Shear wave elastography contribution in ultrasound diagnosis management of breast lesions

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**Purpose:** To determine the diagnosis performance of shear wave elastography in the differentiation of benign and malignant breast lesions and the factors influencing the elasticity values. To suggest an appropriate management of breast lesions using the ultrasound-elastography combination.

**Patients and methods:** Monocentric retrospective study of 167 breast lesions classified by conventional ultrasound as BI-RADS category 3 or higher that underwent an elastography study and histological analysis.

**Results:** The analysis of qualitative parameters, according to the classification established in this study, allows us to obtain a sensitivity of 91.1% and a specificity of 92.3%. These values are very close to or better than the quantitative parameters Emax and Emean. Different Emax thresholds values were established based on the long axis of the lesion and its palpable character, which appeared to be significant factors influencing elasticity. The management of breast lesions by combining ultrasound and elastography, as proposed here, allows us to keep the sensitivity of an ultrasound (96%), while doubling its specificity (86.2% versus 43%).

**Conclusion:** With the complementary nature of their performance, the combination of conventional ultrasound and shear wave elastography can improve the management of breast lesions. The qualitative classification proposed appears to be relevant assistance in lesion characterization.

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Shear wave elastography is a new imaging technique that makes it possible to determine the elasticity of tissues both qualitatively and quantitatively. According to Young’s modulus, the elasticity of a tissue is directly related to the propagation speed of the shear wave in the tissue as per the formula \( E = 3 \rho c^2 \) (where \( E \): elasticity of the tissue, \( \rho \): volume density of the tissue and \( c \): the propagation speed of the shear wave) [1].

This technique, which is complementary to ultrasound, aims to improve specificity [2]. Elastography makes it possible to determine the hardness of the lesion, which is an essential characteristic that is generally provided by the clinical breast exam. It allows this analysis to be extended to intra-clinical lesions.

Unlike static elastography, shear wave elastography does not require any manual compression to map the tissue elasticity. Even if the pressure values can be accentuated in case of manual compression on the transducer, this technique appears much less operator dependent and therefore has excellent intra- and interobserver reproducibility [3,4].

The objectives of this study are as follows:
- to determine the diagnostic performance of shear wave elastography in the differentiation of benign and malignant breast lesions, compared to that of conventional breast ultrasound;
- to characterize the factors influencing the lesion elasticity values;
- to suggest a type of lesion management via the ultrasound — elastography combination.

Patients and methods

Patients, data collection

This is a monocentric retrospective study concerning a series of 142 patients who consulted at the Centre Régional de Lutte Contre le Cancer d’Auvergne [Auvergne Regional Anti-Cancer Center] between January and June 2012. Among these patients, 167 breast lesions detected by ultrasound [mode B] were analyzed with elastography. These lesions had been classified based on conventional ultrasound data as BI-RADS 3, 4 or 5 and required an additional histological analysis. Certain lesions classified as BI-RADS 3 based on ultrasound criteria were sampled either because the breast evaluation (clinical context, mammographies or MRI) showed suspicious criteria or because the patient had a personal or family profile that put them at risk, or because of the patient’s wishes. The lesions that were initially classified as BI-RADS 3 that were not biopsied were included due to their stability and the absence of morphological changes for at least 2 years. They were therefore considered to be benign.

Shear wave elastography was performed with the Aixplorer® ultrasound (ShearWave™ Elastography, SuperSonic Imagine, Aix-en-Provence, France), using two transducers: one linear SL 4–15 MHz transducer and one 3D SLV 5–16 MHz transducer.

The acquisitions were carried out by placing the transducer without compression by asking the patient to hold her breath and by waiting at least 3 seconds for the image to stabilize. The study of the external quadrants was facilitated by the oblique decubitus.

These precautions appeared necessary to avoid any compression, as the elasticity values can be accentuated if there is excessive manual compression on the transducer.

A minimum of 3 different acquisitions was necessary to include the lesion. A 3D elastographic acquisition was also carried out for 84 lesions (50%).

Five operators, who had 2 to 3 months prior experience in the use of elastography, participated in the study. These radiologists had between 4 and 32 years of radiology experience (TK: 4 years; WM: 4 years; VD: 16 years; VB: 30 years and SL: 32 years).

For each acquisition, the quantitative analysis was conducted by the set up of a region of interest (Q-Box) with suitable dimensions over the hardest intra- or perilesional area (Q-Box Lesion), and a second Q-Box in an adjacent fat lobe (Q-Box Fat). For each lesion, we therefore obtained a minimum of 3 measurements for the following parameters: Emax lesion (kPa), Emean lesion (kPa), Emean fat (kPa), ratio (Emean lesion/Emean fat).

The qualitative analysis was carried out using the standard color scale (0–180 kPa) increasing from blue to red with lesion hardness. We chose not to modify this color scale, which seemed suited to the study of breast lesions. For each color map, we analyzed homogeneity, maximum color, presence of a maximum hardness area located inside or around the lesion and the presence of an intralesional echo. To simplify the study, we proposed a qualitative lesion classification (Qual) in 5 types (Table 1), like the one created by Itoh et al. for static elastography [5].

After that, we carried out a retrospective study of the conventional ultrasound images (mode B) and elastography images. Conventional ultrasound (mode B) had been performed for all of the lesions before the elastography. The analysis of each lesion required a minimum of two orthogonal images, in which the long axis and the depth of the lesion compared to the skin surface were measured. Then the shape, orientation, contours, border, echo pattern and posterior acoustics features were analyzed using the criteria of the BI-RADS ultrasound classification [6]. We chose to group lesions that had indistinct, microlobular, angular or spiculated contours under the term "undefined" contours. To determine the BI-RADS category of each lesion, we used the criteria proposed by Costantini et al. [7], which complied with those used by Raza et al. [8] (Table 2).

The histological study was carried out either on percutaneous samples by ultrasound-guided biopsies for 101 lesions (60%), or by surgical pieces for 63 lesions (38%). Only 3 lesions (2%) did not have a histological analysis (known lesions that had been stable for more than 2 years).

Methods

Firstly, we studied the distribution of the collected parameters depending on the benign or malignant character of the lesions. Then, we screened for the presence of a statistical relationship between these criteria and the elastographic parameters, with a value of \( P < 0.05 \) being considered significant. We used the Chi² test, the t-test, the ANOVA test, the Kruskal-Wallis H test and correlation analyses.
Table 1  ShearWave™ Elastography: qualitative classification (Qual).

<table>
<thead>
<tr>
<th>Types</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogeneity</td>
<td>Homogeneous</td>
<td>Not very homogeneous</td>
<td>Heterogeneous</td>
<td>Heterogeneous</td>
<td>Heterogeneous</td>
</tr>
<tr>
<td>Maximum color</td>
<td>Blue</td>
<td>Green</td>
<td>Yellow</td>
<td>Red</td>
<td>Red</td>
</tr>
<tr>
<td>Hard area</td>
<td>0</td>
<td>0</td>
<td>Intra- or Perilesional</td>
<td>Intra- or Perilesional</td>
<td>Perilesional</td>
</tr>
<tr>
<td>Intralesional echo</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
<td>Absent (no echo)</td>
</tr>
</tbody>
</table>

Secondly, by analysis of the ROC curves, we studied the diagnostic performance of the ultrasound BI-RADS classification and the quantitative and qualitative elastographic parameters. We selected, as with a large majority of studies, to consider BI-RADS 3 classified lesions as benign and BI-RADS 4 and 5 lesions as malignant, despite the great heterogeneity of category 4, the malignant potential of which demands a histological study. A threshold value was established for each parameter. By logistic regression, we determined the most effective elastographic parameters for differentiating between benign lesions and malignant lesions.

Finally, we analyzed the impact of the potential modifications in management caused by elastography by applying the determined threshold values.

**Results**

**Analysis of the parameters depending on the benign or malignant character of the lesions**

This series concerning 142 patients made it possible to study 167 breast lesions corresponding to 65 benign lesions (39%) and 102 malignant tumors (61%) (Table 3). The mean age of the patients was 57.7 years (min.: 22 — max.: 88) with a significantly higher mean age ($P < 10^{-7}$) for patients with a malignant tumor (62.5 years compared to 50.2 years for benign lesions). Eighty-nine lesions (53%) were palpable with a mean size evaluated clinically to be 2.6 cm, and 78 lesions (47%) were infra-clinical. The vast majority of benign lesions (75%) were infra-clinical, while only 61% of the malignant lesions were palpable. The malignant tumors therefore accounted for 79% of palpable lesions but also made up 45% of the infra-clinical lesions.

**Conventional ultrasound**

The mean ultrasound size of the lesions was 14.5 mm (4—73 mm), with a significant difference ($P = 0.01$) between the benign lesions (15.7 mm) and the malignant tumors (12.7 mm).

The mean depth of the lesions was 8.2 mm (2—22 mm), with no significant difference ($P = 0.4$) between benign lesions (8.0 mm) and malignant tumors (8.4 mm).

The irregular shape, an orientation that was not parallel to the skin, undefined contours, the hyper-echogenic halo and the posterior acoustic shadowing were associated in a significant manner with malignant lesions. Only the ech-structure had no significant relationship with the benign or malignant character. The predictive values for malignancy are presented in Table 3.

Concerning the BI-RADS ultrasound classification, for the BI-RADS 3 category, a positive predictive value of malignancy of 9% was observed, while it should, in principle, be less than 2% [9].

**Shear wave elastography**

All of the lesional elastographic parameters made it possible to differentiate in a significant manner between benign lesions and malignant tumors (Table 4). We observed mean Emax values of $61.6 \pm 10.9$ kPa for benign lesions compared to $187.1 \pm 37.6$ kPa for malignant tumors. In addition, on acquisitions performed with the linear transducer, we observed a significant increase in elasticity values of the adjacent fat when we were dealing with a malignant
## Table 3  Predictive values of malignancy and mean Emax values of the clinical and ultrasound criteria.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Total</th>
<th>Benign (n)</th>
<th>Malignant (n)</th>
<th>NPV (%)</th>
<th>PPV (%)</th>
<th>Elastography (kPa)</th>
<th>Test H</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td><strong>Clinical examination</strong></td>
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<td></td>
</tr>
<tr>
<td>Palpation</td>
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<tr>
<td>Palpable</td>
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<td>47</td>
<td>16</td>
<td>21</td>
<td>79</td>
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<td>49</td>
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<td>45</td>
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<td>Oval</td>
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<td>44</td>
<td>47</td>
<td>64</td>
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<td>7</td>
<td>3</td>
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<td>50</td>
<td>11</td>
<td>72</td>
<td>87</td>
<td>180.9</td>
<td></td>
</tr>
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<tr>
<td>Parallel</td>
<td>118</td>
<td>71</td>
<td>56</td>
<td>62</td>
<td>47</td>
<td>124.9</td>
<td>$P = 5.10^{-3}$</td>
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<tr>
<td>Not parallel</td>
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<td>29</td>
<td>9</td>
<td>40</td>
<td>82</td>
<td>167.1</td>
<td></td>
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<td>29</td>
<td>38</td>
<td>11</td>
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<tr>
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<td>71</td>
<td>27</td>
<td>91</td>
<td>77</td>
<td>166.4</td>
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<td>Borders</td>
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<tr>
<td>Thin</td>
<td>118</td>
<td>71</td>
<td>63</td>
<td>55</td>
<td>53</td>
<td>111.9</td>
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<td>Hyper-halo</td>
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<td>29</td>
<td>2</td>
<td>47</td>
<td>96</td>
<td>198.3</td>
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<td><strong>Posterior acoustic</strong></td>
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<tr>
<td>Enhancement</td>
<td>20</td>
<td>12</td>
<td>14</td>
<td>6</td>
<td>70</td>
<td>102.8</td>
<td>$P = 4.10^{-5}$</td>
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<td>Normal</td>
<td>86</td>
<td>52</td>
<td>44</td>
<td>42</td>
<td>51</td>
<td>116.2</td>
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<tr>
<td>Mixed</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td>117.5</td>
<td></td>
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<tr>
<td>Shadowing</td>
<td>59</td>
<td>35</td>
<td>6</td>
<td>53</td>
<td>90</td>
<td>180.3</td>
<td></td>
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<tr>
<td><strong>Echo pattern</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hypoechogenic</td>
<td>106</td>
<td>63</td>
<td>42</td>
<td>64</td>
<td>60</td>
<td>129.3</td>
<td>$P = 0.09$</td>
</tr>
<tr>
<td>Isoechogenic</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td></td>
<td>39.7</td>
<td></td>
</tr>
<tr>
<td>Hyper-echogenic</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td>140.5</td>
<td></td>
</tr>
<tr>
<td>Complex</td>
<td>57</td>
<td>34</td>
<td>20</td>
<td>37</td>
<td>65</td>
<td>155.5</td>
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<td><strong>BI-RADS</strong></td>
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<td>BI-RADS 3</td>
<td>33</td>
<td>20</td>
<td>30</td>
<td>3</td>
<td>91</td>
<td>9</td>
<td>$P &lt; 10^{-7}$</td>
</tr>
<tr>
<td>BI-RADS 4</td>
<td>72</td>
<td>43</td>
<td>33</td>
<td>39</td>
<td>46</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>BI-RADS 5</td>
<td>62</td>
<td>37</td>
<td>2</td>
<td>60</td>
<td>3</td>
<td>97</td>
<td></td>
</tr>
</tbody>
</table>

## Table 4  Mean values of the elastographic parameters according to the benign or malignant character of the lesions.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Acquisitions</th>
<th>Benign [95% CI]</th>
<th>Malignant [95% CI]</th>
<th>Test H</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emax (kPa)</td>
<td>Linear</td>
<td>61.6 [50.7; 72.5]</td>
<td>187.1 [149.5; 224.7]</td>
<td>$P &lt; 10^{-7}$</td>
</tr>
<tr>
<td></td>
<td>3D</td>
<td>77.0 [51.6; 102.4]</td>
<td>176.3 [127.2; 225.4]</td>
<td>$P &lt; 10^{-7}$</td>
</tr>
<tr>
<td>Emean (kPa)</td>
<td>Linear</td>
<td>51.7 [42.6; 60.8]</td>
<td>159.6 [126.9; 192.3]</td>
<td>$P &lt; 10^{-7}$</td>
</tr>
<tr>
<td></td>
<td>3D</td>
<td>58.9 [38.6; 79.2]</td>
<td>147.4 [105.0; 189.8]</td>
<td>$P &lt; 10^{-7}$</td>
</tr>
<tr>
<td>Ratio</td>
<td>Linear</td>
<td>4.94 [4.09; 5.79]</td>
<td>10.19 [8.42; 11.96]</td>
<td>$P &lt; 10^{-7}$</td>
</tr>
<tr>
<td></td>
<td>3D</td>
<td>6.30 [4.87; 7.73]</td>
<td>13.82 [10.98; 16.66]</td>
<td>$P = 1.5 \times 10^{-6}$</td>
</tr>
<tr>
<td>Emean fat (kPa)</td>
<td>Linear</td>
<td>13.8 [11.1; 16.5]</td>
<td>18.8 [15.3; 22.3]</td>
<td>$P = 4.8 \times 10^{-6}$</td>
</tr>
<tr>
<td></td>
<td>3D</td>
<td>16.8 [13.0; 20.6]</td>
<td>13.9 [10.2; 17.6]</td>
<td>$P = 0.58$ (NS)</td>
</tr>
<tr>
<td>Qualitative (Qual)</td>
<td>Linear</td>
<td>1.7 [1.4; 2.0]</td>
<td>4.1 [3.3; 4.9]</td>
<td>$P &lt; 10^{-7}$</td>
</tr>
<tr>
<td></td>
<td>3D</td>
<td>2 [1.5; 2.5]</td>
<td>4 [3.0; 5.0]</td>
<td>$P &lt; 10^{-7}$</td>
</tr>
</tbody>
</table>

CI: confidence interval; NS: not significant.
Histological analysis

The 65 benign lesions included 30 fibroadenomas, 3 inflammatory lesions, 29 other mastopathies and 3 follow-up lesions.

Of the 102 malignant lesions, we observed 78 cases of IDC, 41 of which with related DCIS, 3 cases of DCIS without an invasive component, 15 cases of ILC including 4 with related LCIS, 3 mixed carcinomas, 2 mucinous carcinomas and 1 malignant non-Hodgkin’s lymphoma (involvement of an intra-mammary lymph node).

The mean Emean values for each type of histology are presented on Fig. 1.

Analysis of the criteria modifying the elastographic parameters

First of all, no significant change was observed in elasticity parameters based on age. In fact, the increase in elastographic values with age appeared to be related to the more common presence of malignant tumors in the older patients.

Independently of the benign or malignant character of the lesions, there was a clear significant difference between the mean Emax values of palpable lesions (186.0 kPa) and those of intra-clinical lesions (94.5 kPa) \((P < 10^{-7})\) (Table 3). In addition, the clinical size of the palpable lesions was significantly correlated to the elasticity; the more the clinical size increased, the more the Emax increased \((P < 10^{-7})\).

Concerning the elastographic aspect, the long axis of the lesion gave rise to a significant increase in the elasticity parameters \((P < 10^{-6})\), regardless of whether the lesion was benign or malignant. We observed significant differences in Emax for all of the ultrasound lesion characterization parameters, except for the echo pattern (Table 3). There was a significant increase in Emax with the BI-RADS category (Table 3). With regard to the depth of the lesion, it did not have a significant influence on the elastographic parameters \((P = 0.99)\).

Finally, concerning the histological results, the elastographic parameters all differed significantly between benign lesions and malignant tumors. On the other hand, there was no significant difference between the different histological types of malignant tumors (except for lymphoma), or between the different histological types of the benign lesions. For the malignant tumors, there was a significant increase in the quantitative Emean parameter \((P = 0.016)\) and the qualitative classification \((P = 0.04)\), with the SBR histo-prognosis grade (Fig. 2) as well as the cell proliferation factor Ki67 \((P = 0.048)\) for Emean. However, no significant variation was found in the elastographic parameters based on the percentage of in situ lesions associated with invasive carcinomas, hormonal receptors and the HER 2 status.

Diagnostic performance and threshold values

By analyzing the ROC curves, we observed that except for the ratio, the elastographic parameters (Emax, Emean and Qual) on the acquisitions made by the linear wand allowed for, without a penalizing reduction in sensitivity (Se BI-RADS US = 96% vs. Se Emax = 93.1%, Se Emean = 93.1% and Se Qual = 91.1%), an increase in specificity of more than 43 points, i.e. at least a doubling of the specificity of
the BI-RADS ultrasound classification (Sp BI-RADS US = 43.1% vs. Sp Emax = 87.7%, Sp Emean = 86.2% and Sp Qual = 92.3%) (Table 5). In logistic regression, the qualitative classification (Qual) appeared to be the most effective. In addition, the study of the diagnostic performance of Qual for the first acquisition carried out yielded similar values to those obtained by the 3 successive acquisitions with AUCs of 0.924 vs. 0.932, respectively. The 3D acquisition improved the sensitivity of the ratio (Se 3D ratio = 100% vs. Se linear Ratio = 87.1%) and of the qualitative classification compared to the acquisition with the linear transducer (Se 3D Qual = 94.4% vs. Se linear Qual = 91.1%), but led to a significant decrease in the specificity of these parameters (Sp 3D ratio = 51.7% vs. Sp linear Ratio = 80% and Sp 3D Qual = 79.3% vs. Sp linear Qual = 92.3%). Only Emean for 3D acquisition had maintained a sensitivity and a specificity that was slightly higher compared to those of the acquisition by linear transducer (Se 3D Emean = 90.7% and Sp 3D Emean = 89.7%). By distinguishing between infra-clinical lesions and palpable lesions, we observed that compared to conventional ultrasound, by changing the threshold values for Emax and Qual, the specificity was doubled (infra-clinical lesions: Sp BI-RADS US = 44.9% vs. Sp Emax = 89.8% and Sp Qual = 89.8%; palpable lesions: Sp BI-RADS US = 37.5% vs. Sp Emax = 81.3%, and Sp Qual = 81.3%) with no penalizing decrease in sensitivity (infra-clinical lesions: Se BI-RADS US = 89.7% vs. Se Emax = 87.2% and Se Qual = 87.2%; palpable lesions: Se BI-RADS US = 100% vs. Se Emax = 100%, and Se Qual = 100%). For the infra-clinical lesions, the threshold Emax value had to be lowered from 106 to 84 kPa, and the threshold Qual value was maintained at 3. For the palpable lesions as well as for the lesions > 2 cm, the threshold Emax value had to be increased to 132 kPa and the threshold Qual value to 4. For the infra-centimetric lesions, compared to conventional ultrasound, we observed a decrease in sensitivity (Se BI-RADS US = 84.6% vs. Se Emax = 76.9% and Se Qual = 73.1%) when maintaining the obtained threshold values, which was not improved by a reasonable decrease in the threshold values.

Resulting management changes

By applying the determined Emax and Qual threshold values for all of the lesions, we suggested a subdivision of the BI-RADS 4 category as per the following criteria:

- BI-RADS 4a: lesion classified BI-RADS 4 in ultrasound and with elasticity values in favor of benignness (Emax < 106 kPa or Qual < type 3);
- BI-RADS 4b: lesion classified BI-RADS 3 in ultrasound and with elasticity values in favor of malignancy (Emax ≥ 106 kPa or Qual ≥ type 3);
- BI-RADS 4c: lesion classified BI-RADS 4 in ultrasound and with elasticity values in favor of malignancy (Emax ≥ 106 kPa or Qual ≥ type 3) (Table 6).

These resulting management changes are summarized on Fig. 3.

### Table 5 Diagnostic performance (analysis of the ROC curves).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameters</th>
<th>Se</th>
<th>Sp</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>AUC</th>
<th>Threshold values</th>
</tr>
</thead>
<tbody>
<tr>
<td>All lesions (n = 167)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>BI-RADS US</td>
<td>96</td>
<td>43.1</td>
<td>72.4</td>
<td>87.5</td>
<td>0.842</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Emax</td>
<td>93.1</td>
<td>87.7</td>
<td>92.2</td>
<td>89.1</td>
<td>0.933</td>
<td>106 kPa</td>
</tr>
<tr>
<td></td>
<td>Emean</td>
<td>93.1</td>
<td>86.2</td>
<td>91.3</td>
<td>88.9</td>
<td>0.933</td>
<td>82 kPa</td>
</tr>
<tr>
<td></td>
<td>Ratio</td>
<td>87.1</td>
<td>80</td>
<td>87.1</td>
<td>80</td>
<td>0.855</td>
<td>5.6</td>
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<tr>
<td></td>
<td>Qual</td>
<td>91.1</td>
<td>92.3</td>
<td>94.8</td>
<td>87</td>
<td>0.932</td>
<td>3</td>
</tr>
<tr>
<td>All lesions (n = 82)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Emax</td>
<td>90.6</td>
<td>82.8</td>
<td>90.6</td>
<td>82.8</td>
<td>0.914</td>
<td>100 kPa</td>
</tr>
<tr>
<td></td>
<td>Emean</td>
<td>90.7</td>
<td>89.7</td>
<td>94.2</td>
<td>83.9</td>
<td>0.940</td>
<td>86 kPa</td>
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<tr>
<td></td>
<td>Ratio</td>
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<td>51.7</td>
<td>81.8</td>
<td>100</td>
<td>0.825</td>
<td>4.2</td>
</tr>
<tr>
<td></td>
<td>Qual</td>
<td>94.4</td>
<td>79.3</td>
<td>89.5</td>
<td>89.5</td>
<td>0.914</td>
<td>3</td>
</tr>
<tr>
<td>Infra-clinical lesions (n = 89)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>BI-RADS US</td>
<td>89.7</td>
<td>44.9</td>
<td>56.5</td>
<td>84.6</td>
<td>0.796</td>
<td>4</td>
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<tr>
<td></td>
<td>Emax</td>
<td>87.2</td>
<td>89.8</td>
<td>87.2</td>
<td>89.8</td>
<td>0.904</td>
<td>84 kPa</td>
</tr>
<tr>
<td></td>
<td>Qual</td>
<td>87.2</td>
<td>89.8</td>
<td>87.2</td>
<td>89.8</td>
<td>0.919</td>
<td>3</td>
</tr>
<tr>
<td>Palpable lesions (n = 78)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>BI-RADS US</td>
<td>100</td>
<td>37.5</td>
<td>86.1</td>
<td>100</td>
<td>0.858</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Emax</td>
<td>100</td>
<td>81.3</td>
<td>95.4</td>
<td>100</td>
<td>0.950</td>
<td>132 kPa</td>
</tr>
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<td></td>
<td>Qual</td>
<td>100</td>
<td>81.3</td>
<td>95.4</td>
<td>100</td>
<td>0.884</td>
<td>4</td>
</tr>
<tr>
<td>Lesions &lt; 1 cm (n = 57)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>BI-RADS US</td>
<td>84.6</td>
<td>41.9</td>
<td>55</td>
<td>76.5</td>
<td>0.731</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Emax</td>
<td>76.9</td>
<td>90.3</td>
<td>87</td>
<td>82.4</td>
<td>0.873</td>
<td>106 kPa</td>
</tr>
<tr>
<td></td>
<td>Qual</td>
<td>73.1</td>
<td>96.8</td>
<td>95</td>
<td>81.1</td>
<td>0.887</td>
<td>3</td>
</tr>
<tr>
<td>Lesions &gt; 2 cm (n = 30)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>BI-RADS US</td>
<td>100</td>
<td>54.5</td>
<td>79.2</td>
<td>100</td>
<td>0.907</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Emax</td>
<td>100</td>
<td>81.8</td>
<td>91.7</td>
<td>100</td>
<td>0.959</td>
<td>132 kPa</td>
</tr>
<tr>
<td></td>
<td>Qual</td>
<td>100</td>
<td>81.8</td>
<td>90.5</td>
<td>100</td>
<td>0.866</td>
<td>4</td>
</tr>
</tbody>
</table>


<sup>a</sup> With linear transducer.

<sup>b</sup> With 3D transducer.
Table 6  Management modifications as per Emax (threshold value = 106 kPa) and as per Qual (threshold value = 3).

<table>
<thead>
<tr>
<th>Histological type</th>
<th>BI-RADS 3</th>
<th>BI-RADS 4</th>
<th>BI-RADS 5</th>
<th>BI-RADS 3 (stable)</th>
<th>BI-RADS 4</th>
<th>4a (downgraded)</th>
<th>4b (upgraded)</th>
<th>4c (stable)</th>
<th>BI-RADS 5 (stable)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benign</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>30</td>
<td>33</td>
<td>2</td>
<td>29</td>
<td>26a (27d)</td>
<td>1b</td>
<td>7c (6d)</td>
<td>2 (2a,e)</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>30</td>
<td>19</td>
<td>11</td>
<td>0</td>
<td>19</td>
<td>9a (10d)</td>
<td>0</td>
<td>2c (1d)</td>
<td>0</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1a</td>
<td>0</td>
<td>2c (1d)</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>29</td>
<td>8</td>
<td>19</td>
<td>2</td>
<td>7</td>
<td>16a</td>
<td>1b</td>
<td>3c</td>
<td>2 (2a,c)</td>
</tr>
<tr>
<td>Monitoring</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Malignant</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Total</td>
<td>102</td>
<td>3</td>
<td>39</td>
<td>60</td>
<td>3c</td>
<td>2b (1d)</td>
<td>0</td>
<td>37 (38d)</td>
<td>60 (2a,c)</td>
</tr>
<tr>
<td>IDC</td>
<td>78</td>
<td>2</td>
<td>29</td>
<td>47</td>
<td>2c</td>
<td>2b (1d)</td>
<td>0</td>
<td>27 (28d)</td>
<td>47 (2b,c)</td>
</tr>
<tr>
<td>DCIS</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>ILC</td>
<td>15</td>
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<td>4</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Other</td>
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<td>0</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>MNHL</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1c</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>167</td>
<td>33</td>
<td>72</td>
<td>62</td>
<td>32</td>
<td>28</td>
<td>1</td>
<td>44</td>
<td>62</td>
</tr>
<tr>
<td>Benign</td>
<td>65</td>
<td>30</td>
<td>35 (FP)</td>
<td>55 (56d)</td>
<td>10 (9d)</td>
<td>5 (4d) (FN)</td>
<td>97 (98d)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant</td>
<td>102</td>
<td>3 (FN)</td>
<td>99</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a Lesions correctly reclassified by elastography.
b Lesions incorrectly reclassified by elastography.
c Lesions incorrectly classified by ultrasound and not modified by elastography.
d Management changes as per Qual if different from Emax.
e Lesions classified BI-RADS 5 by ultrasound, downgraded by elastography.
Therefore, according to $E_{\text{max}}$, 28 lesions classified as BI-RADS 4 by ultrasound and with elasticity values in favor of benignity were grouped together in the category BI-RADS 4a. Among them, we observed 2 malignant lesions, i.e. a PPV of malignancy of 7.1%. According to Qual, only one malignant lesion was downgraded into the BI-RADS 4a category, i.e. a PPV of malignancy of 3.6%. Forty-four lesions classified as BI-RADS 4 and confirmed by elasticity values were grouped together in the category BI-RADS 4c with, for an $E_{\text{max}}$, a PPV of malignancy of 84.0% (37/44 lesions), and for a Qual, a PPV of malignancy of 86.4% (38/44 lesions). Qual also made it possible to correctly downgrade a benign lesion classified in category BI-RADS 4c by $E_{\text{max}}$. Only one lesion initially classified as BI-RADS 3 by ultrasound had elasticity values in favor of malignancy and this was the only lesion classified in category BI-RADS 4b. However, this lesion was a benign lesion. None of the 3 malignant lesions classified as BI-RADS 3 could be upgraded either by $E_{\text{max}}$ or by Qual. Elastography therefore did not make it possible to lower the high PPV of malignancy of our category BI-RADS 3, which remained at 9.4% (3/32 lesions). The management of lesions classified as BI-RADS 5 by ultrasound was not modified regardless of the result of the elastography.

In all: if we consider the BI-RADS 3 and 4a categories as benign lesions, these changes in management cause by the complementary use of ultrasound and elastography made it possible to obtain for $E_{\text{max}}$: a sensitivity of 95.1%, a specificity of 84.6%, a PPV of 90.7% and a NPV of 91.7%, and for Qual: a sensitivity of 96.1%, a specificity of 86.2%, a PPV of 91.6% and a NPV of 93.3%. These results show that the complementary nature of these two techniques makes it possible to maintain the high sensitivity of ultrasound, while doubling its specificity.

**Discussion**

Complementary to conventional ultrasound, the diagnostic performance of elastography directly competes with that of conventional ultrasound. In our series, conventional ultrasound had, excellent sensitivity (96%), i.e. a value that complies with those in the literature, which finds values of up to 98.4% for Stavros et al. [10]. On the other hand, the specificity of ultrasound remains moderate (43.1%), i.e. a value between that of 32.9% found by Costantini et al. [7] and that of 67.8% found by Stavros et al. [10]. Concerning the evaluated ultrasound criteria, compared to the study conducted by Hong et al. [11], we obtained PPVs of malignancy that were higher for the irregular form (87% vs. 62%) and for the non-parallel orientation (82% vs. 69%). As the ACR suggests [6], grouping together the lesions with undefined contours, in addition to the practical and more realistic aspect demonstrated by Abdullah et al. [12], made it possible for us to present a satisfactory PPV of malignancy of 77%. As per the study carried out by Costantini et al. [7], the perilesional hyper-echogenic halo and the posterior acoustic attenuation also appeared to us to be excellent predictive criteria of malignancy with PPVs evaluated at 96% and 90%, respectively. However, we observed NPVs for malignancy that were lower compared to the study by Hong et al. [11] concerning the oval shape (64% vs. 84%), parallel orientation (47% vs. 78%) and defined contours (78% vs. 90%). The posterior acoustic enhancement also appeared to be a good predictive criterion for benignness with a NPV evaluated at 70%, i.e. a value that was identical to the one found by Costantini et al. [7]. The absence of a significant relationship between echo pattern and the benign/malignant character confirmed its non-discriminating character [7]. Except for
the spiculated contours, which appear to be a sufficient single criterion for malignancy that has been known since
the study by Stavros et al. [10], the combination of several criteria is necessary to improve the ultrasound characteri-
zation of lesions [13]. Despite this, we obtained a rate of malignancy that was too high for the ultrasound BI-RADS
3 category (9%) [9], close to the one found by Costantini et al. [7] (7.7%), which proves that conventional ultrasound
must remain integrated with the complete breast examination that will retain the most pejorative criterion. We chose
not to subdivide the BI-RADS 4 category because, as Lazarus et al. [14] and Abdullah et al. [12] demonstrated, this sub-
division, which was created to facilitate communication with patients and medical correspondents reduces interobserver
reproducibility. The malignancy rate of the BI-RADS 5 ultra-
sound category evaluated at 97% appeared to comply with the reference framework [9], which shows the reliability of
the criteria retained for the diagnosis of malignant lesions.

By more than doubling the specificity percentage of con-
tventional ultrasound, the primary objective of elastography
has been reached.

Concerning the quantitative parameters, we report specificity values that are considerably greater for Emax and
Emean, which were 87.7% and 86.2%, respectively, com-
pared to 78% and 83% for Evans et al. [15], 84.9% (Emean)
for Chang et al. [16]. This increase in specificity occurred
without a penalizing decrease in sensitivity, as it is 93.1%
for Emax and Emean, i.e. a value between 88.8% for Chang
et al. [16] and 97% for Evans et al. [15]. All lesions together,
we therefore retain threshold values of 106 kPa for Emax
and 82 kPa for Emean. The ratio in our study had inferior
diagnostic performance. Our mean values appeared to com-
ply with those of the literature with, for benign lesions,
an Emean of 51.7 kPa and for malignant tumors, an Emean
of 159.6 kPa, compared to 45.3 kPa and 146.6 kPa, respec-
tively, for Athanasiou et al. [17], and 46.1 kPa and 153.3 kPa
for Chang et al. [16]. As per the data recently reported by
Evans et al. [18], we found a significant correlation between
Emean and the SBR histo-prognostic grade, as well as a more
marked difference in Emean values between grade I and
grade II than between grade II and grade III (Fig. 2). This
study also shows that the size of the invasive tumor, the
damage to axillary lymph nodes, the type of tumor and vas-
cular involvement are significantly correlated with Emean.

Though in our study we also found Emean values that were
higher for lobar carcinomas than for ductal carcinomas or
for mixed carcinomas, we did not demonstrate, unlike Evans
et al. [18], a significant difference between the different
types of tumors (Fig. 1). In our study, the highest mean
Emean value is found for ductal carcinomas in situ. This
value, which is surely related to the low number of patients
(n = 3), does not appear to comply with those in the liter-
ature, which are inferior to those of invasive carcinomas
[16,19].

Concerning the qualitative parameters, the use of the
classification created above (Table 1) allowed us to obtain an
excellent specificity value of 92.3%, while keeping a sensitiv-
ity of 91.1%. Tozaki et al. report a similar sensitivity (91.3%),
but lower specificity (80.6%) for a classification in 4 consider-
ably different types [20]. We therefore retained the type 3 of
our classification as the discriminating threshold. By keep-
ing the standard color scale established for breast lesions
(0–180 kPa), we used the maximum color of the lesional
and perilesional map to classify the lesions. This param-
eter, which was also retained in the BE1 study [19], appears
to us to be a simple and rapid discriminating criterion, as
it avoids the performance of qualitative measurements and
is objective and therefore reproducible. In addition, with
the use of this qualitative classification, the conduct of a
single acquisition appears sufficient. Work is currently on-
going to try to explain why this maximum hardness zone
of malignant tumors is most often located around the lesion
[18]. We also report a significant increase in the elasticity
of the fat adjacent to the malignant tumors compared to
the fat surrounding benign lesions, which supports the idea
of a stroma-tumor interaction.

Concerning the factors that modify elasticity, we
observed a significant increase in elasticity values with the
increase in the size of the lesion. This relationship, which
has already been noted by Chang et al. [16], and also found
by Evans et al. [18] for invasive carcinomas, encourages us
to suggest greater threshold values (132 kPa) for lesions > 2 cm.
In the same way, the significant increase in elasticity values
with the palpable character of the lesion orients us towards
lower threshold values (84 kPa) for infra-clinical lesions, and
higher threshold values (132 kPa) for palpable lesions.
We did not demonstrate changes in elastographic parameters
by lesion depth, unlike the BE1 study, which found a slight
reduction in Emax when depth increased [19]. However, our
study only included 3 lesions with a depth of more than
20 mm.

The changes in management induced by elastography
were carried out according to the Emax criterion recog-
nized by the BE1 study as the best quantitative criterion
[19], and according to our qualitative classification, due to
its discreetly higher specificity. The subdivision of the BI-
RADS 4 category as per the elastography results allowed us
to maintain the high sensitivity of the ultrasound, which is
an essential piece of data in senology in particular, while
combining it with the high specificity of elastography.
We therefore suggest classifying in the BI-RADS 4a category
the lesions classified as BI-RADS 4 in ultrasound with an Emax
value < 100 kPa or Qual value < type 3, with a PPV of mali-
gnancy of less than 10%. The lesions classified as BI-RADS 4 in
ultrasound and confirmed by an Emax value > 100 kPa or Qual
value > type 3 had a high PPV for malignancy compatible with
category BI-RADS 4c. The analysis of the only lesion in our
series that was initially classified as BI-RADS 3 in ultrasound
and with elasticity values in favor of malignancy is therefore
to be taken with caution and requires a reevaluation with
a larger number of patients. However, BI-RADS category 4b
appears necessary to us for these lesions that would benefit
from the increase in specificity of elastography. To maintain
the higher sensitivity of ultrasound, the lesions classified as
BI-RADS 5 in ultrasound should not be sub-classified by elas-
tography. If the two benign lesions present in the BI-RADS
5 category were correctly downgraded by elastography, two
malignant tumors could be incorrectly identified.

According to Cosgrove et al. [4], based on a series of 758
lesions, shear wave elastography appears to be a technique
with an excellent intra- and interobserver reproducibility,
with agreement values going from κ = 0.84 to 0.91 for the
Emax and Emean quantitative parameters and for the qual-
itative parameters.
These results allow us to think that elastography appears to be a reproducible means for subdividing the ultrasound BI-RADS 4 category. However, this subdivision, though it increases reproducibility, does not give rise to a direct change in management, as lesions classified as BI-RADS 4 require histological proof. The PPV of malignancy of our BI-RADS 4a category does not allow us to avoid a biopsy of these lesions. To suggest a reclassification of lesions in the BI-RADS 3 category by elastography, the BE1 study demands that only lesions classified as BI-RADS 3 by elastography be considered, with a malignancy rate less than 10% for the BI-RADS 4a category as a pre-requisite. This restriction appears to us to be difficult to apply in practice due to the absence of known and objective ultrasound criteria that allow us to classify a lesion in the BI-RADS 4a category in ultrasound.

Considering the determined threshold values, we had in our series 7 malignant lesions that had Emax values below the threshold. Of these, we observed 5 SBR grade I IDCs (including 2 lesions in the same patient), a malignant non-Hodgkin’s lymphoma and one papilloma colonized by a grade III IDC. The grade I IDCs were all infra-clinical and had an axis length of less than or equal to 10 mm with a mean size of 7.2 mm. The mean values of their Emax were 78 kPa. Of these 5 lesions, 2 had initially been classified in BI-RADS category 5 in ultrasound. In the BE1 study, 3 cancers were also found among 115 lesions with an Emax between 20 and 30 kPa. However, decreasing the Emax threshold value to 20 kPa does not appear possible due to the strong downgrading of specificity. Concerning the lymphoma discovered in an intra-mammary lymph node, we can refer back to the elastographic analysis of the axillary lymph nodes conducted by Tourasse et al. which shows an Emax threshold value of approximately 25 kPa. By using the threshold values determined for breast lesions, the lymph node tumor involvement does not appear to be detectable by elastography. The colonization of the papilloma traps the elastography, which apparently retains the papillary structure of the lesion.

Inversely, our series included 8 benign lesions that had elastographic criteria for malignancy. Of these, we observed 5 lesions that resulted from various mastopathies, the common characteristic of which was the presence of a primarily dense conjunctive tissue. We also had 2 palpable fibroadenomas, the largest of the study, with an axis length greater than equal to 25 mm, and a case of sclerosing adenosis. For Evans et al., benign lesions with high elasticity values are the radial scar, inflammation around abscesses, surgical scars and sequelae of radiotherapy that cause cutaneous thickening. This idea concerning inflammatory lesions motivated us to classify them in a category separate from the other benign lesions, and made it possible for us to confirm that it was the benign lesions that had highest elasticity values (Fig. 1). The only radial scar in our series showed low elasticity values, below the thresholds, but corresponded to a lesion of histological discovery measuring 1 mm inside a dystrophic lesion that was occult upon mammography.

Our study had several limitations. The first is that it is a retrospective study. The retrospective interpretation of recorded ultrasound and elastography images as representative as they may be is still inferior to a dynamic analysis during the examination. The second limitation is the number of patients in our series, which is insufficient to come to conclusions with regard to certain subgroups of lesions, particularly for the BI-RADS 4b category. There is also a recruitment bias related to the activity of the center with a larger proportion of malignant lesions. Finally, we did not study the interobserver variability, as 70% of the examinations were conducted by the same operator.

**Conclusion**

Complementary to ultrasound, shear wave elastography makes it possible to obtain, by analysis of the quantitative Emax and Emean parameters, an excellent specificity without a penalizing reduction in sensitivity. The original qualitative classification of lesions proposed in this article, while maintaining similar diagnostic performance, makes it possible to avoid the carrying out of quantitative measurements and to consider the conduct of one acquisition only. Even if the relevance of the BI-RADS 4b category remains to be determined, the subdivision of the BI-RADS 4 ultrasound category by elastography allows us to provide objective and therefore reproducible criteria. This complementary management makes it possible, if we consider the BI-RADS 4a category as benign, to maintain the ultrasound sensitivity while doubling its specificity. However, the malignancy rate of the BI-RADS 4a category in our series, while lower than that of the BI-RADS 3 category, does not allow us to propose monitoring for these lesions, even if it appears possible in view of the benefit/risk ratio and cost/benefit ratio much less in favor of histological samples. However, these results and these classification proposals from a retrospective study must be validated in a prospective manner if we are to be able to use them in current practice.

**Disclosure of interest**

The authors declare that they have no conflicts of interest concerning this article.

**References**


