably benign breast lesions identified on magnetic resonance imaging, *J. Ultrasound Med. Off. J. Am. Inst. Ultrasound Med.* 31 (2012) 1033–1040.
- [20] C. Spick, P.A.T. Baltzer, Diagnostic utility of second-look US for breast lesions identified at MR imaging: systematic review and meta-analysis, *Radiology* 273 (2014) 401–409, <https://doi.org/10.1148/radiol.14140474>.
- [21] R.M. Mann, C.K. Kuhl, K. Kinkel, C. Boetes, Breast MRI: guidelines from the European society of breast imaging, *Eur. Radiol.* 18 (2008) 1307–1318, <https://doi.org/10.1007/s00330-008-0863-7>.
- [22] F. Sardanelli, C. Boetes, B. Borisch, T. Decker, M. Federico, F.J. Gilbert, T. Helbich, S.H. Heywang-Köbrunner, W.A. Kaiser, M.J. Kerin, R.E. Mansel, L. Marotti, L. Martincich, L. Mauriac, H. Meijers-Heijboer, R. Orecchia, P. Panizza, A. Ponti, A.D. Purushotham, P. Regitnig, M.R. Del Turco, F. Thibault, R. Wilson, Magnetic resonance imaging of the breast: recommendations from the EUSOMA working group, *Eur. J. Cancer Oxf. Engl.* 1990 46 (2010) 1296–1316, <https://doi.org/10.1016/j.ejca.2010.02.015>.
- [23] P. Clauser, K. Pinker, T.H. Helbich, P. Kapetas, M. Bernathova, Pa.T. Baltzer, Fat saturation in dynamic breast MRI at 3 Tesla: is the Dixon technique superior to spectral fat saturation? A visual grading characteristics study, *Eur. Radiol.* 24 (2014) 2213–2219, <https://doi.org/10.1007/s00330-014-3189-7>.
- [24] C. D'Orsi, E. Sickles, E. Mendelson, E. Morris, ACR BI-RADS® atlas, breast imaging reporting and data system, *Am. Coll. of Radiol.* (2013).
- [25] T. Onega, A.N.A. Tosteson, J. Weiss, J. Alford-Teaster, R.A. Hubbard, L.M. Henderson, K. Kerlikowske, M.E. Goodrich, C. O'Donoghue, K.J. Wernli, W.B. DeMartini, B.A. Virnig, Costs of diagnostic and preoperative workup with and without breast MRI in older women with a breast cancer diagnosis, *BMC Health Serv. Res.* 16 (2016) 76, <https://doi.org/10.1186/s12913-016-1317-6>.
- [26] B.K. Patel, R.J. Gray, B.A. Pockaj, Potential cost savings of contrast-enhanced digital mammography, *Am. J. Roentgenol.* 208 (2017) W231–W237, <https://doi.org/10.2214/AJR.16.17239>.
- [27] P. Clauser, R. Mann, A. Athanasiou, H. Prosch, K. Pinker, M. Dietzel, T.H. Helbich, M. Fuchsjäger, J. Camps-Herrero, F. Sardanelli, G. Forrai, P.A.T. Baltzer, A survey by the European Society of Breast Imaging on the utilisation of breast MRI in clinical practice, *Eur. Radiol.* 28 (2018) 1909–1918, <https://doi.org/10.1007/s00330-017-5121-4>.
- [28] C. Spick, H. Bickel, S.H. Polanc, P.A. Baltzer, Breast lesions classified as probably benign (BI-RADS 3) on magnetic resonance imaging: a systematic review and meta-analysis, *Eur. Radiol.* (2017), <https://doi.org/10.1007/s00330-017-5127-y>.
- [29] L.R. LaTrenta, J.H. Menell, E.A. Morris, A.F. Abramson, D.D. Dershaw, L. Liberman, Breast lesions detected with MR imaging: utility and histopathologic importance of identification with US, *Radiology* 227 (2003) 856–861, <https://doi.org/10.1148/radiol.2273012210>.
- [30] M.M. Aracava, R. Chojniak, J.A. Souza, A.G.V. Bitencourt, E.F. Marques, Identification of occult breast lesions detected by magnetic resonance imaging with targeted ultrasound: a prospective study, *Eur. J. Radiol.* 83 (2014) 516–519, <https://doi.org/10.1016/j.ejrad.2013.12.017>.
- [31] P.A.T. Baltzer, M. Benndorf, M. Dietzel, M. Gajda, I.B. Runnebaum, W.A. Kaiser, False-positive findings at contrast-enhanced breast MRI: a BI-RADS descriptor study, *AJR Am. J. Roentgenol.* 194 (2010) 1658–1663, <https://doi.org/10.2214/AJR.09.3486>.
- [32] R.L. Gutierrez, W.B. DeMartini, P.R. Eby, B.F. Kurland, S. Peacock, C.D. Lehman, BI-RADS lesion characteristics predict likelihood of malignancy in breast MRI for masses but not for nonmasslike enhancement, *AJR Am. J. Roentgenol.* 193 (2009) 994–1000, <https://doi.org/10.2214/AJR.08.1983>.
- [33] P.A.T. Baltzer, M. Dietzel, W.A. Kaiser, Nonmass lesions in magnetic resonance imaging of the breast: additional T2-weighted images improve diagnostic accuracy, *J. Comput. Assist. Tomogr.* 35 (2011) 361–366, <https://doi.org/10.1097/RCT.0b013e31821065c3>.
- [34] M. Tozaki, K. Fukuda, High-spatial-resolution MRI of non-masslike breast lesions: interpretation model based on BI-RADS MRI descriptors, *AJR Am. J. Roentgenol.* 187 (2006) 330–337, <https://doi.org/10.2214/AJR.05.0998>.
- [35] L.S.J. Sim, J.H.C.L. Hendriks, P. Bult, S.M.C. Fook-Chong, US correlation for MRI-detected breast lesions in women with familial risk of breast cancer, *Clin. Radiol.* 60 (2005) 801–806, <https://doi.org/10.1016/j.crad.2004.12.005>.
- [36] P. Clauser, L.A. Carbonaro, M. Pancot, R. Girometti, M. Bazzocchi, C. Zuiani, F. Sardanelli, Additional findings at preoperative breast MRI: the value of second-look digital breast tomosynthesis, *Eur. Radiol.* 25 (2015) 2830–2839, <https://doi.org/10.1007/s00330-015-3720-5>.