Utility of elastography for differential diagnosis of benign and malignant thyroid nodules

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ABSTRACT

OBJECTIVE: 1) To classify the appearance of thyroid nodules displayed on ultrasound elastography; 2) to explore the sensitivity and specificity of this examination for differentiating benign and malignant nodules, with histopathologic analysis as the reference standard; and 3) to evaluate its utility for avoiding unnecessary procedures.

STUDY DESIGN: Diagnostic test assessment.

SETTING: Community hospital.

SUBJECTS AND METHODS: Forty-seven thyroid nodules in 44 consecutive patients were examined with ultrasound elastography. The images we obtained were classified into four patterns. In addition, the mean strain index of the thyroid nodule and that of the sternocleidomastoid muscle were measured, and the nodule-to-muscle strain ratio was calculated. As the reference findings, the presence or absence of calcification, irregular margins, and hypoechochogenicity of the thyroid nodules were examined using B-mode ultrasound.

RESULTS: Elastography patterns 3 and 4 were predictive of malignancy, with 73 percent sensitivity (95% confidence interval [CI]: 39%-94%) and 64 percent specificity (95% CI: 46%-79%). Additionally, all nodules without calcification and those that presented with patterns 1 or 2 were benign. A strain ratio greater than 1.5 was set as the predictor of thyroid malignancy. This criterion showed 90 percent sensitivity (95% CI: 59%-100%) and 50 percent specificity (95% CI: 33%-67%).

CONCLUSION: Although elastography can assist in the differential diagnosis of thyroid nodules, its diagnostic performance is not ideal at present. Further improvements in the technique and the diagnostic criteria are necessary for this examination to provide a useful contribution to diagnosis.

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subjects. US elastography was performed concurrently with US-guided FNAB.

Forty-seven thyroid nodules were found in 44 patients. All subjects who had FNAB results that were read as malignant or intermediate underwent surgery, with the exception of two subjects. One of the unoperated subjects was diagnosed with anaplastic carcinoma, and the other was diagnosed with papillary carcinoma but had terminal colon carcinoma. This study was reviewed and approved by the Research Ethic Committee at Hitachi General Hospital.

**Equipment**

Conventional B-mode US and elastographic examinations were performed using a Hitachi LOGOS EUB 7500 System machine and a 14-6 MHz linear probe (Hitachi Medical, Tokyo, Japan). Dedicated software (Combined Autocorrelation Method; Hitachi Medical Systems) was used to provide an accurate measurement of tissue measurement of tissue distortion.

**Imaging Methods**

First, conventional US images of thyroid nodules were obtained with patients positioned lying on their backs with their necks slightly extended. The presence or absence of calcification, irregular margins, and hypoechogenicity of the thyroid nodules was determined. After the B-mode US examination, US elastography was performed.

We made every effort for the ROI to be the same. In addition, the ROI was set so that the nodule and sufficient surrounding normal structure were included in the area. The technique used for the elastographic examination was application of light compression with the US probe to the anterior neck. To keep the strain distribution uniform, compressions were applied to the area with 1- to 2-mm thickness and two to four times per second in all subjects. Because the stiffness obtained with this examination is relative in the ROI, non-nodular tissues were set to make up at least 30 percent of the ROI. If nodules cover most of the ROI, the data are less reliable.

The visualization patterns of nodules on the elastographic images were classified as four pattern types according to the classification proposed by Fukunari (Fig 2). Patterns 3 and 4 were assumed to be characteristic findings of malignancy. In addition, the mean strain index of thyroid nodule and that of the sternocleidomastoid muscle (SCM) were measured, and the nodule-to-muscle strain ratio (SR) was calculated. A SR greater than 1.5 was set as the predictor of nodule malignancy. This cutoff point was decided by the ROC curve so that sum of sensitivity and specificity was maximized.

**Results**

**Pathologic Findings**

On FNAB, 36 of the 47 nodules were diagnosed as benign, and 11 nodules were diagnosed as malignant. The malignant nodules included six papillary thyroid carcinomas, one follicular carcinoma, one poorly differentiated carcinoma, one malignant lymphoma, one spindle epithelial tumor with thymus-like differentiation, and one anaplastic carcinoma. The cases of anaplastic carcinoma and papillary carcinoma were diagnosed with FNAB; the other cases were diagnosed pathologically.

**B-mode US Classification**

Thyroid nodules were classified into two groups based on the presence or absence of calcification. Thirty-one of 47 nodules had no calcification, and 28 of those nodules were diagnosed as benign tumors by FNAB. The remaining 16 of the 47 nodules had calcification, and eight of those nodules were diagnosed as malignant (Table 1). The presence of...
Calcification was predictive of malignancy with 73 percent sensitivity (95% confidence interval [CI]: 39%-94%) and 78 percent specificity (95% CI: 61%-90%).

Thyroid nodules were also classified into two groups based on the presence or absence of irregular margins. Thirty-five of 47 nodules had no irregular margin, and 27 of those nodules were diagnosed as benign tumors by FNAB. The remaining 12 of the 47 nodules had irregular margins, and only three of those nodules were diagnosed as malignant (Table 2). The presence of an irregular margin was predictive of malignancy with 27 percent sensitivity (95% CI: 6%-61%) and 75 percent specificity (95% CI: 58%-88%).

In addition, thyroid nodules were classified into two groups based on their B-mode echogenicity: nodules with hypoechogenicity and those with other echogenicity (isoechoic or mixed with liquid and solid component). Thirty-one of 47 nodules had no hypoechogenicity, and 26 of those nodules were diagnosed as benign tumors by FNAB. The remaining 16 of the 47 nodules had hypoechogenicity, and six of those nodules were diagnosed as malignant (Table 3). The presence of hypoechogenicity was predictive of malignancy with 55 percent sensitivity (95% CI: 23%-83%) and 72 percent specificity (95% CI: 55%-86%).

**US Elastography**

Twenty-six of the 47 nodules showed pattern 1 or 2, and 23 of those nodules were diagnosed as benign. Twenty-one of 47 nodules showed pattern 3 or 4, and eight of those nodules were diagnosed as malignant (Table 4). Patterns 3 and 4 were thus predictive of malignancy, with 73 percent sensitivity (95% CI: 39%-94%) and 64 percent specificity (95% CI: 46%-79%). All nodules without calcification and showing elastographic pattern 1 or 2 were considered benign.

Nineteen of 47 nodules had a SR < 1.5; 18 of these nodules were benign. Among 28 of 47 nodules having a SR ≥ 1.5, 10 were malignant (Table 5). This criterion had 90 percent sensitivity (95% CI: 59%-100%) and 50 percent specificity (95% CI: 33%-67%).

**Discussion**

It has been stated that four to seven percent of the adult population has a palpable thyroid nodule. Even though most of those nodules are benign, the possibility of cancer must always be considered. Although US examination is useful for detecting thyroid nodules, its usefulness fails when differentiating benign and malignant lesions. Intranodular snowstorm-like microcalcifications significantly correlate with papillary carcinoma, but this finding is absent in a great number of malignant nodules. Irregular margins, hypoechogenicity on B-mode US, and intranodal flow demonstrated on color flow Doppler (CFD) sonography are also findings predicting thyroid malignancy. In the present study, color flow Doppler sonography was not performed, but other findings on B-mode US were not so useful for diagnosing thyroid malignancy compared with microcalcifications.

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**Table 1**

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<th>Association between calcification and malignancy in nodules</th>
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<tr>
<td><strong>Benign nodules, n (%)</strong></td>
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<td>--------------------------</td>
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<tr>
<td>Calcification (−)</td>
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<td>Calcification (+)</td>
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<td>Total</td>
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Odds ratio, 9.33 (95% CI: 1.64-63.86).

**Table 2**

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<th>Association between irregular margin and malignancy in nodules</th>
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<td><strong>Benign nodules, n (%)</strong></td>
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<td>---------------------------</td>
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<tr>
<td>Irregular margin (−)</td>
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<tr>
<td>Irregular margin (+)</td>
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<td>Total</td>
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Odds ratio, 1.13 (95% CI: 0.16-6.14).

**Table 3**

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<th>Association between hypoechogenicity and malignancy in nodules</th>
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<td><strong>Benign nodules, n (%)</strong></td>
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<tr>
<td>Hypoechogenicity (−)</td>
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<td>Hypoechogenicity (+)</td>
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<td>Total</td>
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Odds ratio, 3.12 (95% CI: 0.62-15.88).

**Table 4**

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<th>Association between elastographic pattern and malignancy in nodules</th>
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<td><strong>Benign nodules, n (%)</strong></td>
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<td>Patterns 1 and 2</td>
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<td>Patterns 3 and 4</td>
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Odds ratio, 4.72 (95% CI: 0.89-31.39).
To differentiate benign and malignant nodules, it is necessary to use US-guided FNAB. However, that is an invasive procedure and is subject to sampling errors. Even when needle placement is presumably correct, approximately 15 to 20 percent of nodules yield an inadequate or nondiagnostic cytology. Thus, reliable criteria for determining which nodules should be followed up and which should be aspirated are needed. Although palpation is the oldest and most frequently used screening method for detecting thyroid nodules and stiffness of thyroid nodules correlates with malignancy, it is subjective and depends on the skill of the examiner.

US elastography is a newly developed dynamic technique that evaluates the degree of distortion of a tissue under the application of an external force. Because softer parts of tissue deform more readily than the stiffer parts, this technique enables objective evaluation of tissue stiffness from the deformation rate.

US elastography has already been shown to be useful in the differential diagnosis of breast and prostate carcinomas. The aim of the present study was to determine whether US elastography might assist in the differential diagnosis of thyroid nodules.

We found that its performance was not ideal for diagnosing malignant tumors. However, because all the nodules in this study that had no calcification and presented pattern 1 or 2 were benign, we can say that US elastography is useful for avoiding unnecessary FNAB on nodules in those classifications. Needless to say, more cases needed to be evaluated, and more discussion is necessary.

For US elastography to become a more useful examination, we should consider the following problems.

First, stricter exclusion criteria should be set. Cystic nodules should be excluded, for they are mostly composed of fluid, and US elastography cannot give useful information. Asteria et al evaluated 86 consecutive thyroid nodules in 67 patients by US elastography and achieved excellent results with 94 percent sensitivity and 81 percent specificity. In that study, completely cystic nodules were excluded. Nodules with a calcified shell should also be excluded because the US beam does not cross the calcification. In addition, calcification is the initial finding that indicates malignancy, so it is safe for such nodules to be aspirated. Actually, FNAB is minimally invasive, and it is the most accurate means for diagnosing thyroid malignancy.

Second, the ROI should be taken into consideration when evaluating the results. In this study, we selected horizontal slices of the thyroid gland because it is necessary for SCM to be included in the ROI as the control region. However, this slice includes the carotid artery. Because palpation of the carotid artery influences the strain distribution, a sagittal slice of the thyroid gland may be more appropriate for US elastography. Ideally, every nodule should be evaluated using multiple sections, and, in each ROI, nodules that present different patterns should be excluded.

Finally, the SR measuring method needs to be reviewed. In this study, diagnostic performance using SR was not optimal. One of the reasons that the SCM is not appropriate for the control region is that the elasticity of the SCM varies even if patients are positioned uniformly. Lyshchik et al evaluated 52 consecutive thyroid nodules in 31 patients by US elastography. The nodule-to-gland SR was calculated. Those authors found that a SR > 4 was the predictor of thyroid gland malignancy (96% specificity and 82% sensitivity). Although Lyshchik et al’s study was done using offline processing, which differs from the method we used, the excellent results obtained are helpful for evaluating US elastography. However, in that case, the nodules dominated more than 80 percent of the thyroid gland, and minimal nontumor material remains in the thyroid gland. It may be wise to exclude such nodules. In the present study, thyroid nodules > 40 mm were excluded, but there remains little normal thyroid region even when diameter of the nodule is approximately 35 mm. Therefore, a stricter size limit is needed if thyroid nodules have to be evaluated by nodule-to-gland SR.

In conclusion, although some problems remain to be solved, US elastography is nonstressful for patients, easy to perform, and requires no more than a few minutes of additional examination time compared with that of conventional US. In this study, this technique in combination with B-mode US played a role in the exclusive diagnosis of benign nodules. After reviewing the details we have discussed in this study, we concluded that US elastography can become a very useful examination to avoid unnecessary procedures.
Disclosures

Competing interests: None.
Sponsorships: None.

References