# Innovations in Modern Endocrine Surgery

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*Editors*

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ISBN 978-3-030-73950-8 ISBN 978-3-030-73951-5 (eBook)
https://doi.org/10.1007/978-3-030-73951-5



This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

*David J. Terris*

*To my family, friends, colleagues, trainees, and the many patients who were so generous in allowing me to learn from them over three decades. And finally, a special acknowledgment to three very important people in my life – Amy, Bill, and Dick*

*Michael C. Singer*

*To my parents, David and Judy Singer, and in-laws, Sam and Brenda Gewurz, whose common values of love of family, concern for the welfare of others, and living lives of principle have provided a framework for my personal and professional life. Your impact knows no bounds.*

# Preface

Over the past two decades, the care of patients with thyroid and parathyroid diseases has been transformed. Molecular, diagnostic, radiological, and surgical developments that touch on all elements of the care of these patients have resulted in improved outcomes and satisfaction.

While surgeons performing thyroid and parathyroid surgery may endeavor to remain abreast of all the advances in the field, staying current can be challenging. This book was conceived as a single resource for surgeons seeking to understand the latest developments and trends in the field. This book is the first to focus on the range of innovations that have been critical to the emergence of modern endocrine surgery. Fortunately, the authors of many of the chapters are the experts who have been the primary proponents of the individual innovations. This allows them to place these developments in their proper context, crucial to understanding their value and proper application.

Equipped with the knowledge provided by this text, surgeons can assess their own practice and choose to integrate innovations that may improve their patients' outcomes.

Detroit, MI, USA — Michael C. Singer
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# Part I
# Diagnosis and Preoperative Work-up of Thyroid Disease

# Chapter 1
# Ultrasound for Thyroid Nodule Risk Stratification


**Poorani N. Goundan and Stephanie L. Lee**

## Introduction

Ultrasound (US) is the imaging modality of choice and the standard of care for evaluating thyroid nodules. While thyroid nodules are a common occurrence, only about 5% are malignant. Historically, in order to stratify a patient's risk for thyroid cancer, physicians would consider their clinical history, family history, and physical examination. However, these factors provided only a limited ability to discriminate between benign and malignant nodules. The development of a noninvasive tool for cancer risk assessment became a necessity to reduce the number of invasive procedures including biopsy and surgical resection [1, 2].

In the 1950s, Blume and colleagues showed that one of the earlier versions of US technology, A-mode scanning, could provide the distance of a refractile surface to a US probe. Based on this capability, the detection and measurement of a single dimension of a thyroid nodule was possible [3]. The introduction of B-mode imaging allowed the creation of two-dimensional images by combining serial A-mode images [4]. It was in the 1960s that US technology was first applied to the evaluation of thyroid nodules. Fujimoto et al., in 1967, published their data on 184 patients and described four basic patterns of thyroid nodules: cystic, sparsely spotted, increased attenuation without internal echos and malignant [5]. Essentially, the technology at the time could identify large nodules, but did not provide adequate resolution to discriminate between benign and malignant nodules.

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M. C. Singer, D. J. Terris (eds.), *Innovations in Modern Endocrine Surgery*,
https://doi.org/10.1007/978-3-030-73951-5_1

The development and application of gray-scale imaging in the 1970s allowed for more granular characteristics of thyroid nodules to be recognized and improved correlation with histopathologic findings [6, 7]. Over the following decades, gray-scale US has been further refined with the development of higher-frequency probes and post-imaging enhancement such as tissue harmonic and compound spatial imaging [8, 9]. In an effort to further increase the discriminatory value of US and aid in estimating malignancy risk, gray-scale imaging has been combined with other US modalities, including Doppler analysis and elastography, and with fine-needle aspiration (FNA). To consolidate our knowledge regarding US features and the risk of cancer, several risk stratification systems have been developed [10–14].

This chapter will discuss the current role thyroid US plays in the management of thyroid nodules and will highlight possible future directions of this technology.

## Ultrasound Setting and Image Acquisition

In order to obtain quality and consistent images, patient positioning and US settings need be optimized prior to acquiring US images. The patient's neck should be hyperextended, which may be facilitated by placing a pillow behind their shoulders. High-resolution US typically uses US frequencies between 10 and 15 MHz or higher for imaging the thyroid gland. The focus and frequency of the sound waves and gain should be adjusted to the level of structures being imaged. Adjustment of the focus to the depth of the nodule is critical to detect and characterize the fine details of the nodule, echogenicity and margins of a nodule (Fig. 1.1). A complete US exam of the thyroid gland includes visualization of thyroid and perithyroidal structures and characterization of the cervical lymph nodes. A final US report should include a description of the thyroid gland parenchyma and its dimensions, a detailed description of relevant thyroid nodules, and information regarding the presence or absence of abnormal cervical adenopathy.

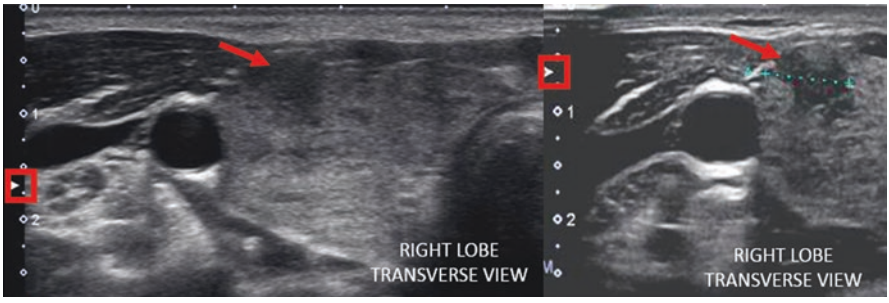



**Fig. 1.1** Difference in quality and resolution of images between (**a**) sub-optimal US settings using a 14 MHz probe and incorrect focus (red box) and (**b**) optimal US settings using an 18 MHz probe and correct focus (red box) in a thyroid gland with a hypoechoic anterior nodule with infiltrative margins (arrow) with a heterogeneous background of Hashimoto's thyroiditis

## Gray-scale Ultrasound Characteristics of Thyroid Nodules

Individual US characteristics have variable sensitivity, specificity and positive predictive value (PPV) for thyroid cancer (Table 1.1) [15–19]. The description, US examples, and interpretation of cancer risk of these characteristics are discussed in Table 1.2. High-risk US features for malignancy include a solid composition, hypoechogenicity, taller than wide dimensions, irregular margins, and microcalcifications. Interrupted peripheral macrocalcification, particularly when seen with extranodular soft tissue extrusion, is a high-risk US feature, while isolated intranodular macrocalcification is not [20, 21]. Most US features that we associate with thyroid cancer identify the most common type of thyroid cancer, papillary thyroid cancer (PTC), in particular the classic type. Other less prevalent thyroid cancers including follicular thyroid cancers (FTC), follicular variants of PTC, and noninvasive follicular neoplasms with papillary-like features (NIFTP) may be hypoechoic but are more often iso- or hyperechoic and are not associated with microcalcifications [18, 22, 23]. While medullary thyroid cancers tend to be hypoechoic and contain intranodular calcifications, their US features are less well defined [24].

There are several US features that are associated with benign nodules (Figure 1.2a–c). Purely cystic or spongiform nodules never or rarely require FNA, as their risk of malignancy is very low. A colloid comet, a US artifact due to reverberation of echo signals in colloid, is a benign finding. However, these can be difficult to distinguish from hyperechoic, non-shadowing microcalcifications, which are potentially associated with cancer. Importantly, indistinct margins must be distinguished from infiltrative margins. While indistinct margins are not specifically a characteristic of low-risk thyroid nodules, they usually occur in confluent isoechoic adenomatous nodules and are not a high-risk feature for malignancy.

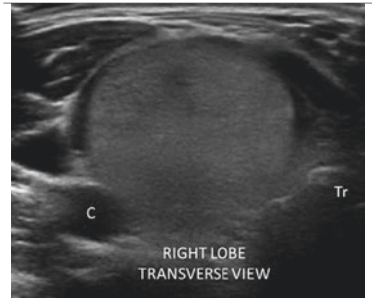
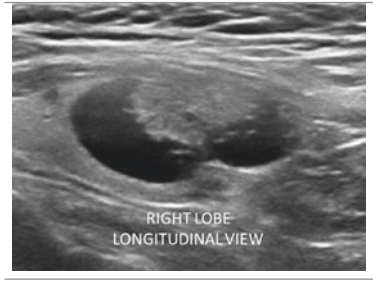
US interpretation is both instrument and operator dependent. Studies have demonstrated interobserver variability that is more evident with certain US features such as nodule volume, margins, and the presence of microcalcifications [25–27]. To try to minimize this interobserver variability seen when interpretation is done by a physician, the use of machine learning for US characteristic and pattern recognition has begun to be investigated [28, 29].

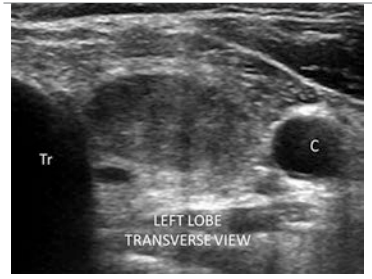
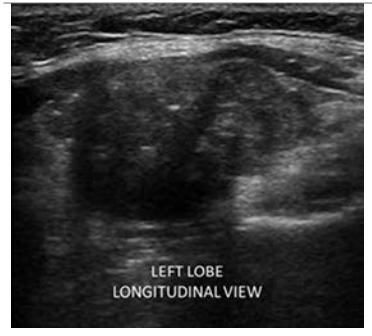
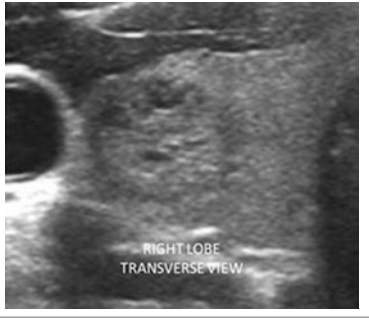
**Table 1.1** Individual ultrasound characteristics of thyroid nodules and risk for thyroid cancer*

| Nodule characteristic | Sensitivity | Specificity | PPV |
|---|---|---|---|
| Hypoechogenicity | 68–87% | 43–81% | 11–61% |
| Marked hypoechogenicity (similar to strap muscle) | 27–69% | 92–98% | 68–96% |
| Solid consistency | 89–91% | 33–58% | 26–39% |
| Microcalcification | 36–59% | 86–98% | 39–85% |
| Macrocalcification | 2–10% | 96–98% | 25–65% |
| Irregular/microlobulated margins | 48–84% | 83–92% | 30–81% |
| Taller than wide configuration on transverse view | 32–64% | 91–100% | 67–100% |

* [15–19]

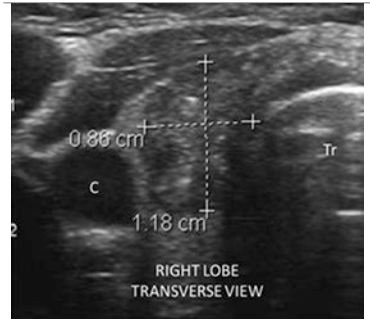
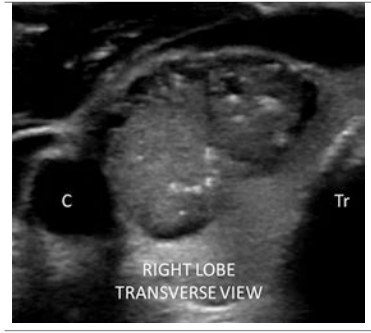
**Table 1.2** Interpretation of Individual "high-risk" thyroid nodule US characteristics

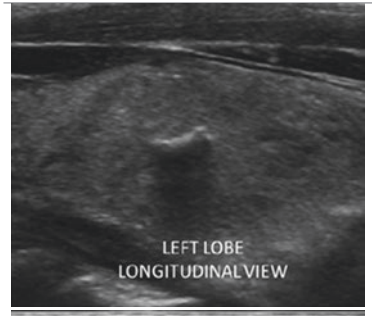
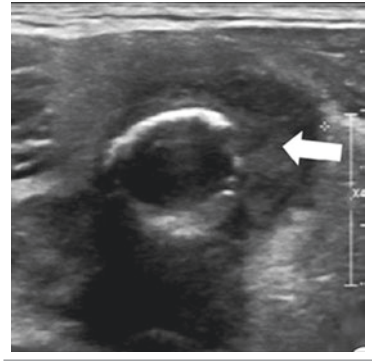
| Ultrasound characteristic | Definition | Interpretation/discussion |
|---|---|---|
| *Solid composition* | | |
|  | Entire nodule has a predominantly solid component | This is not specific for thyroid cancer, but nearly all cancers are solid |
|  | If a mixed solid cystic nodule, assess the characteristics of the solid component, and estimate the angle made between nodule wall. Nodules with an acute angle (<90°) between nodule wall and solid component are likely high risk than if an obtuse angle is present | |

| | | |
|---|---|---|
| *Hypoechogenicity* | | |
|  | Isoechoic is defined as equal echogenicity of the normal thyroid parenchyma and the submandibular gland<br>Mild hypoechogenicity is when nodule echogenicity is reduced compared to surrounding thyroid parenchyma<br>Marked hypoechogenicity is when the nodule echogenicity is similar to that of the overlying strap muscles | In conditions when the thyroid parenchyma is hypoechoic, detection of a hypoechoic nodule, especially one with infiltrative margins, can be difficult |
| *Irregular margins* | | |
|  | Either microlobulated or infiltrative margins | An indistinct margin, referring to a nodule margin that is not clearly visualized, is not an irregular margin and is not a high-risk US feature. It is often found in adenomatous nodules<br>  |

(continued)

**Table 1.2** (continued)

| Ultrasound characteristic | Definition | Interpretation/discussion |
|---|---|---|
| *Taller than wide configuration* | | |
|  | This is usually described in the transverse view. It refers to the anteroposterior diameter being equal to or greater than the transverse diameter of the thyroid nodule (AP ≥ TR) | |
| *Microcalcification* | | |
|  | Microcalcification are non-shadowing punctate hyperechoic foci | There are many other hyperechoic genic foci seen in thyroid nodules (such as comet tail artifact and focal fibrosis) that can be mistaken for microcalcification |

| | | |
|---|---|---|
| *Macrocalcification* | | |
|  <br>  | Macrocalcification appears as larger hyperechogenic US reflection with posterior shadowing | Isolated intranodular macrocalcification is not a high-risk feature except for medullary thyroid cancer<br>Interrupted peripheral rim of calcification with soft tissue extrusion (white arrow) is a concerning US feature |

*C* carotid artery, *Tr* trachea

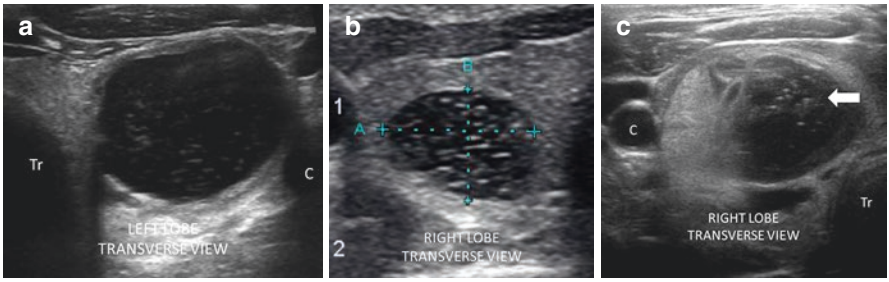



**Fig. 1.2** (**a**–**c**) Low-risk thyroid nodule ultrasound feature. (**a**) Cystic nodule: an anechoic or hypoechoic lesion with posterior enhancement and no solid tissue. (**b**) Spongiform nodule: nodule with more than 50% of the nodule occupied by microcystic spaces with linear posterior wall reflection enhancement. (**c**) Comet tail artifact: a reverberation artifact seen within a cystic nodule

## Doppler Flow in Thyroid Nodule Evaluation

Doppler flow imaging (Doppler) provides additional information about the vascularity of thyroid nodules. Color flow Doppler images indicate direction and speed of vascular flow within tissue. Power Doppler, on the other hand, does not take into consideration differences in frequency shifts and represents the total amount of flow irrespective of direction. Power Doppler is more sensitive in picking up low flow and is favored by some [30]. However, it also has a higher background signal, and some practitioners consequently prefer the higher specificity of color flow Doppler analysis.

Thyroid nodule vascularity can be graded on a scale of 1–4 (Figure 1.3a–d): no flow (grade 1), peripheral flow (grade 2), low central flow (grade 3), and high central flow (grade 4). In 2010, Moon et al. published data showing that vascularity was not a helpful predictor for malignancy [31]. This was conflicted with the results of prior studies. In 1083 nodules, intranodular vascularity was present in 17% and absent in 60% of malignant nodules vs. 31% and 60%, respectively, in benign nodules. The cancers in this study were predominantly PTC and included small nodules (i.e., less than 1 cm). Most studies evaluating vascular flow of thyroid malignancies have a predominance of classical variant of PTC, which can make the sensitivity of intranodular vascular flow low as a marker for malignancy. When looking specifically at follicular lesions, there is evidence to suggest a role for Doppler detection of intranodular vascular flow [32, 33]. In one study, in 305 nodules that were classified as follicular lesions on FNA, intranodular flow was seen in only 5% of benign adenomatous nodules (grade 3 vascularity), 34% of follicular adenomas, and 86% of follicular carcinomas (grade 3–4 vascularity) [32]. Other studies have, however, showed considerable overlap between the vascular pattern of benign lesions and follicular cancers and a lack of a predictive value of vascular distribution [34, 35].

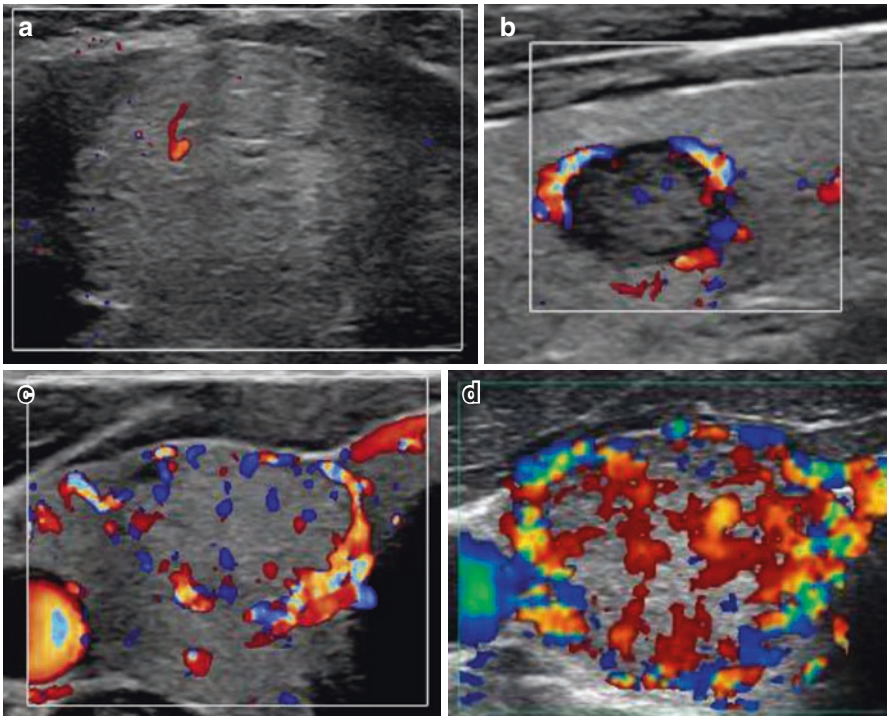



**Fig. 1.3** Vascular grade of thyroid nodules. (**a**) Grade 1: No or scant vascularity. (**b**) Grade 2: predominantly perinodular vascularity. (**c**) Grade 3: low intranodular vascular flow. (**d**) Grade 4: high intranodular vascular flow

## Elastography

Elastography assesses the degree of stiffness of tissue utilizing sound waves to measure the amount of compression from external pressure. In strain elastography, the most commonly used technique relied on intermittent manual external pressure being applied with the US probe. This introduced a significant limitation of being operator dependent. Subsequently, quantitative elastography techniques have been developed to reduce this confounding factor. When a strain ratio is calculated from the mean strain of the nodule and the surrounding tissue, there is some improvement in interobserver variability [36]. Elasticity contrast index, which utilizes the pulsation of the adjacent carotid artery as a source of pressure, is another semiquantitative method developed and studied in thyroid nodules [37]. Shear wave elastography utilizes an ultrasonic pulse from the probe rather than manual compression to obtain a numerical value for stiffness based on change in wave propagation speed. This method has been demonstrated to be less operator dependent and more reproducible [38].

Studies have shown the utility of combining elastography with conventional gray-scale US characteristics in risk assessment. When elastography was combined

with five conventional US risk characteristics (hypoechogenicity, microcalcification, taller than wide configuration, irregular margins, and intranodular vascularization), the overall sensitivity improved (compared to analysis with only gray-scale US characteristics) from 85% to 97%, and the negative predictive value increased from 91% to 97% [39]. Similarly, in 142 nodules with indeterminate cytological classification on FNA, elastography demonstrated a specificity of 91.8% but a sensitivity of 96.8% [40]. Overall, multiple studies have demonstrated the potential use of elastography as a predictor of benign disease in thyroid nodules. In a prospective study looking at the use of shear wave elastography only, a threshold of 3.45 m/s produced a sensitivity of 79.3% and specificity of 71.5%. The cancer prevalence in the cohort was 11.5%, and the PPV and negative predictive value (NPV) were found to be 26.7% and 96.3%, respectively [41].

While elastography may provide additional, useful information, it does have drawbacks. In addition to interobserver variability, shear wave elastography does have a marked operator learning curve. Additionally, both strain and shear wave elastography cannot be used when significant cystic areas or calcification is present in thyroid nodules. Furthermore, their results are affected by nodule depth and surrounding tissue fibrosis, which limits the broad utility of these imaging methods.

## Risk Stratification System

Recognizing that sensitivity and specificity of individual US features are not adequate to predict benignity or malignancy of thyroid nodules, risk stratification systems, which incorporate multiple US features, have been developed. Several of these systems, which were based on the Breast Imaging Reporting and Data System (BI-RADS) system followed for breast imaging, adopted the name Thyroid Imaging Reporting and Data System (TI-RADS). One of the earliest versions of this was developed and described by Horvath and colleagues in 2009 [42]. Since then, several research groups and professional societies have developed different iterations of TI-RADS. The American College of Radiology (ACR) TI-RADS assigns points for individual US features, and the total score determines the risk category – a higher score indicating a higher risk for cancer [11].

In contrast, the American Thyroid Association (ATA) guidelines rely on pattern recognition in determining cancer risk in a nodule [12]. This is similar to the pattern recognition approach taken by the Korean Society of Radiology (K-TI-RADS), the European Thyroid Association (EU-TI-RADS) and the American Association of Clinical Endocrinologist (with the American College of Endocrinology and Associazione Medici Endocrinologi Medical) [10, 13, 14]. All methods follow the same principle of assigning a higher risk category for nodules with a greater number of high-risk US features. When combined with a threshold diameter to consider biopsy, these systems are designed at improving diagnostic accuracy of US and FNA and reducing the number of unnecessary thyroid nodule biopsies performed [10–14]. It is important to point out that, as noted previously, the high-risk US

**Table 1.3** American Thyroid Association stratification of sonographic patterns and risk of malignancy

| Sonographic pattern | US feature |
|---|---|
| High suspicion | Hypoechoic echogenicity (solid nodule or solid portion of a partially cystic nodule) with one or more of the following:<br>Irregular margins<br>Microcalcifications<br>Taller than wide dimension<br>Peripheral rim of calcification with soft tissue extrusion<br>Extrathyroid extension<br>Presence of abnormal or suspicious cervical lymphadenopathy |
| Intermediate suspicion | Hypoechoic solid nodule with smooth margins without other high-risk US features |
| Low suspicion | Isoechoic or hyperechoic solid nodule or partially cystic nodule with eccentric solid area, without high-risk US features |
| Very low suspicion | Spongiform or partially cystic nodules without any high, intermediate, or low suspicion US features |
| Benign | Purely cystic nodule |

characteristics used to determine if a nodule requires biopsy are more specific for the hypoechoic classical PTC compared to the more isoechoic follicular variant PTC, the more isoechoic follicular thyroid cancer, and NIFTP.

When comparing the two commonly used thyroid nodule risk stratification systems in the Unites States, i.e., the ATA US risk stratification and ACR TI-RAD (Tables 1.3, 1.4, and 1.5) [11, 12]:

(a) Ahmadi et al. showed in their review of 323 thyroid nodules (27.2% malignant) the sensitivity and specificity for detection of cancer of the ATA guideline recommendations to be 77.3% and 76.6%, respectively, and the ACR TI-RADS 78.4% and 73.2% [43]. Gao et al. reviewed 2455 nodules (66.1% malignant) and determined a higher sensitivity of 95.5% for the ATA guidelines compared to 81.6% for the ACR TI-RADS [44]. In general, based on statistical analysis, a risk stratification system that combines multiple US features compared to individual high-risk characteristics will increase specificity but also reduce the sensitivity of the test. This results from the fact that while few thyroid cancers will have all the high-risk sonographic features, those that do have these characteristics are very likely to be malignant.

(b) The ATA system utilizes US patterns to classify nodules into risk categories. Because of this, several nodules are not considered classifiable if the definition of each risk category is strictly followed. Nodules in this "unclassified" category include iso- or hyperechoic nodules with additional high-risk US characteristics such as irregular margins or microcalcification. In one study, this represented 54 of 1077 thyroid nodules that were found to have an increased risk (OR 7.2, CI: 2.44–21.24) for high-risk cytology compared to the nodules with lower US suspicion features [45].

**Table 1.4** Summary of ACR Thyroid Imaging Reporting and Data System (TI-RADS)

| Step one: Assign points for US feature | | | TI-RADS category |
|---|---|---|---|
| Composition (choose one) | Cystic or spongiform [a](zero points)/mixed solid and cystic (one point)/solid (two points)<br>(if composition cannot be determined, assign two points) | Add points from each category | TR1 (benign): zero points |
| Echogenicity (choose one) | Anechoic (zero points)/hyper-or isoechoic (one point)/hypoechoic (two points)/very hypoechoic (three points)<br>(if echogenicity cannot be determined, assign one point) | | TR2 (not suspicious): two points |
| Shape (choose one) | Wider-than tall (zero points)/Taller than wide (three points) | | TR3 (mildly suspicious): three points |
| Margin (choose one) | Smooth or ill defined (zero points)/lobulated or irregular (two points)/extrathyroidal extension (three points)<br>(if margin cannot be determined, assign zero points) | | TR4 (moderately suspicious): four to six points |
| Echogenic foci (all that apply) | None or large comet tail artifacts (zero points)/macrocalcification (one point)/peripheral (rim) calcifications (two points)/punctate echogenic foci (three points) | | TR5 (highly suspicious): ≥ seven points |

[a]If spongiform, do not add additional points for echogenicity, shape, margin or echogenic foci

**Table 1.5** Comparison of ATA and ACR TI-RADS thyroid nodule risk stratification systems and biopsy recommendations (with theoretial risk of malignancy)

| ATA (2015) | | ACR TI-RADS (2017) | |
|---|---|---|---|
| Benign (0%) | No FNA | TR1: benign (<2%) | No FNA |
| Very low suspicion (<3%) | Consider FNA if ≥2 cm or observation | TR2: not suspicious (<2%) | No FNA |
| Low suspicion (5%–10%) | FNA if ≥1.5 cm | TR3: mildly suspicious (5%) | FNA if ≥2.5 cm<br>Follow if ≥1.5 cm (US at 1 and 3 years)[b] |
| Intermediate suspicion (10%–20%) | FNA if ≥1 cm | TR4: moderately suspicious (5%–20%) | FNA if ≥1.5 cm<br>Follow if ≥1 cm (US at 1, 2, 3, and 5 years)[b] |
| High suspicion (>70%–90%) | FNA if ≥1 cm | TR5: highly suspicious (at least 20%) | FNA if ≥1 cm<br>Follow if ≥0.5 cm (US every year for 5 years)[b] |

[a]If adenopathy suspicious for metastatic cancer is seen on US, both the ACR TI-RADS and ATA guidelines recommend FNA of the lymph node [11, 12]

[b]Can stop imaging at 5 years if there is no change in nodule size; if a nodule's ACR TI-RADS level increases on follow-up imaging, then repeat US in 1 year irrespective of initial TI-RADS level

(c) Both the ATA system and ACR TI-RADS suggest a size threshold of 1 cm for recommending a biopsy for a nodule in their highest-risk categories (i.e., high suspicion and TR5, respectively). Sub-centimeter tumors, in the absence of local invasion or adenopathy or distant metastasis, often are indolent [46].

(d) The ATA guideline provides a lower size threshold, of 1.5 cm and 1 cm, regarding when to recommend biopsy for low and intermediate suspicion nodules. For equivalent ACR TI-RADS categories of mildly suspicious TR3 and moderately suspicious TR4, biopsy is recommended for nodules greater than 2.5 cm and 1.5 cm, respectively. Multiple studies have demonstrated that the ACR TI-RADS results in a greater number of nodules in which biopsies are avoided compared to the ATA system. This relative reduction by the ACR TI-RADS has been reported to be around 40%–50%, with a false negative rate between 2% and 3% [44, 47]. In one study, however, in nodules which would not have been biopsied if following TI-RADS, the malignancy rate was as high as 11.3%. Interestingly, the rate was similar when the ATA guidelines were applied (10.1%). These false-positive cases tend to be iso- or hyperechoic nodules, as described earlier. Of note, data suggests that papillary and follicular thyroid cancers that are >2–2.5 cm in size have been associated with an increased cumulative risk for distant metastasis [48, 49].

(e) As part of the thyroid nodule evaluation guidelines, the ATA recommends thyroid scintigraphy if TSH levels are low. This is not outlined in the ACR TI-RADS and can lead to biopsy of "hot" nodules that have to have a low risk of malignancy. In this setting, some have expressed concerns about an increased risk of false-positive cytology (atypia of undetermined significance/follicular lesion) on FNAs performed on autonomous nodules. However, this has not been seen consistently [50, 51].

(f) The ACR TI-RADS recommends serial US for TR3–5 nodules that do not meet the criteria for FNA for up to 5 years at varying frequency depending on the risk category. If there is stability in size and US characteristics, the US can be stopped at 5 years. It does not provide specific recommendations regarding follow-up for nodules with a prior benign biopsy.

The ATA guidelines do address this scenario. Following a benign biopsy, they recommend repeating a US for nodules with a high suspicion pattern in 1 year and for nodules with low to intermediate suspicion patterns in 1–2 years. For nodules with a very low suspicion pattern (spongiform or cystic) and for nodules with two benign biopsy results, follow-up US may not be required. In a nodule with a benign biopsy result, suspicious US features rather than growth should possibly determine the need for repeat biopsy [52]. It should be noted that the serial US exams recommendations in the ATA and TI-RADS classification systems are for risk of malignancy and not for sequential growth of a benign nodule. Although it is likely that low risk subcentimeter nodules do not require long-term followup, larger nodules have a potential for growth and developement of obstructive symptoms and require intermittent evaluation for growth [53].

(g) Both the ATA guidelines and ACR TI-RADS recognize extrathyroidal extension as a high-risk feature that should place a thyroid nodule in a higher risk category. Nodule size would then determine if a biopsy would be indicated. The authors, however, recommend biopsy of any suspicious nodule with extrathyroidal extension irrespective of its size. Biopsy of abnormal cervical lymph nodes, if detected while evaluating a thyroid nodule, is recommended regardless of the nodule size.

(h) The ATA guidelines and ACR TI-RADS do not incorporate elastography or vascularity as a tool in the assessment of thyroid nodules. In a stratification system developed by Russ and colleagues, a five-tier TI-RADS classification system that included the use of elastography with gray-scale US characteristics demonstrated a slightly improved sensitivity of 98.5% (in 991 cases) compared to 95.7% when only gray-scale US characteristics were included (in 3658 cases) [54]. The use of elastography has not been universally adopted because of the cost of the equipment and operator and machine variability. Some classification systems, however, such as the French thyroid TI-RADS, have included it [55, 56].

## Conclusion

The current evaluation of thyroid nodules includes assessment of thyroid function, gray-scale characteristics of a thyroid nodule combined with other US modalities, including Doppler analysis and elastography, and with fine-needle aspiration. The TI-RADS thyroid nodule risk assessment reduces biopsies compared to the ATA system but may be associated with more missed cancers (follicular thyroid cancer, follicular variant of PTC and NIFTP that are usually isoechoic). Newer techniques including contrast-enhanced US, three-dimensional US imaging, and quantitative US have been or are currently being studied to expand the sonographic techniques to evaluate thyroid nodules [57–59]. Many groups are exploring the application of deep machine learning and artificial intelligence to improve the diagnostic accuracy of the current risk stratification systems and to avoid errors in interpretation of images [28, 29]. However, despite that gray-scale US includes machine and operator limitations, it remains the imaging modality of choice for evaluating thyroid nodules for the risk of malignancy.

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