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BREAST

Six-year prospective evaluation of second-look US with volume navigation for MRI-detected additional breast lesions

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Abstract

Objective The aim of this study is to present a 6-year prospective evaluation of second-look ultrasound (US) using volume navigation (V Nav) for MRI-detected additional breast lesions.

Methods After IRB approvals in both institutions, 1930 consecutive prone MRI breast examinations in 1437 patients were prospectively evaluated. All patients with an MRI-detected additional lesion underwent second-look US, and if occult, contrast-enhanced MRI in supine position was performed for US and MRI co-registration. For patients with breast hypertrophy, MRI-guided biopsy was performed directly. Pathologic examination was the standard of reference. One-way ANOVA and chi-square tests were used.

Results In 490 MRI examinations (25.4%, 490/1930), at least one additional breast lesion was detected for a total of 722 only MRI-detected lesions. Second-look US identified 549 additional lesions (23 ± 8 mm); 362 (65.9%, 362/549) proved benign at pathology and 187 (34.1%, 187/549) malignant. Second-look US with V Nav identified 151 additional lesions (17 ± 9 mm, p = n.s.); 67 (44.4%, 67/151) proved benign at pathology and 84 (55.6%, 84/151) malignant. MRI-guided biopsy was performed on 22 additional breast lesions (22 ± 8 mm, p = n.s.); pathology revealed 20 (90.9%, 20/22) benign lesions and 2 (9.1%, 2/22) malignant ones. Mass lesions were significantly higher in the second-look US group ($p < 0.001$). No significant difference in lesion dimension was found between the three groups ($p = 0.729$).

Conclusions Second-look US with V Nav can be effective in detecting a large number of additional breast lesions occult at second-look US and to biopsy a significant number of malignant lesions safely and irrespective of distance from skin or lesion position.

Key Points

- *Second-look US with volume navigation is effective in detecting occult additional lesions.*
- *Permits safe biopsies irrespective of position and depth*
- *Reduces the need for MRI-guided biopsy*

Keywords Breast ultrasonography · Magnetic resonance imaging · Breast tumours · Multimodal imaging · Image-guided biopsy

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Abbreviations

BI-RADS™	Breast Imaging Reporting and Data System
CT	Computed tomography
DCIS	Ductal carcinoma in situ
Gd-BOPTA	Gadobenic acid
IDC	Invasive ductal carcinoma
ILC	Invasive lobular carcinoma
LAVA	Liver acquisition volume acceleration
MRI	Magnetic resonance imaging
THIVE SPAIR	Three-dimensional turbo field echo sequence with T1-weighted high-resolution isotropic examination volume and spectral attenuated inversion recovery
US	Ultrasound
V Nav	MRI volume navigation
VAB	Vacuum-assisted biopsy

Introduction

Second-look breast ultrasound (US) is used in clinical practice to reassess a patient after the detection of additional lesions using another technique, generally a contrast-enhanced MR imaging [1–6].

Targeted second-look ultrasound, proposed to increase MRI specificity, makes it possible to identify correlated lesions at a pooled rate of 57.5%, considering both mass and non-mass lesions, both benign and malignant, with a different impact on the rates [7]. Indeed, the rate of malignant lesions occult at second-look ultrasound is not negligible [7], probably related to the inclusion criteria, prevalence of disease, and risk factors [8].

From a theoretical point of view, this large number of additional lesions, a pooled rate of 42.5% accordingly to literature [7], could be due to the following: either false negative at conventional imaging, subsequently detected by contrast media breast MRI; or false positive at MR imaging, later proved to be benign at pathology or after the 2-year follow-up. There are two possible explanations for this: an 'objective' or technical reason related to the type of energy used to highlight breast lesions and a 'subjective' or human-related reason connected with the skill of the operator in detecting the corresponding lesion using each technique. Numerous other explanations could be mentioned, two of which are certainly related to the signal of the lesion—echogenicity for US or density in x-ray mammography or contrast enhancement at MRI—compared to the background breast signal and spatial displacement in the different breast imaging techniques.

At present, some biases could be overcome in clinical practice by using a new technique which can combine live ultrasound of the breast and MR imaging obtained in supine position with similar parameters to the prone examination. After MRI co-registration, obtained by coupling three pairs of markers, the multiplanar reconstructed MRI image of the corresponding US image is displayed on the monitor with high reproducibility and low rates of misalignment [9–11].

The aim of this study is to present the results of a 6-year assessment of second-look US of additional breast lesions with volume navigation (V Nav) using supine contrast-enhanced MRI co-registered during live US examination, to analyse its clinical value using pathology as reference, and to assess the need for MRI-guided biopsies.

Patients and methods

Study population

From January 2009 to December 2015—with the exclusion of a 12-month period (January 2010 to December 2010) due to the transfer of the technology from one hospital to another—1981 MRI examinations of the breast in 1437 patients (53 ± 12 years, range 21–94) were performed and prospectively evaluated. Institutional Review Board approval from both institutions and patient informed consent were obtained pursuant to the aims of the study.

All MRI examinations were performed in the second week of the menstrual cycle in the case of premenopausal women, in a prone position with a dedicated breast coil and with the administration of a contrast medium as per the state of the art standard [12, 13].

Before the MRI examination, all patients underwent a clinical examination and conventional imaging: mammography and ultrasound of the breast. The former was performed in the case of young women (under the age of 40) only if a malignant lesion was suspected.

The study inclusion criterion was the detection of an additional lesion, a new lesion not previously detected using conventional imaging, visible at MRI examination classified as BI-RADS 3–5 evaluated by consensus by two radiologists from a pool of five (with more than 10 years' experience in breast imaging and intervention). Exclusion criteria were lack of pathology results or incomplete follow-up.

Correlation with second-look US

For patients with an additional lesion, a second-look US was performed by the same radiologist who evaluated the MRI examination. US-guided biopsy was immediately performed in the case of concordance between second-look US and MRI examination. A solution of vegetal charcoal or tissue marker of pyrolytic carbon-coated zirconium oxide (Biomarc, Vigeo srl) was systematically positioned before ending the procedure according to the radiologist's indications.

No correlation with second-look US

In subjects with an additional lesion occult at second-look US, breast volume was clinically evaluated in supine position; the bra size was registered. Moreover, breast hypertrophy estimated using two anthropomorphic measurements [14] was used to select subjects for second-look US with V Nav or MRI-guided biopsy, especially if the additional lesion was localised at the external quadrants and at a distance from the skin.

Second-look US with V Nav

Before proceeding to the various steps of second-look US with V Nav, three softgel capsules of natural d-α-tocopherol (vitamin E 400 UI, Smart Nutrition Ltd.) were coupled over a corresponding coloured surgical skin marker (DeRoyal Industries Inc.) drawn on the breast with the known additional lesion. All subjects were in supine position, as is standard for US examination, with the upper extremities extended above the head. Each skin marker was drawn the same size as the capsule and subjectively positioned at 9, 12, and 3 o'clock radially to the nipple. The capsules were fixed with a polyolefin single-coated surgical tape (3M Health Care), as described in literature [10].

MRI examinations were performed on two 1.5-T MR scanners (Achieva, Philips Healthcare; Signa HDxt, GE Healthcare) in supine position during the second evaluation as follows: three-dimensional turbo field echo sequence with T1-weighted high-resolution isotropic examination volume and spectral attenuated inversion recovery or liver acquisition volume acceleration (THRIVE SPAIR, LAVA), 180–220 axial 1-mm partitions (TR/TE = 5.7/2.7 ms; flip angle = 10°; field of view = 400 mm; matrix = 380 × 400 mm; NEX = 0.8; acquisition time 10′ 08″) with 122-s time resolution; 1 precontrast and 4 postcontrast phases, after automated intravenous administration (2 ml/s) of 0.05 mmol/kg of Gd-BOPTA (Multihance, Bracco Diagnostics Inc.) followed by a flush of 20 ml saline solution using a cubital vein (30 ml if dorsal metacarpal vein was used). All subjects were studied in the second week of the menstrual cycle in the case of premenopausal women and after a maximum of 7 days from the first evaluation in the remainder. Breast MRI was performed in supine position with arms extended above the head, using a double synergy body coil with sensitivity encoding (SENSE) covering both breasts. Breast compression was minimised using a dedicated mattress and two straps.

Postcontrast native and postcontrast subtracted sequences were uploaded on a dedicated postprocessing console for image evaluation choosing the optimal vascular phase, seeking the best view of the additional lesion. Selected MRI volume was saved in a re-writable digital versatile disk or universal serial bus for uploading to the US equipment.

Finally, all capsules were removed and the remaining skin markers were covered with a transparent dressing (3M Health Care) to prevent any modification before and during the US examination.

Live US exams were performed using a platform configured with V Nav (LOGIQ E9, GE Healthcare) and using a 6–15-MHz transducer with a geometry permitting visualisation of a wide field of view. A high frame rate (≥ to 30 frames/s) and all the postprocessing capabilities were maintained.

The V Nav equipment consisted of a magnetic tracking system used to determine the position of a pair of freehand sensors relative to a fixed transmitter using a defined operating volume. More specifically, an electromagnetic transmitter was positioned close to the subject under examination, and two electromagnetic sensors were mounted on the transducer bracket. Transmitter and sensors were connected to a position-sensing unit embedded in the US equipment to track probe position and orientation within the electromagnetic field. The live US image was co-registered to the MRI breast volume by coupling markers: softgel capsule on the MR image and the corresponding skin marker on the subject.

Both types, US and MR image, could be displayed side by side or in a blended overlaying format on the US monitor, the so-called fusion image. The same magnification factor had to be used for fusion imaging. In the remaining settings, the MRI magnification factor was lower and used as a 'road map'. After co-registration, a US-guided biopsy with V Nav was immediately performed systematically leaving a tissue marker of pyrolytic carbon-coated zirconium oxide (Biomarc, Vigeo srl) before ending the procedure.

MRI-guided biopsy

In the group of lesions occult at second-look US with breast hypertrophy [14], MRI-guided biopsy was performed, according to the guidelines published by Heywang-Köbrunner et al [15], in the second week of the menstrual cycle in the case of premenopausal women and within a maximum of 15 days for the remainder. Again, a tissue marker of pyrolytic carbon-coated zirconium oxide (Biomarc, Vigeo srl) was systematically positioned before ending the procedure.

Pathology of all additional lesions was obtained. Percutaneous biopsies were performed using a reusable automated core biopsy device with a 14-gauge needle (Magnum®, Bard Biopsy Systems.) with at least four samples for mass lesions. For non-mass lesions using US-guided biopsies with V Nav or MRI-guided biopsy, a vacuum-assisted breast biopsy system with a 14-gauge or 10-gauge needle (Vacora®, Bard Biopsy Systems.) was used, obtaining at least six samples in accordance with the radiologist's evaluation.

In the case of a benign pathology result in the US-guided biopsy group, a US examination and mammography were performed after 3 months. Likewise, in the case of benign

pathology result in the V Nav and MRI-guided biopsy group, a prone MR imaging to verify lesion enhancement and tissue marker position was performed after 3 months.

In the event of discrepancies between pathology results and BI-RADS™ classification or tissue marker localisation, a repeated biopsy was performed.

Statistical analysis

ANOVA one-way test was used to compare lesion dimensions in three groups. The calculation of Bonferroni-adjusted *p* values was used for pairwise comparison. Chi-square test for proportion evaluation was used for any association between lesion enhancement type and pathology result. Both tests are available on http://www.socscistatistics.com/tests/anova/default2.Aspx and http://www.socscistatistics.com/tests/chisquare2/Default2.aspx (accessed on October 15, 2017). An alpha level of 5% (0.05) was used to determine statistical significance.

Results

In the period of the study, 51 subjects (2.6%, 51/1981) interrupted the MRI examination. One thousand nine hundred thirty standard consecutive breast MRIs were prospectively evaluated. Clinical indications for contrast-enhanced breast MRI and rates are listed in Table 1. One thousand four hundred forty MRIs out of 1930 examinations (74.6%, 1440/1930) revealed no additional lesions: 1059 (54.9%, 1059/1930) revealed negative or benign results while 381 exams (19.7%, 381/1930) confirmed a known malignancy with no additional lesions. In the remaining 490 MRI breast examinations (25.4%, 490/1930), at least one additional lesion was detected for a total of 722 breast lesions, with a prevalence of 37.4% (722/1930) MRI-detected additional breast lesions.

Five hundred forty-nine lesions out of 722 (76.0%, 549/722) were revealed by second-look US and biopsied accordingly; 362 (65.9%, 362/549) proved benign on pathology and 187 (34.1%, 187/549) malignant. One hundred seventy-three out of 722 (24.0%, 173/722) lesions were occult at US, and consequently, second-look US using V Nav (87.3%, 151/173) or MRI-guided biopsy (12.7%, 22/173) was performed. All 173 additional breast lesions were visible both at contrast-enhanced supine MRI breast examination and at MRI-guided biopsy (i.e. no vanishing lesions were reported).

In 151 additional lesions, a US with V Nav-guided biopsy was performed and pathology revealed 67 (44.4%, 67/151) benign and 84 (55.6%, 84/151) malignant lesions. In the remaining 22 additional lesions, an MRI-guided biopsy was performed and pathology revealed 20 (90.9%, 20/22) benign and two (9.1%, 2/22) malignant lesions. In Graph 1, a flowchart of the workflow is presented. Lesion distribution is summarised in Table 2. Tables 3 and 4 present lesion characteristics at pathology.

Table 1 MR imaging indications

Indications	N	%
FU	557	28.86
TL	530	27.46
PREOP	437	22.64
POP	123	6.37
PRO	107	5.54
HR	88	4.56
NEOCHT	67	3.47
CUP	21	1.09
	1930	100

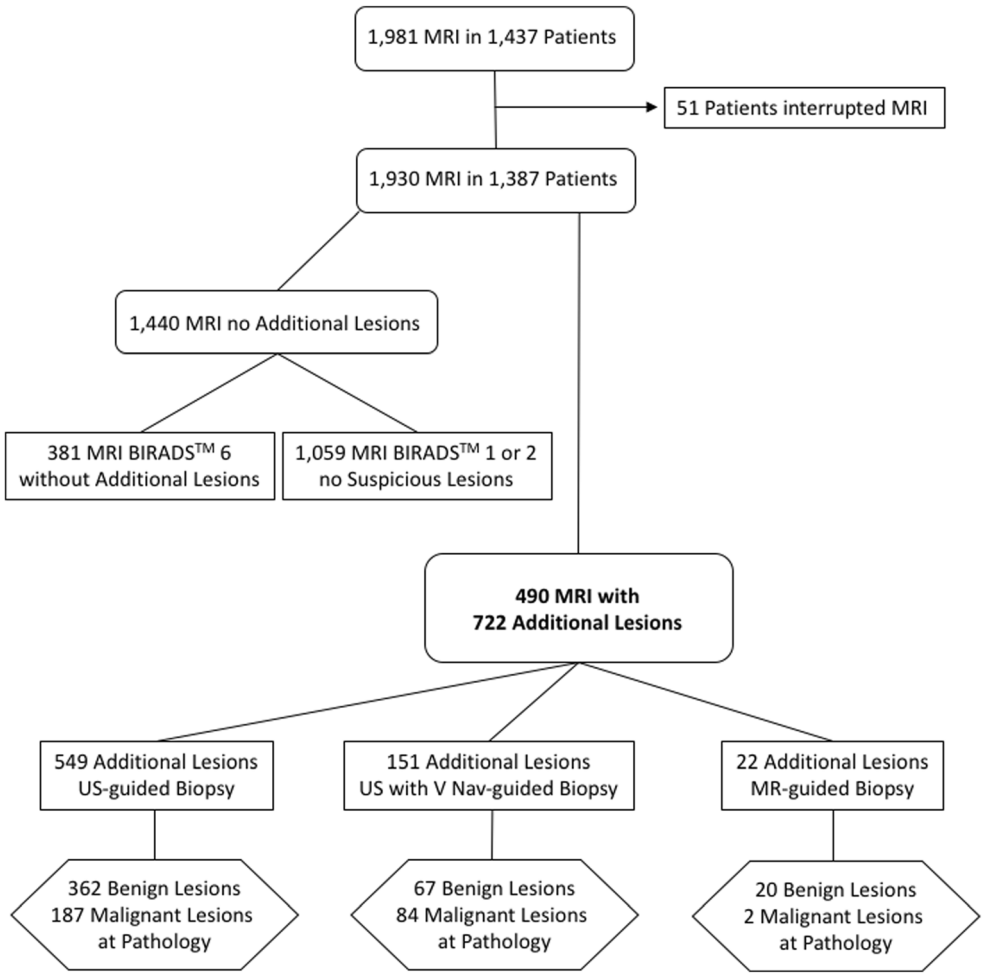
FU follow-up of previous cancer, *TL* third-level examination cases not clear at conventional imaging, *PREOP* preoperative examination, *POP* postoperative examination, *PRO* prosthesis evaluation, *HR* high-risk subjects, *NEOCHT* neoadjuvant chemotherapy, *CUP* carcinoma with unknown primary

Statistical analysis revealed a significantly higher number of mass lesions in the second-look US group ($p < 0.001$) and a higher number of benign lesions ($p < 0.001$). No significant difference was found for lesion dimension in each pairwise comparison: US versus US with V Nav, US versus MRI-guided biopsy, and US with V Nav versus MRI-guided biopsy ($p = 0.729$).

Results at follow-up

Furthermore, in three lesions (two subjects, previously referred to US-guided procedure), the US biopsy was repeated (0.5%, 3/549) using V Nav due to the discrepancy between the lesion pathology result and the radiologist's suspicions, revealing three benign lesions (two fibroadenomas of 7 and 9 mm and a sclerosing adenosis of 7 mm). In one lesion (one subject, previously referred to US with V Nav-guided procedure), the biopsy was repeated using MRI-guided biopsy because of discrepancy (0.2%, 1/549) revealing an intramammary lymph node of 6 mm.

After 2 years of follow-up, none of the benign additional lesions referred to US with V Nav biopsy or MRI-guided biopsy revealed any malignancy. In three cases referred to US-guided biopsy, follow-up revealed a malignancy: one ductal carcinoma in situ (DCIS) of 24 mm previously diagnosed as an atypical ductal hyperplasia, one invasive lobular carcinoma (ILC) of 14 mm previously attributed to fibrocystic changes, and one invasive ductal carcinoma (IDC) + DCIS of 27 mm previously considered a sclerosing adenosis.



Graph 1 Flowchart of the workflow

Discussion

The occurrence of an additional lesion after breast MRI is not rare. In our study, it occurred in about 25% of all MRI examinations with a prevalence of 37% (722/1930) of additional lesions classified as BI-RADS™ 3–5.

For all these breast lesions, a second-look US is mandatory according to literature [13, 16–18]. However, due to the large variability of displacement of the breast tissue, the chance of finding a lesion correlation during a second-look US examination ranges from 58% [7] to 64% [10] as reported in literature. Recently, Telegrafo et al suggested a method for finding a lesion correlation by measuring the distance to the nipple. However, they reported a variability ranging from 0.2 to 3.2 cm, suggesting an evaluation of the entire quadrant in which the lesion is detected by MR imaging [19]. Moreover, when a pathologic examination is required, a percutaneous guided biopsy is essential [7, 12, 15] marking the lesion for future MRI correlation when required.

MRI-guided procedure is undoubtedly the primary technique used to obtain pathology results from a lesion occult at second-look US. However, the cost of the examination in

Table 2 Additional lesion characteristics

Type of second look	Add L	B3	m	nm	%	M (mm)	SD (mm)	BEN	MAL
US	549	195	495	54	76	23	8	362	187
US with V Nav	151	44	65	86	21	17	9	67	84
Only MRI	22	9	8	14	3	22	8	20	2
	722	248			100			449	273

US ultrasound, *US with V Nav* ultrasound with MRI volume navigation, *Add L* additional lesions, *B3* lesions classified BI-RADS™ 3 at MRI, *m* mass lesions, *nm* non-mass lesions, *M* mean, *SD* standard deviation, *BEN* benign lesions, *MAL* malignant lesions

Table 3 Benign lesions at pathology

Benign lesions	BEN1	M1 (mm)	SD1 (mm)	BEN2	M2 (mm)	SD2 (mm)	BEN3	M3 (mm)	SD3 (mm)
FA	193	33	13	30	23	11	4	20	5
FC	62	24	10	11	15	9	6	17	7
SA	24	32	12	7	11	12	4	20	4
IFL	23	36	7	2	26	4			
IM LYN	19	16	6	8	10	7	1	14	
FT	17	21	7				2	23	4
PAP	13	21	7	7	16	8	3	19	4
PHL	6	16	9						
ADH	3	18	4	2	14	7			
LIN (1-2)	2	15	3						
	362			67			20		

FA fibroadenoma, *FC* fibrocystic changes, *SA* sclerosing adenosis, *IFL* breast inflammation or periductal inflammation, *IM LYN* intramammary lymph node, *FT* fibrosclerotic tissue, *PAP* papilloma or lesions with papillary aspects, *PHL* phylloid tumour, *ADH* atypical ductal hyperplasia, *BEN1* number of benign lesions at US biopsy, *BEN2* number of benign lesions at US with MRI volume navigation biopsy, *BEN3* number of benign lesions at MRI-guided biopsy, *M1 M2 M3* mean values in the group of US US with V Nav and MRI-guided procedure respectively, *SD1 SD2 SD3* standard deviation values in the group of US US with V Nav and MRI-guided procedure respectively

terms of the time for which the MR equipment is used (from the performance of the biopsy up to reconditioning of the premises) and of MRI-compatible materials is certainly higher, especially in relation to the high rate of false positives [20, 21]. Moreover, the inability to reach lesions located near the chest wall or the nipple area and the high degree of expertise required to perform it make the development of a complementary method necessary.

Several experiences have reported good results using breast MRI in supine position [9, 10, 22, 23] or breast CT [24] for co-registration during live US examination. All studies reported a corresponding lesion dislocation of less than 1 cm^2 irrespective of lesion position—distance from nipple or skin—with a low inter- and intraobserver variability [9, 10]. Pons et al reported similar results regarding the breast and the axilla, for lymph node evaluation, using US-guided breast biopsy with V Nav [11].

To our knowledge, this is the largest prospective study in which additional lesions following breast MRI were studied comparing a 'subjective' second-look US and an 'objective'

Table 4 Malignant lesions at pathology

Malignant lesions	MAL1	M1 (mm)	SD1 (mm)	MAL2	M2 (mm)	SD2 (mm)	MAL3	M3 (mm)	SD3 (mm)
IDC	66	20	9	27	16	11			
ILC	36	34	11	10	33	8	1	41	
IDC + DCIS	27	26	7	22	22	8			
ILC + LCIS	22	22	12						
DCIS	12	25	11	17	15	12	1	22	
ILC + DCIS	11	34	9	2	36	13			
MIL	9	10	4	4	11	9			
IC NOS	3	23	9	2	13	4			
MP	1	16							
	187			84			2		

IDC invasive ductal carcinoma, *ILC* invasive lobular carcinoma, *ILC + LCIS* invasive ductal carcinoma with extensive lobular cancer in situ, *DCIS* ductal carcinoma in situ, *MIL* metastatic intramammary lymph node, *IC NOS* invasive carcinoma not otherwise specified, *MP* malignant phylloid tumour, *MAL1* number of malignant lesions at US-guided biopsy, *MAL2* number of malignant lesions at US with MRI volume navigation biopsy, *MAL3* number of malignant lesions at MRI-guided biopsy, *M1 M2 M3* mean values in the group of US US with V Nav and MRI-guided procedure respectively, *SD1 SD2 SD3* standard deviation values in the group of US US with V Nav and MRI-guided procedure respectively

one, obtained by co-registration between supine breast MRI and live US. A follow-up of at least 2 years and the repeat biopsy for discordant cases were also included.

Technical improvements, probably due to the different sequences and equipment used, make it possible to obtain images of sufficient quality to detect additional lesions during dynamic contrast-enhanced MRI of the breast in supine position. Two different types of MRI equipment were used in our study to obtain supine breast MRI for co-registration without any loss of information caused by artefacts, as previously reported [25] as recently described by Alderliesten et al to demarcate breast cancer for breast-conserving surgery [26] or Nakamura et al for conservative breast surgery [27].

The study confirmed that lesion dimension is not significant between the three groups; however, the higher number of no-mass lesions ($p < 0.001$) occult at second-look US appears to indicate specific attention to lesion appearance: shape and signal at US compared to the tissue background (see Figs. 1 and 2). During US examination, lesion signals can be underestimated or, more probably, completely missed at routine examination. Moreover, lesion shape in the US image may not be clearly suspicious as compared with the irregular margins of the MRI (see Fig. 3). Finally, the intraductal component associated with invasive cancer cannot be revealed or detected during second-look US, which shows only the invasive part of the lesion (see the video).

In the group of lesions occult at second-look US (24%, 173/722), the prevalence of malignant lesions was 49% (86/173, 84 using US biopsy with V Nav and two with MRI-guided breast biopsy), amounting to almost one malignant lesion for every benign one (86/87) and almost one malignant lesion every five benign ones (17.2%, 86/499) considering all additional lesions. This result confirms literature data showing that second-look US cannot detect sufficient correlation to additional lesion diagnosis [7].

The application of V Nav technique requires an extra MRI examination, as well as MRI-guided biopsy, since at present, it is impossible to obtain a supine reconstruction of the MRI breast volume acquired in prone position. However, it saves time in the use of the MRI room for the interventional procedure and the cost of vacuum-assisted biopsy (VAB). In fact, as suggested by Heywang-Köbrunner et al, vacuum-assisted biopsy should be performed during MRI-guided biopsy obtaining from 12 to 24 samples [15].

Recently, Aribal et al have reported that V Nav technique is a feasible alternative to MRI-guided biopsy of breast lesions occult at second-look US [27].

In our study, only 22 lesions underwent MRI-guided biopsy in 6 years, demonstrating the reduced need for this technique, mandatory in subjects with breast hypertrophy. Moreover, in view of the scarcity of centres performing MRI-guided biopsies, as reported in a recent survey [28], this new technique could assume an important role, offering an alternative to MRI-guided biopsy for a large number of additional lesions, as reported in our study.

A future issue will be patient position during breast MRI: if the supine position could demonstrate the same diagnostic value as the examination in prone position, an 'objective' second-look US or a similar approach could easily be performed also in the operating room [29].

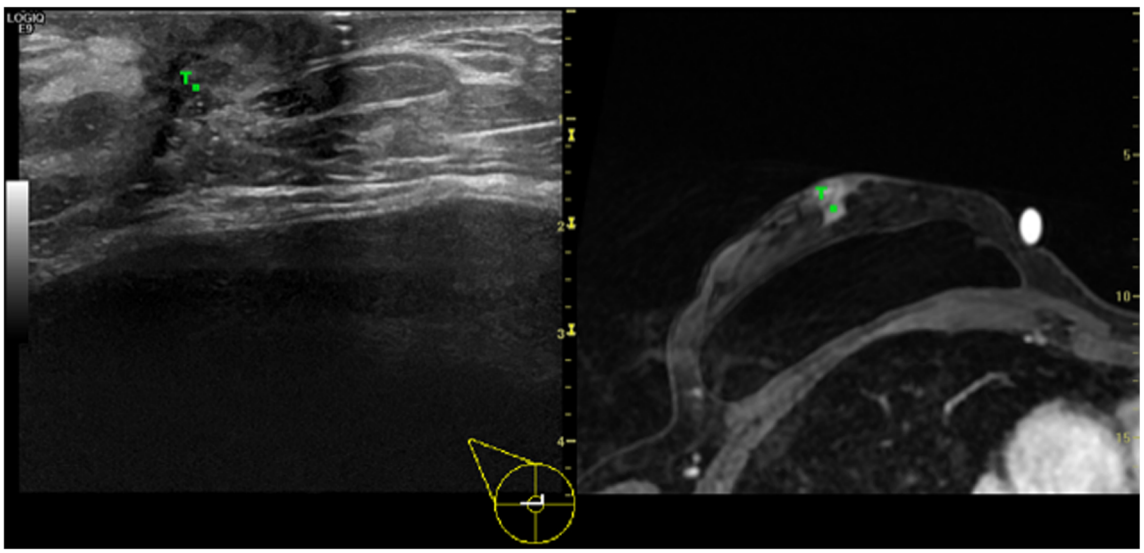


Fig. 1 Ultrasound image (left side) with the corresponding multiplanar reconstructed MR image (right side) of a 39-year-old woman with previous surgery for large ductal in situ carcinoma of the right breast operated with a skin-nipple spearing mastectomy and prosthesis reconstruction. After the 2-year follow-up, MR imaging showed a rounded enhancing lesion behind the nipple without any discharge, undetected at second-look US. Second-look US with volume navigation revealed the corresponding lesion (T, target) impossible to detect using other techniques. Pathology obtained with ultrasound-guided biopsy with volume navigation demonstrated a papilloma (T)

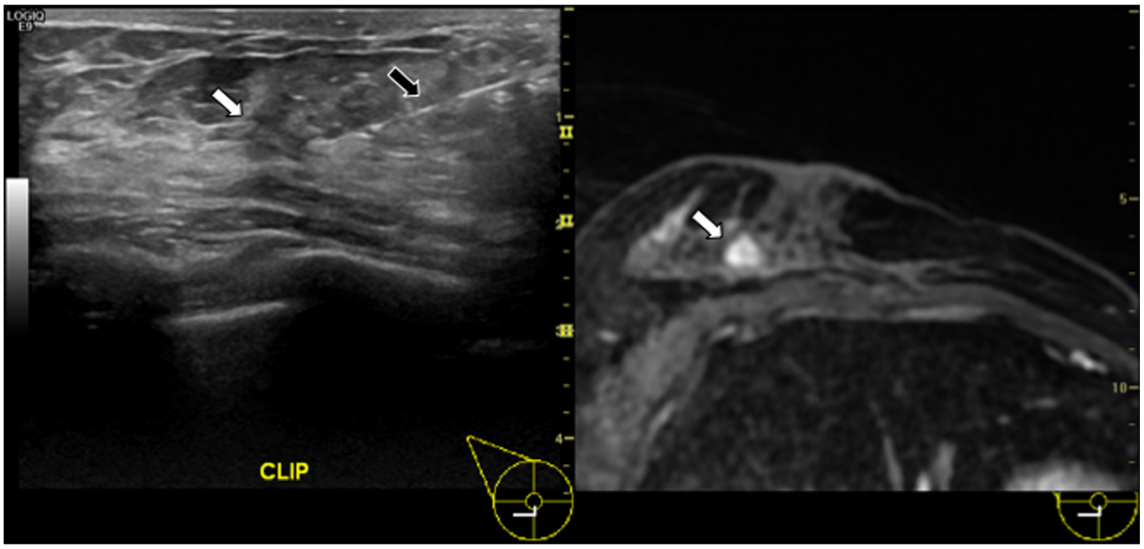


Fig. 2 Ultrasound image (left side) with the corresponding multiplanar reconstructed MR image (right side) of a 52-year-old woman with rounded-irregular enhancing lesion in the lower external quadrant of the right breast, undetected at second-look US. Second-look US with volume navigation (V Nav) revealed the corresponding suspicious lesion impossible to detect using other techniques. The tissue marker needle is clearly visible on the US image (black arrow). Pathology obtained with ultrasound-guided biopsy with V Nav demonstrated an invasive lobular carcinoma of 9 mm (white arrows)

The most important characteristic of lesions occult at US seems to be the echogenicity compared to the background signal, even more than dimension. Tables 2, 3, and 4 show the different lesion dimensions and pathologic features of the groups. A significantly higher number of benign lesions were detected during second-look US compared to the V Nav or MRI-guided biopsy group even if, in absolute terms, the numbers are considerably smaller.

However, US and MRI co-registration does have an important disadvantage: the displacement of the tissue during the US evaluation and biopsy. In fact, after obtaining US and MRI co-registration, patient movements or probe pressure on the skin could increase image misalignment. Nevertheless, this can be reduced by avoiding high pressure on the breast skin during US evaluation, maintaining the probe perpendicularly to the surface and verifying the correct alignment between skin marker and MRI reference on the corresponding image.

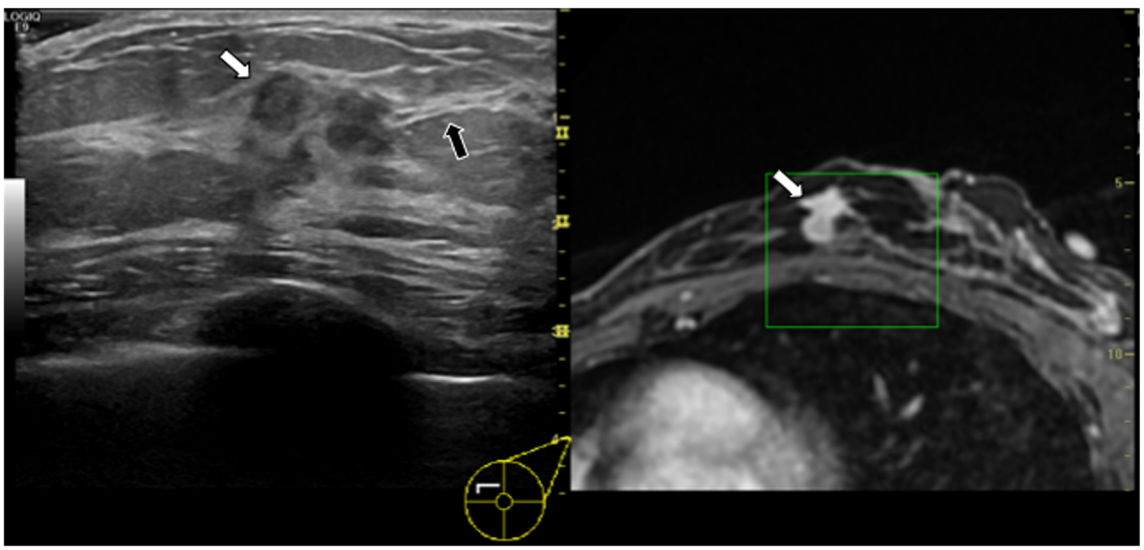


Fig. 3 Ultrasound image (left side) with the corresponding multiplanar reconstructed MR image (right side) of a 44-year-old woman with rounded-irregular enhancing lesion in the upper external quadrant of the left breast, undetected at second-look US. Second-look US with volume navigation (V Nav) revealed the corresponding suspicious lesion without a clear correlation at second-look US. The biopsy needle is visible on the US image (black arrow). Pathology obtained with ultrasound-guided biopsy with V Nav demonstrated an invasive ductal carcinoma of 16 mm (white arrows). The green box represents the corresponding US area on MR image showing additional lesion shape and conspicuity

One major limitation of the technique is that it cannot be performed in the case of breast hypertrophy, with excessive tissue of over 1.5 kg (3.3 lb). In view of its characteristics, more than the bra size, the evaluation of two anthropomorphic measurements is extremely useful for directly candidating the patient to MRI-guided biopsy. In our series, breast hypertrophy was present in a very small group of patients. It involved 12% (22/173) of all additional lesions occult at US, 3% (22/722) of all additional lesions with a prevalence of 1% (2/173) of malignant lesions considering all additional breast lesions occult at US. A minor limitation is represented by respiratory movements during the examination.

In conclusion, an 'objective' second-look US can effectively be obtained with MRI co-registration using V Nav. This could be a reliable technique in view of the technological improvement yielding high image quality of breast MRI in supine position. The cost-benefits of US with V Nav-guided biopsy compared with MRI-guided biopsy are mainly due to the time saving in the use of the MR equipment, freeing this for interventional procedures, and the lower cost of materials which do not need to be MR-compatible when US is used with V Nav-guided biopsy. The application of this technique makes it possible to detect a large number of additional breast lesions, occult at second-look US, and to biopsy a significant number of malignant lesions safely and irrespective of the distance from the skin or lesion position.

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Compliance with ethical standards

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Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Prospective
- Diagnostic study/observational
- Multicentre study

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