Hong Kong J Radiol. 2018;21:107-13 | DOI: 10.12809/hkjr1816829

ORIGINAL ARTICLE

The Impact of Thyroid Sonoelastography in Preventing Irrational Needle Biopsies in Evaluation of Benign Thyroid Nodules

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ABSTRACT

Objective: *Ultrasound elastography involves combining the diagnostic advantages of high-frequency ultrasound examination and the accuracy of thyroid cancer diagnosis based on the nodule's stiffness. This study aimed to evaluate the elastographic appearances of different types of thyroid gland nodules and to explore the real diagnostic value and clinical utility of thyroid ultrasound elastography with histopathological analysis as a reference standard.*

Methods: *A total of 72 sonographically visible thyroid nodules were included and their elastographic appearance being classified into six classes. Results of strain or quasistatic elastography were compared with pathological results on fine-needle aspiration cytology/biopsy and statistical analysis performed with calculation of sensitivity, specificity, as well as positive and negative predictive values.*

Results: *A total of 42 nodules were diagnosed as malignant and 30 as benign on elastography. On histopathological analysis, 37 nodules were found malignant including 31 cases of papillary carcinoma and six of follicular carcinoma. The sensitivity, specificity, positive and negative predictive values of thyroid ultrasound elastography with histopathological diagnosis as reference standard were 97.29%, 82.85%, 85.71% and 96.67%, respectively.*

Conclusion: *Thyroid elastography can greatly reduce the rate of thyroid biopsies especially in benign-appearing lesion.*

Key Words: *Biopsy; Thyroid nodule*

中文摘要

甲狀腺超聲彈性成像在預防良性甲狀腺結節評估中的不合理針刺活檢

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目的：超聲彈性成像結合了高頻超聲檢查的診斷優勢和基於結節僵硬度的甲狀腺癌診斷的準確性。本研究旨在評估不同類型甲狀腺結節的彈性成像表現，並探討以組織病理學分析為參照標準的甲狀腺超聲彈性成像的實際診斷價值和臨床應用。

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Submitted: 13 Mar 2017; Accepted: 31 May 2017.

Disclosure of Conflicts of Interest: The authors have no conflicts of interest to disclose.

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

方法：研究中包括72個超聲可見的甲狀腺結節。結節的彈性成像外觀分為六種類型。將應變或準靜態彈性成像的結果與細針抽吸細胞學／活組織檢查的病理結果進行比較，並通過計算靈敏度、特異性，以及陽性和陰性預測值進行統計分析。

結果：彈性成像診斷42個結節為惡性，30個為良性。組織病理學分析發現37個結節為惡性，包括31例乳頭狀癌和6例濾泡狀癌。以組織病理學診斷為參考標準的甲狀腺超聲彈性成像的敏感性、特異性，以及陽性和陰性預測值分別為97.29%、82.85%、85.71%和96.67%。

結論：甲狀腺彈性成像可以大大降低甲狀腺活檢，尤其是良性病變的比率。

INTRODUCTION

Thyroid nodules is a very frequent finding in the general population with a prevalence of about 13% to 67% on evaluation by sonography.[1] Thyroid nodules need to be categorised as benign or malignant for management and prognosis point of view. Ultrasound elastography involves combining the diagnostic advantages of high-frequency ultrasound examination and the accuracy of thyroid cancer diagnosis based on a nodule's stiffness.[2] It is based on the principle that harder and less mobile lesions on clinical palpation is more likely to be malignant. When a nodule is compressed by external pressure, its softer parts deform more readily than its harder part. The amount of this displacement in depth is measured by ultrasound in quasistatic/strain elastography and displayed visually in different colours. This study aimed to evaluate the elastographic appearances of different types of thyroid gland nodules, and to explore the real diagnostic value and clinical utility of thyroid ultrasound elastography with histopathological analysis as a reference standard.

METHODS

This prospective study was carried out on 55 patients with 72 sonographically visible thyroid nodules from August 2010 to February 2012. Informed patient consents were obtained. We also did ultrasound elastography of 10 controls with normal thyroid on high-frequency ultrasound. Exclusion criteria included previous biopsy or intervention; lesions that were clearly cystic on B-mode ultrasonography; very large lesions that could not be completely included in the region of interest; a mostly calcified nodule on B-mode imaging; or where a pathological diagnosis could not be obtained.

Elastography was performed by a single radiologist of more than 5 years of experience, with a Toshiba I Style Aplio XG Ultrasound Unit (Tokyo, Japan) using 6 to 12 MHz multifrequency transducer under same settings as B-mode ultrasonography. The ultrasound probe was placed on the neck with gel applied to the skin. Repeated short bouts of steady firm pressure were applied for 5 to 6 times at the region of interest. The point of pressure application was selected such that the image frame included the nodule, the normal gland, and parts of adjacent neck muscles. Selection of the image frame was done by the graphical representation of compression (by the machine itself), and the image with the most symmetrical and uniform compression was used. The elastography scale ranges from red (greatest strain, i.e. softest component), green (average strain), to blue (no strain, i.e. hardest component).

The elastographic appearances of the nodules were classified into six types based on their colour appearance at elastography. Class 1: Soft nodules that appear homogeneously green, similar to the healthy gland and adjacent neck muscles (Figure 1a); Class 2: Mostly elastic displaying predominantly green with few mosaic areas of yellow (increased strain) and red, and no areas of blue (Figure 1b); Class 3: Central part of the nodule is blue (i.e. hard) with complete peripheral rim of green (i.e. elasticity) [Figure 1c]; Class 4: Homogeneously hard nodule: predominantly blue with few mosaic areas of green (Figure 1d); Class 5: Hard, homogeneous nodules: entire nodule is blue (Figure 1e); and Class 6: No elasticity in the nodule and surrounding area: both nodule and its surroundings are blue (Figure 1f).

Classes 1, 2, and 3 represent the elastographic appearance of benign thyroid nodules, and Classes 4, 5, and 6 represent malignant nodules. The results of elastography were correlated with their pathological results from fine-needle aspiration cytology (FNAC)/biopsy. Statistical analysis was performed to determine its sensitivity, specificity, as well as positive and negative predictive values.

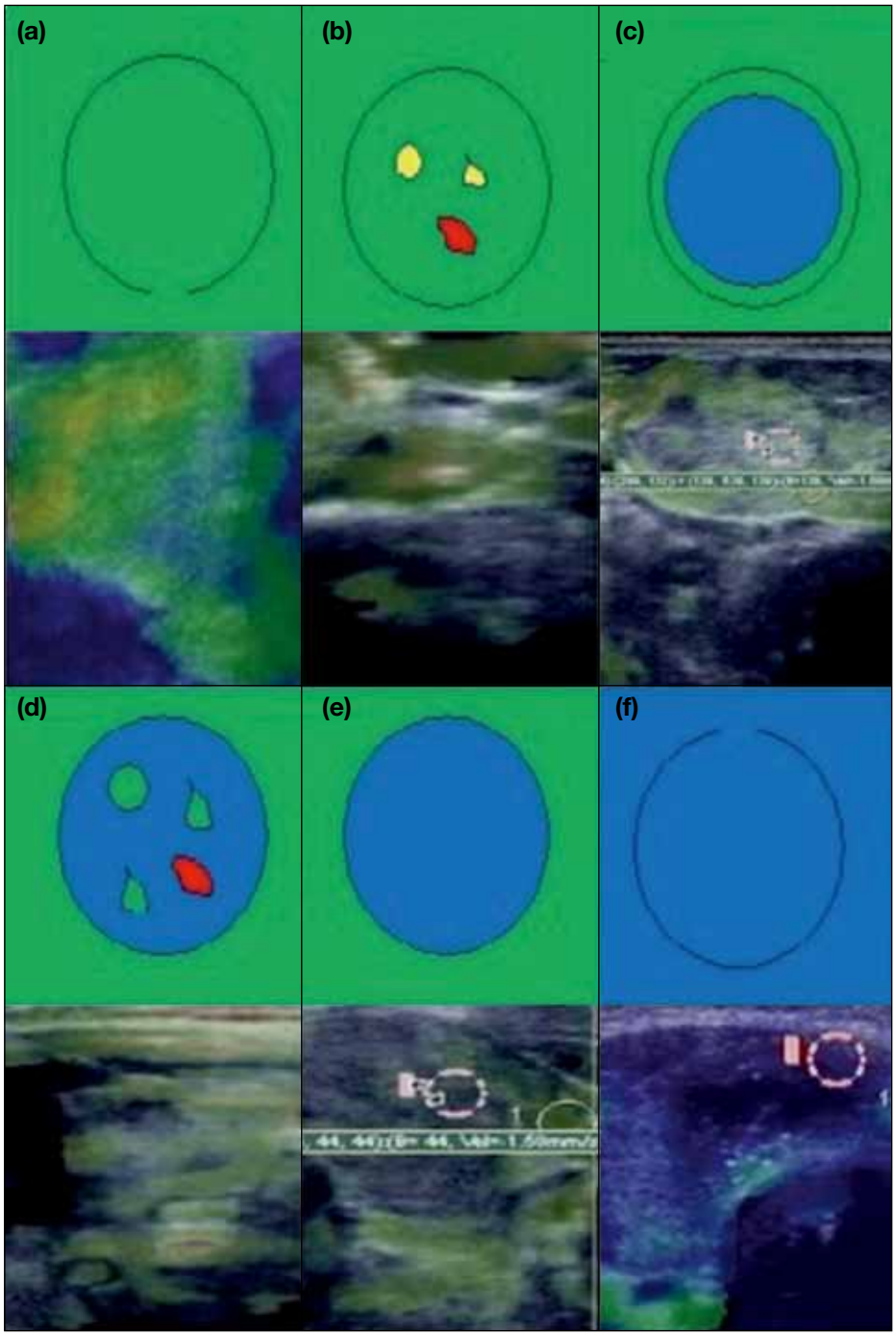

Figure 1. Diagrammatic representation of thyroid nodules classification on elastography.

RESULTS

The 55 patients had 72 thyroid nodules that were investigated. Ultrasound elastography of 10 controls with normal thyroid on high-frequency ultrasound was also performed. Forty-two nodules were diagnosed as malignant and 30 as benign by elastography. On histopathological analysis, 37 nodules were found malignant, including 31 cases of papillary carcinoma and six cases of follicular carcinoma. The 35 benign nodules included 20 colloid and 15 follicular adenomas. Of the 42 malignant nodules on elastography, all 31 cases of papillary carcinoma were correctly diagnosed as malignant, bearing Class 5 or 6 appearances (Figure 2). The five cases of follicular carcinoma had Class 4 appearances (Figure 3). There were six false positives with Class 5 appearances which were ultimately diagnosed on histopathology as benign (4 hyperplastic nodules, 2 colloid cysts). Elastography diagnosed 30

nodules as benign—15 nodules had Class 3 appearances (Figure 4), which were found to be follicular adenomas on histopathology. A case of follicular carcinoma was wrongly diagnosed as benign with Class 2 appearances. It had a predominantly cystic appearance with solid eccentric component, resulting in a mixed appearance on elastography with background of predominant green (Figure 5). Fourteen cases of colloid cyst/hyperplastic nodule had Class 1 or 2 appearances (Figure 6 and Table 1). The sensitivity, specificity, positive and negative predictive values of thyroid ultrasound elastography, when referenced with histopathological diagnoses, were 97.29%, 82.85%, 85.71% and 96.67%, respectively (Table 2). Elastography performed on 10 controls with normal thyroid on B-mode ultrasonography revealed that the deeper areas of the thyroid gland, as well as the areas near the carotid artery were marred by artefacts and frequently did not exhibit a homogeneous green colour. These areas had mixed yellow and red appearances.

DISCUSSION

The ultrasound features of hypoechogenicity, irregular margins, and microcalcifications in thyroid nodules have been shown to have prognostic value for predicting thyroid malignancy,[3] though they can be seen in benign nodules as well. Even when combined with colour Doppler, the sensitivity and specificity do not increase significantly, and the number of nodules referred for FNACs remain similar.[4,5]

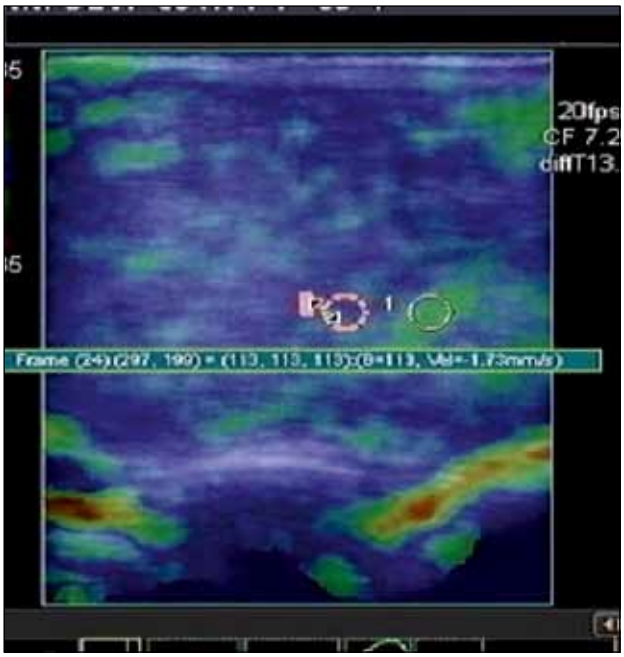

Figure 3. Follicular carcinoma in a 65-year-old female giving Class 4 appearance on sonoelastography.

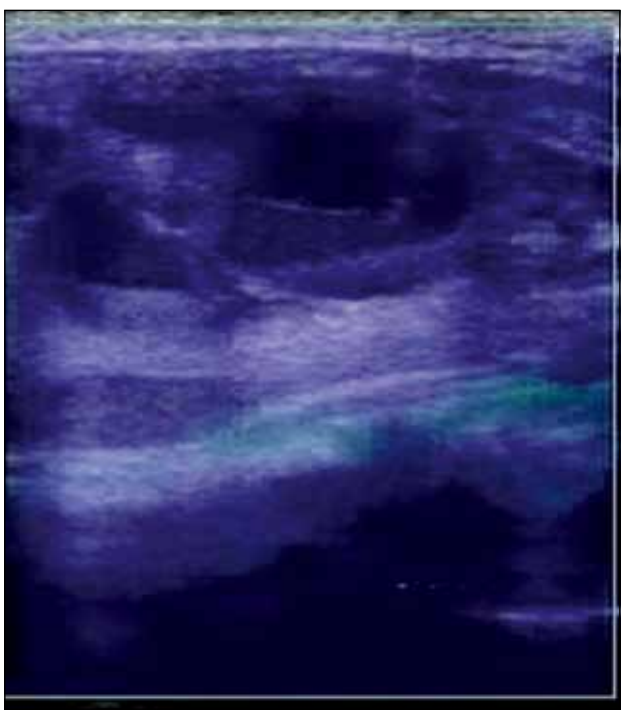

Figure 2. Class 6 appearance on sonoelastography of a case of papillary carcinoma.

Figure 4. Class 3 nodule on elastography diagnosed as follicular adenoma on histopathology.

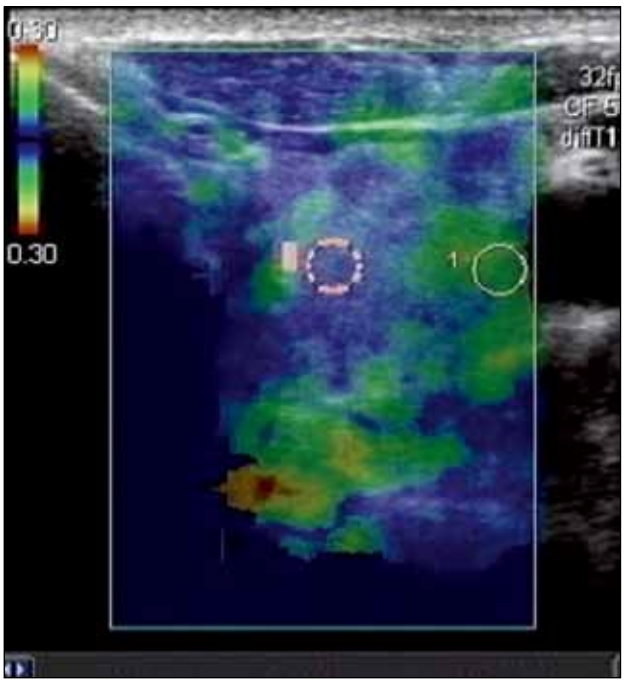

Figure 5. A case of follicular carcinoma in a 45-year-old male which was wrongly interpreted as benign on elastography with Class 2 appearance.

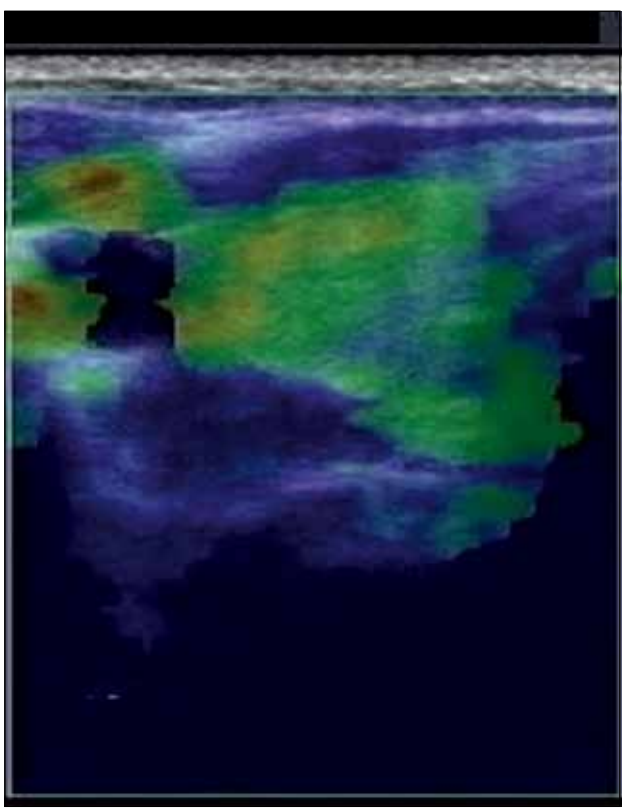

Figure 6. Elastography image of a hyperplastic nodule with Class 2 appearance.

Table 1. Elastography appearance of thyroid nodules (n = 72).

Class	No. of nodules
1	9
2	6
3	15
4	5
5	16
6	21

Table 2. Elastography versus histopathology results.

	Malignant	Benign	Total
Positive test	36	6	42
Negative test	1	29	30
Total	37	35	72

Elastography measures the amount of tissue deformation (strain) under applied pressure, and thereby, in principle, may increase the accuracy of thyroid cancer diagnoses based on the nodule's stiffness.[2,6]

A study by Dighe et al[7] using quantitative measurements generated from ultrasound elastography showed 100% sensitivity, 79.4% specificity, 60% positive predictive value, and 100% negative predictive value of this modality. As per the researchers' views, ultrasound elastography reliably characterised a substantial number of benign nodules, thereby significantly reducing the number of unnecessary biopsies.

Similar studies on ultrasound elastography have yielded variable results with some studies showing great clinical utility while others show dismal performances.[8-10] Our realistic estimation was that the utility of elastography would be somewhere in between. Our study endeavoured to specifically answer the following questions:

1. Is elastography sensitive or specific in the determinations of whether a thyroid nodule is benign or malignant?
2. Can it reduce the number of biopsies without missing a thyroid cancer?
3. What are the shortcomings of this study and procedure? Which areas of involvement would make scanning suboptimal, requiring more guarded interpretations?
4. Is characterisation of thyroid nodules possibly based

on elastographic appearances?
5. How can we modify or improve this procedure?

From our observations, we hypothesised that patients with Class 1 (homogeneous green) and Class 3 (central blue with peripheral rim of green colour) appearances may be safely assumed to be benign and can be followed with ultrasound to assess the change in characteristics over time, thereby reducing the number of biopsies in our study population by 33.33%. Rubaltelli et al[11] concluded that the entirely elastic pattern was observed only in relation to benign nodules, restricting the number of cases with recourse to fine-needle aspiration. Our study not only showed that an entirely elastic nodule with homogeneous green colour was benign, but that the appearance of central blue with complete peripheral rim of green colour was seen only in cases of follicular adenoma. This latter finding has not been previously reported.

Nodules showing complete elastic pattern but with mosaic appearances (Class 2) may occasionally miss a hidden follicular carcinoma as seen in our single false-negative case. Although sonoelastography has been found to be very efficient at the diagnosis of papillary carcinoma—100% accuracy in our study, its major limitation, in our opinion, is its lack of sensitivity for diagnosing follicular carcinoma. In cases of multinodular goitre, sonoelastography may help in deciding which nodule to target for FNAC/biopsy, specifically those with hard appearances. Using elastography, we hypothesised that it may be possible to detect malignancy even in small non-palpable thyroid nodules. This may be of great prognostic value to the patient as a significant percentage of small malignant nodules may metastasise.[12]

Because existing imaging modalities (ultrasound, colour Doppler, computed tomography, magnetic resonance imaging) cannot accurately differentiate between malignant and benign nodules, FNAC/biopsy is performed on almost all nodules. Even after combining ultrasound and colour Doppler, the number of nodules referred for FNACs is not reduced. Thyroid sonoelastography can ensure significant reduction of health expenditure by giving a diagnosis of benignity with high specificity and sensitivity (Class 1 and Class 3 nodules), thereby reducing the cost of unnecessary FNAC/biopsy.[13] However this technique lacked accuracy when a large part of the nodule was calcified or cystic, and such cases should be excluded to reduce a false hard appearance on elastography. Moreover, it is important to note that deeper areas of the thyroid gland, and areas near the carotid artery are often marred by artefacts, resulting in mixed yellow and red appearances.

A significant limitation of our study was its subjective nature where the amount of compression could not be quantified, thus making the study results susceptible to inter- and intra-observer variability. However, this study was performed by a single sonographer with considerable experience in this technique. Also, the uneven surface of the neck also made it difficult to apply uniform compression. Our sonographer lightly placed the linear transducer with a small footprint on the patient's neck and applied uniform pressure during image acquisition. Our study on the role of sonoelastography was primarily intended to confidently diagnose benign nodules of the thyroid gland that can decrease the burden of cases sent for FNAC/biopsy. It was different from those earlier studies which were primarily aimed at diagnosing and differentiating malignant nodules. Our study shows that sonoelastography is more valuable for excluding malignancy—sensitivity of 97.29% and specificity of 82.85%. Also, the incidence of malignant lesions can be attributed to its small sample size, selection bias, and late presentation in a largely illiterate population which does not seek medical care until the problem becomes severe.

CONCLUSION

Sonoelastography has shown its role as a non-invasive screening tool to reduce the number of FNACs being performed on benign nodules. In conjunction with the B-mode ultrasound and colour Doppler, thyroid sonoelastography may lead to significant improvement in the management and follow-up of thyroid nodules.[14]

It is concluded that Class 1 and Class 3 nodules can be assumed benign, and can be followed up by sonoelastography without FNAC. Elastography is highly accurate in the diagnosis of papillary carcinoma as most of these nodules have a Class 5 or 6 appearance. Large cystic lesions or very large nodules are not the ideal cases for elastography. Sonoelastography is of high utility in multinodular goitre as it can help select the most suspicious nodule for FNAC, thus reducing false-negative results. It can also help in selecting the hardest part of a nodule to sample. Non-palpable small nodules are ideal for sonoelastography evaluation. Mosaic

images (i.e. Classes 2 and 4) need to be interpreted with caution. Follicular carcinoma frequently have a mosaic appearance. Follicular adenoma may also have a mosaic Class 4 appearance. Elastography is marred with artefacts in deeper regions of the thyroid, and at areas near the carotid artery. Hence if a nodule is located in these regions, FNAC may be warranted depending on its sonographic features.

The technique has some limitations, some of which have been overcome, like the quantification of strain by shear-wave elastography, acoustic radiation force impulse. Also, development of uniform scoring or classification system for thyroid tumours like for breast lesions is required. The modality is also relatively less sensitive to follicular carcinoma as compared to papillary carcinoma.

At present, elastography is useful when combined with high-frequency ultrasound. It requires little additional time, costs, and should be considered a useful technique for reducing unnecessary FNAC or biopsies in benign lesions.

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