



Diagnostic performance of 2D-shear wave elastography in the diagnosis of breast cancer: a clinical appraisal of cutoff values

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Abstract

Purpose To assess the role of 2D-shear wave elastography (2D-SWE) in differentiating benign from malignant focal breast lesions (FBLs), providing new vendor-specific cutoff values.

Methods 158 FBLs (size: 3.5–50 mm) detected in 151 women (age: 21–87 years) were prospectively evaluated by means 2D-SWE. For each lesion, an expert radiologist assessed US BI-RADS category and calculated the following four 2D-SWE parameters: (1) elasticity maximum ($E_{\max}$); (2) mean elasticity (E_{mean}); (3) minimum elasticity ($E_{\min}$); (4) elasticity ratio (E_{ratio}). US-guided core-biopsy was considered as standard of reference for all the FBLs classified as BI-RADS 4 or 5. For each 2D-SWE parameter, the optimal cutoff value for a diagnostic test was calculated using the Youden method. Diagnostic performance of the US BI-RADS and 2D-SWE parameters was calculated accordingly.

Results 83/158 (52.5%) FBLs were benign and 75/158 (47.5%) were malignant. Statistically significant higher stiffness values were observed in malignant FBLs for all 2D-SWE parameters than in benign ones ($p < 0.001$). 2D-SWE cutoff values were 82.6 kPa, 66.0 kPa and 53.6 kPa, respectively, for $E_{\max}$, E_{mean} , $E_{\min}$ and 330.8% for E_{ratio} . The 2D-SWE parameter showing the best diagnostic accuracy was $E_{\max}$ (85.44%). Considering US BI-RADS 3 ($n = 60$) and 4a ($n = 32$) FBLs, $E_{\max}$ and E_{mean} showed the best diagnostic accuracy (85.87% for both), without a statistically significant decrease in sensitivity ($p = 0.7003$ and $p = 1$, respectively).

Conclusion Our study provides new vendor-specific cutoff values for 2D-SWE, suggesting its possible clinical use in the adjunctive assessment of category US-BI-RADS 3 and 4a breast masses.

Keywords Breast · Ultrasonography · Elasticity imaging techniques · Shear wave imaging

Introduction

First described in 1987 by Krouskop et al., the capability of ultrasound (US) to non-invasively assess the mechanical properties of soft tissues, such as the stiffness or displacement in response to an imparted force (US elastography), has been investigated in various organs and tissues, including breast [1–3]. On the assumption that breast cancer is stiffer than surrounding breast fibroglandular tissue, various elastographic techniques, either qualitative (i.e., Strain Elastography: SE), semi-quantitative or quantitative (i.e., Shear wave Elastography: SWE), have been developed over time to characterize focal breast lesions (FBLs) with encouraging results [4–7].

In particular, SWE has been proved to increase the specificity of B-mode US in the characterization of FBLs, thus

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reducing unnecessary biopsies of low-suspicion masses [8]. Nevertheless, a recent meta-analysis, while confirming that SWE is effective for distinguishing benign from malignant FBLs, suggested further studies to extend this finding and to confirm appropriate cutoff values of SWE [9]. Actually, cutoff values used to assess tissues elasticity are vendor-specific and various parameters with different methods may be calculated for SWE, such as $E_{\max}$, E_{mean} , $E_{\min}$, E_{SD} , E_{ratio} , E_{color} and E_{color} homogeneity [10–12].

To this regard, the purpose of this study was to assess the role of 2D-shear wave elastography (2D-SWE) in differentiating benign from malignant FBLs providing new vendor-specific cutoff values.

Materials and methods

Study design and patient population

Institutional ethical committee approval was obtained, and full written informed consent was obtained for this prospective study. Our study complied with the terms of the Declaration of Helsinki [13].

Between January 2019 and November 2019, 158 FBLs (size range: 3.5–50 mm; mean size $\pm$ SD: 15.4 mm $\pm$ 8.7 mm) were detected in 151 women (age range: 21–87 years; mean age $\pm$ SD: 53.6 $\pm$ 14.5 years) who underwent high resolution US by means of an ultrasound unit provided with a 3–12 MHz linear transducer (RS85 Samsung Medison, Co. Ltd.).

Indications for breast US included: (1) a palpable mass detected on physical examination; (2) dense breasts; (3) detected lesions from adjunct mammography examination; (4) patients with mastodynia; (5) young patients having family history or (6) in a follow-up for benign breast nodules.

Exclusion criteria included lack of adequate standard of reference (refusal to undergo biopsy or inconsistent follow-up).

Image selection and evaluation

An experienced breast radiologist (20 years of experience in breast imaging, including ultrasound) after performing B-mode US also made the elasticity assessment with 2D-SWE for each of the 158 FBLs by means of the same ultrasound unit using a 2–9 MHz linear transducer (RS85 Samsung Medison, Co. Ltd.).

2D-SWE was performed while placing the probe vertically on the skin, avoiding to exert heavy pressure as well as probe movement. A real-time assessment of the lesion was

performed in a dual screen mode, allowing at the same time a conventional B-mode observation and a qualitative elasticity assessment. To this purpose and to ensure the high image quality needed for 2D-SWE, a specific box is superimposed on the lesion allowing a visual evaluation of image quality by means of a color code: ranging from yellow (good image quality) to red (bad image quality). Furthermore, a reliability measurement index (RMI) is calculated and displayed on the US equipment screen. In our study, an RMI equal or greater than 0.6 was considered to be sufficient to provide adequate image quality.

Then, the radiologist chose the best scan plane to evaluate lesion stiffness and froze the image. Elasticity measurement was performed placing a circular ROI sized 2 mm within the lesion in the stiffest area as depicted by a color-coded map in a rectangular box, ranging from 0 (dark blue: soft) to 180 kPa (red: stiff) [7]. 2D-SWE analysis provided the following four parameters: (1) elasticity maximum ($E_{\max}$); (2) mean elasticity (E_{mean}); (3) minimum elasticity ($E_{\min}$); (4) elasticity ratio (E_{ratio}). The first three parameters are expressed in kPa. Eratio is expressed as percentage, indicating the ratio between the lesion's mean elasticity value and that of fat, by positioning another circular ROI of the same size at the same level in the surrounding breast tissue.

Standard of reference (SOR) and statistical analysis

For the purpose of this study, US-guided core-biopsy was considered as SOR for all the FBLs classified as BI-RADS 4 or 5, either before or after 2D-SWE assessment.

For all lesions classified as BI-RADS 2 and 3, US findings at six, 12, and 24-months follow-up was considered as SOR. In particular, stability or size decrease during follow-up was considered typically benign US findings.

Diagnostic performance of the US BI-RADS assessment alone and in conjunction with $E_{\max}$, $E_{\min}$, E_{mean} and E_{ratio} was measured through sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPP) and diagnostic accuracy (DA), with corresponding 95% confidence intervals. The equality of the above measures of diagnostic performance was assessed through the z-test for proportions. The overall diagnostic confidence was assessed through the area under receiver operating characteristic curve (AUC).

For each 2D-SWE parameter, the optimal cutoff value for a diagnostic test was calculated using the Youden method that maximizes the sum of the sensitivity and specificity, and then sensitivity, specificity, NPP, PPV and DA were re-calculated [14].

Statistical analyses were performed by using STATA/IC 15.1 (StataCorp LLC).

Results

According to SOR, 83 out of 158 (52.5%) FBLs were benign and 75 out of 158 (47.5%) were malignant (Table 1). Overall, statistically significant higher stiffness values were observed in malignant FBLs for $E_{\max}$, E_{mean} , $E_{\min}$ and E_{ratio} ($p < 0.001$), in comparison with benign FBLs (Table 2).

Table 3 details the diagnostic performance of the expert reviewer on the basis of US BI-RADS assessment only and the 2D-SWE evaluation based on the cutoff values in kPa for $E_{\max}$ (82.6), E_{mean} (66.0), $E_{\min}$ (53.6) and in percentage for E_{ratio} (330.8%) as calculated by the Youden method. Figure 1 depicts the correspondent area under the receiver operating characteristic curve (AUROC) analysis, showing for $E_{\max}$, E_{mean} and $E_{\min}$ but not for E_{ratio} higher values than BI-RADS.

An increase in specificity was observed for all the four studied 2D-SWE parameters in comparison with US

BI-RADS assessment, but without reaching statistical significance (Table 3). A statistically significant decrease in sensitivity was observed for E_{ratio} (62.67) ($p < 0.0001$) and $E_{\min}$ ($p = 0.0343$) (Table 3). The 2D-SWE parameter showing the best diagnostic accuracy was $E_{\max}$ (85.44%) (Table 3).

Table 4 shows the 2D-SWE evaluation based on the cut-off values as calculated by the Youden method to the FBLs categorized as US BI-RADS 3 ($n = 60$) or 4a ($n = 32$) by the expert reviewer. In this subgroup, in comparison with US BI-RADS assessment, a statistically significant increase in specificity was observed for $E_{\max}$ (89.19% versus 75.68%; $p = 0.0308$) without a statistically significant decrease in sensitivity (72.22% versus 77.78%; $p = 0.7003$) (Table 4). The 2D-SWE parameters showing the best diagnostic accuracy were $E_{\max}$ and E_{mean} (85.87% for both parameters) (Table 4).

In particular, by using the $E_{\max}$ cutoff (82.6 kPa), 9 out of 60 US BI-RADS 3 FBLs were upgraded to BI-RADS 4a. Three out of these latter 9 FBLs were actually malignant masses and were correctly upgraded (Fig. 2A,B). The remaining 6 out of 9 FBLs were benign masses and were incorrectly upgraded (Fig. 3A,B). Conversely, 20 out of 32 US BI-RADS 4a FBLs were downgraded to BI-RADS 3. Sixteen out of these latter 20 FBLs were actually benign masses and correctly downgraded (Fig. 4A,B). The remaining 4 out of 20 FBLs were malignant masses and were incorrectly downgraded (Fig. 5A,B).

By using the E_{mean} cutoff (66 kPa), 10 out of 60 US BI-RADS 3 FBLs were upgraded to BI-RADS 4a. Three out of these latter 10 FBLs were actually malignant masses and correctly upgraded, whereas the remaining 7 out of 10 FBLs were benign masses and incorrectly upgraded. Conversely, 19 out of 32 US BI-RADS 4a FBLs were downgraded to BI-RADS 3. Sixteen out of these latter 19 FBLs were actually benign masses and correctly downgraded, whereas the remaining 3 out of 19 FBLs were malignant masses and incorrectly downgraded.

Table 1 Final diagnosis of 158 FBLs as by standard of reference

Benign (83)	Malignant (75)
Fibroadenoma (67)	Invasive ductal carcinoma (43)
Complicated cyst (4)	Invasive ductal carcinoma and DCIS (11)
Scar tissue (2)	Invasive lobular carcinoma (10)
Fibrosis (2)	Mucinous carcinoma (4)
Benign phyllodes tumor (1)	Tubular carcinoma (2)
Fibromatosis (1)	Metaplastic carcinoma (2)
Radial scar (1)	Medullary carcinoma (1)
Galactocele (1)	DCIS (1)
Angiolipoma (1)	Non-Hodgkin Lymphoma (1)
Abscess (1)	
Usual ductal hyperplasia (1)	
Adenosis (1)	

Figures in parentheses are actual number of lesions

Table 2 Comparison of elasticity values between benign and malignant focal breast lesions

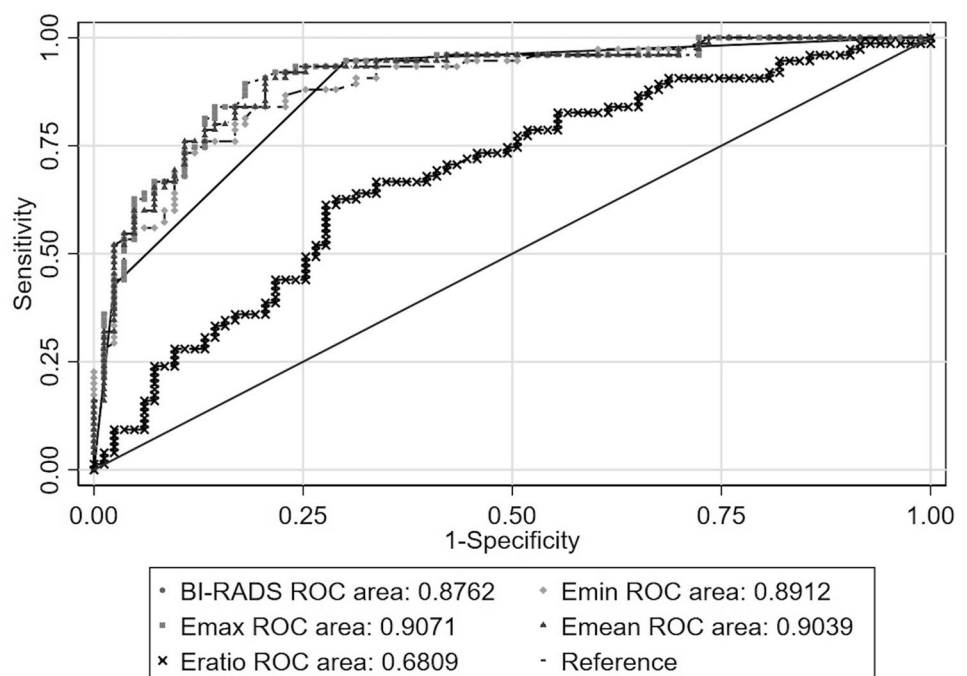
Elasticity 2D-SWE parameters	BENIGN FBLs (83/158) Mean $\pm$ SD Me (Q1; Q3)	MALIGNANT FBLs (75/158) Mean $\pm$ SD Me (Q1; Q3)	P value
$E_{\min}$	38.56 $\pm$ 24.93 35.3 (20.5; 47.3)	98.33 $\pm$ 44.09 93.2 (64.2; 128.5)	< 0.001
E_{mean}	50.18 $\pm$ 20.82 45.85 (29.3; 62.85)	115.90 $\pm$ 41.18 116.8 (83.65; 148.95)	< 0.001
$E_{\max}$	61.55 $\pm$ 32.94 56.5 (38.1; 78.4)	132.55 $\pm$ 40.21 140.5 (96.7; 169.4)	< 0.001
E_{ratio}	346.78 $\pm$ 351.34 242.2 (145.8; 440.5)	564.34 $\pm$ 544.33 393.8 (238.9; 670.2)	< 0.001

2D-SWE 2-Dimensional-Shear Wave Elastography, FBLs focal breast lesions, SD standard deviation, ME median, Q1 first quartile, Q3 third quartile, $E_{\min}$ minimum elasticity, E_{mean} mean elasticity, $E_{\max}$ Elasticity maximum, E_{ratio} Elasticity ratio

Table 3 Comparison of diagnostic performance of US BI-RADS and 2D-SWE on 158 FBLs

158 FBLs	TN	TP	FN	FP	Sen (%)	Spe (%)	NPV (%)	PPV (%)	DA (%)
BI-RADS	58	71	4	25	94.67	69.88	93.55	73.96	81.65
					86.90–98.53	58.82–79.47	84.30–98.21	64.00–82.38	74.72–87.35
2D-SWE Optimal cutoff (95% C.I.) $E_{\max}$ 82.6 kPa	68	67	8	15	89.33	81.93	89.47	81.71	85.44
					80.06–95.28	71.95–89.52	80.31–95.34	71.63–89.38	78.96–90.54
					$P=0.2281$	$P=0.0695$	$P=0.3975$	$P=0.2169$	$P=0.3636$
E_{mean} 66.0 kPa	66	68	7	17	90.67	79.52	90.41	80.00	84.81
					81.71–96.16	69.24–87.59	81.24–96.06	69.92–87.90	79.25–90.02
					$P=0.3473$	$P=0.1531$	$P=0.5063$	$P=0.3367$	$P=0.4522$
$E_{\min}$ 53.6 kPa	67	63	12	16	84.00	80.72	84.81	79.75	82.28
					73.72–91.45	70.59–88.56	74.97–91.90	69.20–87.96	75.42–87.89
					$P=0.0343$	$P=0.1054$	$P=0.1043$	$P=0.3681$	$P=0.8842$
E_{ratio} 330.8%	47	59	28	24	62.67	71.08	67.82	66.20	66.67
					50.73–73.57	60.09–80.52	56.94–77.44	53.99–77.00	58.77–73.93
					$P<0.0001$	$P=0.8654$	$P=0.0002$	$P=0.2569$	$P=0.0024$

US ultrasound, 2D-SWE 2-Dimensional-Shear Wave Elastography, FBLs focal breast lesions, TN true negative, TP true positive, FN false negative, FP false positive, Sen sensitivity, Spe specificity, NPV negative predictive value, PPV positive predictive value, DA diagnostic accuracy, C.I. confidence interval, $E_{\max}$ Elasticity maximum, E_{mean} mean elasticity, $E_{\min}$ minimum elasticity, E_{ratio} Elasticity ratio, kPa kiloPascal

Fig. 1 Receiver operating characteristic curve of diagnostic performance for distinguishing benign from malignant masses of 2D-SWE parameters in comparison with US BI-RADS

By using the $E_{\min}$ cutoff (53.6 kPa), 11 out 60 US BI-RADS 3 FLBs were upgraded to BI-RADS 4a. Three out of these latter 11 FBLs were actually malignant masses and correctly upgraded whereas the remaining 8 out 11 FBLs were benign masses and incorrectly upgraded. Conversely, 18 out 32 US BI-RADS 4a FLBs were downgraded to BI-RADS 3. Fifteen out of these latter 18 FBLs were actually benign masses and correctly downgraded, whereas the

remaining 3 out 18 FBLs were malignant masses and incorrectly downgraded.

By using the E_{ratio} cutoff (330.8%), 15 out 60 US BI-RADS 3 FLBs were upgraded to BI-RADS 4a. One out of these latter 15 FBLs was actually a malignant mass and correctly upgraded whereas the remaining 14 out 15 FBLs were benign masses and incorrectly upgraded. Conversely, 17 out 32 US BI-RADS 4a FLBs were downgraded to BI-RADS 3. Eleven

Table 4 Comparison of diagnostic performance of US BI-RADS and 2D-SWE on 92 (3 and 4a) FBLs

92 FBLs 3 (60) and 4a (32)		TN	TP	FN	FP	Sen (%)	Spe (%)	NPV (%)	PPV (%)	DA (%)
BI-RADS		56	14	4	18	77.78	75.68	93.33	43.75	76.09
BI-RADS and 2D-SWE Optimal cutoff	$E_{\max}$ 82.6 kPa	66	13	5	8	52.36–93.59	64.31–84.90	85.39–97.11	32.67–55.49	66.06–84.37
						72.22	89.19	92.96	61.90	85.87
						46.52–90.31	79.80–95.22	86.19–96.54	44.30–76.85	77.05–92.26
						$p=0.7003$	$p=0.0308$	$p=0.9325$	$p=0.1960$	$p=0.0909$
						77.78	87.84	94.20	60.87	85.87
	E_{mean} 66.0 kPa	65	14	4	9	52.36–93.59	78.16–94.29	87.21–97.48	44.56–75.06	77.05–92.26
						$p=1.000$	$p=0.0554$	$p=0.8382$	$p=0.2103$	$p=0.0909$
						77.78	85.14	94.03	56.00	83.70
						52.36–93.59	74.96–92.34	86.85–97.41	41.16–69.84	74.54–90.58
						$p=1.000$	$p=0.1472$	$p=0.8719$	$p=0.3586$	$p=0.4747$
	E_{ratio} 53.6 kPa	63	14	4	11	50.00	71.62	85.48	30.00	67.39
						26.90–73.10	61.35–81.89	76.72–94.25	13.60–46.40	57.81–76.97
						$p=0.0828$	$p=0.5756$	$p=0.1601$	$p=0.2627$	$p=0.1903$
	E_{ratio} 330.8%	53	9	9	21					

US ultrasound, 2D-SWE 2-Dimensional-Shear Wave Elastography, FBLs focal breast lesions, TN true negative, TP true positive, FN false negative, FP false positive, Sen sensitivity, Spe specificity, NPV negative predictive value, PPV positive predictive value, DA diagnostic accuracy, C.I. confidence interval, $E_{\max}$ Elasticity maximum, E_{mean} mean elasticity, $E_{\min}$ minimum elasticity, E_{ratio} Elasticity ratio, kPa kiloPascal

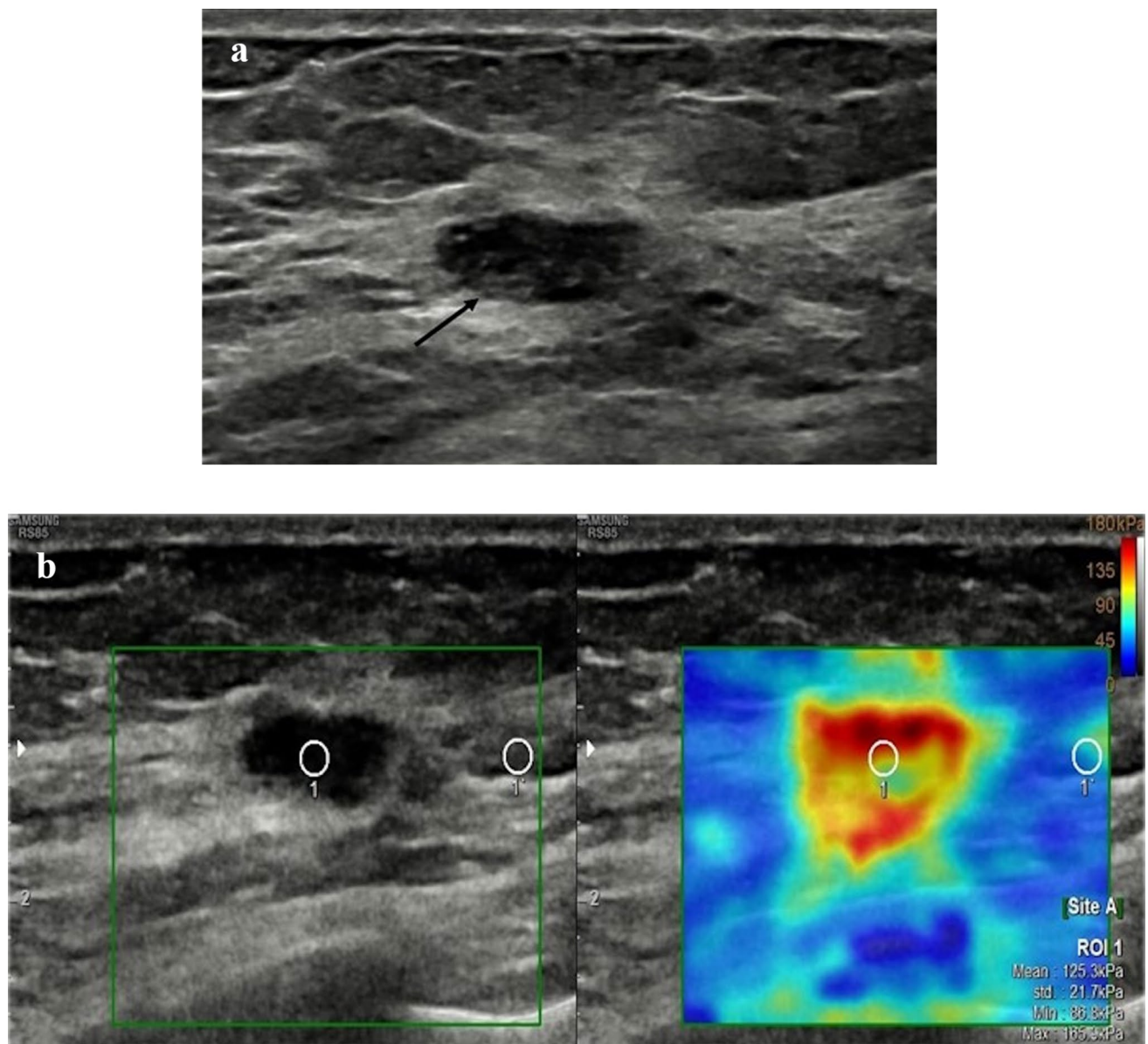


Fig. 2 **A, B** Asymptomatic 38-year-old woman. B-mode **A** US shows an oval-shaped, hypoechoic mass (black arrow), sized 1 cm with parallel orientation and substantially circumscribed margin, categorized as BI-RADS 3 by the expert radiologist. 2D-SWE **B** revealed a markedly stiff lesion. 2D-SWE parameters ($E_{\max}$, E_{mean} , $E_{\min}$ and E_{ratio})

were 165.9 kPa, 125.3 kPa, 86.8 kPa and 215.8%, respectively. Breast tissue nearby the lesion is also stiffer than normal. Consequently, the lesion was upgraded from BI-RADS 3 to BI-RADS 4a. Core-needle biopsy proved the mass to be a Luminal B Her—invasive ductal carcinoma

out of these latter 17 FBLs were actually benign masses and correctly downgraded, whereas the remaining 6 out of 17 FBLs were malignant masses and incorrectly downgraded.

Discussion

Since their first application in the late eighties, US elastography techniques have been used to assess breast tumors stiffness [2]. In spite of the progressively increasing use of such

techniques in the assessment of focal breast masses, their real contribution in the characterization of breast cancer still remains not completely clear. Cutoff values used to assess tissue elasticity are vendor-specific and different parameters may be calculated for SWE with different methods. Stiffness measurement itself may be provided either in meters per second, according to the shear wave velocity, or in kilopascal, according to Young's modulus. This latter measurement implies a unit conversion and introduces an element of variability depending on the manufacturer system [15].

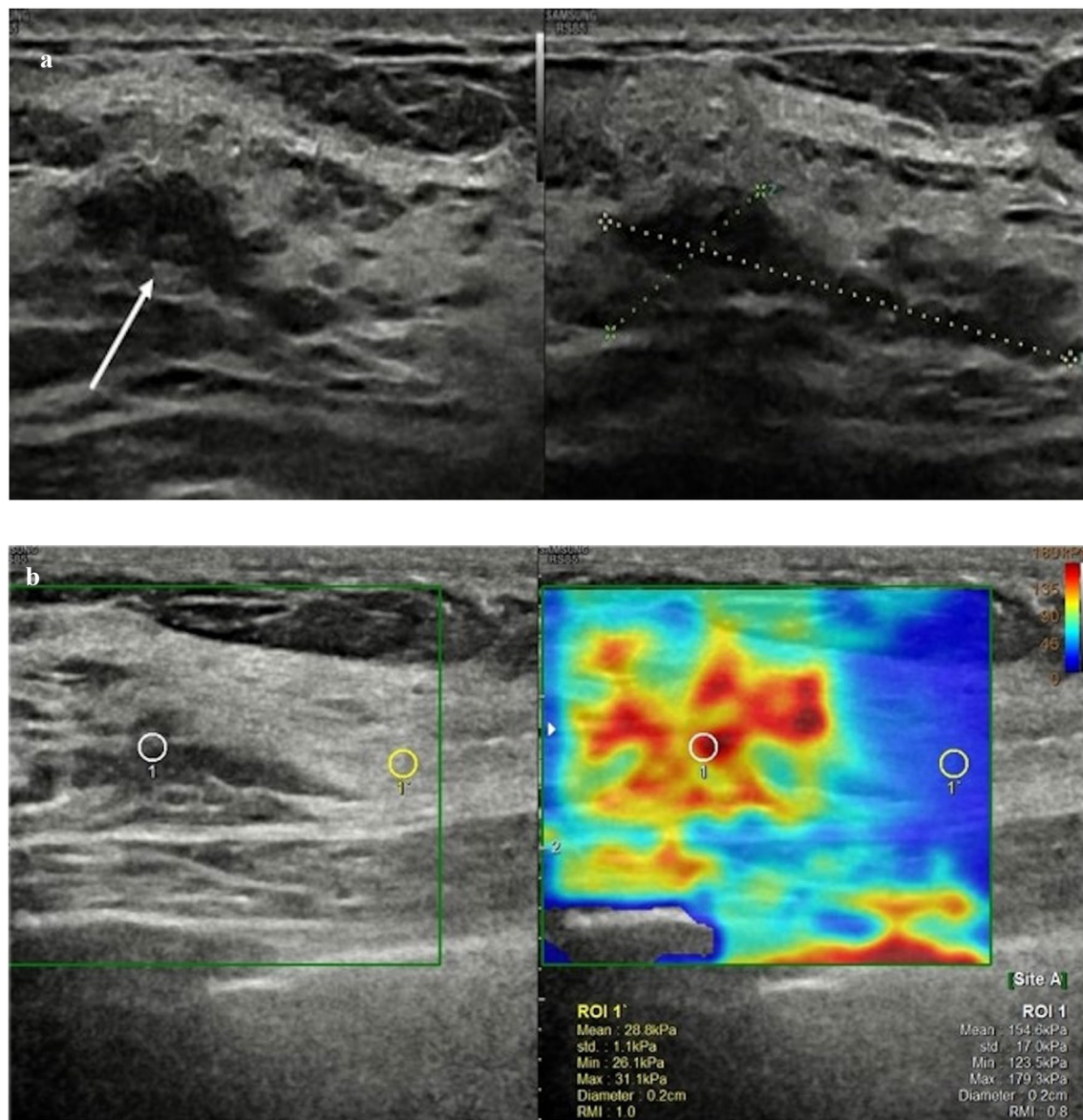


Fig. 3 A, B Asymptomatic 42-year-old woman. B-mode A US shows a non-mass hypoechoic area (white arrow), with parallel orientation, irregular shaped, with multiple oblong bundles mimicking a star as depicted in the anti-radial (left) and radial (right) probe positioning. 2D-SWE B reveals a markedly stiff lesion with stiffness propagating

to the surrounding breast tissues with corresponding 2D-SWE parameters ($E_{\max}$, E_{mean} , $E_{\min}$ and E_{ratio}) of 179.3 kPa, 154.6 kPa, 123.5 kPa and 523.6%, respectively. This lesion was upgraded from BI-RADS 3 to BI-RADS 4a. Core-needle biopsy proved the mass to be a radial scar

The latest available edition of the BI-RADS lexicon from the American College of Radiology (dated 2013) considers elasticity assessment just an associated feature of morphologic evaluation and advise not let the former to supersede the latter [16]. On the other hand, according to the 2018 update of EFSUMB guidelines as well as the 2015 WFUMB guidelines, a BI-RADS 3 lesion appearing stiffer on breast ultrasound elastography should be considered for biopsy [17, 18]. Furthermore, 2015 WFUMB guidelines state that downgrading by means of stiffness evaluation a US BI-RADS 3 or 4a breast mass is reasonable, but downgrading a US

BI-RADS 4b, 4c, or 5 lesion is not recommended [18]. In clinical practice, considering the very high probability of benignity for a US BI-RADS 3 lesion and the very low suspicion for a US BI-RADS 4a lesion of being malignant, the ability of avoiding unnecessary biopsies would allow to save costly and relatively invasive procedures.

In our series, quantitative 2D-SWE parameters significantly differed between benign and malignant breast masses, thus supporting previously reported data obtained with different ultrasound equipment [19–24]. In our experience, 2D-SWE analysis performed by an expert reviewer has led

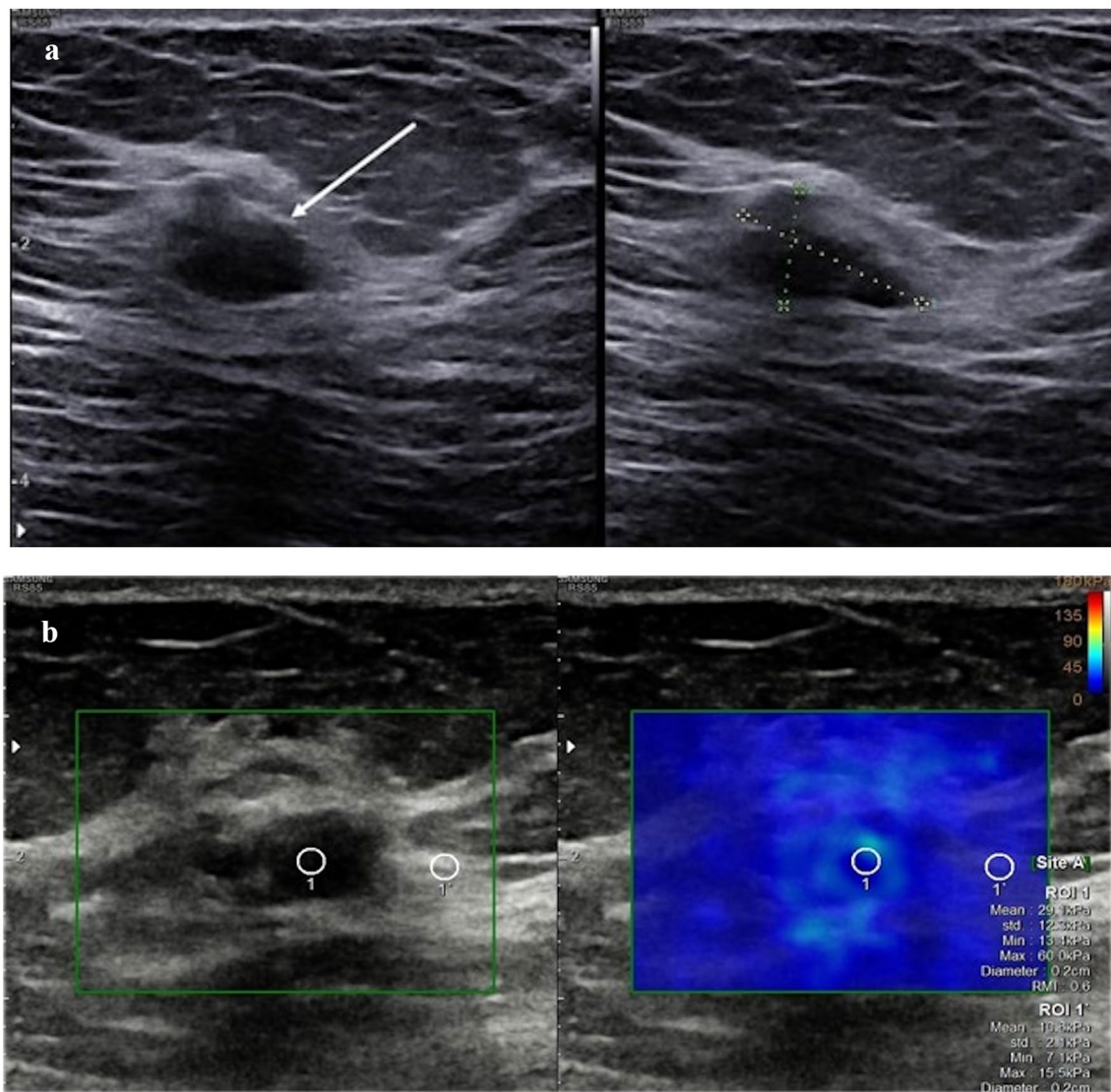


Fig. 4 **A, B** Asymptomatic 52-year-old woman. B-mode US depicts a 1 cm hypoechoic oval-shaped mass (white arrow) with parallel orientation but partially indistinct margins and categorized as BI-RADS 4a by the expert radiologist. 2D-SWE **B** shows the lesion as soft and

corresponding 2D-SWE parameters ($E_{\max}$, E_{mean} , $E_{\min}$ and E_{ratio}) were 60.0 kPa, 29.1 kPa, 13.4 kPa and 275.3%, respectively. This lesion was downgraded from BI-RADS 4a to BI-RADS 3. Final diagnosis was fibroadenoma

to an increase of specificity—albeit not statistically significant—for all the four studied parameters, but at the expense of sensitivity. In particular, a statistically significant decrease for $E_{\min}$ and E_{ratio} was observed. As a consequence, 2D-SWE assessment alone would have led to a not significant reduction of unnecessary biopsies but it would have generated a significant increase in missed breast cancer.

Interestingly enough, when limiting our analysis to category 3 and 4a FBLs and adding 2D-SWE assessment to US BI-RADS categorization, a statistically significant increase in specificity was observed for $E_{\max}$ without a statistically significant decrease in sensitivity. These results are in line with a recent meta-analysis concluding that adding SWE to

B-mode US increases the specificity in the characterization between benign and malignant breast lesions and decreases the number of unnecessary biopsies [9].

Of note, in our series, a not negligible number of breast cancer would have been missed both with the use of US BI-RADS lexicon ($N=4$) and 2D-SWE assessment, ranging from 4 to 9 cases depending on the considered 2D-SWE parameter. In particular, four breast cancers would have been missed: one metaplastic carcinoma, which is usually soft at pathology. The other three missed cancers were one triple negative invasive ductal carcinoma and two Luminal B/Her negative invasive and in situ ductal carcinomas, respectively. All these last three lesions showed 2D-SWE parameters

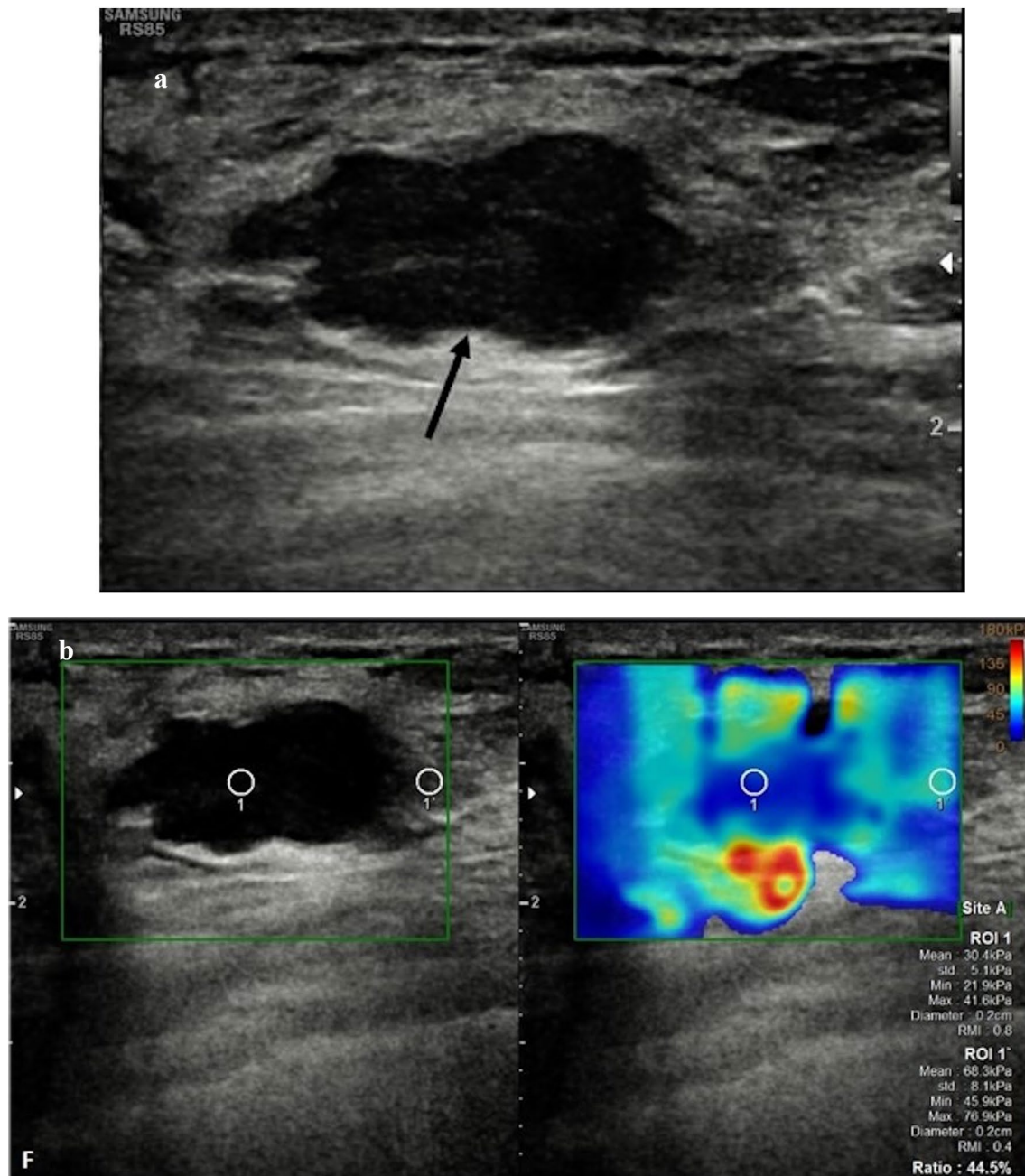


Fig. 5 **A, B** 47-year-old woman. B-mode US depicts a 2.2 cm irregular-shaped, lobulated, markedly hypoechoic mass (black arrow), with parallel orientation, circumscribed margin and posterior enhancement. Expert radiologist classified it as BI-RADS 4a. 2D-SWE (**B**) shows a soft lesion, although with an increased stiffness of surround-

ing breast tissues, and corresponding 2D-SWE parameters ($E_{\max}$, E_{mean} , $E_{\min}$ and E_{ratio}) were 41.3 kPa, 30.4 kPa, 21.9 kPa and 44.5%, respectively. This lesion was downgraded from BI-RADS 4a to BI-RADS 3. Final diagnosis was metaplastic carcinoma

slightly lower to the cutoffs. To this regard, a trend toward lower $E_{\max}$ and E_{mean} has been reported in more aggressive phenotypes, such as triple negative tumors [25].

In our series, unnecessary biopsies of benign lesions would have occurred both with the US BI-RADS lexicon ($N=18$) or with 2D-SWE assessment, ranging from 8 to 21 depending on the 2D-SWE parameter used. In particular,

in the US BI-RADS 3 and 4a groups, all the benign FBLs incorrectly classified as malignant were fibroadenomas, regardless of the 2D-SWE parameter considered. These results are supported by Elseedawy et al., who found a relationship between 2D-SWE false-positives results and hyalinized or calcified fibroadenomas [26]. Two more fibrosis and one fibromatosis lesions were assessed as suspicious,

with or without 2D-SWE. Histology may explain this evidence, since both these entities are characterized by varying amounts of collagen [27, 28].

On the other hand, in our series, one case of galactocele was classified BI-RADS 2 at B-mode US and appeared stiff at 2D-SWE evaluation. This evidence is in agreement with the case reported by Toprak et al., suggesting that stiffness was due to the presence of dense proteinaceous contents [29].

Although $E_{\max}$ was the only parameter showing a statistically significant increase in specificity in our series in addition to US-BI-RADS, it would have led to one more missed cancer. To this regard, also E_{mean} improved the specificity rate, with a considerable reduction of false positive cases (9 vs. 18), but without varying sensitivity significantly. This evidence is in agreement with the recent meta-analysis of Park et al., who reported for E_{mean} , in comparison with $E_{\max}$, a slightly lower improvement in specificity (24% vs. 28%) but a less decrease in sensitivity (1% vs. 5%) [9].

Although several studies on breast 2D shear wave have been already conducted, diverse quantitative parameters have been reported with a wide range of cutoffs values depending on different vendors [12, 30–32]. Furthermore, heterogeneity also remains in studies performing 2D-SWE of breast masses with the same ultrasound equipment [12, 24, 30, 33, 34]. As a consequence, it is highly recommended that each site assesses the most appropriate cutoff values and uses continued monitoring to adjust the cutoff as needed [35]. To our knowledge, this is the first work reporting 2D-SWE cutoffs values for the characterization of breast masses with a vendor-specific ultrasound equipment as indicated in the pertinent section and not yet fully evaluated in literature. To this regard, our cutoffs values are consistent to those obtained with a different ultrasound equipment by Choi et al. and Kim et al., who included in their study, respectively, 428 and 177 breast lesions sized less than 2 cm or to those obtained with a further different ultrasound equipment by Seo et al. and Youk et al., who, respectively, analyzed 45 and 79 breast lesions, including lesions larger than 2 cm [36–39].

A recent meta-analysis of quantitative parameters has shown that a co-variate cutoff value for $E_{\max}$ and E_{mean} equal or higher than 70 kPa yielded significantly higher sensitivity than a lower cutoff (< 70 kPa) [9]. To this regard, the new cutoff values found with the vendor-specific equipment used in this study do not differ significantly, being 82.6 kPa for $E_{\max}$ and 66 kPa for E_{mean} . In a study by Youk et al. encompassing 79 breast masses, cutoff values of 90 kPa for $E_{\max}$ and 61.9 kPa for E_{mean} allowed no false-negative cases when downgrading US BI-RADS category 4a lesions [39].

Our study presents some limitations. Firstly, we were not able to perform a direct comparison of tumoral elasticity by means of histological analysis. Such an analysis could

have provided more insight about the real correspondence between 2D-SWE and tumoral stiffness, but it would not have directly affected the results of the present study.

Second, although advisable, we could not perform a concordance analysis. However, literature data already exist showing excellent concordance for $E_{\max}$ assessment [40].

Third, our study included a Caucasian population of women; hence, further studies encompassing different populations are needed to evaluate the reproducibility of our results in other geographical areas.

In conclusion, our study provides new vendor-specific cutoff values for 2D-SWE characterization of breast masses, suggesting a strategy for down- and up-grading, respectively, the US BI-RADS category of 4a and 3 lesions by adding 2D-SWE analysis to morphologic B-mode assessment.

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Declarations

Conflict of interest Tommaso Vincenzo Bartolotta is lecturer and scientific advisor for Samsung. Other authors declare that they have no conflict of interest. This research was supported by research equipment from SAMSUNG MEDISON Co., Ltd.

Ethical approval Institutional ethical committee approval was obtained, and full written informed consent was obtained for this prospective study. Our study complied with the terms of the Declaration of Helsinki.

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