

Screening of breast lesions: a comparative study between mammography, B-mode ultrasonography, sonoelastography and histological results*

Rastreamento de lesões mamárias: estudo comparativo entre a mamografia, ultrassonografia modo-B, elastografia e resultado histológico

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Abstract Objective: To compare the capacity of mammography, sonoelastography, B-mode ultrasonography and histological analysis to differentiate benign from malignant breast lesions. **Materials and Methods:** A total of 12 histopathologically confirmed breast lesions were documented. The lesions were assessed by means of mammography, B-mode ultrasonography and sonoelastography, and histopathological analysis was utilized as a gold standard. Sensitivity and specificity were calculated. A receiver operating characteristic (ROC) curve was constructed to evaluate the diagnostic performance of the mentioned techniques. **Results:** Sensitivity and specificity in the differentiation between benign and malignant lesions were respectively 100% and 50% for mammography, 100% and 71% for B-mode ultrasonography, and 67% and 83% for sonoelastography. The area under the ROC curve was calculated for the three imaging modalities and corresponded to 0.792 for mammography, 0.847 for B-mode ultrasonography, and 0.806 for sonoelastography. **Conclusion:** Sonoelastography demonstrated higher specificity and lower sensitivity as compared with mammography and B-mode ultrasonography. On the other hand, B-mode ultrasonography had the largest area under the ROC curve. Sonoelastography has demonstrated to be a promising technique to detect and evaluate breast lesions, and could potentially reduce the number of unnecessary biopsies.

Keywords: Breast B-mode ultrasonography; Breast lesions; Mammography; Sensitivity; Specificity; Sonoelastography.

Resumo Objetivo: Comparar a capacidade de diferenciação de lesões benignas versus malignas por parte da mamografia, ultrassonografia modo-B e elastografia. **Materiais e Métodos:** Um total de 12 lesões mamárias confirmadas histologicamente foi documentado. A avaliação das lesões foi realizada por meio da mamografia, ultrassonografia modo-B e elastografia. Os resultados histopatológicos foram utilizados como técnica padrão ouro. As sensibilidades e as especificidades foram calculadas. A curva receiver operating characteristic (ROC) foi realizada para avaliar o desempenho diagnóstico das técnicas utilizadas. **Resultados:** A sensibilidade e a especificidade na diferenciação entre lesões mamárias benignas e malignas foram 100% e 50%, respectivamente, para a mamografia, e 100% e 71% para a ultrassonografia modo-B. A elastografia obteve sensibilidade de 67% e especificidade de 83%. A área abaixo da curva ROC foi calculada para as três técnicas imaginológicas, sendo 0,792 para a mamografia, 0,847 para a ultrassonografia modo-B e 0,806 para a elastografia. **Conclusão:** A elastografia mostrou ter maior especificidade e menor sensibilidade comparativamente à mamografia e à ultrassonografia modo-B. A ultrassonografia modo-B foi a técnica que demonstrou maior área abaixo da curva ROC. A elastografia mostra-se uma técnica promissora na detecção de doença mamária e, potencialmente, poderá reduzir biópsias desnecessárias.

Unitermos: Elastografia; Especificidade; Lesões mamárias; Mamografia; Sensibilidade; US modo-B mamária.

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INTRODUCTION

Breast cancer is the most common neoplasm in the female population, comprising about 16% of all tumors affecting women. Its incidence is quite variable worldwide. In North America, its incidence has been calculated to be 99.4 cases per 100,000 women. In regions such as Eastern Europe, South America, the Southern African region and Western Asia, the reported incidence is moderate, however, it is increasing⁽¹⁾. Such a fact is followed by a decrease in mortality, which is intimately related to early detection of breast diseases and to the increasing availability of appropriate treatment⁽²⁾.

In Portugal, the recorded incidence is approximately 4,000 new cases/year⁽³⁾.

Mammography is a diagnostic technique aimed at producing detailed images from the internal structures of the breast so as to allow for early diagnosis of breast diseases. The mammographic study comprises the acquisition of two basic views, namely, craniocaudal and mediolateral oblique views. Supplementary views may be acquired whenever the presence of a suspected lesion is detected⁽⁴⁾.

In the diagnosis of breast lesions, B-mode ultrasonography (US) has demonstrated to be quite relevant as a complement with other diagnostic modalities. Whenever possible, the sonographic study should always be preceded by a complete mammographic study⁽⁵⁾. It is a screening method for younger women with dense breasts at mammography (BI-RADS 3 and 4)⁽⁶⁾. The acquisition technique varies among patients, indications, location and type of lesion. Sonographic findings should be documented in two orthogonal planes (longitudinal and cross-sectional) to allow the visualization of all their characteristics.

Currently, sonoelastography has shown to be a promising technique in the follow-up of suspicious breast lesions in elderly patients, and in the intervals of the mammographic follow-up, thus allowing for guidance in diagnosis and prognosis. At younger ages, such a technique allows the addition of information to the diagnosis of solid lesions, avoiding unnecessary biopsies. It is complementary with B-mode US in the diagnosis of breast diseases. Its main

advantages include absence of ionizing radiations, providing more specific data on the possible lesion, besides not requiring a significant increase in time for the investigation of suspected lesions⁽⁷⁾. Such a method allows for quantifying the tissues elasticity degree by means of pressure exerted on them^(6,8). The lesions are quantified according to a color scale. A transducer that superimposes the color data on the B-mode US images is utilized⁽⁹⁾. The color scale ranges from red to blue, and is associated with the benignity/malignancy degree, with the absence of deformation being characterized by the blue color associated to the malignancy degree^(6,10).

Breast biopsy is defined as an invasive procedure aimed at confirming the breast lesion detection. Such a procedure relies on the collection of breast tissue specimens which are then histologically analyzed. There are several types of biopsies, which are utilized according to lesion type, size and depth in relation to the skin surface. The post-procedural follow-up depends upon the type of histological finding⁽¹¹⁾.

Thus, the present study is aimed at determining the capability of mammography, B-mode US and sonoelastography to differentiate benign from malignant breast lesions relying on histological results as the gold-standard technique.

The present study reveals itself as an opportune investigation, considering that breast sonoelastography is a relatively recent technique whose diagnostic accuracy is scarcely described in the literature. In case the reliability of the technique in differentiating benign from malignant lesions is proven, the number of unnecessary breast biopsies currently performed could be reduced.

MATERIALS AND METHODS

The present study population comprised a group of female patients with unilateral or bilateral breast disease who were submitted to imaging studies at the Radiology Services of Hospital do Faro, E.P.E. and at H.P.P. – Hospital Santa Maria de Faro. The sample comprised 12 breast lesions documented by means of mammography, B-mode US and sonoelastography images. The histological results from the biopsies

performed on the studied lesions were considered as the gold-standard, so as to increase the specificity of the results. The lack of any of the previously mentioned diagnostic imaging study was defined as an exclusion criterion for the present study.

The mean age of the patients was 54.8 ± 10.4 years, ranging from 43 to 73 years.

Tables were prepared to simplify the data collection. Such tables include the essential characteristics of the lesions which allowed their classification as benign or malignant with basis on the four diagnostic modalities. By means of observation and analysis of the images from the three imaging methods, as well as the correct filling of the above mentioned tables, it was possible to establish the degree of probability of benignity/malignancy of the studied lesions.

The collected data were exclusively and solely utilized in the present study, and the patients' identity, anonymity and confidentiality were safeguarded.

Mammography

All the patients were submitted to mammography. The images were acquired in GE Medical System Senographe DMR[®] and GM Medical System Apollon[®] mammography apparatuses, with craniocaudal and oblique mediolateral acquisitions, which allowed for the demonstration of the outer and inner quadrants, the upper and lower quadrants, and the inframammary angle, respectively.

The mammographic images were analyzed according to the Breast Imaging Reporting and Data System (BI-RADS[®]) from the American College of Radiology. By means of such a system, it is possible to standardize the terms utilized in mammography reports, making it clear, concise and easily understandable⁽⁸⁾.

The classification of mammographic findings comprises seven categories directly related to the approach recommendations, as follows⁽⁸⁾:

- Category 0 – Currently utilized in cases whose results depend upon comparison with the previous results or a recall for technical error. Such a category may also be utilized in those cases requiring further investigation by means of US or magnetic resonance imaging (MRI), for diagnosis clarification.

- Category 1 – Refers to images negative for malignancy, with no evidence of significant focal radiographic alterations.
- Category 2 – Utilized in situations where the mammographic findings are characteristically benign.
- Category 3 – Mammographic findings with high probability of benignity, with positive predictive value (PPV) $\geq 98\%$.
- Category 4 – Lesions presenting probability of malignancy, but with no typical characteristic of carcinoma.
- Subcategory 4a – Lesions with intermediate malignancy suspicion, with indication for biopsy for histological correlation.
- Subcategory 4b – Amorphous calcifications, nodules with partially circumscribed and partially indistinct contours.
- Subcategory 4c – Lesions under moderate suspicion of malignancy, with expectation of histological result positive for malignancy.
- Category 5 – Lesions whose malignancy probability is high (PPV > 95%).
- Category 6 – Lesions whose malignancy has already been previously histopathologically confirmed and that have not been submitted to any definitive treatment yet.

B-mode US and sonoelastography

The B-mode US and sonoelastography images were obtained by GE Medical System Logic 9[®] and Siemens Acuson Antares[®] US apparatuses, with the utilization of a high-frequency linear transducer. The frequencies ranged between 7.5 and 14 MHz, depending upon the depth of the lesion and breast thickness. The lesions under study were documented in two orthogonal planes (longitudinal and cross-sectional).

Once the elastography mode is selected, the scale of colors is superimposed over the B-mode image⁽⁹⁾. Both images are simultaneously presented on the equipment screen in real time, with the B-mode being presented on the left side and the sonoelastogram being presented at the right side of the screen.

As regards sonoelastography, measurements were performed before and after uniform tissue compression, so as to evaluate the multi-directional deformation of the suspicious breast tissue.

The evaluation of the B-mode US images, similarly to mammography, is performed according to the BI-RADS classification. On the other hand, sonoelastographic images, namely the elastic tissue properties, are quantitatively analyzed according to the Ueno elasticity five-score system (Figure 1)^(8,12-15), as follows:

- Level 1 – Uniformly elastic lesion, green colored. A variation of this type is the diagnostic image of a cyst (1*), where three layers are presented (blue, green and red).
- Level 2 – Fundamentally elastic lesion, with some zones of elasticity absence, characterized by a green and blue mosaic pattern.
- Level 3 – Peripheral elasticity and absence of elasticity in the central region of the lesion, with green color at the peripheral zone and blue color within the lesion.
- Level 4 – Absence of elasticity in the entire lesion, which is visualized entirely in the blue color.
- Level 5 – Absence of elasticity not only in the entire lesion but also in surrounding tissues, with a blue region more extensive than the lesion itself being visualized.

The levels attributed at sonoelastography may be compared with the BI-RADS classification. Levels 1 and 2 at sonoelastography correspond to BI-RADS category 2. The remaining levels at sonoelastography present a one-to-one correspondence with the BI-RADS classification⁽⁹⁾. Thus, level 1 at sonoelastography represents findings negative for malignancy, level 2, benign findings, level 3, probably benign findings, level 4 demonstrates findings suspicious for malignancy, and level 5 represents findings that are highly suspicious for malignancy⁽¹⁶⁾. Therefore, one can affirm that the elasticity level of lesion is intimately correlated with the BI-RADS classification, since low elasticity levels correspond to high BI-RADS categories. The contrary is also true⁽¹⁷⁾.

Histology

The histological results were available for all patients. Percutaneous US-guided core biopsies with automated biopsy device were performed in nine patients (75%) and

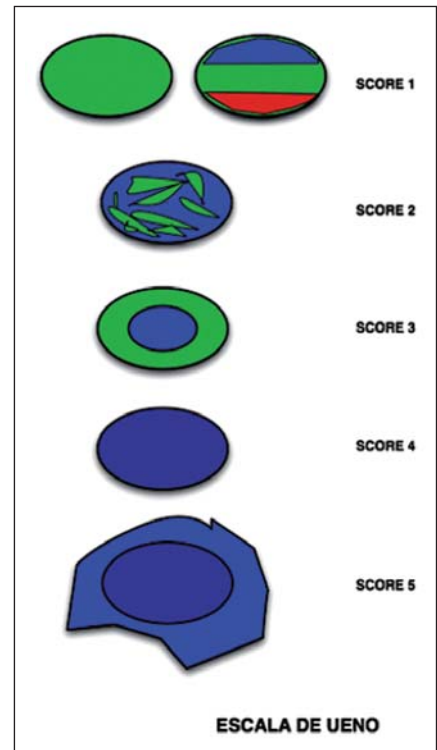


Figure 1. Ueno score system, where elasticity levels are schematically demonstrated⁽¹³⁾.

stereotactic biopsies were performed in three patients (25%). The specimens were collected and histologically analyzed in a laboratory.

Statistical analysis

The obtained results were analyzed with the softwares Microsoft Excel 2010[®] and Statistical Package for the Social Sciences (SPSS) V 20.0[®].

The Microsoft Excel 2010[®] software was utilized for the calculation of sensitivities, specificities, PPVs and negative predictive values (NPVs) for the three imaging methods.

The SPSS V 20.0[®] was utilized to calculate central trend measurements (means) and dispersion measures (standard deviations). The receiver operating characteristic (ROC) curve was also obtained for all the techniques under study. In such a curve, the sensitivity values are represented on the ordinate axis, while on the abscissa axis the 1 – specificity values are represented for all defined cutoff points. The knowledge of the area under the curve allows for the quantification of the accuracy of the diagnostic tests. The *t*-test was also calculated for the

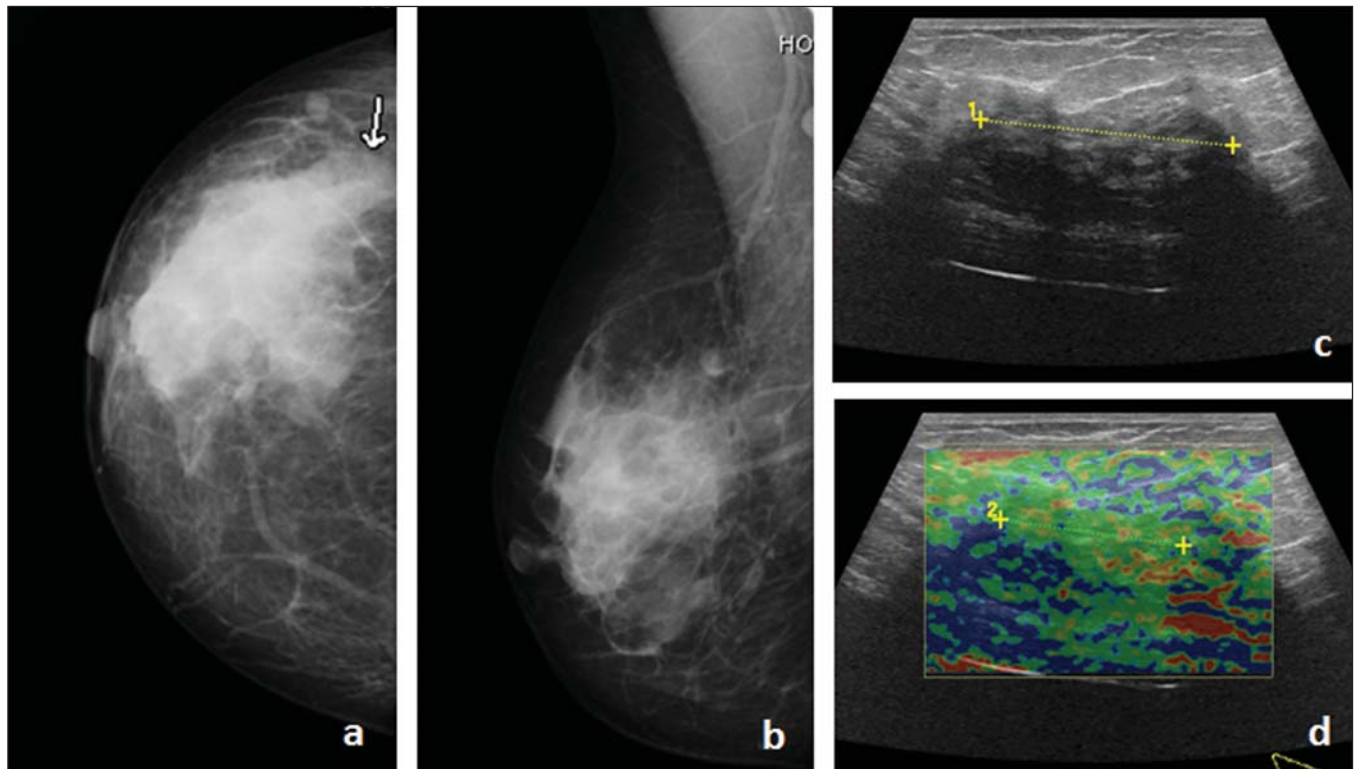


Figure 3. Female 56-year-old patient with a recent history of mastitis in the right upper outer quadrant. Mammography with craniocaudal (a) and oblique mediolateral (b) views revealing an irregular hyperdense region with partially obscured contours, classified as BI-RADS 4b. Sonographic image (c) revealed an ovoid hypodense area with partially obscured margins, causing a acoustic shadow cone, classified as BI-RADS 3. Sonoelastography (d) demonstrated a fundamentally elastic lesion, with some elasticity absence zones, classified as level 2 according the Ueno score system. Histopathological analysis demonstrated the presence of fibroadipose tissue.

Table 1 Sensitivity, specificity, PPV and NPV for the imaging methods under study.

	Sensitivity	Specificity	PPV	NPV
Mammography	100%	50%	67%	100%
B-mode US	100%	71%	71%	100%
Sonoelastography	67%	83%	80%	71%

According to Figure 4, the area under the mammography ROC curve was calculated as being 0.792. B-mode US presented an area of 0.847 under the ROC curve, while sonoelastography presented an area of 0.806 under the ROC curve.

Also, the mean values and respective standard deviations of the Ueno classifications for both benign and malignant lesions were calculated for sonoelastography. Mean values of 2.17 ± 0.408 for benign lesions, and 3.33 ± 1.033 for malignant lesions were observed. In order to determine if the mean value of the Ueno classification for malignant lesions is significantly higher than the mean Ueno classification for benign lesions, the *t*-test was applied for the difference between mean

values, and a $p < 0.05$ value was obtained, thus a higher and statistically significant mean value was found for the Ueno classification of malignant lesions.

DISCUSSION

Considering that an incorrect diagnosis of breast diseases is many times directly related to a failure in perception of the lesion by the investigator, it becomes essential to evaluate the diagnostic capability of the imaging methods for detecting true-positive results (sensitivity) and true-negative results (specificity).

With the progress in medical technologies, it is already possible to utilize sonoelastography in routine diagnoses. Such

method presents some advantages, namely, the data obtained is immediately evaluated and superimposed over the B-mode US images, and it does not require more time than conventional B-mode US.

Previous studies demonstrated low sensitivity and high specificity of sonoelastography as compared with B-mode US^(9, 14,18). As regards mammography, data on the calculation of sensitivity and specificity in comparison with other imaging methods are still scarce in the literature.

Based on the above mentioned data and according to the present results, one observes that sonoelastography presents sensitivity and specificity to differentiate breast lesions, and also that the three imaging methods under study do not present the same sensitivity and specificity for the same lesions.

The present study is in agreement with the results reported by Thomas et al.⁽⁹⁾, since B-mode US obtained higher sensitivity (100% in the present study and 94% as reported by Thomas et al.⁽⁹⁾) and higher

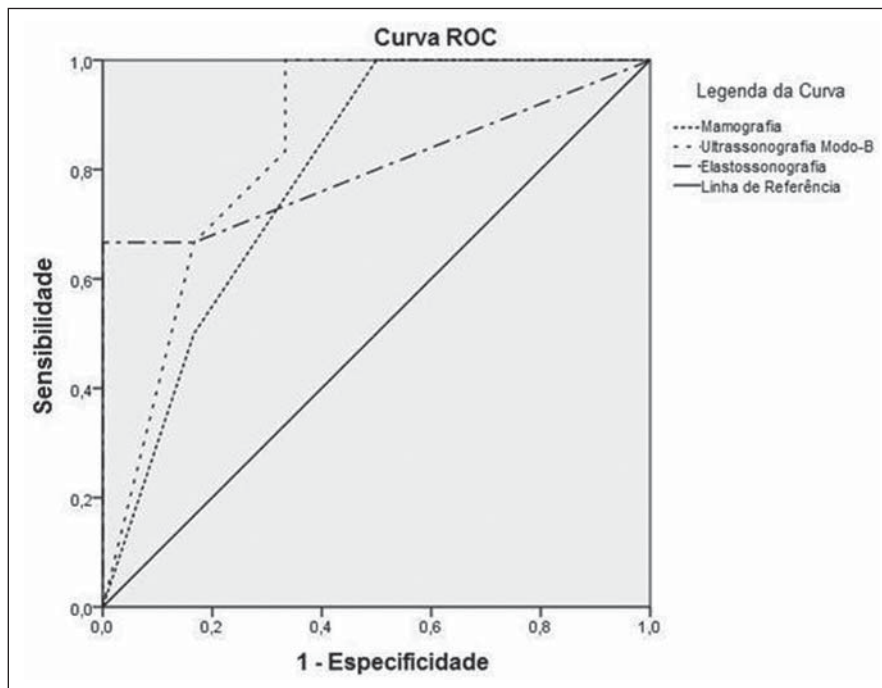


Figure 4. ROC curves representing the sensitivity and specificity values for mammography, B-mode US and sonoelastography.

NPV (100% in the present study and 95% reported by Thomas et al.⁽⁹⁾), while sonoelastography showed lower specificity (83% in the present study and 87% reported by Thomas et al.⁽⁹⁾). As regards PPV, the study developed by Thomas et al.⁽⁹⁾ is in disagreement with the present study, since according to those authors, mammography obtained the highest value (89%), while in the present study sonoelastography presented the highest value (80%). The study developed by Lee et al.⁽¹⁴⁾ is in agreement with the present study, since B-mode US obtained the highest sensitivity value (95.8%) and sonoelastography obtained the highest specificity value (45.7%), and PPV, 23.7%. Only the NPV is different from the present study results, with a higher value being obtained by sonoelastography (97.6%), as compared with B-mode US result of 100% obtained in the present study⁽¹⁴⁾. The study developed by Mansour et al.⁽¹⁶⁾ is completely in disagreement with the present study, since the results obtained by those authors are contradictory, namely the higher specificity (86.2%) and higher PPV (81.4%) were obtained with B-mode US and the higher sensitivity (92.3%) and higher NPV (93.4%) were obtained with sonoelastography.

Thus, it is possible to conclude that the association of the various techniques allows for the improvement of the accuracy in breast lesions diagnosis, since all the imaging methods contribute to the diagnosis. Such association also allows for the reduction of the number of biopsies currently performed.

The mean values of the Ueno classifications for benign and malignant lesions at sonoelastography were calculated, and the *t*-test was utilized to calculate the difference between mean values. The results from present study are in agreement with those reported by Lee et al.⁽¹⁴⁾, demonstrating lower mean values (1.72 ± 0.78 for benign lesions, and 3.02 ± 1.33 for malignant lesions as compared with the mean values of 2.17 ± 0.408 for benign lesions and 3.33 ± 1.033 for malignant lesions in the present study). After the *t*-test, a *p* value lower than alpha ($p < 0.001$ as compared with the $p < 0.05$ obtained in the present study), also confirming a statistically significant difference between the mean values for malignant and benign lesions.

The ROC curve represents a powerful tool for quantifying the performance of imaging methods. One verified that B-mode US was the method with the largest

area under the ROC curve (0.847), followed by sonoelastography (0.806) and mammography (0.792). According to the classification attributed to the areas under the ROC curve, mammography presented a reasonable performance, while both B-mode US and sonoelastography performances were classified as good. It is possible to observe that the values obtained with B-mode US and sonoelastography are quite similar, allowing the assertion that based on such analysis, both methods present a similar diagnostic performance. The results from the present study are different from those reported by Lee et al.⁽¹⁴⁾, with the area under the ROC curve for B-mode US (0.616) lower than that from sonoelastography (0.784), with a weak and reasonable performance, respectively for the two methods. The results reported by Schaefer et al.⁽¹²⁾ are also different from the results from the present study, with an area under the ROC curve for B-mode US (0.820) lower than that for sonoelastography (0.884), with both methods presenting a good performance.

CONCLUSION

The present study allows for the conclusion that sonoelastography presents a good diagnostic sensitivity and high diagnostic specificity in the differentiation between benign and malignant lesions, thus allowing for a reduction in the current number of breast biopsies. Although the imaging methods described in the present study do not present the same sensitivity and specificity for the same lesions, their combination may clearly improve the accuracy of the diagnosis of breast lesions.

The main limitation of the present study was the reduced sample size, conditioned by the reduced number of breast biopsies performed over the data collection period.

As a recommendation for future studies, the authors suggest that prospective studies are undertaken about the theme in question with a larger sample and in different clinical centers, in order to determine whether a quantitative analysis of the images may be useful to overcome some shortcomings of the method. The authors also wish to propose that breast MRI be included in the studies, so as the compari-

son can cover the whole range of imaging methods.

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