Value of US Correlation of a Thyroid Nodule with Initially Benign Cytologic Results

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Purpose:
To investigate the value of ultrasonographic (US) features in thyroid nodules with initially benign cytologic results.

Materials and Methods:
The institutional review board approved this retrospective study and required neither patient approval nor informed consent for the review of images and records. From October 2003 to February 2006, 6118 focal thyroid nodules in 6025 consecutive patients underwent US-guided fine-needle aspiration biopsy (FNAB). This study included 1343 nodules 1 cm or larger in 1302 patients that were diagnosed as benign at initial cytologic evaluation and underwent pathologic or follow-up study. We compared the risk of malignancy according to US findings and calculated the likelihoods of different subgroups having benign nodules.

Results:
In total, 26 (1.9%) malignant and 1317 (98.1%) benign nodules were found according to reference standards. If initial cytologic results showed benign thyroid nodules, the likelihood of the nodule actually being benign was 98.1%. When a thyroid nodule had benign results at both initial and repeat FNAB, the likelihood increased to 100%. The likelihood of having a benign thyroid nodule with suspicious US features was lower (79.6%) than having a benign thyroid nodule with negative US features (99.4%, P < .001). In the nodule with benign features at initial US, the risk of malignancy for a thyroid nodule with an increase in size at follow-up US was slightly higher (1.4%) than that of a thyroid nodule with no interval change or decrease in size, but it was not significantly different (0.5%, P = .354).

Conclusion:
Repeat FNAB should be performed for thyroid nodules that have suspicious US features, even if the initial cytologic results indicate that it is a benign lesion.
When diagnosing focal thyroid nodules, fine-needle aspiration biopsy (FNAB) is an essential tool to help decide whether a nodule requires surgery. However, FNAB has inevitable limitations in helping diagnose a thyroid nodule, such as false-positive (1, 2), false-negative (1–3), and inadequate (1, 2, 4, 5) results. Although the Papanicolaou Society of Cytopathology Task Force on Standards of Practice recommends that the false-negative (FN) rate not exceed 2% and the false-positive rate not exceed 3% for FNAB cytologic evaluation of the thyroid (6), the reported FN rate of FNAB ranges from 2.3% to 6.2% (7–9) and the false-positive rate of FNAB ranges from 0.2% to 11.6% (7–11). To reduce the FN rate of FNAB, repeat aspiration can be performed, and some investigators insist that they are important to avoid missing a cancer in thyroid nodules with initial benign cytologic results (12–14). However, organizations such as the American Thyroid Association (15), American Association of Clinical Endocrinologists (16), and Associazione Medici Endocrinologi (17) suggest that the original cytologic diagnosis be accepted until the nodule grows or changes in appearance. Instead of routine repeat aspiration, several researchers (17–20) recommended the judicious use of repeat aspiration and clinical follow-up. Several investigators (21–23) have demonstrated that combined ultrasonographic (US) and cytologic information could achieve more timely detection of thyroid cancer; however, to our knowledge, these studies had small sample sizes (21–23), wide ranges of nodule sizes (21–23), or no concrete guidelines for the management of thyroid nodules with benign cytologic results (22, 23). The aim of our study was to investigate the value of US features in thyroid nodules with initially benign cytologic results.

### Materials and Methods

#### Study Population

Our institutional review board approved this retrospective study and required neither patient approval nor informed consent for the review of images and records. However, informed consent for FNAB was obtained from all patients prior to biopsy. From October 2003 to February 2006, 6118 focal thyroid nodules in 6025 consecutive patients underwent US-guided FNAB at Severance Hospital (Seoul, Korea). Of 4065 focal thyroid nodules with benign cytologic results, 3540 measured 1 cm or greater in maximum diameter at initial aspiration. Benign cytologic results included colloid nodules, adenomatous hyperplasia, lymphocytic thyroiditis, Graves disease, and postpartum thyroiditis. Of the nodules examined, 2136 were excluded owing to a lack of further evaluation, such as surgery, follow-up FNAB, or follow-up US; 60 nodules were excluded because they showed an increase in size at follow-up US but underwent no further cytologic or pathologic evaluation. One nodule was excluded because it showed follicular neoplasm at follow-up cytologic evaluation but was not treated by means of surgery. This study included 1343 thyroid nodules in 1324 patients (1193 women, 131 men) (Fig 1). Mean age of all patients was 48.9 years (range, 14–81 years), mean age of male patients was 49.3 years (range, 16–76 years), and mean age of female patients was 48.8 years (range, 14–81 years). The mean lesion size was 22.2 mm (range, 10–60 mm).

#### Imaging Surveillance

US images were obtained by using a 7- to 15-MHz linear array transducer (HDI 5000; Philips Medical Systems, Bothell, Wash.), an 8- to 15-MHz linear array transducer (Acuson Sequoia; Siemens Medical Solutions, Mountain View, Calif), or a 5- to 12-MHz linear array transducer (IU22; Philips Medical Systems) for evaluation of thyroid glands and necks. Conebeam imaging was performed for all cases that used the HDI 5000 or IU22 transducer.

Real-time US was performed by one of three radiologists (K.M.J., K.J.Y., and K.E.K., with 4, 6, and 10 years experience in thyroid imaging, respectively) who were aware of the clinical history of the patient. At our institution, all US measurements of a mass were obtained at the longest aspect. The length, width, and depth of each nodule were evaluated on US images. Nodule volume was calculated by using the formula for a prolate ellipsoid (length × width × depth × π/6) (24–26). Two radiologists (K.J.Y. and K.E.K.) dedicated to thyroid imaging independently reviewed US features that were obtained at both initial and follow-up US. If there was disagreement about characteristics, the radiologists reached a consensus after discussion. We did not evaluate interobserver variability because they had

#### Advances in Knowledge

- The likelihood of a truly benign nodule when the initial fine-needle aspiration biopsy (FNAB) result was benign was 98.1%; this likelihood increased to 100% when the nodule was benign at both initial and repeat FNAB.
- The risk of malignancy was lower for negative US features (0.6%) when compared with positive US features (20.4%) in a thyroid nodule with benign cytologic results.

#### Implication for Patient Care

- Repeat FNAB should be performed for thyroid nodules with suspicious US features, even when the initial results indicate that the lesion is benign.
experience (more than 4 years of attendance at the same conferences) in communicating their analysis of US features of thyroid nodules and had established a consensus lexicon for US criteria. Focal thyroid nodules were interpreted by using US features, including internal components, echogenicity, margin, calcifications, and shape. Internal components were defined as solid, mixed, or cystic. A mass with mixed components indicated that the mass had both solid and cystic components. US analyses for masses with mixed components were evaluated on the basis of internal solid components. Malignant US features were defined as marked hypoechogenicity (decreased echogenicity compared with the surrounding strap muscle), a microlobulated or irregular margin, microcalcifications, and a greater anteroposterior than transverse dimension. A suspicious malignant nodule (positive US result) was defined if one of the above findings were present. If a nodule showed no suspicious features, it was classified as probably benign (negative US result). US features were determined on the basis of our previously published criteria (27). At follow-up US, we evaluated changes in size and shape of the thyroid nodules. We categorized a thyroid nodule as increased in size when its maximum diameter increased by more than 3 mm or its volume increased by more than 15% (26).

**US-guided FNAB and the Reference Standard**

After US evaluation of the thyroid gland, US-guided FNAB was performed by the same radiologists who evaluated the thyroid gland by using US alone. FNABS were performed either for thyroid nodules with suspicious US features or the largest thyroid nodule if no suspicious US features were detected. US FNAB was performed with a 23-gauge needle (Korea Vaccine, Seoul, Korea) attached to a 20-mL disposable plastic syringe (Kovax-Syringe, Korea Vaccine) and aspirator (CAMECO, Sebre Medical, Vellinge, Sweden). Each lesion was aspirated at least twice (range, 2–4 times). Materials obtained from the aspiration biopsy were expelled on glass slides and smeared. All smears were immediately placed in 95% alcohol for Papanicolaou staining. The remainder of the material was rinsed in saline for processing as a cell block. The cytopathologist was not on site during the biopsy. Additional special staining was performed on a case-by-case basis according to the cytopathologist’s needs. Five cytopathologists interpreted the FNAB slides. Malignant nodules were confirmed by means of surgery or repeat FNAB, while nodules were classified as benign if confirmed as benign by means of surgery or repeat aspiration or if nodules showed no interval change or decreased size at follow-up US.

There were 26 malignant and 1317 benign nodules. Of these, 122 were confirmed by means of surgery, 543 by means of repeat FNAB, and 678 at follow-up US. Of 122 thyroid nodules in 122 patients who underwent surgery, 23 were malignant (Table 1). The mean interval between initial and follow-up FNAB was 15.6 months (range, 3–51 months) in 543 thyroid nodules. The interval between first and repeat aspiration was more than 90 days for all patients to avoid nuclear atypia related to aspiration (28). More than two follow-up FNABs were performed in 94

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**Table 1**

<table>
<thead>
<tr>
<th>Histopathologic Result</th>
<th>No. of Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant nodule (n = 23)</td>
<td></td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>19 (82.6)</td>
</tr>
<tr>
<td>Follicular variant of papillary carcinoma</td>
<td>3 (13)</td>
</tr>
<tr>
<td>Minimally invasive follicular carcinoma</td>
<td>1 (4.4)</td>
</tr>
<tr>
<td>Benign nodule (n = 99)</td>
<td></td>
</tr>
<tr>
<td>Adenomatous hyperplasia</td>
<td>87 (87.9)</td>
</tr>
<tr>
<td>Follicular adenoma</td>
<td>8 (8.1)</td>
</tr>
<tr>
<td>Thyroiditis</td>
<td>4 (4.1)</td>
</tr>
</tbody>
</table>

Note.—Percentages are in parentheses.
of 753 nodules. The mean interval between initial and follow-up US was 26.7 months (range, 3–60 months) in 678 thyroid nodules.

Statistical Analysis
We used the $\chi^2$ test to compare the risk of malignancy according to sex and US groupings. We also evaluated the risk of malignancy according to age and size by using the Student $t$ test for independent samples. Significance was assumed when the two-sided $P$ value was less than .05. Logistic regression analysis was performed to assess the odds ratio for the risk of malignancy. Odds ratios with relative 95% confidence intervals (CIs) were also calculated.

We calculated the likelihood of having a benign nodule in different subgroups that were subdivided by the number of aspirations, US features, and follow-up data. After estimating the likelihood for different conditions, we first compared the likelihood in thyroid nodules with initially benign cytologic results with those of the remaining subgroups. Second, we compared the likelihood of thyroid nodules with initially benign cytologic results at least twice with a nodule from the remaining subgroups. Finally, we compared the likelihood of thyroid nodules with initially benign cytologic results, negative US results, and no interval change at follow-up US with nodules that had initially benign cytologic results, negative US results, and increased size at follow-up US. We made these comparisons by using the $\chi^2$ test. Analysis was performed by using software (SAS, version 9.1.3; SAS Institute, Cary, NC).

Results
Final Cytopathologic Results
Ninety-seven nodules underwent operation without undergoing follow-up FNAB or follow-up US (Fig 2). The mean interval between initial FNAB and surgery was 2.7 months (range, 1–5 months). The reasons for performing surgery were as follows: relatively large nodule size (>2 cm, $n = 50$); other associated thyroid nodules with malignant or suspicious cytologic results ($n = 17$), suspicious US features ($n = 17$), and because of patient request ($n = 13$). The remaining 1246 nodules underwent follow-up US (Fig 2). Repeat aspirations were performed for 603 nodules. The causes for repeat aspiration were: the clinician’s or patient’s request ($n = 190$), relatively large nodule size (>2 cm, $n = 221$), suspicious US features ($n = 54$), or growth at follow-up US ($n = 138$). Twenty-five of 1246 nodules were treated by means of surgery during follow-up owing to malignant or suspicious cytologic results ($n = 9$), indeterminate cytologic results ($n = 5$), relatively large nodule size (>2 cm; $n = 9$), patient anxiety ($n = 1$), and increased size seen at follow-up US ($n = 1$).

There were 26 (1.9%) malignant and 1317 (98.1%) benign nodules (Table 2). The benign nodules were 22.3 mm ± 10.8, and were significantly larger than the malignant nodules (18.2 mm ± 8.7) ($P < .001$). However, there was no significant relationship between the risk of malignancy and either sex or age. Logistic regression analysis demonstrated that the odds ratios were 0.956 (95% CI: 0.912, 1.002; $P = .06$), 1.021 (95% CI: 0.987, 1.057; $P = .23$), 0.592 (95% CI: 0.201, 1.745; $P = .34$), and 45.588 (95% CI: 18.377, 111.874; $P < .001$) for size, age, sex, and US groupings, respectively.

Comparison with US Findings and Risk of Malignancy
There were 93 nodules with positive features and 1250 nodules with negative features determined on the basis of US (Table 2). The rate of malignancy was 1.9% (26 of 1343; 95% CI: 0.0127, 0.0282) for focal thyroid nodules with benign cytologic results. The risk of malignancy was lower for negative US features (0.6%; 95% CI: 0.0023, 0.0115) compared with positive US features (20.4%; 95% CI: 0.1277, 0.3005).

Table 2
Results of Groupings of Focal Thyroid Nodules Diagnosed as Benign at US FNAB

<table>
<thead>
<tr>
<th>Reference Standard</th>
<th>No. of Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant ($n = 26$)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>19</td>
</tr>
<tr>
<td>Negative</td>
<td>7</td>
</tr>
<tr>
<td>Benign ($n = 1317$)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>74</td>
</tr>
<tr>
<td>Negative</td>
<td>1243</td>
</tr>
</tbody>
</table>

Figure 2: Diagnostic algorithm for 1343 nodules.
The risk of malignancy in a thyroid nodule with negative results at initial US and increased in size at follow-up US was higher (1.4%; 95% CI: 0.0017, 0.0510) than the risk of thyroid nodules with negative results at initial US and showed no interval change or decrease in size (0.5%; 95% CI: 0.0015, 0.0105), but there was no significant difference ($P = .1778$) (Table 3). Of 139 nodules that increased in size at follow-up US, two were cancer: a papillary carcinoma and a follicular variant of papillary carcinoma, according to histologic results. The mean interval between initial US and follow-up US was 27.3 months (range, 7–70 months). The likelihood of having a nodule that had benign results at initial cytologic evaluation was significantly lower than the likelihood of thyroid nodules having benign cytologic results at least twice ($P = .001$) and that of thyroid nodules with benign cytologic and negative US results ($P = .002$, Table 3). The likelihood of a nodule that had benign cytologic results at least twice was not significantly higher than the likelihood of thyroid nodules having benign cytologic and negative US results without interval change ($P = .179$, Table 3). However, the likelihood of nodules demonstrating benign cytologic results at least twice was significantly higher than that of thyroid nodules with negative results at initial US and increased in size at follow-up US ($P = .001$) (Table 3, Figs 3 and 4).

### Table 3

<table>
<thead>
<tr>
<th>Benign Cytologic Result</th>
<th>No. of Nodules</th>
<th>No. of Ultimately Benign Nodules</th>
<th>Likelihood of Nodule Being Benign (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>At first aspiration</td>
<td>1343</td>
<td>1317</td>
<td>98.1</td>
<td>0.9718, 0.9873</td>
</tr>
<tr>
<td>At least twice</td>
<td>545</td>
<td>545</td>
<td>100</td>
<td>0.9933, 1.0000</td>
</tr>
<tr>
<td>At first aspiration + positive US result</td>
<td>93</td>
<td>74</td>
<td>79.6</td>
<td>0.6995, 0.8723</td>
</tr>
<tr>
<td>At first aspiration + negative US result</td>
<td>1250</td>
<td>1243</td>
<td>99.4</td>
<td>0.9885, 0.9977</td>
</tr>
<tr>
<td>At first aspiration + negative US + no interval change at follow-up US</td>
<td>1111</td>
<td>1106</td>
<td>99.5</td>
<td>0.9895, 0.9985</td>
</tr>
<tr>
<td>At first aspiration + negative US + increased in size at follow-up US</td>
<td>139</td>
<td>137</td>
<td>98.6</td>
<td>0.9490, 0.9983</td>
</tr>
</tbody>
</table>

![Figure 3](image)

**Figure 3:** US (a, transverse; b, longitudinal) scans in 51-year-old woman show 2.4-cm well-defined mixed-echoic hypoechoic nodule (arrows) in right lobe of thyroid gland. Initial cytologic result was adenomatous hyperplasia, confirmed after 11 months at repeat aspiration.

![Figure 4](image)

**Figure 4:** US (a, transverse; b, longitudinal) scans in 49-year-old woman show 1.0-cm irregular, hypoechoic nodule (arrows) with microcalcifications (arrowheads) in right lobe of thyroid gland. Initial cytologic result was adenomatous hyperplasia; surgical results confirmed papillary carcinoma.
nodule with benign cytologic and negative US results with interval change ($P = .041$, Table 3).

**Repeat Aspiration**

The results of repeat aspirations are shown in Figure 5. There were 562 adequate and 41 inadequate results. Changes in cytologic diagnoses were demonstrated in 12 nodules (from benign to suspicious for malignancy or malignancy) and in five nodules (from benign to follicular neoplasm). Of 603 thyroid nodules with repeat aspirations, 54 had suspicious US features and 549 did not (Fig 6). However, all 545 thyroid nodules with benign cytologic results at repeat aspiration revealed benign results on the basis of standard results, irrespective of US features (Fig 5).

**Discussion**

FNAB is a method used worldwide to diagnose thyroid nodules but it has limitations, such as false-positive (1,2), FN (1–3), and inadequate results (1,2,4,5). The causes of false-positive and FN results are the nature of the lesions, intrinsic limitations of the procedure, and the manner, skill, and experience of the operator (7). False-positive results can also result from interpretation errors made by the cytologists (7). Because some malignant cytologic features, such as chromatin clearing and nuclear grooves, can be seen in benign thyroid nodules (29), false-positive cytologic outcomes cannot be avoided in some cases. The main problem with FN results for a thyroid nodule is that it can result in delayed diagnosis of thyroid cancer. Although most thyroid cancers are slow growing and have a good prognosis, even a small thyroid cancer can metastasize to other organs (30–32). Therefore, it is important to reduce the FN rate of FNAB. Higher FN rates tend to occur when using palpation rather than US guidance during examination (33,34). FNAB FN results can also result from the subtle cytologic features of papillary thyroid carcinoma, especially follicular variants (7,35). Therefore, cytologic-clinico-radiologic correlation can be an important follow-up step to control these errors (23). In this study, we observed a FN rate of 1.9%, which was lower than those in previous reports (range, 2.3%–6.2%) (7–9).

Many reports described suspicious US features, such as microlobulated or irregular margins (27,36–40), hypoecho- genicity (27,36–38), microcalcifications (27,36,37,39,42,43), solid nature (37,39,44), a taller-than-wide shape (27,41), and intratumoral vascularity (36,38,44). To differentiate benign from malignant nodules, several authors suggested combined analysis of several US features (27,36,45). In our study, we used the US classification described by Kim et al (27) because of its simplicity and high diagnostic accuracy.

To decrease the FN rate of FNAB, some authors recommend routine repeat aspirations (12,13). However, routine rebiopsy may not be a viable option because of its low cost-effectiveness. Many organizations, such as the American Thyroid Association (15) and American Association of Clinical Endocrinologists, (16) and several authors (46,47) suggest that thyroid nodules with benign cytologic results can be monitored with follow-up observations until they show an increase in size at US. It would be helpful to have guidelines to determine when each of the above approaches is appropriate. Several authors (17–20,23) recommend the judicious use of repeat aspiration and clinical follow-up. Oertel et al (18) suggested that repeat
aspiration should be performed for a thyroid nodule with initial benign cytologic results under the following conditions: (a) an increase in size, firmness, or other worrisome clinical changes; (b) the nodules did not respond to suppressive therapy; (c) the patient or the physician requested the procedure; and (d) results that did not make sense to the referring physician. However, Oertel et al did not provide statistical data. To reduce the FN rate of FNAB effectively, US information could be useful in thyroid nodules with benign cytologic results depending on whether repeat aspiration could be performed and could reduce the FN rate at the nodule. A recent report demonstrated that the risk of malignancy was different for thyroid nodules with the same cytologic results according to the presence of suspicious US features. However, this report included only surgically confirmed thyroid nodules and had a relatively small sample size with a wide range of nodule sizes. In our study, we included thyroid nodules that were both pathologically confirmed and followed up with US. We found that malignant nodules were smaller than benign nodules.

In our study, the likelihood of a truly benign nodule when the initial FNAB result was benign was 98.1%. When a thyroid nodule was benign at both initial and repeat FNAB, the likelihood increased to 100%. Oertel et al demonstrated that the likelihood was 90% (512 of 570) in a thyroid nodule with benign results at first FNAB and 98% (124 of 126) in a thyroid nodule with benign results at both initial and repeat FNAB. The likelihoods in our study were slightly higher than those of Oertel et al. This may be a result of a difference in the inclusion criteria between the study groups. Our study included thyroid nodules treated by means of surgery or FNAB or US follow-up while the study by Oertel et al included thyroid nodules treated by means of surgery only. Although the likelihood of an ultimately benign nodule was statistically higher for a thyroid nodule with benign results at both initial and repeat FNAB when compared with initial FNAB only (18), repeat aspiration of all thyroid nodules with benign results at initial FNAB is inadvisable owing to its low cost-effectiveness. Therefore, we evaluated the most efficient approach to decrease the FN rate of FNAB and avoid unnecessary repeat FNAB by using US features for evaluation. As expected, the likelihood of a nodule being benign was statistically higher (99.4%) for thyroid nodules with benign results at first FNAB and positive US features (79.6%, \( P < .001 \)). Furthermore, when thyroid nodules with initially benign FNAB results and negative US features showed no interval changes at follow-up US, the likelihood of the lesions being benign was extremely high (99.5%). When a thyroid nodule with negative US features increased in size at follow-up US, the risk of malignancy was 1.4% (two of 139). However, there was no significant risk of malignancy for a thyroid nodule with negative US features between no interval changes and increase in size at follow-up US. There were no significant differences between the likelihoods of a thyroid nodule that showed benign cytologic results two or more times and initial benign cytologic results with negative US features without interval change at follow-up US. In our study, we found that US features were extremely helpful in deciding whether repeat aspiration should be performed; therefore, we suggest repeat aspiration be performed on a thyroid nodule with benign cytologic results when it has suspicious US features.

Results from many reports (15,16, 18,46,47) suggest that an increase in nodule size is an important factor for determining whether repeat aspiration should be performed or not, even though an increase in nodule volume not indicate a malignancy (26). There is no consensus on what threshold level should be used to characterize clinically important nodule growth. Results from some reports (26,48) suggest that the definition of nodule growth should be a 15% increase in nodule volume or a 20% increase in nodule diameter with a minimum increase in two or more dimensions of at least 2 or 3 mm. We defined an increase in size as an increase of at least 3 mm on US images or a 15% increase in nodule volume. Of 139 nodules that increased in size and led to several biopsies, only two of these actually turned out to be cancerous. This suggests that our policy of closely following nodules and looking for growth has little value.

There were several limitations to this study. First, five cytopathologists interpreted the FNAB slides at our hospital, resulting in variability in interpretations of FNAB results. This kind of interobserver variability has been reported for follicular-patterned thyroid nodules (49–52). Second, we did not evaluate the causes of FN results. Several reports demonstrated that these causes included sampling errors, suboptimal smears, nonstrict criteria of specimen accuracy, and the inevitable limitations of cytologic interpretation (7,35,33,54). Retrospective cytologic evaluations of FN results can be helpful in reducing diagnostic error. Third, 60 nodules that showed growth at follow-up US were excluded owing to a lack of further cytologic or pathologic evaluation. Therefore, we could not calculate the exact rate of malignancy for thyroid nodules that showed an increased size at follow-up. Fourth, we could not evaluate the timeframe of repeat aspiration in a thyroid nodule with a suspicious US feature, although the interval between first and repeat aspiration should be more than 90 days to avoid nuclear atypia related to aspiration (28). Further prospective studies will be needed. Fifth, we regarded nodules with no growth at follow-up with a mean of 7–70 months as benign. Realistically, some of these nodules likely contained cancers that could have been found if all of the nodules had undergone biopsy. The final limitation of our study was that we followed up only a subset of our population. Because a large proportion (2136 cases) of our initial population did not undergo follow-up, there could be bias in the sample owing to attrition.

In conclusion, if the initial biopsy is negative and there is no suspicious US feature in a thyroid nodule, the risk...
of malignancy is extremely low (0.6%). However, if the nodule has suspicious US features, it needs to be subjected to repeat biopsy, and one could expect a positive rate of 20%. Therefore, repeat FNAB should be performed for thyroid nodules with suspicious US features, even when the initial FNAB results indicate that the lesion is benign.

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