New Sonographic Criteria for Recommending Fine-Needle Aspiration Biopsy of Nonpalpable Solid Nodules of the Thyroid

OBJECTIVE. The purpose of our study was to provide new sonographic criteria for fine-needle aspiration biopsy of nonpalpable solid thyroid nodules.

MATERIALS AND METHODS. Sonographic scans of 155 nonpalpable thyroid nodules in 132 patients were prospectively classified as having positive or negative findings. Sonographic findings that suggested malignancy included microcalcifications, an irregular or microlobulated margin, marked hypoechogenicity, and a shape that was more tall than it was wide. If even one of these sonographic features was present, the nodule was classified as positive (malignant). If a nodule had none of the features described, it was classified as negative (benign). The final diagnosis of a lesion as benign (n = 106) or malignant (n = 49) was confirmed by fine-needle aspiration biopsy and follow-up (>6 months) in 83 benign nodules, by fine-needle aspiration biopsy and surgery in 44 malignant and 15 benign lesions, and by surgery alone in five malignant and eight benign lesions. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated on the basis of our proposed classification method.

RESULTS. Of 82 lesions classified as positive, 46 were malignant. Of 73 lesions classified as negative, three were malignant. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy based on our sonographic classification method were 93.8%, 66%, 56.1%, 95.9%, and 74.8%, respectively.

CONCLUSION. Considering the high level of sensitivity of our proposed sonographic classification, fine-needle aspiration biopsy should be performed on thyroid nodules classified as positive, regardless of palpability.

The introduction of high-resolution sonography has made it possible to detect many nonpalpable nodules in the thyroid [1, 2]. The incidence of such lesions in the general population appears to be high—approximately 10–40% [3–5]. Most of these incidental thyroid nodules are benign, but the discovery of nonpalpable nodules raises concerns about their possible malignancy. Many studies have documented considerable overlap of characteristic findings in benign and malignant lesions [2, 6–9]. Some authors have recommended that sonography be used solely to determine the presence of the focal lesion, to determine whether a lesion is cystic or solid, and for needle guidance [6–9].

To our knowledge, no reports on specific sonographic characteristics of nonpalpable thyroid malignancy have been published to date. We undertook this work to assess the potential role of sonography in the differentiation of benign from malignant nonpalpable thyroid lesions and to provide new sonographic criteria for the indication of fine-needle aspiration biopsy in nonpalpable solid thyroid lesions.

Materials and Methods
Between December 1997 and May 1998, sonography of the thyroid was performed on 1,140 patients for nonthyroid indications, including thyroid screening during breast sonography (n = 1,057) and complaints of swallowing difficulties, hoarseness, or neck discomfort (n = 83). We found 322 focal thyroid nodules in 170 patients: 199 solid nodules, 108 cystic nodules (anechoic), and 15 lesions with mixed cystic and solid portions. We included only solid nodules in this study. When experienced surgeons palpated the thyroids of patients with solid nodules, 155 nodules in 132 patients were nonpalpable (a single thyroid nodule in 119 patients and multiple nodules in 13 patients). The resulting study group consisted of 120 women (90.9%) and 12 men (9.1%). Their ages ranged from 20 to 77 years (mean age, 48 years).

Sonography was performed by one radiologist with an HDI 3000 scanner (Advanced Technology Laboratories, Bothell, WA) using electronically focused near-field probes with a bandwidth of 7–12 MHz.
Malignant sonographic characteristics were defined as microcalcifications, an irregular or microlobulated margin, marked hypoechogenicity, and a shape that was more tall than it was wide. Microcalcifications (Figs. 1 and 2) suggesting malignancy were defined as tiny, punctate hyperechoic foci—either with or without acoustic shadows. Peripheral, eggshell-like calcifications were not considered malignant. Irregular (Fig. 3) or microlobulated (Fig. 1) margins were also considered to be malignant findings. Microlobulation was defined as the presence of many small lobules on the surface of a nodule. Marked hypoechogenicity (Fig. 4) was defined as decreased echogenicity compared with the surrounding strap muscle. Most nonpalpable thyroid nodules were hypoechogenic, and most of them were benign. Subsequently, we discriminated between markedly hypoechogenic and hypoechogenic lesions and considered marked hypoechogenicity as a malignant finding. A nodule with a shape more tall than wide (Fig. 5) was defined as being greater in its anteroposterior dimension than its transverse dimension. We considered this finding to be positive for malignancy if any part of the nodule was more tall than wide.

The sonographic characteristics we used were based on previously published criteria [6–9] and on nonpublished criteria from our retrospective study. We prospectively classified nodules as positive or negative. If a single feature suggestive of malignancy was present, the nodule was classified as positive. If a nodule had no suspicious features, it was classified as negative (benign). The final diagnosis of benign (n = 106) or malignant (n = 49) was determined using fine-needle aspiration biopsy and follow-up (>24 months) of 83 benign nodules. Follow-up was done by fine-needle aspiration biopsy and surgery on 44 malignant and 15 benign lesions and by surgery alone on five malignant and eight benign lesions. All solid nodules were aspirated in patients with two or more solid nodules. Diagnosis of malignancy at histology included papillary carcinoma (n = 48) and metastasis from carcinoma of the breast (n = 1).

We calculated the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for individual sonographic characteristics and classifications.

Results

The size of the 155 nodules ranged from 3 to 28 mm (mean size, 7.5 mm). We found no statistical difference between the benign and malignant nodules with regard to size. The sonographic findings in malignant and benign nodules are summarized in Table 1. All findings appear to be statistically significant. The correlation of sonographic classifications with histologic findings is shown in Table 2. The sensitivity of the sonographic classification was 93.8%, specificity was 66%, positive predictive value was 56.1%, negative predictive value was 95.9%, and the overall accuracy was 74.8%. Table 3 summarizes the diagnostic index for individual sonographic criteria of malignant nodules. Most malignant nodules had multiple...

### Table 1: Sonographic Findings in 155 Malignant or Benign Thyroid Nodules

<table>
<thead>
<tr>
<th>Sonographic Characteristics</th>
<th>Malignant Nodules (%) (n = 49)</th>
<th>Benign Nodules (%) (n = 106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcalcification</td>
<td>29 (59.1)</td>
<td>15 (14.2)</td>
</tr>
<tr>
<td>Irregular or microlobulated margin</td>
<td>27 (55.1)</td>
<td>28 (26.4)</td>
</tr>
<tr>
<td>Marked hypoechogenicity</td>
<td>13 (26.5)</td>
<td>6 (5.6)</td>
</tr>
<tr>
<td>More tall than wide</td>
<td>16 (32.7)</td>
<td>8 (7.5)</td>
</tr>
</tbody>
</table>

Note: All findings appear to be statistically significant (p < 0.05, using the chi-square test).

<table>
<thead>
<tr>
<th>Table 2: Comparison of Sonographic and Histologic Findings</th>
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<tbody>
<tr>
<td>Sonographic Classification</td>
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<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>Malignant</td>
</tr>
<tr>
<td>Malignant</td>
</tr>
<tr>
<td>Benign</td>
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<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Note: In these 155 nodules, our sonographic classification method resulted in a sensitivity of 93.8% (46/49), specificity of 66% (70/106), positive predictive value of 56.1% (46/82), negative predictive value of 95.9% (70/73), and accuracy of 74.8% (116/155).
Sonography of Nonpalpable Nodules of the Thyroid

Sonographically suspicious findings. The mean number of suspicious findings per malignant nodules was 2.6. The accuracy of each sign was 72.9–77.4%, but the sensitivity was low, ranging from 26.5% to 59.1%.

Three nodules classified in the negative category were confirmed at pathology as papillary carcinoma. On sonography, a well-defined, oval hypoechoic nodule was seen in two of these lesions, and a well-defined, oval isoechoic nodule was seen in the third (Fig. 6).

Discussion

Increased use of high-frequency sonography has led to the identification of nonpalpable thyroid nodules during nonthyroid sonographic examination of the neck. The discovery of one or more nodules in an otherwise clinically normal thyroid gland raises concerns about malignancy. Most such incidental lesions are histologically benign. Kuma at al. [10] examined the long-term outcome of benign thyroid nodules that were untreated. Among 134 patients with cytologically benign thyroid nodules who were followed for 9–11 years, most nodules (133/134, 99.3%) remained benign. This finding clearly shows that benign thyroid nodules remain benign for a long time.

TABLE 3 Diagnostic Index for Individual Sonographic Criteria of Malignant Thyroid Nodules

<table>
<thead>
<tr>
<th>Sonographic Characteristics</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcalcification</td>
<td>29/49 (59.2)</td>
<td>91/106 (85.8)</td>
<td>29/41 (70.7)</td>
<td>91/114 (79.8)</td>
<td>120/155 (77.4)</td>
</tr>
<tr>
<td>Irregular or microlobulated margin</td>
<td>27/49 (55.1)</td>
<td>88/106 (83)</td>
<td>27/45 (60)</td>
<td>88/110 (80)</td>
<td>115/155 (74.2)</td>
</tr>
<tr>
<td>Marked hypochochogenicity</td>
<td>13/49 (26.5)</td>
<td>100/106 (94.3)</td>
<td>13/19 (68.4)</td>
<td>100/136 (73.5)</td>
<td>113/155 (72.9)</td>
</tr>
<tr>
<td>More tall than wide</td>
<td>16/49 (32.7)</td>
<td>98/106 (92.5)</td>
<td>16/24 (66.7)</td>
<td>98/131 (74.8)</td>
<td>114/155 (73.5)</td>
</tr>
</tbody>
</table>

Note.—Most malignant nodules had multiple sonographic findings suggestive of malignancy (mean number of suspicious findings per malignant nodule, 2.6). The accuracy of each sign was 72.9–77.4%, but the sensitivity was low, ranging from 26.5% to 59.1%.
Kim et al.

Many reports have discussed sonographic findings of the thyroid mass; however, a considerable overlap of characteristics in benign and malignant lesions was found [6–8]. Although most surgeons recommend fine-needle aspiration biopsy for palpable thyroid nodules [11], the optimal method for managing nonpalpable thyroid nodules is a matter of controversy [11–13].

We tried to identify the characteristic sonographic findings of nonpalpable malignant nodules because, to our knowledge, no studies on sonographic characterization of nonpalpable solid thyroid nodules are available. Recently, Brander et al. [14] reported on their 5-year follow-up of thyroid nodules detected on sono-

graphic screening. No thyroid malignancies were detected among patients in whom echo abnormalities were found during the primary sonographic screening, and these researchers concluded that incidentally found thyroid nodules were clinically unimportant. However, their series was restricted by the size of the study group \(n=69\) and the small number of solid hypoechoic nodules that were found \(n=16\). Brander et al. did not provide the details of their sonographic findings.

Microcalcification is a common finding in patients with palpable thyroid papillary carcinoma. It is not often seen in a nonpalpable nodule; however, microcalcification was found to be the most sensitive and accurate criterion in our study. Sonography is not highly sensitive in revealing microcalcifications unless they occur within masses. At pathology, tiny, punctate microcalcifications are correlated with the calcification of psam-
moma bodies. Solbiati et al. [15] suggested that detection of microcalcifications in thyroid nodules with high-frequency sonography, although uncommon, can be considered nearly specific for malignancy.

An irregular or microlobulated margin is a general finding of malignancy. Microlobulation is more common than an ill-defined margin in nonpalpable thyroid malignancy, and it may be associated with smaller mass and a less invasive character. Several studies have mentioned hypo-
echogenicity as a finding suggestive of malignancy [6–9]. However, most nonpalpable thyroid nodules are hypoechoic—and most of those are benign. Therefore, we attempted to differentiate markedly hypoechoic lesions from other hypoechoic lesions, and only mark-
edly hypoechoic lesions were considered a finding indicative of malignancy. We defined markedly hypoechoic nodules as being much less echogenic than the medium-level echogeneity of the strap muscles. The healthy thyroid gland shows homogeneous hyperechogenicity compared with the surrounding muscle. Because most thyroid nodules show hypoechogenicity when compared with the parenchyma of the thyroid, this comparison does not provide much useful information. Subcutaneous fat on the anterior aspect of the thyroid gland shows uniform hypoechogenicity, but the amount of fat varies among individuals. Furthermore, the comparison is difficult in patients with little fat. The strap muscle is uniformly present in all patients; therefore, we chose the strap muscle as the comparative standard for the evaluation of the echogenicity of solid nodules.

We regarded a nodule shape more tall than wide as a finding suggestive of malignancy. Researchers have documented that nodules in the breast that are taller than they are wide are more likely to be malignant [16–18]. The growth of most benign nodules has been found to remain within normal tissue planes, whereas malignant nodules grow across normal tissue planes [16]. We applied this finding in thyroid nodules and showed that it was not a sensitive but a very specific finding, and thus it could be used as an ancillary finding of nonpalpable thyroid malignancies. In three cases, a shape more tall than wide was the only sign of malignancy (Fig. 6).

Surprisingly, sonographic findings suggestive of malignancy in our thyroid study were very similar to those in the breast. To our knowledge, our study is the first to report this assumption; additional and extensive studies are required to validate this hypothesis.

The goal of treatment should be to avoid extensive and costly evaluations in the most pa-
tients with benign disease without missing the minority of patients who have thyroid cancer. In this study, we found no single criterion that could distinguish benign from malignant thyroid nodules with 100% reliability. However, although individual suspicious findings had low-to-moderate sensitivity, our sonographic classification, by which a nodule is classified as positive if even a single suspicious sonographic finding is present, was found to be highly sensitive, reaching 93.8% sensitivity. Only 6.2% of malignant lesions were misclassified as benign. These results, if widely reproducible, could have a substantial impact on the evaluation of incidental thyroid lesions.

Controversy exists on the optimal treatment for occult papillary carcinomas. Most papillary carcinomas show an indolent course and excel-

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**Fig. 7.** Diagram of algorithm for evaluation of incidental thyroid lesions.
Sonography of Nonpalpable Nodules of the Thyroid

References