Magnetic Resonance Imaging 57 (2019) 317–322

Contents lists available at ScienceDirect

Magnetic Resonance Imaging

journal homepage: www.elsevier.com/locate/mri

Original contribution

Is it worth to perform preoperative MRI for breast cancer after mammography, tomosynthesis and ultrasound?

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ARTICLE INFO

Keywords:
Breast cancer
Magnetic resonance imaging
Breast density
Digital Mammography
Breast Ultrasonography

ABSTRACT

Background: The use of preoperative breast MRI remains controversial despite being the most sensitive technique for the detection of breast malignancies.
Purpose: To evaluate the benefit of preoperative breast MRI after performing the three conventional techniques (DM, US, DBT). To analyze the influence of breast density in the sensitivity of the different imaging techniques.
Material and methods: Retrospective review of 280 histologically confirmed breast cancers in 192 women. We reviewed the medical records and evaluated the change of treatment induced by MRI. Also, we assessed the reports of DM and the combination of the different imaging techniques, and categorized them according to ACR density (a–d) and as negative (BI-RADS 1-3) or positive (BIRADS 4 or 5). The gold standard was the pathologic assessment of the surgical specimen. The sensitivity of the different techniques was compared using McNemar test.
Results: Among these 192 women the use of MRI did not significantly increase the mastectomy rate (from 16.6% to 17.6%; $p = 0.5$). The addition of any technique demonstrated a higher sensitivity than DM alone. The sensitivity of DM alone was 52.5% while using all the techniques, including MRI, was 94.3% ($p < 0.001$). Regardless of breast density pattern, the addition of any technique significantly increased the sensitivity of DM ($p < 0.001$).
Conclusions: The addition of MRI to the three conventional techniques increased the sensitivity but did not significantly modify the rate of mastectomies. Additional techniques increased the sensitivity of DM in both dense and non-dense breasts.

1. Introduction

Digital Mammography (DM) is the basal study for all the patients who undergo a preoperative assessment of breast cancer. However, the sensitivity of DM is decreased in dense breasts due to tissue overlapping and DM can fail to detect multifocal or multicentric cancers. Digital Breast Tomosynthesis (DBT) and US are complementary techniques capable of increasing the sensitivity of mammography, especially in dense breasts. Moreover, DBT is very sensitive to architectural distortion and spiculation, while US detects the majority of masses in dense breasts.

Numerous studies have proven magnetic resonance imaging (MRI) as the most sensitive technique for the detection of breast malignancies, with an estimated sensitivity around 95% [1,2]. Breast MRI is capable of identifying multifocal/multicentric malignancies not evident in conventional imaging, being able to detect occult additional tumors in up to 37% of patients. Also, breast MRI can detect up to 3% of occult breast cancer in the contralateral breast [3]. This is important because it may influence the therapeutic strategy [4–7].

However preoperative use of breast MRI is still controversial because it can detect tumors of uncertain behavior including overdiagnosis. This circumstance could lead to unnecessary mastectomies. There is a lack of evidence that the increase in the detection rate of MRI improves patient outcomes. In fact, randomized trials showed that addition of MRI had no benefit on reduction of reoperation rate [8,9]. Mariscotti et al. [10] retrospectively reviewed 200 patients with breast cancer and found no significant increase in sensitivity by adding MRI to the three conventional techniques (DM + US + DBT).

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https://doi.org/10.1016/j.mri.2018.12.005
Received 3 October 2018; Received in revised form 20 November 2018; Accepted 19 December 2018

Table 1
Sensitivities of the different techniques.

Sensitivities	DM	DMUS	DMDBT	DMUSDBT	MRI[a]
All tumors	52.5%	82.5%	72.5%	86.4%	94.3%
Dense	42.7%	79.6%	65.0%	84.1%	92.3%
Non dense	65.0%	86.2%	82.1%	89.4%	95.9%

DM: Digital Mammography. DMUS: Digital Mammography + Ultrasound. DMDBT: Digital Mammography + Digital Breast Tomosynthesis. DMUSDBT: Digital Mammography + Ultrasound + Digital Breast Tomosynthesis.

[a] MRI was reported with the previous information of the three conventional techniques (DM + US + DBT).

Our study had two main objectives, the first one was to retrospectively evaluate the benefit of preoperative breast MRI after performing the three conventional techniques (DM, US, DBT) and its impact on the surgical treatment. The second objective was to evaluate the influence of breast density patterns in the sensitivity of the different imaging techniques.

2. Material and methods

2.1. Patient selection

The institutional review board of our institution approved this retrospective analysis, and the need for informed consent was waived. At our center, 192 women with 280 consecutive newly-diagnosed cancers (lesion based), histologically confirmed, were included in a database from October 2011 to September 2016. Our center is a second-opinion hospital which attends both symptomatic and asymptomatic women. We do not perform population-based screening but an opportunistic screening on patients coming from our gynecology department. All the patients underwent DM as initial technique and afterwards, US, DBT and MRI were performed.

2.2. Study design

We retrospectively reviewed the reports of the patients included in our database. In our reports, we routinely describe the mammographic density of the breast as well as the lesions detected by mammography and the additional lesions detected by US and/or tomosynthesis. Both US and tomosynthesis examinations were originally interpreted knowing the mammographic findings. Furthermore, the MRI report was also performed taking into account the information of the conventional techniques.

We registered the BI-RADs categories for each detected cancer with the combination of the different imaging techniques (DM, DM + US; DM + DBT; DM + US + DBT; DM + US + DBT + MRI). Final BI-RADS category (1–5) was the highest of the different combined techniques (lesion based study). For the analysis, those cases classified as BI-RADS categories 4 and 5 were considered positive, whereas categories 1, 2 and 3 were considered negative. Moreover, the density of the breast was registered according to ACR density patterns (a–d).

In order to analyze the impact on the surgical treatment, we evaluated the medical records of the patients and assessed the proposed treatment after the combination of three conventional techniques (DM + US + DBT). Routinely, in our center, we localize the lesions with ultrasound and paint the projection on the skin in order to plan the surgical technique. Photographs of both breasts are obtained in all cases. Two radiologists and two surgeons decide in consensus the surgical technique to be performed in every case. If there is a disagreement the surgeon decides the best surgical option. For lesions not visible in US, such as microcalcifications, we estimate with ultrasound the possible localization and paint the orthogonal projection on the skin. Due to the introduction of oncoplastic techniques, larger specimens can be removed without performing a mastectomy.

The impact on the surgical treatment of the additional MRI was evaluated. Patients with neoadjuvant chemotherapy (due to a lesion > 30 mm) were not included for this purpose.

Both DM and DBT studies were performed using a Siemens Mammomat Inspiration unit (Siemens Medical Solutions, Erlangen, Germany). Standard 45° mediolateral oblique (MLO) and craniocaudal (CC) DM views were acquired. Given that our DBT system uses a wide angle (50°) and requires around 25 s for the acquisition, we only performed one single view (MLO) to save radiation dose and time. Additional CC view was performed if the index lesion was better depicted on CC views, which occurred in approximately 5% of patients.

All whole-breast US examinations were performed using a MyLab60 unit (Esaote, Genoa, Italy) with a multi-frequency (5–13 MHz) linear array transducer. Second look targeted US were performed in cases with initially normal US but positive DBT and in cases with positive MRI. Breast cancers detected with second look targeted US after initial negative US were considered US negative.

All breast cancers underwent routinely preoperative MRI on a 1.5-Tesla MR system (AERA, Siemens Medical Solutions, Erlangen, Germany) in the prone position, with no breast compression and using a dedicated four-channel breast coil. Our MRI protocol included the following sequences and parameters: an axial STIR T2 weighted sequence (slice thickness, 4 mm; TR/TE, 4600/74; field of view [FOV], 380 × 380 mm; matrix, 384 × 376); an axial T2 diffusion-weighted imaging (DWI) sequence (slice thickness, 4 mm; TR/TE, 6300/82; FOV, 340 × 340 mm; matrix, 192 × 90), and a dynamic acquisition three-dimensional (3D) axial sequence (T1 fl3d tra dynaVIEWS 1þ5, fat sat; slice thickness, 1.5 mm; TR/TE, 4.8/1.8; FOV, 300 × 300 mm; matrix, 384 × 342) after the administration of 0.1 mmol/kg of body weight of gadolinium (Gadovist, Bayer-Healthcare, Leverkusen, Germany).

2.3. Pathologic assessment

Although all the lesions detected by the imaging techniques were biopsied under US, stereotactic or MRI guidance, the gold standard for our study was the pathologic assessment of the surgical specimen. Initially the specimens were assessed with hematoxylin-eosin stain and secondly, an immunohistochemical study was performed.

2.4. Statistical analysis

A McNemar test was used to compare the mastectomy rate with and without the information of the MRI. The same test was used to compare the sensitivity of the different techniques in the whole sample as well as in the different breast density patterns. For comparison reasons breast density patterns c & d were considered as “dense” breasts and breast density patterns a & b as “non-dense”. Data analysis was performed using SPSS 21.0 software (IBM Corp; Armonk, NY, USA). A p value of < 0.05 was considered to indicate a significant difference.

3. Results

The total number of patients was 192 with a mean age of 57 (range 32–88) years. Among them, the final histological diagnosis were 34 ductal carcinomas in situ (DCIS, 12.1%), 208 invasive ductal carcinomas (IDC, 74.3%), 38 invasive lobular cancers (ILC, 13.6%).

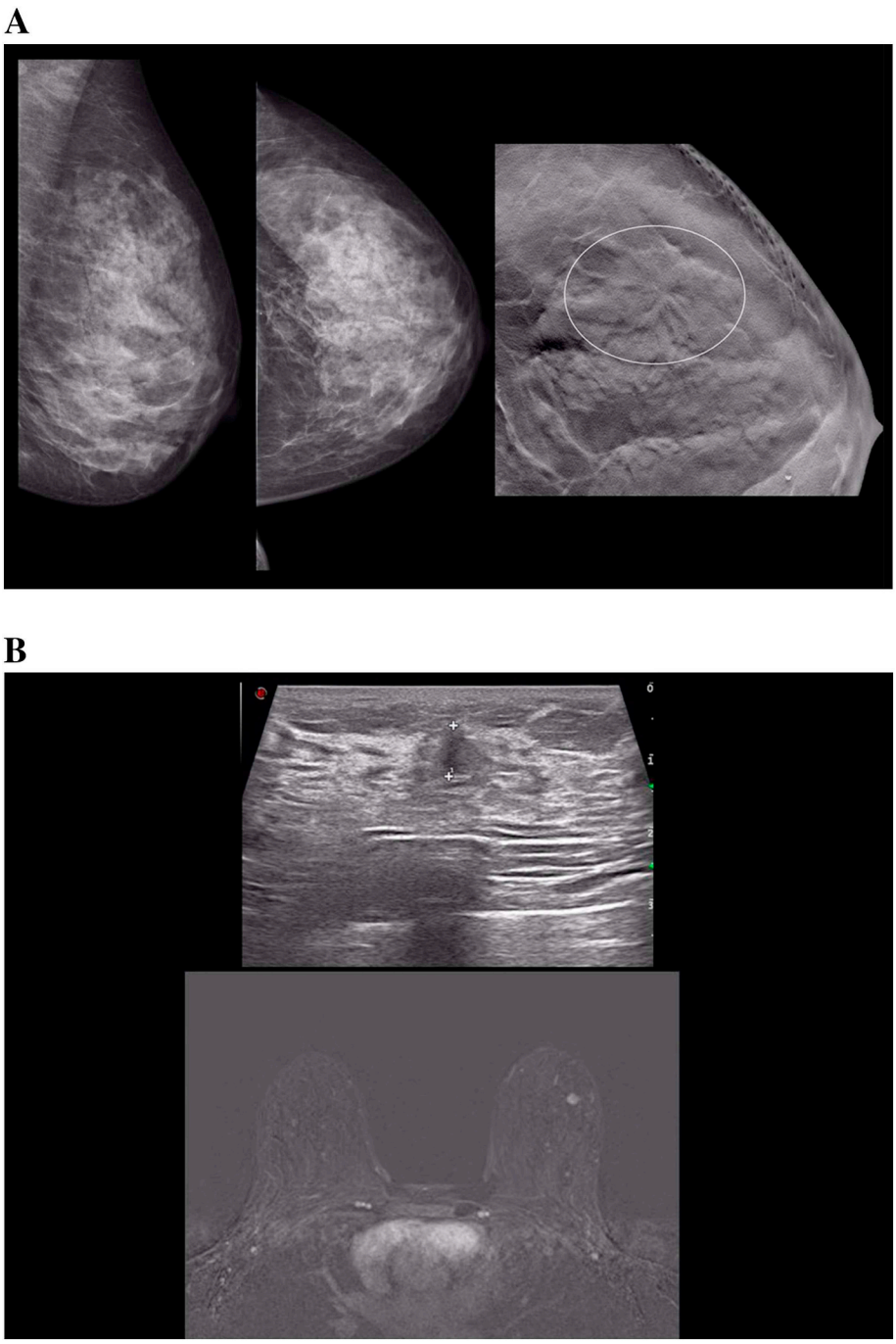

Fig. 1. a. A 52-year-old lady underwent routine mammography at our center. The mammographic study was considered normal as well as the initial US exam. However, the DBT study detected an architectural distortion (white circle).
b. Second look US detected a non-parallel irregular mass, suspicious for malignancy. The biopsy confirmed an invasive ductal carcinoma, Luminal A subtype (ER: 100%, PR: 100%, Ki67: 3%). MRI confirmed a suspicious mass enhancement with no additional lesions.

The mean size of the tumors was 13.94 (range 1–65) mm. There were 54 tumors smaller than 6 mm and 226 tumors greater than or equal to 6 mm. Preoperative breast MRI detected 42 tumors (77.8%) smaller than 6 mm.

The distribution of the immunohistochemical patterns of the lesions was as follows: 129 (46.1%) cancers were luminal A tumors, 78 (27.9%) luminal B tumors, 32 (11.4%) triple negative, 9 (3.2%) pure HER-2.

According to the American College of Radiology (ACR) density patterns, pattern a was seen in 6 (2.1%), pattern b in 119 (42.5%), pattern c in 121 (43.2%) and pattern d in 34 (12.1%). Thus, 155 (55.4%) were “dense” breasts (c & d) and 125 (44.6%) were “non-dense” breasts (a & b).

Regarding surgery, among these 192 women, 154 (80.2%) of them underwent breast conserving surgery (BCS) and 38 (19.8%) underwent

Table 2
Comparison of sensitivities of the different techniques in the whole sample (McNemar test).

All tumors	Sensitivity	p value
DM vs DMUS	52.5% vs 82.5%	$p < 0.001$
DM vs DMDBT	52.5% vs 72.5%	$p < 0.001$
DM vs DMUSDBT	52.5% vs 86.4%	$p < 0.001$
DMUS vs DMDBT	82.5% vs 72.5%	$p < 0.001$
DMUSDBT vs MRI[a]	86.4% vs 94.3%	$p < 0.001$

DM: Digital Mammography. DMUS: Digital Mammography + Ultrasound. DMDBT: Digital Mammography + Digital Breast Tomosynthesis. DMUSDBT: Digital Mammography + Ultrasound + Digital Breast Tomosynthesis.

[a] MRI was reported with the previous information of the three conventional techniques (DM + US + DBT).

mastectomy. Excluding 5 patients with neoadjuvant chemotherapy, out of the remaining 187 women, 31 mastectomies would have been indicated with the information of DM + US + DBT, while after performing MRI, the number of proposed mastectomies was 33. Thus in our study, the use of MRI did not significantly increase the mastectomy rate (from 16.6% to 17.6%; $p = 0.5$).

For the whole sample, the combination of any of the three techniques demonstrated a higher sensitivity than DM alone. Out of the 280 tumors, DM alone detected 147 (52.5%) and all the techniques, including MRI detected 264 (94.3%) (Table 1; Fig. 1).

Moreover, the combination DM + US showed a better sensitivity than DM + DBT, showing significant differences ($p < 0.001$) (Table 2; Fig. 2).

In dense breasts (ACR density patterns c & d) the addition of any technique improved the sensitivity of DM alone, and the sensitivity of the combination of all the techniques, including MRI, was higher than DM + US + DBT (92.3% vs 84.1%; $p = 0.011$). On the other hand, in non-dense breasts (ACR patterns a & b), there were no significant differences between DM + US vs DM + DBT (86.2% vs 82.1%; $p = 0.267$). The sensitivity of DM + US + DBT + MRI was also higher than DM + US + DBT (95.9% vs 89.4%; $p = 0.039$) in non-dense breasts (Table 3).

4. Discussion

We have conducted a retrospective study evaluating the impact of MRI after performing the three conventional techniques (DM, US, DBT) in a preoperative assessment of breast cancer. According to our data, the highest sensitivity was achieved with all the techniques, including MRI (94.3%) and the use of MRI did not significantly increase the mastectomy rate.

Nowadays, although MRI has the highest sensitivity of all imaging techniques (over 95%) [5], the use of preoperative breast MRI is still controversial for several reasons such as the increase in the mastectomy rate [7]. Even though the use of MRI results in the detection of smaller cancers and the occurrence of fewer interval cancers, some authors still found limited evidence to support the idea that use of MRI improves patient outcomes [11]. Their results indicated that those undergoing preoperative breast MRI had a significantly greater mastectomy rate than those not having MRI exams (52% vs 38%; $p < 0.0001$) [12]. However, according to our data, the use of MRI did not significantly increase the mastectomy rate (from 16.6% to 17.6%; $p = 0.5$). This could be explained because we have studied the addition of MRI to the three conventional techniques (DM + US + DBT). Due to the higher sensitivity of US and DBT, most additional cancers that could change the initial management had been detected before MRI. Also, our surgeons use oncoplastic techniques for selected cases that could reduce the mastectomy rate.

One of the limitations of breast MRI is the low spatial resolution which could fail to detect very small cancers. However, in our sample, MRI detected 42 (77.8%) of the 54 tumors smaller than 6 mm.

In our sample, out of the 280 tumors, DM alone detected 147 (52.5%). This low sensitivity was due to the design of this study (lesion-based) and 55.4% of the cases were dense breasts. The combination of any techniques showed a higher sensitivity than DM alone. For example, DM + US had a sensitivity of 82.5% and DM + DBT of 72.5%. When we performed the three of them (DM + US + DBT) we achieved a sensitivity of 86.4% (Table 1).

Our results are similar to those in the literature. Zonderland et al. [13] concluded that additional US significantly increased the sensitivity of DM and Skaane et al. [14] described that the use of DM + DBT resulted in a significantly higher cancer detection rate (up to 27%). Moreover, when we compared which additional technique was the best, DM + US had a better sensitivity than DM + DBT, showing significant differences ($p < 0.001$) (Table 2). This is an important fact, because nowadays both US and DBT are profusely used as complementary techniques after DM. If we could only perform one of them, US would be the preferable one. However, US is an operator-dependent and time consuming technique. According to our data, the most sensitive combination (excluding MRI) was DM + US + DBT.

It is well known that the sensitivity of DM drops in dense breasts. Moreover, density itself is a risk factor of developing breast cancer in the future. More than 40% of the women between 40 and 74 years have dense breasts [15]. According to Pisano et al. [16], the introduction of DM increased the sensitivity in women below 50 years old with dense breasts, however the sensitivity for this group was still low (59%). In our sample the sensitivity of DM alone was 42.7% in dense breasts and 65% in non-dense breasts. In both dense and non-dense breasts, the addition of any technique showed a higher sensitivity than DM alone, and the sensitivity of the combination of all the techniques, including MRI, was higher than DM + US + DBT (Table 3).

In non-dense breasts (patterns a & b), there were no significant differences between DM + US and DM + DBT (86.2% vs 82.1%; $p = 0.267$) (Table 3). Nevertheless, in dense breasts, the combination of DM + US showed a higher sensitivity than DM + DBT (79.6% vs 65%; $p = 0.016$). This could be explained by the ability of US to detect cancers that are completely surrounded by fibroglandular tissue. It has been described that DBT requires a certain amount of fat to detect lesions, and DBT could fail to detect a tumor surrounded by dense tissue [17].

Mariscotti et al. [10] retrospectively reviewed 200 patients with breast cancer and found no significant increase in sensitivity by adding MRI to the three conventional techniques (97% vs 98.8%). However, our results indicate that the addition of MRI remains as the best combination to diagnose breast tumors, with a statistically significant higher sensitivity than the association of the DM + US + DBT (94.3% vs 86.4%; $p < 0.001$). Thus, we encourage the routine use of preoperative breast MRI.

Our study is limited because it was performed reviewing the medical reports of the different imaging techniques, so the images themselves were not reviewed. Due to the design of this study, specificities could not be achieved. Furthermore, the results of this lesion by lesion preoperative study cannot be applied to a population based screening.

In conclusion, the addition of MRI to the three conventional techniques significantly increased the sensitivity but did not significantly modify the mastectomy rates. Additional techniques increased the sensitivity of DM not only in dense breasts but also in a & b patterns.

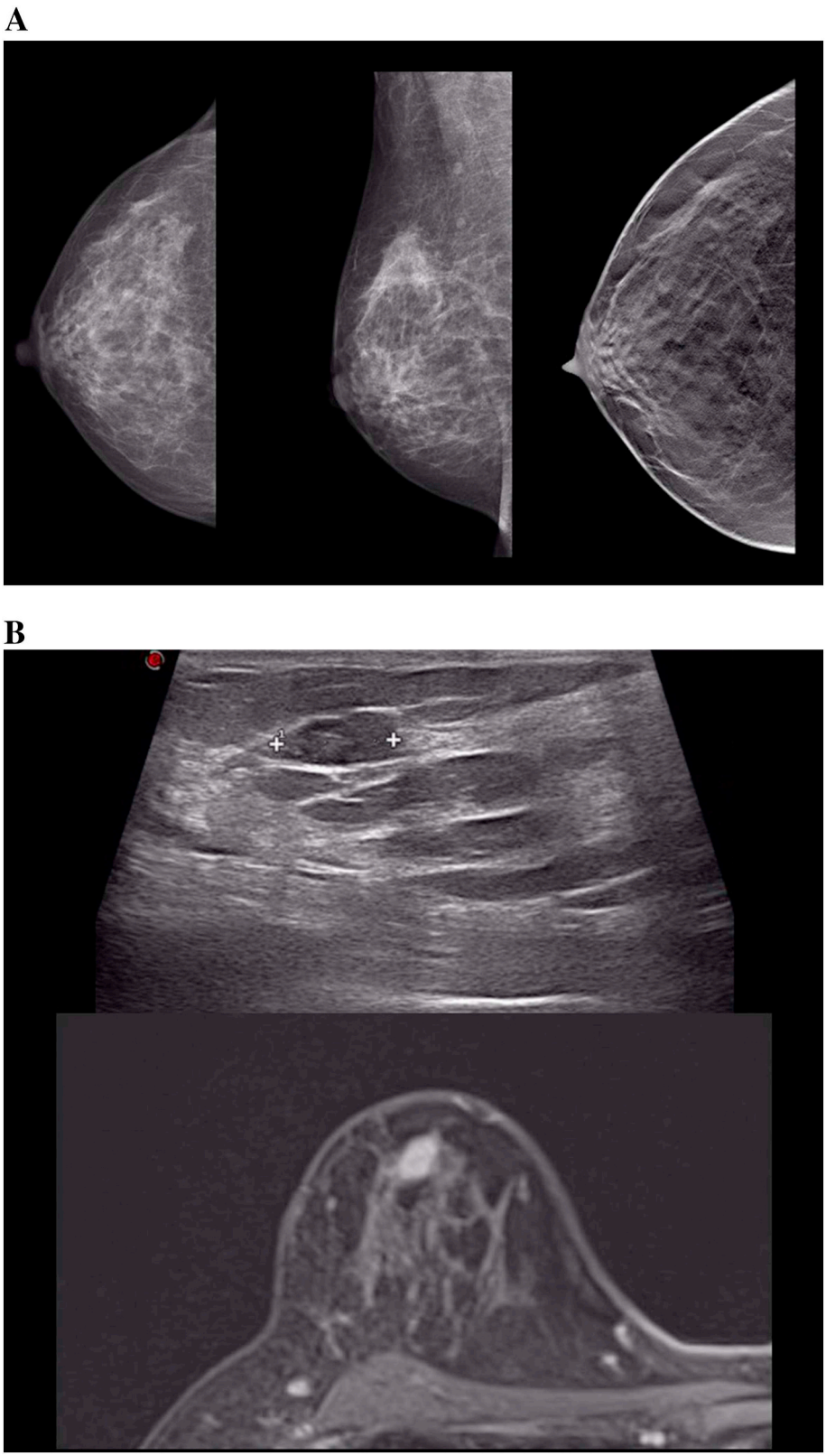

Fig. 2. a. A 50-year-old asymptomatic lady attended at our institution for a routine follow-up. A mammographic examination (two views) and DBT (cc view) were performed, showing no lesions.
b. Additional US showed a circumscribed oval mass. An US-guided biopsy was performed (14G CNB). Pathology was an invasive ductal carcinoma, triple negative. This lesion was a mass enhancement on MRI with no satellite lesions.

Table 3
Sensitivities and p values of the different techniques regarding breast density pattern.

	Sensitivity	p value
Dense (ACR PATTERN c & d)		
DM vs DMUS	42.7% vs 79.6%	$p < 0.001$
DM vs DMDBT	42.7% vs 65.0%	$p < 0.001$
DM vs DMUSDBT	42.7% vs 84.1%	$p < 0.001$
DMUS vs DMDBT	79.6% vs 65.0%	$p = 0.016$
DMUSDBT vs MRI[a]	84.1% vs 92.3%	$p = 0.011$
Non-dense (ACR PATTERN a & b)		
DM vs DMUS	65.0% vs 86.2%	$p < 0.001$
DM vs DMDBT	65.0% vs 82.1%	$p < 0.001$
DM vs DMUSDBT	65.0% vs 89.4%	$p < 0.001$
DMUS vs DMDBT	86.2% vs 82.1%	$p = 0.267$
DMUSDBT vs MRI[a]	89.4% vs 95.9%	$p = 0.039$

DM: Digital Mammography. DMUS: Digital Mammography + Ultrasound. DMDBT: Digital Mammography + Digital Breast Tomosynthesis. DMUSDBT: Digital Mammography + Ultrasound + Digital Breast Tomosynthesis.

[a] MRI was reported with the previous information of the three conventional techniques (DM + US + DBT).

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