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**Abbreviation:**

FNA = fine-needle aspiration

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## Management of Thyroid Nodules Detected at US: Society of Radiologists in Ultrasound Consensus Conference Statement<sup>1</sup>

The Society of Radiologists in Ultrasound convened a panel of specialists from a variety of medical disciplines to come to a consensus on the management of thyroid nodules identified with thyroid ultrasonography (US), with particular focus on which nodules should be subjected to US-guided fine needle aspiration and which thyroid nodules need not be subjected to fine-needle aspiration. The panel met in Washington, DC, October 26–27, 2004, and created this consensus statement. The recommendations in this consensus statement, which are based on analysis of the current literature and common practice strategies, are thought to represent a reasonable approach to thyroid nodular disease.

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The Society of Radiologists in Ultrasound convened a panel of specialists from a variety of medical disciplines to come to a consensus about management of thyroid nodules identified at thyroid ultrasonography (US). The panel met in Washington, DC, October 26–27, 2004, and created this consensus statement. While many facets of the management of thyroid nodular disease could have been considered by such a panel, this conference was convened to determine which thyroid nodules should undergo US-guided fine-needle aspiration (FNA) and which need not undergo FNA.

Several US characteristics have been studied as potential predictors of thyroid malignancy (1–6). Although there are certain trends in the US distinction of benign and malignant thyroid nodules, there is also overlap in their appearances. Because of the inconsistent predictive value of US features, most agree that FNA and cytopathologic evaluation of a thyroid nodule are usually required before a patient undergoes surgical resection for a possible thyroid malignancy. The widespread use of FNA and cytopathologic analysis has improved the detection of thyroid cancer and has led to a decreased frequency of thyroid surgery and increased cancer rates at thyroidectomy (7–10). However, the importance of early diagnosis of thyroid cancer in patients at low risk remains uncertain because thyroid cancers are typically slow growing and are associated with low morbidity and mortality.

This consensus panel attempted to define recommendations based on nodule size and US characteristics for those thyroid nodules that should undergo US-guided FNA and for those nodules that need not undergo FNA. In this statement, we not only present the recommendations of the consensus panel along with background information and explanations but also suggest topics for future research.

### METHODS AND CONFERENCE PREPARATIONS

The panel consisted of the director (M.C.F.), codirector (C.B.B.), and 19 panelists, all of whom have specialty experience in thyroid nodule evaluation and/or treatment. The panel members were from several medical disciplines, including radiology, endocrinology, cytopathology, and surgery. Prior to the conference, 14 recent articles related to thyroid nodular disease and US evaluation of thyroid nodules were selected by the conference director and codirector and were sent to conference participants (1–4,6,9,11–18). In

addition, a summary of several studies and an abstract that assessed US features associated with thyroid cancer and provided adequate data to determine sensitivity, specificity, and positive and negative predictive values were compiled and provided to participants (1–6) (Table 1).

The consensus conference took place on October 26–27, 2004, in Washington, DC. An audience consisting of invited representatives from medical specialty societies and industry observed the proceedings. The 1st day of the conference was devoted to presentations and discussion on the epidemiology of thyroid nodules and cancer, US characteristics of thyroid cancer, cytopathology issues related to thyroid FNA, and medical and surgical management of nodular thyroid disease. At the end of the 1st day, a subset of panelists spent the evening drafting a consensus statement. This statement was discussed by the entire group the following morning until the group arrived at a consensus.

## BACKGROUND AND SUMMARY OF THE LITERATURE

### Clinical Epidemiology of Thyroid Nodules and Cancer

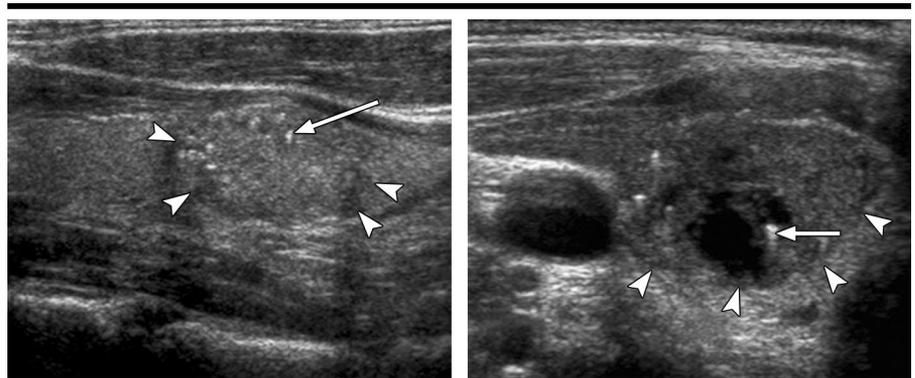
Thyroid nodules are very common: They are found in 4%–8% of adults by means of palpation, in 10%–41% by means of US (19–23), and in 50% by means of pathologic examination at autopsy (24). The prevalence of thyroid nodules increases with age. The likelihood that a nodule is malignant is affected by a variety of risk factors. Malignancy is more common in nodules found in patients who are younger than 20 or older than 60 years of age than in patients between 20 and 60 years of age (25). Physical examination factors associated with increased likelihood of malignancy include firmness of the nodule, rapid growth, fixation to adjacent structures, vocal cord paralysis, and enlarged regional lymph nodes (25). In addition, a history of neck irradiation or a family history of thyroid cancer increases the risk that a thyroid nodule is malignant (26).

The overall incidence of cancer in patients with thyroid nodules selected for FNA is approximately 9.2%–13.0%, no matter how many nodules are present at US (3,25,27,28). This recent finding, based on the evaluation of large groups of patients undergoing thyroid US and US-guided FNA, contradicts the commonly held belief that the presence of

**TABLE 1**  
**US Features Associated with Thyroid Cancer**

| US Feature*                        | Sensitivity (%) | Specificity (%) | Positive Predictive Value (%) | Negative Predictive Value (%) |
|------------------------------------|-----------------|-----------------|-------------------------------|-------------------------------|
| Microcalcifications (1–5)          | 26.1–59.1       | 85.8–95.0       | 24.3–70.7                     | 41.8–94.2                     |
| Hypoechoogenicity (2–5)            | 26.5–87.1       | 43.4–94.3       | 11.4–68.4                     | 73.5–93.8                     |
| Irregular margins or no halo (2–5) | 17.4–77.5       | 38.9–85.0       | 9.3–60.0                      | 38.9–97.8                     |
| Solid (4–6)                        | 69.0–75.0       | 52.5–55.9       | 15.6–27.0                     | 88.0–92.1                     |
| Intranodule vascularity (3, 6)     | 54.3–74.2       | 78.6–80.8       | 24.0–41.9                     | 85.7–97.4                     |
| More tall than wide (2)            | 32.7            | 92.5            | 66.7                          | 74.8                          |

\* Numbers in parentheses are reference numbers.



**Figure 1.** Punctate echogenicities in thyroid nodules. **(a)** Sagittal US image of nodule (arrowheads) containing multiple fine echogenicities (arrow) with no comet-tail artifact. These are highly suggestive of malignancy. FNA and surgery confirmed papillary carcinoma. **(b)** Transverse US image of nodule (arrowheads) containing cystic areas with punctate echogenicities and comet-tail artifact (arrow) consistent with colloid crystals in a benign nodule.

multiple nodules decreases the likelihood of thyroid cancer (29). In patients with multiple nodules, the cancer rate per nodule decreases, but the decrease is approximately proportional to the number of nodules so that the overall rate of cancer *per patient*, 10%–13%, is the same as that in patients with a solitary nodule (27,28). While the thyroid cancers found in patients with multiple nodules are often in the dominant or largest nodule, in approximately one-third of cases the cancer is in a nondominant nodule. Thus, FNA interrogation only of the dominant nodule will result in detection only of approximately two-thirds of thyroid cancers in these patients (27).

Many patients present for US for evaluation of a suspected thyroid nodule found incidentally with other imaging tests, such as carotid US or cervical magnetic resonance imaging. In many cases, the nodules are not palpable. Several investigators (2,3,14,28) have demonstrated that the incidence of thyroid cancer in incidentally identified or non-

palpable thyroid nodules is the same as that in patients with palpable nodules.

Compared with the very high prevalence of nodular thyroid disease, thyroid cancer is not common. On the basis of American Cancer Society estimates, in 2005 25 690 new cases of thyroid cancer will be diagnosed, and 1460 patients will die of thyroid malignancy in the United States (30).

The majority (75%–80%) of new cases of thyroid cancer diagnosed in the United States in 2005 will be papillary thyroid cancer. Other histologic types of thyroid cancer include follicular (10%–20%), medullary (3%–5%), and anaplastic (1%–2%) cancers (30,31). The morbidity and mortality rates of thyroid cancer are low compared with the rates for many other cancers, but both increase with advancing age of the patient and stage of the disease (32). The most common follicular cell–derived cancer is papillary thyroid carcinoma, and it is generally accepted that the 30-year survival rate for this malignancy is approximately 95%

**TABLE 2**  
**Recommendations for Thyroid Nodules 1 cm or Larger in Maximum Diameter**

| US Feature  | Recommendation  |
|---|---|
| Solitary nodule   |   |
| Microcalcifications   | Strongly consider US-guided FNA if $\geq 1$ cm  |
| Solid (or almost entirely solid) or coarse calcifications                               | Strongly consider US-guided FNA if $\geq 1.5$ cm  |
| Mixed solid and cystic or almost entirely cystic with solid mural component             | Consider US-guided FNA if $\geq 2$ cm   |
| None of the above but substantial growth since prior US examination                     | Consider US-guided FNA  |
| Almost entirely cystic and none of the above and no substantial growth (or no prior US) | US-guided FNA probably unnecessary  |
| Multiple nodules  | Consider US-guided FNA of one or more nodules, with selection prioritized on basis of criteria (in order listed) for solitary nodule* |

Note.—FNA is likely unnecessary in diffusively enlarged gland with multiple nodules of similar US appearance without intervening parenchyma. Presence of abnormal lymph nodes overrides US features of thyroid nodule(s) and should prompt US-guided FNA or biopsy of lymph node and/or ipsilateral nodule.

\* Panel had two opinions regarding selection of nodules for FNA. The majority opinion is stated here.

(33). Most patients with papillary cancer (80%–85%) are considered to be low risk, with 99% survival at 20 years after surgery (34). Adjuvant radioiodine treatment after complete tumor removal at thyroidectomy improves disease-free survival in high-risk patients, with no clear survival benefit in low-risk patients (32,35,36). Suppression of thyroid-stimulating hormone with exogenous thyroid hormone is a routine postoperative practice that may further improve both overall and disease-free survival in patients with papillary or follicular cancer (37, 38).

### US Features of Thyroid Cancer

A thyroid nodule is a discrete lesion within the thyroid gland that is sonographically distinguishable from the adjacent parenchyma (Fig 1). For each thyroid nodule, gray-scale and color Doppler US are used to evaluate the US features, which include size, echogenicity (hypoechoic or hyperechoic), and composition (cystic, solid, or mixed), as well as presence or absence of coarse or fine calcifications, a halo, irregular margins, and internal blood flow.

Many studies have been published in which the ability to predict whether a thyroid nodule is benign or malignant on the basis of US findings was assessed (1–5,12,13,28,39–41). Nodule size is not predictive of malignancy, because the likelihood of cancer in a thyroid nodule has been shown to be the same regardless of the size measured at US (2,3,5,28). Several US features have been found to be

associated with an increased risk of thyroid cancer (Table 1), including presence of calcifications, hypoechogenicity, irregular margins, absence of a halo, predominantly solid composition, and intranodule vascularity. However, the sensitivities, specificities, and negative and positive predictive values for these criteria are extremely variable from study to study, and no US feature has both a high sensitivity and a high positive predictive value for thyroid cancer. The feature with the highest sensitivity, in the range of 69.0%–75.0%, is solid composition; however, this feature has a fairly low positive predictive value in that a solid nodule has only a 15.6%–27.0% chance of being malignant. The feature with the highest positive predictive value, 41.8%–94.2%, is the presence of microcalcifications; however, microcalcifications are only found in 26.1%–59.1% of cancers (low sensitivity). The combination of factors improves the positive predictive value of US to some extent (3,4). In particular, a predominantly solid nodule (<25% cystic) with microcalcifications has a 31.6% likelihood of being cancer, as compared with a predominantly cystic nodule (>75% cystic) with no calcification, which has a 1.0% likelihood of being cancer (5).

Color Doppler US has also been evaluated as a diagnostic tool for predicting thyroid cancer, with the hypothesis that flow that is predominantly at the periphery of a nodule is suggestive of a benign nodule, while flow predominantly in the central portion of the nodule is sugges-

tive of malignancy. The results of these studies are mixed, with some reporting that Doppler US is helpful (3,12,42,43) and others reporting that Doppler US did not improve diagnostic accuracy (13,41,44,45). In one study (6) in particular, central flow was seen in a higher percentage of malignant nodules than benign nodules (42% vs 14%). However, like other US features, color Doppler US cannot be used to diagnose or exclude malignancy with a high degree of confidence; rather, the color Doppler US finding of predominantly internal or central blood flow appears to increase the chance that a nodule is malignant.

### Cytopathologic Evaluation

FNA with cytologic evaluation has become the accepted method for screening a thyroid nodule for cancer, and, in the hands of an experienced cytologist, FNA has a high accuracy rate (7). Cytologic specimens are typically classified as negative (or benign), suspicious for cancer or follicular neoplasm, positive (or diagnostic for cancer), or nondiagnostic. In general, the false-positive rate for aspirates classified as positive for cancer is less than 1%. Of the aspirates read as suspicious for cancer, 30%–65% will prove to be cancer at surgery (7). Samples that are not suspicious or diagnostic for malignancy and that contain a smaller number of cells than required for diagnosis of a benign nodule must be considered nondiagnostic. Even in centers with substantial experience, the nondiagnostic rate may be as high as 15%–20% (46). The rate of cancer in surgically resected nodules with nondiagnostic FNA results is 5%–9% (47–49).

FNA is safe, accurate, and inexpensive. Complications of the procedure, such as hematoma or pain, are rare and usually minor. The use of US guidance ensures that the sample is obtained from the nodule in question and permits direction of the needle into the solid portions of partially cystic nodules, which will improve the diagnostic yield (10,17,50).

### CONSENSUS DISCUSSION AND STATEMENT

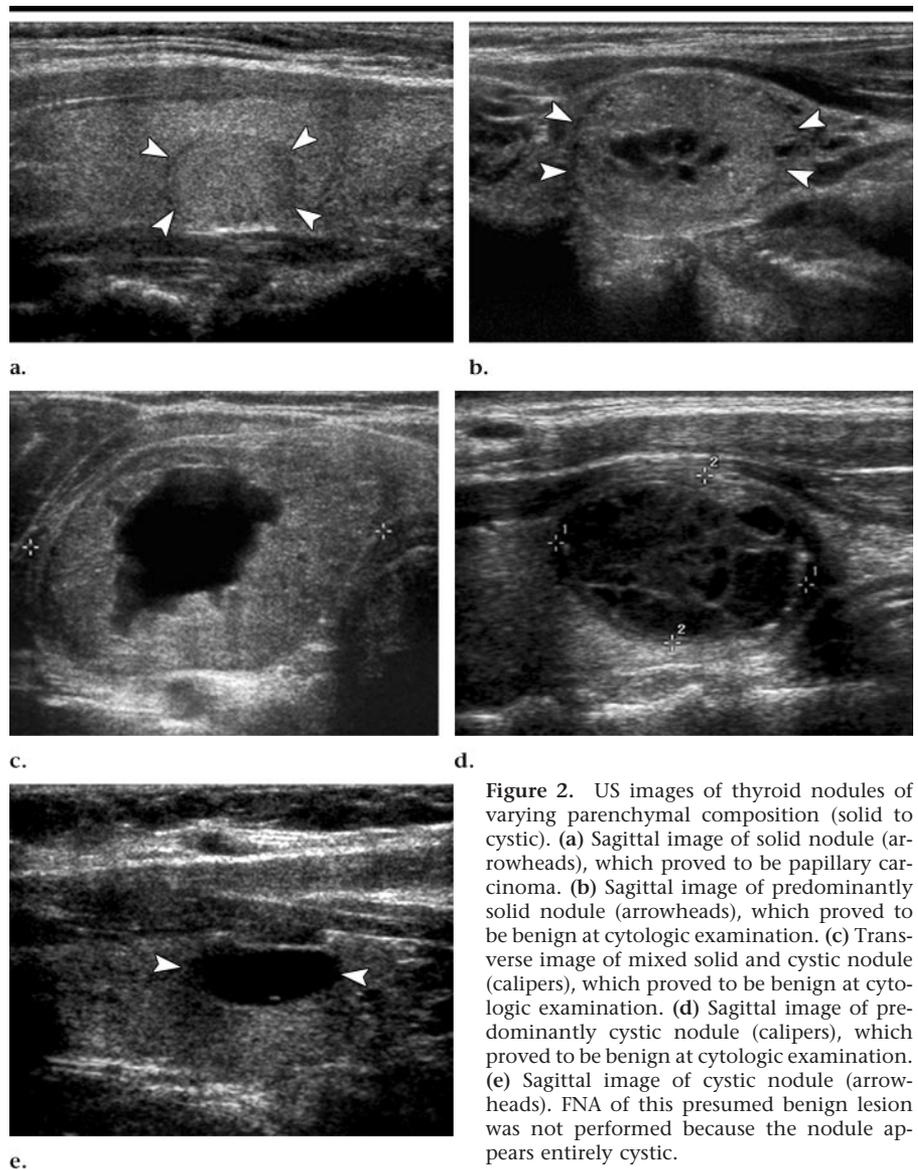
#### Discussion

The consensus statement was developed to assist physicians in deciding which thyroid nodules should undergo US-guided FNA and which nodules need not undergo FNA. The statement was developed on the basis of the state of knowledge and available data at the time

of the conference, and it is understood that as research continues and more information is obtained, recommendations regarding US-guided FNA of thyroid nodules may change. The recommendations allow physicians some flexibility in the selection of which nodules require FNA. The decision to perform or defer US-guided FNA for a particular thyroid nodule in a given patient should be made by the physician according to the individual circumstances.

The goal in evaluating a thyroid nodule is to determine whether it is benign or malignant so that patients with thyroid cancer can receive a diagnosis and undergo treatment at an earlier stage to reduce possible morbidity and mortality due to the disease, while avoiding unnecessary tests and surgery in patients with benign nodules. The panelists aimed to develop recommendations to achieve this goal, taking into account the fact that there are insufficient data to answer a number of related questions: Does diagnosis of microcarcinomas (<1.0 cm) or even of cancers smaller than 2.0 cm improve life expectancy in view of the fact that thyroid cancer tends to grow slowly and most of these patients have an excellent prognosis? Do the benefits of removing papillary thyroid cancers smaller than 1 cm outweigh the risks of more patients undergoing thyroid surgical procedures? If recommendations lead to an increased number of FNAs of thyroid nodules and subsequent thyroid surgery, what are the cost-benefit consequences, and how (if at all) should cost considerations be taken into account? The panelists considered these issues as they created the consensus statement.

For the purposes of these recommendations, a thyroid nodule is defined as any discrete lesion that is sonographically distinguishable from the adjacent thyroid parenchyma. These recommendations apply to nodules 1.0 cm in size or larger because of the uncertainty as to whether or not diagnosis of smaller cancers improves life expectancy, as well as concern that inclusion of smaller nodules would lead to an excessive number of biopsies. The size criteria for nodule selection were chosen on the basis of the risk of cancer associated with the US features. For nodules with US features associated with a higher risk of cancer, the size cutoff is smaller than that for nodules with features associated with benign cytologic findings. In particular, the presence of features most suggestive of malignancy (eg, microcalcifications) should prompt US-guided FNA at a smaller nod-



**Figure 2.** US images of thyroid nodules of varying parenchymal composition (solid to cystic). (a) Sagittal image of solid nodule (arrowheads), which proved to be papillary carcinoma. (b) Sagittal image of predominantly solid nodule (arrowheads), which proved to be benign at cytologic examination. (c) Transverse image of mixed solid and cystic nodule (calipers), which proved to be benign at cytologic examination. (d) Sagittal image of predominantly cystic nodule (calipers), which proved to be benign at cytologic examination. (e) Sagittal image of cystic nodule (arrowheads). FNA of this presumed benign lesion was not performed because the nodule appears entirely cystic.

ule size than for nodules without such features.

### Consensus Statement

The consensus statement is summarized in Table 2.

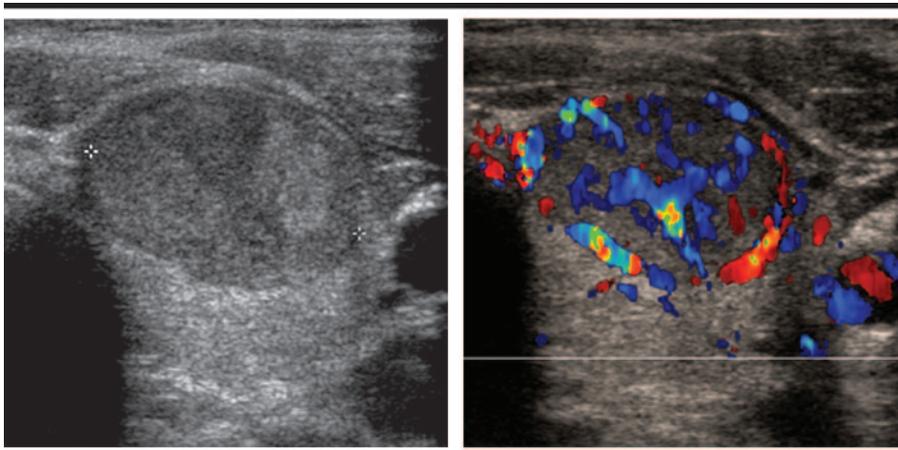
**Preamble.**—These are general recommendations for adult patients who have a thyroid nodule on US images, regardless of how the nodule was initially detected. The recommendations may not apply to all patients, including those who have historical, physical, or any other features suggesting they are at increased risk for cancer or who have a history of thyroid cancer.

**Part I.**—The following are general recommendations for nodules 1.0 cm or greater in largest diameter:

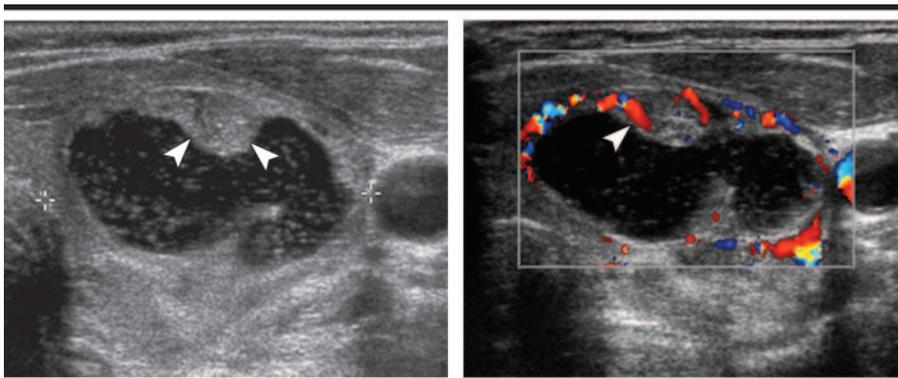
**Solitary nodule.**—Strongly consider FNA for (a) a nodule 1.0 cm or more in largest diameter if microcalcifications are present and (b) a nodule 1.5 cm or more in largest diameter if any of the following apply: (i) nodule is solid or almost entirely solid, or (ii) there are coarse calcifications within the nodule.

Consider FNA for (a) a nodule 2.0 cm or more in largest diameter if any of the following apply: (i) the nodule is mixed solid and cystic, or (ii) the nodule is almost entirely cystic with a solid mural component; or (b) the nodule has shown substantial growth since prior US examination.

FNA is likely unnecessary if the nodule is almost entirely cystic, in the absence of the above-listed features.



**Figure 3.** Role of color Doppler US. (a) Transverse gray-scale image of predominantly solid thyroid nodule (calipers). (b) Addition of color Doppler mode shows marked internal vascularity, indicating increased likelihood that nodule is malignant. This was a papillary carcinoma.



**Figure 4.** Transverse US images of mostly cystic thyroid nodule with a mural component containing flow. (a) Gray-scale image shows predominantly cystic nodule (calipers) with small solid-appearing mural component (arrowheads). (b) Addition of color Doppler mode demonstrates flow within mural component (arrowhead), confirming that it is tissue and not debris. US-guided FNA can be directed into this area. The lesion was benign at cytologic examination.

**Multiple nodules.**—Consider FNA of one or more nodules, with selection prioritized on the basis of the previously stated criteria in the order listed above. FNA is likely unnecessary in diffusely enlarged glands with multiple nodules of similar US appearance without intervening normal parenchyma.

Note that these recommendations are not absolute or inflexible. In certain circumstances, the physician's clinical judgment may lead him or her to determine that FNA need not be performed for nodules that meet the recommendations above. In others, FNA may be appropriate for nodules that do not meet the criteria listed above.

**Part II.**—The recommendation for nondiagnostic aspirates from initial FNA is as follows: Consider a second FNA of nod-

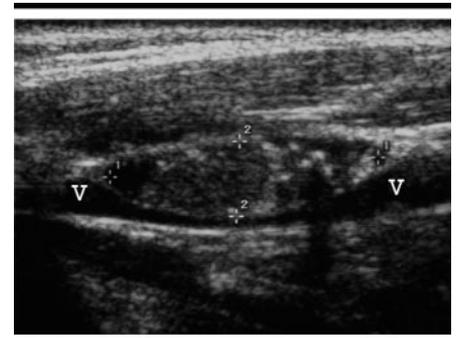
ules meeting criteria for FNA of solitary nodules, as outlined above.

**Part III.**—The presence of abnormal lymph nodes overrides the US features criteria and should prompt biopsy of the lymph node and/or (if necessary) of an ipsilateral thyroid nodule.

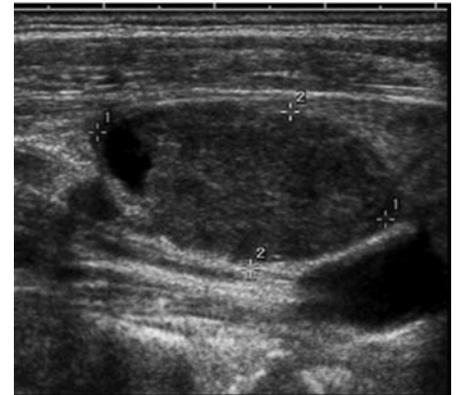
**Explanations**

**Measurements.**—Nodules should be measured with the calipers placed outside of any visible halo. The maximum diameter should be used when considering whether or not US-guided FNA should be performed.

**Calcification.**—The presence of any calcification within the nodule raises the likelihood of malignancy. In particular, microcalcifications in a predominantly



a.



b.

**Figure 5.** Abnormal cervical lymph nodes. (a) Sagittal US image of enlarged node (calipers) with central punctate echogenicities, consistent with microcalcifications, shows mass effect on internal jugular vein (V). Node was proved to be metastatic papillary carcinoma. (b) Sagittal US image of enlarged node (calipers) with cystic component. Node was proved to be metastatic papillary carcinoma.

solid nodule (Fig 2a) are associated with an approximately threefold increase in cancer risk and coarse calcifications are associated with a twofold increase, as compared with predominantly solid nodules without calcifications (5). Microcalcifications likely represent multiple calcified psammoma bodies, which are typical of papillary thyroid cancer (51). Care must be taken to differentiate these fine punctate calcifications, which are individually too small to induce posterior acoustic shadowing, from echogenic foci with posterior comet-tail artifacts, which are commonly seen in benign cystic or partially cystic nodules (40) (Fig 2b). In the absence of comet-tail artifacts, tiny echogenicities must be assumed to be calcifications when considering the risk of cancer. There are insufficient data to know whether intense rim calcification, as opposed to calcifications within the nodule, is associated with malignancy.

**Composition.**—Each nodule should be

evaluated with regard to the fraction of the nodule that is solid versus the fraction that is cystic. Nodules can be classified semiquantitatively, according to the estimated percentage of solid or cystic composition or in descriptive terms based on the predominant composition (eg, solid, predominantly solid, mixed solid and cystic, predominantly cystic, and cystic) (Fig 2). Solid or predominantly solid nodules have a higher risk of malignancy than do mixed or predominantly cystic nodules. Cystic and almost completely cystic nodules have a very low likelihood of being malignant. Nodules with mixed composition have an average risk of malignancy. For this reason, the recommended minimal size for US-guided FNA is lower for solid or predominantly solid nodules than the recommended minimal size for mixed solid and cystic nodules.

**Color Doppler US.**—When color Doppler US is included in the evaluation of a thyroid nodule, available research indicates that marked internal flow suggests an increased likelihood of malignancy, as compared with the absence of marked internal flow. Marked internal flow is defined as more flow in the nodule than in the surrounding thyroid gland and more flow in the central part of the nodule than at the periphery (Fig 3). Appropriate Doppler US technique is imperative for accurate assessment of nodule vascularity, with color Doppler gain settings maximized for slow flow. Color Doppler US is also useful for evaluating mixed cystic and solid nodules and predominantly cystic nodules with a focal area that appears solid. This will help differentiate solid tissue, which will have blood flow, from an avascular blood clot or debris (Fig 4). When US-guided FNA is performed on such nodules, the needle should be directed toward the regions with visible flow, to increase the likelihood of a diagnostic aspirate. While occasionally useful in selecting nodules for US-guided FNA, color Doppler US should not be considered a requirement for the selection of nodules for sampling.

**Interval growth.**—The panelists agreed that US-guided FNA should be considered for nodules demonstrating substantial growth on serial US studies, even if a prior FNA result was benign. Although the natural history for both benign and malignant nodules is growth over time (16), rapid growth of a nodule indicates an increased risk for malignancy (15,52). The panelists did not come to a consensus on how to define substantial growth

for the consensus statement, nor on how to monitor growth.

**Multiple nodules.**—In many patients, more than one nodule is identified or the gland appears diffusely enlarged with multiple nodules of similar US appearance without intervening normal parenchyma. The panel agreed that FNA is likely not necessary in the latter setting. In patients with multiple discrete nodules, the panel had two opinions regarding selection of nodules for FNA. The majority opinion was that the selection should be based primarily on US characteristics other than nodule size (5). Thus, a solid nodule with microcalcifications should be selected for FNA before a larger mixed cystic and solid nodule without calcifications. The minority opinion was that the largest nodule should undergo US-guided FNA, and the selection of other nodules for US-guided FNA should be based on US characteristics.

**Abnormal cervical lymph nodes (excluding submandibular nodes).**—The presence of abnormal cervical lymph nodes overrides the recommendations in parts I and II of the statement and should prompt biopsy of the abnormal lymph nodes and/or an ipsilateral thyroid nodule of any size. On occasion, a patient has an abnormal lymph node representing metastatic thyroid cancer and a sonographically normal gland, because the primary tumor is not visible at US. US diagnosis of an abnormal lymph node depends on size, shape, vascularity, and internal architecture (53,54). The US features associated with the highest risk of cancer include heterogeneous echotexture, calcifications, and cystic areas within the lymph node (Fig 5). A rounded lymph node or one causing a mass effect is also at elevated risk of being malignant. In general, size is a less reliable criterion for malignancy in a lymph node than are shape and architecture, although the chance of malignancy increases as the size of the lymph node increases. Thus, lymph nodes should be considered suspicious if they measure more than 7 mm in the short axis (54).

### Research Topics

The panel identified several important unanswered questions that merit future research.

1. How should *substantial growth* be defined? In particular, if a nodule has a prior FNA diagnosis of being benign, how much growth over what period of time should prompt consideration for repeat US-guided FNA? What measurements or

calculations should be used to monitor growth: maximum diameter, average diameter, or volume?

2. In a patient with multiple nodules, which and how many nodules should undergo US-guided FNA? Strategies for follow-up in patients with multiple nodules should be devised.

3. Are there other US characteristics of a nodule that might be used to prove a nodule is benign, thus precluding FNA in some other patients besides those with almost entirely cystic nodules? Are there combinations of US characteristics that might be used to help direct management?

4. What is the cost-effectiveness of various approaches to the diagnosis of solitary and multiple nodules?

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