Radiology

International Expert Consensus on US Lexicon for Thyroid Nodules

Cosimo Durante, MD, PhD • Laszlo Hegedüs, MD • Dong Gyu Na, MD, PhD • Enrico Papini, MD • Jennifer A. Sipos, MD • Jung Hwan Baek, MD, PhD • Andrea Frasoldati, MD • Giorgio Grani, MD • Edward Grant, MD • Eleonora Horvath, MD • Jenny K. Hoang, MBBS • Susan J. Mandel, MD • William D. Middleton, MD • Rose Ngu, BDS, EDS • Lisa Ann Orloff, MD • Jung Hee Shin, MD • Pierpaolo Trimboli, MD • Jung Hyun Yoon, MD, PhD • Franklin N. Tessler, MD, CM

From the Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy (C.D., G.G.); Department of Endocrinology and Metabolism, Odense University Hospital, Odense, Denmark (L.H.); Department of Radiology, Gangneung Asan Hospital, University of Ulsan College of Medicine, Seoul, Republic of Korea (D.G.N.); Department of Endocrinology and Metabolism, Regina Apostolorum Hospital, Rome, Italy (E.P.); Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, The Ohio State University Wexner Medical Center, Columbus, Ohio (J.A.S.); Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Seoul, Korea (J.H.B.); Endocrinology Unit, Arcispedale S. Maria Nuova IRCCS, Reggio Emilia, Italy (A.F.); Department of Radiology, Keck Hospital of USC, University of Southern California, Los Angeles, Calif (E.G.); Department of Imaging, Universidad del Desarrollo, Clínica Alemana de Santiago, Santiago, Chile (E.H.); Department of Radiology, Johns Hopkins Bayview Medical Center, Baltimore, Md (J.K.H.); Division of Endocrinology, Diabetes and Metabolism, Perelman School of Medicine, University of Pennsylvania, Perelman Center for Advanced Medicine, Philadelphia, Pa (S.J.M.); Mallinckrodt Institute of Radiology, Washington University School of Medicine, St Louis, Mo (W.D.M.); Department of Dental Radiological Imaging, Guy's and St Thomas NHS Foundation Trust & King's College London Dental Institute, London, United Kingdom (R.N.); Department of Otolaryngology — Head and Neck Surgery, Stanford Cancer Center, Stanford University School of Medicine, Stanford, Calif (L.A.O.); Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea (J.H.S.); Clinic for Endocrinology and Diabetology, Ente Ospedaliero Cantonale, Lugano, Switzerland (P.T.); Department of Radiology, Severance Hospital Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul, Republic of Korea (J.H.Y.); and Department of Radiology, The University of Alabama at Birmingham Heersink School of Medicine, 619 19th St S, Birmingham, AL 35249 (F.N.T.). Received June 9, 2023; revision requested July 10; revision received September 11; accepted September 19. **Address correspondence to** F.N.T. (email: *ftessler@uabmc.edu*).

Conflicts of interest are listed at the end of this article.

See also the article by Lee et al and the editorial by Reuter in this issue.

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Multiple US-based systems for risk stratification of thyroid nodules are in use worldwide. Unfortunately, the malignancy probability assigned to a nodule varies, and terms and definitions are not consistent, leading to confusion and making it challenging to compare study results and craft revisions. Consistent application of these systems is further hampered by interobserver variability in identifying the sonographic features on which they are founded. In 2018, an international multidisciplinary group of 19 physicians with expertise in thyroid sonography (termed the International Thyroid Nodule Ultrasound Working Group) was convened with the goal of developing an international system, tentatively called the International Thyroid Imaging Reporting and Data System, or I-TIRADS, in two phases: (phase I) creation of a lexicon and atlas of US descriptors of thyroid nodules and (phase II) development of a system that estimates the malignancy risk of a thyroid nodule. This article presents the methods and results of phase I. The purpose herein is to show what has been accomplished thus far, as well as generate interest in and support for this effort in the global thyroid community.

The widespread use of US, CT, MRI, and PET/CT has led to an increase in incidentally discovered thyroid nodules, which the American Thyroid Association defines as discrete lesions within the thyroid gland that are radiologically distinct (1). Sonography is the most sensitive method for their detection, and thus, nodules are frequently found incidentally at thyroid US performed for nonspecific indications, such as thyroid enlargement. In a study of 635 adults with no history of thyroid disease, 432 (68%) harbored at least one nodule at high-resolution US, of which 400, or 93%, were 5 mm or larger and potentially of clinical interest (2).

Most nodules are benign, particularly when they are discovered incidentally in patients with no risk factors for thyroid cancer (3). Small proven malignancies often have an indolent course, and their detection may constitute overdiagnosis if they would not have caused significant morbidity or mortality during the patient's lifetime (4,5). These factors have prompted the development of risk stratification systems (RSSs) for thyroid nodules, which use US features (descriptors) to estimate the likelihood of malignancy of a nodule (1,6–11).

Many RSSs also provide guidance on whether fine-needle aspiration biopsy is warranted based on the risk level of a nodule according to US criteria, combined with the maximum diameter that would dictate tumor staging (and prognosis) if malignancy were present, tempered by clinical considerations. Multiple professional organizations have created and endorsed their own RSSs, and other systems have been published by individual investigators. No fewer than 20 RSSs are currently in use. Many incorporate the acronym TI-RADS, for Thyroid Imaging Reporting and Data System, patterned after the American College of Radiology (ACR) BI-RADS, or Breast Imaging Reporting and Data System, which has been widely adopted in breast imaging for several decades (12). In addition to estimating malignancy risk and guiding management, these systems are intended to standardize communication and reporting. Unfortunately, the cancer risk and management recommendations for a nodule often differ depending on which system is applied, leading to confusion for physicians and patients (13). As well, it is time-consuming to translate results from one RSS to another, and maintaining

Abbreviations

ACR = American College of Radiology, ETE = extrathyroidal extension, I-TIRADS = International Thyroid Imaging Reporting and Data System, RSS = risk stratification system

Summary

A consensus lexicon for describing thyroid nodules at US will anchor the development of an international risk stratification system, encourage consistent worldwide reporting, and facilitate international efficacy studies.

Key Results

- The plethora of systems for classifying thyroid nodules confuses physicians and patients.
- An international lexicon for describing thyroid nodules and an accompanying online atlas will reduce interobserver variability in reporting and facilitate revisions, comparison studies, and meta-analyses.
- The International Thyroid Imaging Reporting and Data System, or I-TIRADS, lexicon will serve as the basis for a universal risk stratification system.

and periodically revising RSSs entails duplication of effort by content experts. Meta-analyses and comparisons of individual studies are also hampered by the multiplicity of RSSs.

Considerable interobserver variability in determining which descriptors are present in a nodule is even more concerning, as this may lead to inconsistency in estimating the cancer risk of a nodule. In a recent study (14), seven experts assigned features after viewing US clips, which more closely mimic real-world conditions than static images. Interobserver agreement for the finding of eccentric solid components in partially cystic nodules, irregular margins, and punctate echogenic foci was only fair or moderate (14). Therefore, any attempt to resolve the uncertainty caused by discrepant RSS recommendations must be preceded by development and validation of a descriptor dictionary, or lexicon, that addresses the issue of unreliable identification of US features. To tackle these problems, in late 2017, one of the authors of this article (F.N.T.) approached the lead authors of several RSSs to gauge their interest in cooperating to develop a unified RSS, beginning with a lexicon. This led to the creation of a steering committee and project plan, described herein.

Materials and Methods

The initial framework for the project was conceived during a combined teleconference and in-person discussion that was held in conjunction with the 13th Congress of the Asian Federation of Societies for Ultrasound in Medicine and Biology in May 2018. Over subsequent months, the plan was further refined, and a multidisciplinary steering committee was convened to represent eight professional societies that had developed an RSS, either independently or in partnership with other organizations: the American Association of Clinical Endocrinology, or AACE; the American College of Endocrinology, or ACE; the ACR; the Associazione Medici Endocrinologi, or AME (Italian Association of Clinical Endocrinologists); the American Thyroid Association, or ATA; the European Thyroid Association, or ETA; the Korean Society of Thyroid Radiology; and the Korean Thyroid Association.

Two people represented each society, apart from instances where more than one organization had collaborated on an RSS, in which case the same two committee members jointly represented them to avoid undue influence. Society leaders and committees formally endorsed physicians who had already expressed interest in serving or nominated other people to participate. The project plan was refined and finalized via email, teleconferences, and face-to-face conversations at professional meetings, including the European Thyroid Association in September 2018, the World Congress on Thyroid Cancer in June 2019, and the American Thyroid Association in October 2019. One steering committee member resigned early in the process and was not replaced, and the AACE and ACE did not continue to participate. Ten additional physicians with a special interest in thyroid nodule sonography were recruited by word of mouth. All 19 project participants, which include endocrinologists, radiologists, and surgeons from academic and private practices, collectively make up the International Thyroid Nodule Ultrasound Working Group. We have tentatively named the RSS that we are developing the International Thyroid Imaging Reporting and Data System, or I-TIRADS, in keeping with the global scope of our effort.

From the outset, the initiative was conceived as comprising two sequential phases.

Phase I is to create a lexicon of US descriptors for thyroid nodules grouped into six categories like the ones used in other RSSs: composition, echogenicity, shape, margin, extrathyroidal extension (ETE), and echogenic foci/calcifications. A seventh category was assigned to lymph nodes because it would require unique descriptors not pertinent to the other categories. The lexicon was not intended to apply to specific populations (eg, pediatric patients), as these terms are relevant to all thyroid sonograms. Translating constellations of descriptors to malignancy risk while taking demographics into account will be dealt with in the next phase. Figure 1 shows the organizational chart for phase I.

Phase II is to use the categories and descriptors from phase I to determine the probability of cancer for a nodule and arrive at management recommendations. Preliminary discussions on how to proceed with this phase are currently underway.

The task of reviewing the literature and arriving at tentative definitions for descriptors in the seven categories was divided among four subgroups: *(a)* composition and echogenicity, *(b)* echogenic foci/calcifications, *(c)* shape and margin, and *(d)* ETE and lymph nodes. Each subgroup, which included up to five panelists, was managed by a different leader responsible for finding and collating reference material and producing a work product suitable for voting (Fig 1). The literature searches were performed using PubMed *(https://pubmed.ncbi.nlm.nih.gov)*, with keywords chosen to find publications pertinent to each subgroup's area of focus (Table 1). Not surprisingly, this process led to identification of additional sources that were also consulted during the subgroups' deliberations, as well as in subsequent work on the lexicon and preparation of this article. References were provided to members in portable document format for review.

A modified Delphi process in three rounds was used to reach consensus on all the category and descriptor definitions. The procedure was similar to that used by other professional groups to

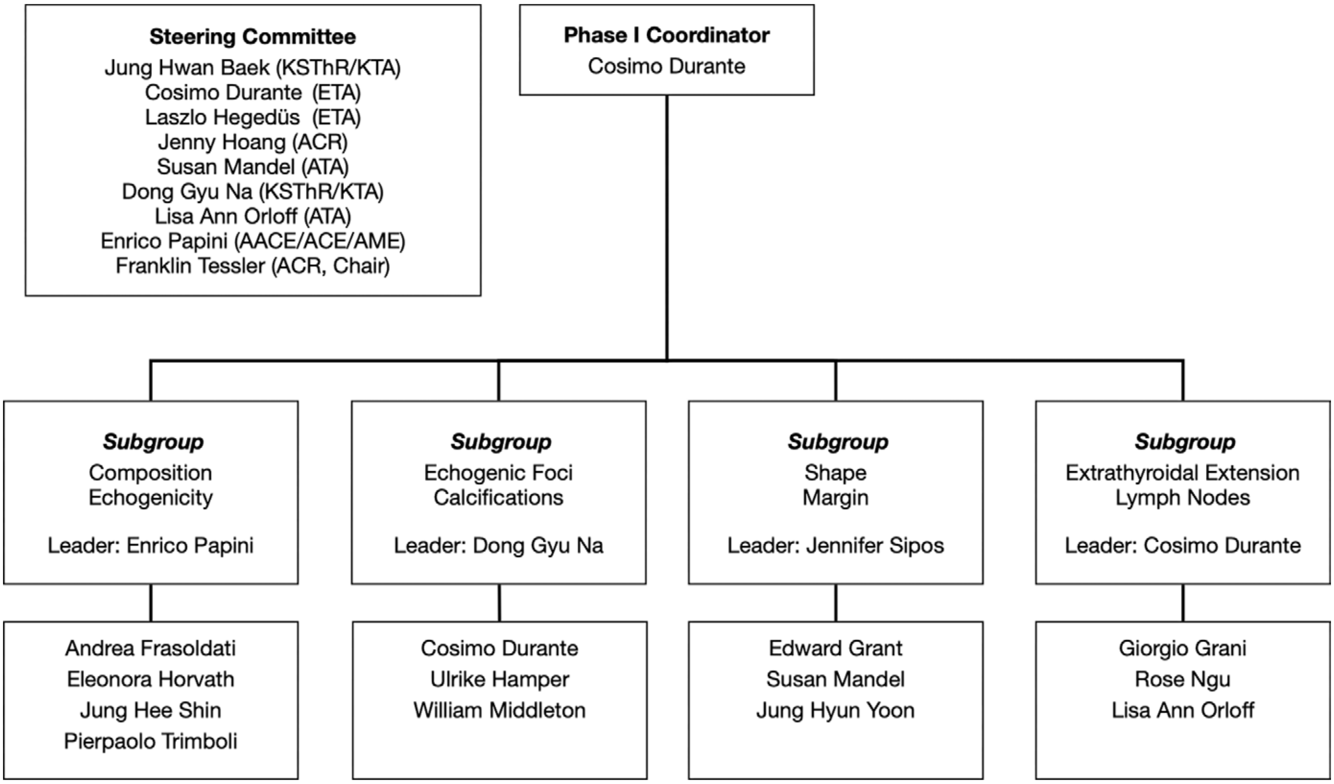


Figure 1: Organizational chart for phase I of the International Thyroid Imaging Reporting and Data System, or I-TIRADS, project. AACE = American Association of Clinical Endocrinology, ACE = American College of Endocrinology, ACR = American College of Radiology, AME = Associazione Medici Endocrinologi, ATA = American Thyroid Association, ETA = European Thyroid Association, KSThR = Korean Society of Thyroid Radiology, KTA = Korean Thyroid Association.

Table 1: Keywords Used in PubMed Literature Searches for I-TIRADS Categories

Category	Keywords
Composition	Thyroid ultrasound, sonography, thyroid imaging, thyroid nodules, structure, composition
Echogenicity	Thyroid ultrasound, sonography, thyroid imaging, thyroid nodules, structure, echogenicity
Margin	Thyroid nodule, diagnostic imaging, ultrasonography, margins, halo
Shape/direction of growth	Thyroid nodule, diagnostic imaging, ultrasonography, shape, taller-than-wide
Echogenic foci/calcifications	Ultrasonography, thyroid nodule, thyroid neoplasms, calcification, echogenic dots, echogenic foci, hyperechoic foci, comet tail
Extrathyroidal extension	Extrathyroidal extension, diagnostic imaging, ultrasound, ultrasonography, ultrasonics
Lymph nodes	Lymph node, thyroid, ultrasound, sonographic, sonography, diagnostic imaging, ultrasonography

Note.—These are high-level keywords that were used in initial PubMed searches, which, in turn, led to use of other search terms and identification of additional references. I-TIRADS = International Thyroid Imaging Reporting and Data System.

develop consensus guidelines, modified to suit the needs and resources of the I-TIRADS project (15). In applying this method, we sought to limit the ability of participants to influence the results; thus, the first two rounds were conducted anonymously.

Round 1 (September to November 2021)

An online survey tool (SurveyMonkey, Momentive) was used to present proposed definitions for seven categories and 25 descriptors. The respondents were provided with digital copies of references selected by the subgroups, along with anonymized comments from subgroup members. Voters rated each definition on a five-point scale: strongly agree, agree, neutral, disagree, or strongly disagree. They were also free to enter optional anonymous comments. Consensus was considered to have been achieved if 80% or more of the voters indicated they agreed or strongly agreed with a definition. Of the 25 descriptors, 20 met the consensus threshold during this round, with five at 100%, two at 95%, six at 90%, and seven at 84%. Five definitions, with scores ranging from 58% to 79%, failed to attain consensus (Table 2).

Round 2 (February 2022)

Next, the round 1 survey results and anonymous comments were sent to all the subgroups. Subgroup leaders were asked to concentrate on the five descriptors that remained below the consensus threshold and suggest edits. The original and alternative

Table 2: Voting Results and Risk of Malignancy for All I-TIRADS Categories

Category and Descriptor	Percentage Agreement for Definition	Voting Round When Consensus Was Achieved	Risk of Malignancy (%)
Composition	100	1	...
Solid	58	2	29.5–35.4 (18,20)
Mixed predominantly solid	58	2	8.2 (18)
Mixed predominantly cystic	84	2	4.4 (18)
Spongiform	90	2	<1 (21)
Pure cyst	90	1	~0 (18)
Echogenicity	68	2	...
Markedly hypoechoic	100	1	57.0 (23)
Mildly hypoechoic	68	2	19.9 (23)
Isoechoic	68	2	3.9 (23)
Hyperechoic	68	2	NA
Anechoic	100	1	NA
Margin	100	1	...
Irregular	100	1	32.1–86.7 (18,38,39)
Smooth	100	1	NA
Ill-defined	100	1	14.8 (32)
Direction of growth	95	1	...
Wider-than-tall	...	3	NA
Taller-than-wide	...	3	65.3–77.5 (18,33,39)
Echogenic foci/calcifications	95	1	...
Punctate echogenic foci/microcalcifications	84	1	16.8–77.9 (36–39)
Macrocalcifications	95	1	13.2–64.8 (36,38,43–45)
Peripheral (rim) calcifications	90	1	5.3–57.7 (38,43,45,46)
Echogenic foci with comet-tail artifact	95	1	NA
Extrathyroidal extension	95	1	...
Gross extrathyroidal extension	90	1	~100 (53)
Suspicious minor extrathyroidal extension	...	3	NA
Capsule contact	84	1	NA
Lymph nodes	...	...	...
Suspicious lymph node	84	1	82.0–100 (55)
Indeterminate lymph node	...	3	NA
Nonsuspicious lymph node	84	1	NA

Note.—Numbers in parentheses are bibliographic reference numbers. Percentage agreement is the proportion of panelists who voted to adopt a definition. Voting round indicates in which round consensus was reached. An 80% threshold was adopted for rounds 1 and 2, with the exception of a 50% threshold for seven descriptors and one category that had reached consensus in round 1 but were revised in round 2, which is why the percentages for some of them are less than 80%. For descriptors that were voted on in round 3, consensus was attained through discussion. I-TIRADS = International Thyroid Imaging Reporting and Data System, NA = not available.

definitions were presented in a second voting round in which physicians rated the new definitions using the same scale as before, this time without comments. As previously, 80% agreement, or strong agreement, indicated consensus. The subgroups were also permitted to propose alternate definitions for seven descriptors on which consensus had been reached in round 1. For the latter items, voters indicated whether they preferred the prior or new definition, with a simple majority required for consensus. In round 2, one of the five descriptors attained consensus, leaving four that did not.

Round 3 (March 2022)

The four descriptors were subjected to further deliberation with use of a password-protected online bulletin board (ProBoards, VerticalScope). A separate discussion thread was created for each descriptor, which allowed participants to nonanonymously propose changes and enter comments at their discretion. This method was used in lieu of conference calls because it allowed for asynchronous conversation, which facilitated discourse among participants in widely separated time zones. Consensus was reached on all four.

Results

The Lexicon

Table 2 shows the results of voting for the definitions of the seven categories and their respective descriptors in the I-TIRADS lexicon for thyroid nodules, as well as the estimated risk of malignancy for each descriptor, where available. Figures 2–8 present the definition of each category, followed by definitions

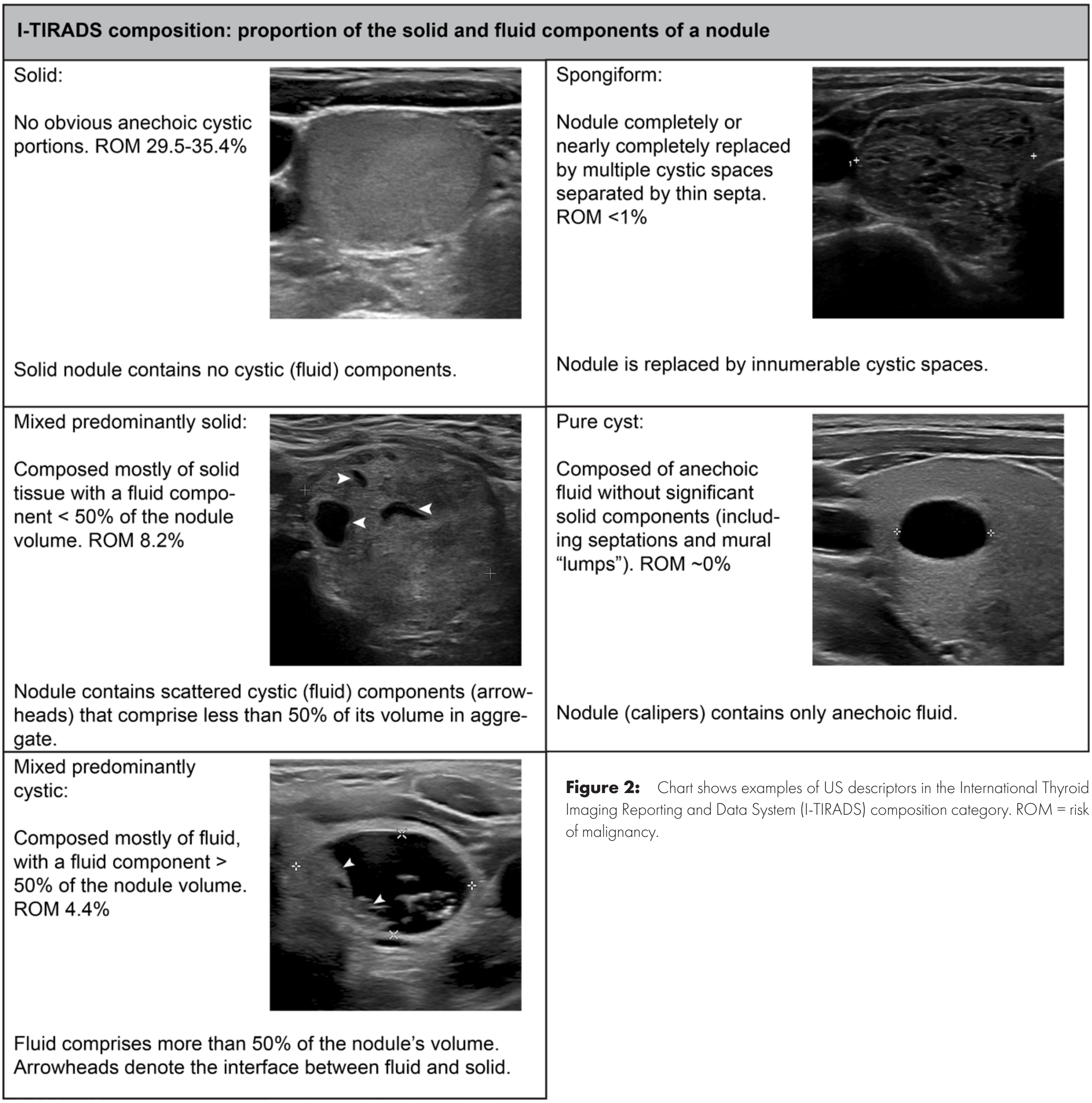


Figure 2: Chart shows examples of US descriptors in the International Thyroid Imaging Reporting and Data System (I-TIRADS) composition category. ROM = risk of malignancy.

and illustrative sonograms for its descriptors. Tables 3 and 4 list the studies cited, along with the study type, number of patients, and reference standard.

Composition

Composition (Fig 2) is defined as the proportion of the solid and fluid components in a nodule. Solid composition is associated with malignancy of thyroid nodules (16–19), with a reported sensitivity of 72.7%–87.0% and a specificity of 53.2%–56.0% (16,19). The malignancy risk of purely solid nodules is substantially higher than that of minimally cystic (cystic component <10%) or partially cystic (cystic component >10%) nodules. A Korean study showed that the malignancy risks of minimally cystic and partially cystic nodules (8.8% and 6.2%, respectively) were significantly lower (<10% risk) than the risk for purely solid nodules (29.5% risk) (20). Because estimation of the proportion of the fluid component in mixed nodules may not be accurate, causing low interobserver agreement, the panel chose to define as *solid* those nodules without any obvious anechoic cystic portions and the others as *mixed*.

The descriptors *predominantly solid* and *predominantly cystic* refer to the relative proportion of each component, with the understanding that this determination is often subjective, particularly if the amounts are nearly equal. *Pure cyst* refers to nodules that contain only fluid, or fluid with only minimal solid components. This, too, is sometimes a subjective determination, but in practice, it is almost never pivotal in classifying a nodule.

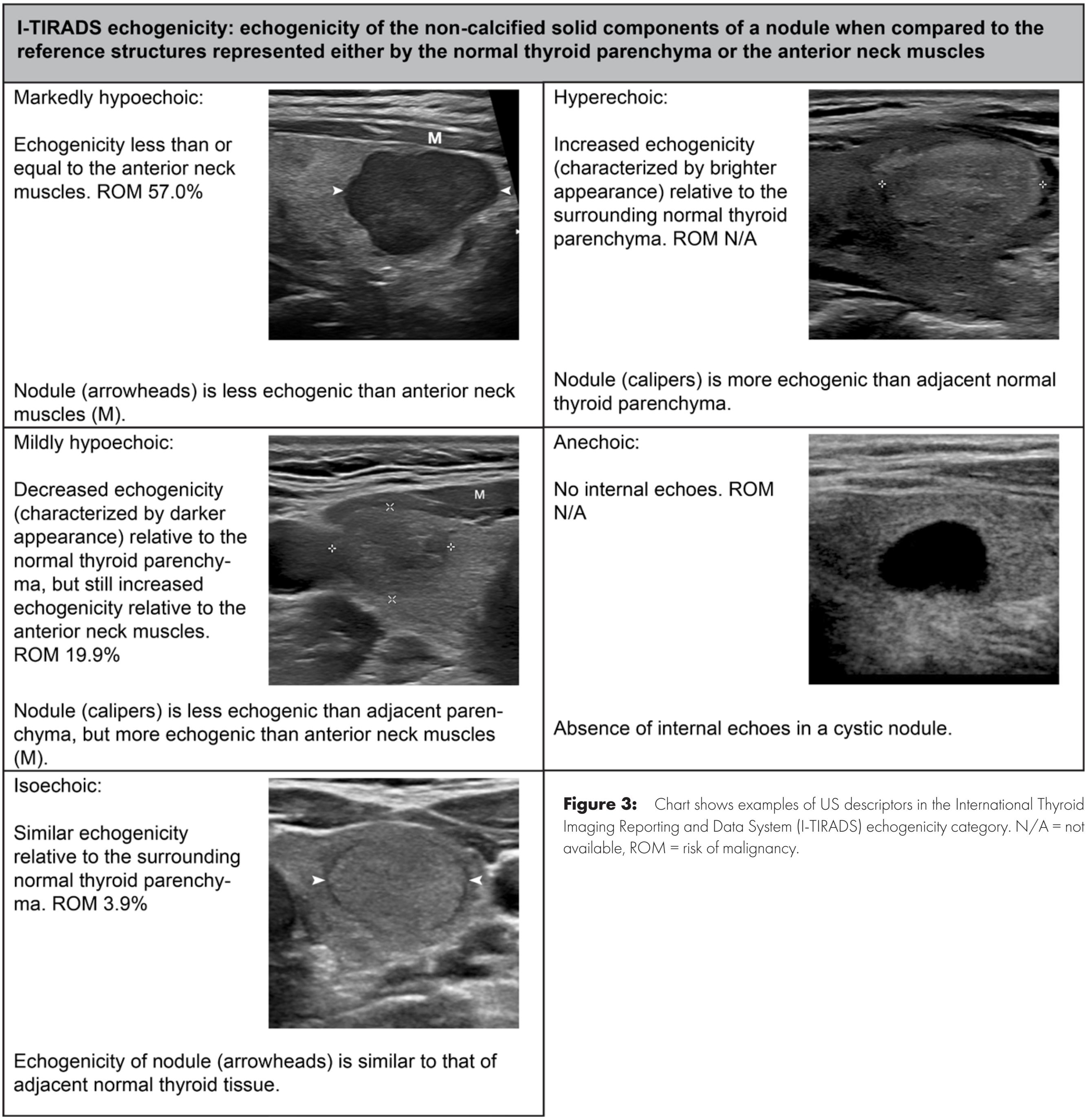


Figure 3: Chart shows examples of US descriptors in the International Thyroid Imaging Reporting and Data System (I-TIRADS) echogenicity category. N/A = not available, ROM = risk of malignancy.

When a spongiform nodule is defined as a nodule having a sponge-like appearance involving nearly the entire nodule volume, the risk of cancer is less than 1% (21). The cystic spaces in spongiform nodules are usually small, but there is overlap with predominantly cystic nodules that contain larger fluid components. Hypoechoic nodules with a partially spongiform appearance have a higher malignancy risk than those that are completely spongiform (22).

The working group elected not to include Doppler US specifically for risk assessment of thyroid nodules because of its variable value in their experience and in the literature. However, Doppler US may be helpful to distinguish viable tissue from necrotic debris, as only the former will exhibit flow. Additionally, as described later, color Doppler US is incorporated into the assessment of cervical lymph nodes.

Echogenicity

Echogenicity (Fig 3) refers to the reflectivity of the noncalcified solid components of a nodule when compared with reference structures. If a nodule is more echogenic than the adjacent thyroid, it is called *hyperechoic*; if it is equally echogenic, it is *isoechoic*. Nodules that are less reflective than the thyroid are classified as *hypoechoic*, with a reported sensitivity of 62.7%–73.0% and specificity of 56.0%–62.3%

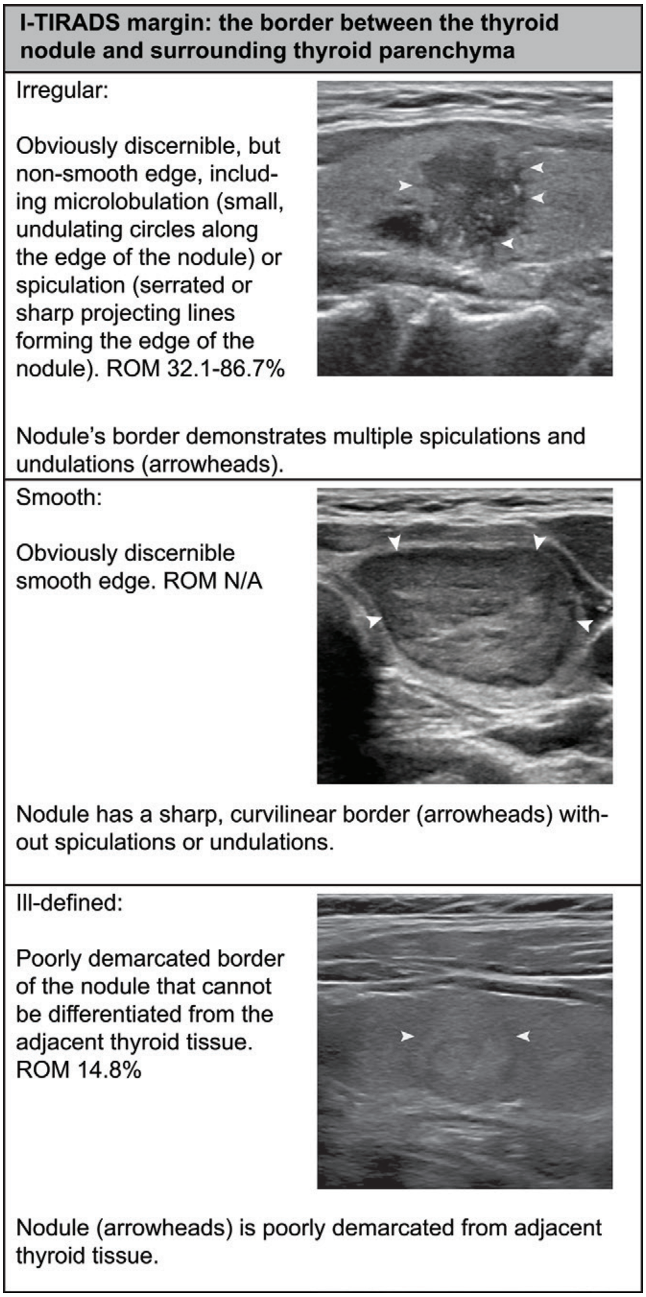


Figure 4: Chart shows examples of US descriptors in the International Thyroid Imaging Reporting and Data System (I-TIRADS) margin category. N/A = not available, ROM = risk of malignancy.

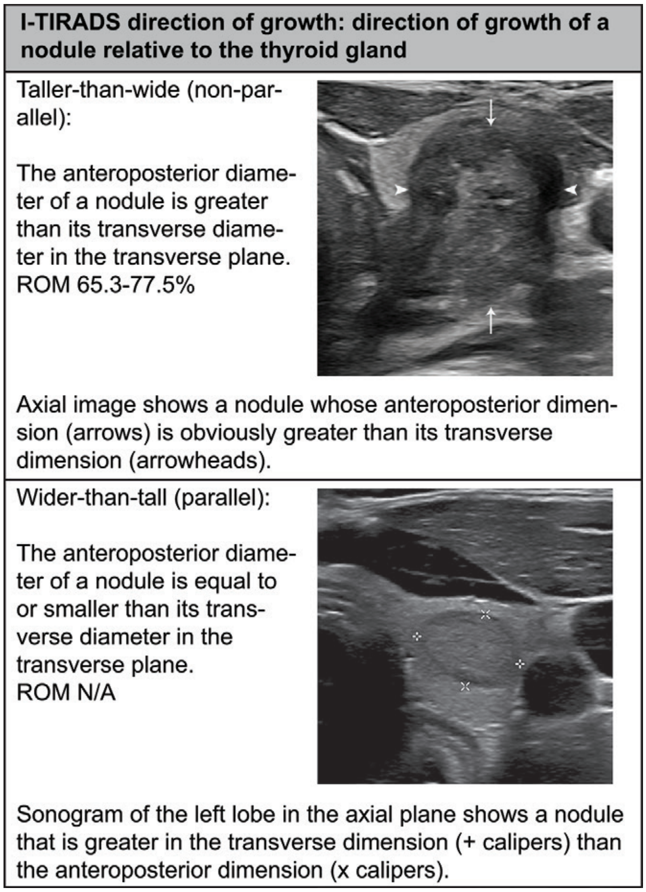


Figure 5: Chart shows examples of US descriptors in the International Thyroid Imaging Reporting and Data System (I-TIRADS) direction of growth category. (The term *shape*, which was used during the search process, was later changed to *direction of growth*, which was believed to be more specific.) N/A = not available, ROM = risk of malignancy.

for malignancy (16,19). Hypoechogenicity may be further subclassified as mild, moderate, or marked, as this further influences the risk of malignancy (16–19). For example, in a recent retrospective study (n = 2255), the malignancy risk of markedly (52.5%) and moderately hypoechoic (58.6%) nodules was significantly higher than that of mildly hypoechoic nodules (19.9%) (23). However, given their similar malignancy risk, the panel elected to combine moderate and marked echogenicity. In the lexicon, *mildly hypoechoic* is defined as decreased echogenicity relative to the normal thyroid parenchyma but still higher than that of the anterior neck muscles, while *markedly hypoechoic* is echogenicity less than or equal to that of the anterior neck muscles. The final descriptor in this category, *anechoic*, is reserved for nodules with no internal echoes such as pure cysts, as defined previously.

A solid nodule may be homogeneous (characterized by uniform echogenicity) or heterogeneous (characterized by variable echogenicity, such as, for instance, in the presence of both hypo- and isoechoic areas). If a nodule exhibits heterogeneous echogenicity, the predominant component determines the echogenicity of the nodule. When the echogenicity of thyroid tissue surrounding a nodule is decreased, as in Hashimoto thyroiditis, the echogenicity of the solid component of the nodule may be assessed relative to normal parenchyma in other parts of the gland, if present. Quantitative estimations (eg, gray-scale analysis or other radiomics techniques) of the degree of echogenicity may be useful to improve interobserver variability; an increase from fair to substantial agreement has been reported (24,25), but they are not widely available. Although the submandibular glands have been proposed as an alternative reference standard, a recent study reported that normal submandibular glands showed decreased echogenicity in more than a quarter of the adult patients (27.0%), rendering them inadequate for this purpose (26).

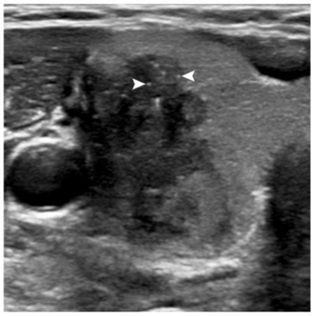
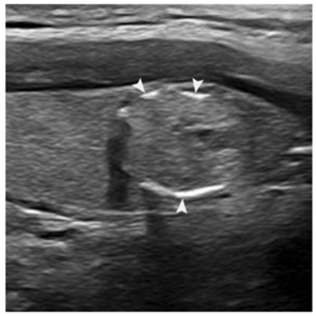
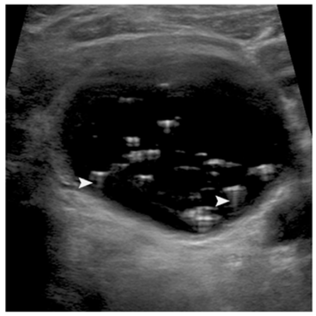
I-TIRADS echogenic foci/calcifications: focal regions within or along the periphery of a nodule that are markedly hyperechoic relative to the rest of the nodule and the surrounding normal parenchyma	
Punctate echogenic foci/microcalcifications: Punctate (≤ 1 mm) hyperechoic foci within the solid components of a nodule. ROM 16.8-77.9%  Nodule contains multiple minute echogenic foci with no acoustic shadowing (arrowheads).	Peripheral (rim) calcifications: Curvilinear hyperechoic line completely or incompletely surrounding the nodule's margin, with or without posterior shadowing. ROM 5.3-57.7%  Lower pole nodule shows incomplete calcifications (arrowheads) along its border.
Macrocalcifications: Large (> 1 mm) hyperechoic foci with posterior acoustic shadowing. ROM 13.2-64.8%  Macrocalcifications. Nodule (calipers) contains large calcific foci with acoustic shadowing (arrowhead).	Echogenic foci with comet tail artifact: Echogenic foci showing comet-like echogenic tails. ROM N/A  Colloid nodule contains multiple echogenic foci, many of which exhibit comet-like artifacts (arrowheads).

Figure 6: Chart shows examples of US descriptors in the International Thyroid Imaging Reporting and Data System (I-TIRADS) echogenic foci/calcifications category. N/A = not available, ROM = risk of malignancy.

Margin

Margin (Fig 4) is defined as the border between the thyroid nodule and surrounding thyroid parenchyma. Nodules that exhibit a sharp margin, without projections into the adjacent tissue, are called *smooth*. Conversely, an irregular margin is associated with an increased risk of malignancy (16–19), with a reported sensitivity of 50.5% and specificity of 83.1% (19). The term *irregular* encompasses small rounded projections (microlobulated) and jagged, spike-like (spiculated) margins. These were combined in a single descriptor to improve interobserver agreement, which is reported to be slight to fair for this feature, especially when using more subtypes (24,27–29). While some studies report that an ill-defined (poorly discernable) margin has an increased likelihood of malignancy (30–32), the strength of this association is lower when compared with microlobulation or spiculation (32).

Direction of Growth

This refers to the direction of growth of a nodule (Fig 5) relative to the thyroid gland as assessed by the ratio of its linear dimensions. The descriptors in this category are *wider-than-tall* (parallel) and *taller-than-wide* (nonparallel), with the latter showing a sensitivity of 26.7%–53.0% and specificity of 93.0%–96.6% for malignancy (16,19). Although some panelists favored evaluating this attribute on either transverse or sagittal images, the former was adopted because the diagnostic performance in both planes is similar and the transverse plane was believed to be easier to understand (33).

Technically, nodules with identical anteroposterior and transverse measurements, which have a round configuration, are neither wider-than-tall nor taller-than-wide. However, for practical purposes, the former descriptor should be applied to such nodules to avoid overcalling taller-than-wide. To mitigate this risk, some panelists suggested establishing a minimum height-to-width threshold, bolstered by evidence that the likelihood of malignancy increases with increasing anteroposterior-to-transverse diameter (34,35). Again, however, for simplicity, the panel decided not to adopt a specific threshold.

Echogenic Foci/Calcifications

Echogenic foci (Fig 6) are focal regions within or along the periphery of a nodule that are markedly hyperechoic relative to the rest of the nodule and the surrounding normal parenchyma. They may vary in size, shape, and location in a nodule. Punctate echogenic foci/microcalcifications (≤1 mm) have an independent association with malignancy (36,37), with a reported sensitivity of 41.6%–75.7%, specificity of 35.1%–92.4%, and positive predictive value of 16.8%–77.9% (36–39). The malignancy risk of nodules containing them depends on the coexistence of descriptors in other US categories, such as composition and echogenicity (38,39). For example, their risk in solid hypoechoic nodules is substantially higher than in solid iso- or hyperechoic or partially cystic nodules (38–40).

Punctate echogenic foci in papillary thyroid cancers are rarely associated with posterior acoustic shadowing (echo voids deep to calcifications) and occasionally show comet-tail artifacts. Therefore, the presence of such artifacts should not preclude application of this descriptor, with the understanding that they are also commonly seen in benign thyroid nodules and may correspond to other pathologic features such as dense colloid or dystrophic calcification, in addition to psammomatous calcifications (41).

Macrocalcifications (>1 mm) are larger than punctate echogenic foci and may be located within the substance of a nodule or along its periphery. Their configuration varies from rounded or nearly so to curvilinear. When they follow the margin of a nodule in a complete or interrupted fashion, they are called peripheral or rim calcifications. Both types may be associated with dense acoustic shadowing that precludes confident assessment of the echogenicity and composition of a nodule; composition may be assumed to be solid when this occurs (42).

Many studies have reported that macrocalcifications confer an increased risk for cancer, with a reported sensitivity of 9.7%–25.0%, specificity 81.6%–96.1%, and positive predictive value of 13.2%–64.8% for malignancy (36,38,39,43,44). However, it is uncertain if macrocalcifications alone are independently associated with malignancy (36,39).

Several studies (38,43,45) have reported that peripheral (rim) calcifications are associated with malignancy, with reported sensitivities of 1.1%–8.9%, specificities of 96.5%–99.4%, and positive predictive values ranging from 16.7% to 57.7%. However, other studies have reported conflicting results (36,46), and it is unclear if this feature confers an increased risk of cancer.

Echogenic foci with triangular comet-tail artifacts often vary in shape and location within a nodule. They are mostly found in the fluid components of cystic nodules and are reliably predictive of benignity (47–49). Similar foci at the margin of the cystic components of partially cystic nodules also favor benignity; however, they can at times be seen in a cystic papillary carcinoma and are not specific for benign or malignant nodules (48). Echogenic foci with comet-tail artifacts in solid tissue have a relatively high malignancy risk and should not be considered a benign feature (49–52).

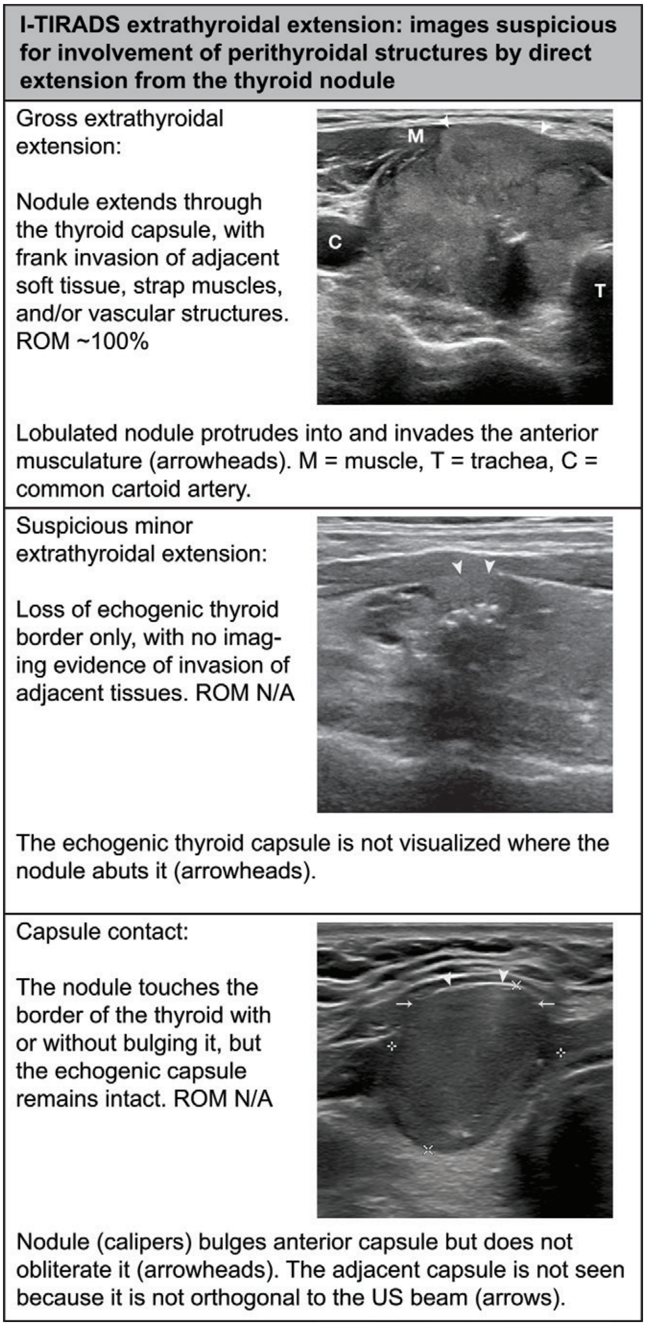


Figure 7: Chart shows examples of US descriptors in the International Thyroid Imaging Reporting and Data System (I-TIRADS) extrathyroidal extension category. N/A = not available, ROM = risk of malignancy.

Extrathyroidal Extension

ETE (Fig 7) describes the spatial relationship between a nodule and the thyroid capsule and perithyroidal structures. (Although the thyroid lacks a complete fibrous capsule, the term was retained, as it has gained widespread acceptance.) The reported sensitivity is 6.8%–86.4%; specificity, 29.8%–100%; and positive predictive value, 39.2%–100% for malignancy, which reflects the degree of certainty that the nodule is truly invasive (53). At the low end, capsule contact is when the nodule touches the border of the thyroid. The echogenic capsule may be bulged, but it remains sonographically intact. Whether a nodule contacts the anterior versus the posterior capsule is relevant to the decision for or against active surveillance (54). However, this feature alone has a positive predictive value too low to justify changes in management of an already planned surgery (53). Suspicious minor ETE, where the capsule is not visible where a nodule abuts it, represents an indeterminate state.

Gross ETE includes a nodule margin that is indistinct and poorly differentiated from the strap muscles (also known as the infrahyoid muscles), the tracheoesophageal groove, or esophagus or forms an obtuse angle with the trachea. Evidence for the predictive value of sonographically detected gross ETE to the trachea or tracheoesophageal groove is limited. Due to the potential impact and morbidity, the Korean recommendations are included herein as suspicious of gross ETE (8). Of note, these tumors are expected to have at least another high-suspicion feature, such as irregular margin, marked hypoechogenicity, punctate echogenic foci, or taller-than-wide shape. When there is gross ETE along the posterior border of the thyroid, US is likely to underestimate the extent of disease. For better surgical planning, complementary cross-sectional imaging with CT or MRI should be considered.

Lymph Nodes

The I-TIRADS lexicon encompasses descriptive terms for regional (cervical) lymph nodes (Fig 8), which are relevant to tumor staging and may influence the need for biopsy of a thyroid nodule. The European Thyroid Association's scheme for lymph node US classification (55), which categorizes nodes based on shape, internal architecture, and other characteristics, was endorsed by the American Thyroid Association and subsequently validated by multiple studies (56,57). The features associated with the I-TIRADS suspicious lymph node descriptor have a reported sensitivity of 5.0%–87.0% and specificity of 43.0%–100% (55). The panel chose to endorse this stratification as a baseline and update it with evidence from more recent studies (58).

Lymph nodes take on different characteristics in different anatomic compartments of the neck. Levels I–VI have different expectations for node size and shape, and even central versus lateral neck nodes may differ (53). Detection of central compartment lymph nodes in patients with an intact thyroid may be more difficult, as their features are harder to recognize than in patients who have undergone thyroidectomy. The coexistence of chronic lymphocytic thyroiditis also may confound lymph node interpretation (59).

As described in Figure 8, nonsuspicious nodes lack suspicious features and have an ovoid shape and/or a visible hilum, while indeterminate nodes fall into an intermediate category. The vast majority turn out to be benign and resolve spontaneously or remain stable over time (57). The risk of malignancy varies according to the clinical context. The positive predictive value of indeterminate features is expected to change according to the pretest probability. For example, indeterminate lymph nodes identified during a screening sonogram with no suspicious findings in the thyroid are at lower risk than those identified in a patient with papillary thyroid cancer.

Features suspicious for thyroid cancer metastases that were included in this category have a high positive predictive value that is consistently reported in the literature. Microlobulated, poorly defined, or irregular margins may increase the suspicion for metastasis (58–60). However, panelists decided not to include these characteristics in the lexicon based on their expert opinion that determining the margin of a lymph node is highly subjective.

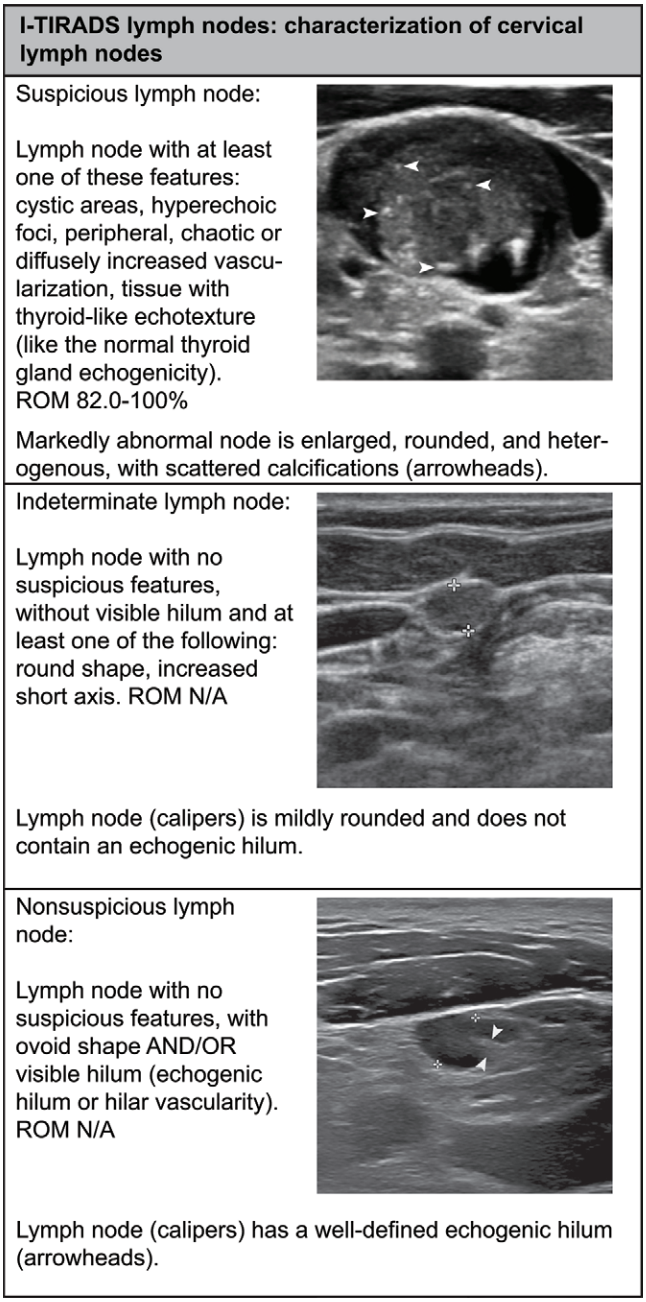


Figure 8: Chart shows examples of US descriptors in the International Thyroid Imaging Reporting and Data System (I-TIRADS) lymph nodes category. N/A = not available, ROM = risk of malignancy.

Discussion

This article presents a lexicon of US descriptors for thyroid nodules, with the intent for it to serve as the foundation for an international risk stratification system, tentatively called the International Thyroid Imaging Reporting and Data System, or I-TIRADS. We also describe the methods used to develop the lexicon, including expert opinion and evidence from the literature.

Our endeavor has highlighted a key rationale for an international system that is likely underappreciated. Developing and updating RSSs often requires considerable labor over several years by teams with requisite expertise, resources, and interest. Simply keeping abreast of the ever-expanding body of relevant scientific literature is extremely time-consuming, as are applying resources, reaching consensus, and publishing the results.

Table 3: Retrospective Studies Cited for I-TIRADS Descriptors

Study First Author and Year	Type of Study	Enrolled Patients	Reference Standard
Ahuja et al, 1996 (47)	Single-center	100	Path
Beland et al, 2011 (48)	Single-center	189	FNA, Path, IFU
Chen et al, 2020 (58)	Single-center	46	Path
Choi et al, 2021 (26)	Single-center	969	...
Frates et al, 2006 (43)	Single-center	1985	FNA
Grani et al, 2015 (24)	Single-center	839	FNA
Grani et al, 2019 (56)	Single-center	226	Clinical, FNA
Ha et al, 2019 (50)	Single-center	954	Path, IFU
Itani et al, 2019 (27)	Single-center	137	Path
Kim et al, 2013 (60)	Single-center	104	FNA, Path, IFU
Kim et al, 2021 (33)	Single-center	1513	FNA, Path
Lamartina et al, 2016 (57)	Single-center	58	Clinical, IFU
Lee et al, 2020 (23)	Single-center	1817	FNA, Path
Lee et al, 2022 (20)	Multicenter	4989	FNA, Path
Lu et al, 2011 (46)	Single-center	1498	Path
Malhi et al, 2014 (44)	Multicenter	903	FNA, Path, IFU
Mattingly et al, 2022 (35)	Single-center	415	Path
Middleton et al, 2017 (38)	Multicenter	3315	FNA, Path
Moon et al, 2008 (36)	Multicenter	831	FNA, Path
Na et al, 2016 (39)	Multicenter	1802	FNA, Path, IFU
Paik et al, 2020 (42)	Multicenter	20	FNA, Path
Park et al, 2010 (28)	Single-center	108	FNA, Path
Popowicz et al, 2009 (37)	Single-center	672	Path
Sohn et al, 2021 (52)	Single-center	832	FNA, Path
Tahvildari et al, 2016 (41)	Single-center	51	Path
Teefey et al, 2021 (40)	Multicenter	3315	FNA, Path
Wildman-Tobriner et al, 2020 (29)	Single-center	92	...
Wu et al, 2018 (49)	Single-center	560	Path
Wu et al, 2021 (25)	Single-center	913	Path
Yoo et al, 2013 (59)	Single-center	124	FNA, Path
Zhang et al, 2015 (32)	Single-center	346	FNA, Path
Zheng et al, 2018 (45)	Single-center	1013	FNA, Path

Note.—FNA = fine-needle aspiration biopsy cytologic examination, IFU = imaging follow-up, I-TIRADS = International Thyroid Imaging Reporting and Data System, Path = histopathologic examination.

Creating an international system, as we are attempting, will reduce or eliminate current duplication of effort worldwide, facilitate incorporating the latest findings into revisions, and prevent further divergence between systems. Additionally, comparing the results of studies is hampered by the lack of agreement regarding what a particular descriptor represents—for example, two groups of investigators may define *punctate echogenic foci* differently. Adopting a universal lexicon will eliminate or substantially reduce this risk. As well, existing RSSs were developed to address papillary thyroid carcinoma; a unified system could perhaps be more easily extended to encompass other phenotypes.

To further gauge interest in and guide our work, in 2020, several of us (C.D., L.H., E.P., J.K.H., and F.N.T.) undertook an international survey about utilization of five of the leading thyroid nodule RSSs: AACE/ACE/AME Medical Guidelines, ACR TI-RADS, ATA Guidelines, EU-TIRADS, and K-TIRADS (13). While over 90% of respondents acknowledged the value of RSSs, the results demonstrated considerable heterogeneity and inconsistency in how they are applied within practices. Among the two-thirds of respondents who indicated RSS use, their choice was highly influenced by the practitioner's medical specialty and geographic location. Importantly, almost one-third reported using more than one RSS in their practice, which can be confusing for patients and physicians, particularly if management recommendations for a given nodule differ substantially.

More than half the survey respondents expressed support for a universal lexicon to address interobserver variability when humans assign the US features on which thyroid nodule RSSs are founded. Variability may be reduced in two ways. First, the words chosen to define a descriptor no doubt affect the consistency with which it is applied. But testing this experimentally would be impractical, and so we relied on expert opinion and consensus-building to devise our definitions.

Second, we believe an online atlas of static images, video clips, and diagrams that illustrate the range of appearances that apply to each descriptor will be far more effective than

Table 4: Studies Other than Retrospective Cited for I-TIRADS Descriptors

Study First Author and Year	Type of Study	Enrolled Patients	Reference Standard
Aydoğan et al, 2019 (21)	Prospective, single-center	96	FNA
Brito et al, 2014 (16)	Meta-analysis	13 736	...
Brito et al, 2016 (54)	Review	...	...
Campanella et al, 2014 (17)	Meta-analysis	>10 000	...
Grani et al, 2020 (34)	Prospective, single-center	553	FNA
Ha et al, 2016 (18)	Prospective, multicenter	750	FNA, Path
Ha and Chung et al, 2021 (8)	Consensus statement	...	...
Kim et al, 2015 (22)	Prospective, single-center	195	FNA, Path
Klang et al, 2015 (51)	Review	...	...
Leenhardt et al, 2013 (55)	Guideline	...	...
Papini et al, 2002 (30)	Prospective, single-center	402	FNA, Path, IFU
Ramundo et al, 2020 (53)	Prospective, single-center	128	Path
Remonti et al, 2015 (19)	Meta-analysis	...	...
Salmaslıoğlu et al, 2008 (31)	Prospective, single-center	550	Path

Note.—FNA = fine-needle aspiration biopsy cytologic examination, IFU = imaging follow-up, I-TIRADS = International Thyroid Imaging Reporting and Data System, Path = histopathologic examination.

definitions alone. The atlas will also include examples of US findings that mimic the features that exhibit high interobserver variability to reduce the likelihood that they will be overcalled (14,61). The figures presented herein are intended to illustrate the value of this resource, which is in the formative stages. Additionally, we are planning a multidisciplinary study to measure and validate the consistency of the lexicon. Indeed, by publicizing our work now, we hope to garner attention from the thyroid US community to participate in this work and support further development of I-TIRADS. Interested individuals may communicate their interest by contacting the corresponding author of this article.

We are aware that practitioners will tend to favor the RSS with which they are most familiar and/or that is promoted by their specialty's professional organization, as demonstrated by the RSS survey (13). To overcome this tendency, it is important to recognize that all current systems are based on similar sonographic findings and that RSSs already have more in common than it may seem. For example, the 2015 American Thyroid Association Guidelines and ACR TI-RADS are fully concordant in seven of the former system's 15 nodule patterns and differ by only 0.5 cm in the recommended biopsy threshold for some nodules. While this concordance is not always manifest in the interpretation of sonographic images, we hope I-TIRADS will reduce variability in nodule classification and risk category assignment. We also recognize that some physicians have questioned the clinical value of RSSs, and we hope to address their concerns (62). Additionally, we are aware that the malignancy risk conferred by US features, alone or in combination, will likely depend on the patient's geographic location and other factors unrelated to images. We intend to tackle this aspect in the next phase of our work. The ACR, AME, ATA, ETA, and Korean Society of Thyroid Radiology/Korean Thyroid Association have formally endorsed our initiative to create an international RSS, although they will appropriately not commit to adopting I-TIRADS until it is completed in phase II. The ETA also acknowledged the lexicon project in its 2023 Clinical Practice Guidelines for Thyroid Nodule Management (63).

The literature on malignancy risk assessment for thyroid nodules at US is constantly growing. Therefore, descriptors and their definitions will have to be revised, deleted, or added as new evidence comes to light over time. Additionally, we elected to not include newer US techniques, such as sonoelastography (64), contrast-enhanced US (65), and three-dimensional imaging (66) in our lexicon, largely because they are not universally available and/or because their use in assessing malignancy risk of thyroid nodules has not yet been standardized. However, we recognize that they may, and probably will, deserve to be incorporated into future revisions of our lexicon and the I-TIRADS RSS that follows. Similarly, we believe that machine learning, radiomics, and related computational methods, which have already shown great promise, will eventually find their way into I-TIRADS (67).

In conclusion, we have presented a US-based lexicon intended to reduce interobserver variability in assigning thyroid nodule descriptors. An online atlas of images and clips, which is under development, will be instrumental in achieving this goal, which will be evaluated with a multicenter study. The lexicon will eventually serve as the foundation for a new international risk stratification system for managing thyroid nodules, tentatively called I-TIRADS, with the hope that it allows future revisions and expansion, facilitates international efficacy studies, and encourages consistency in reporting worldwide.

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manuscript editing, **C.D., L.H., D.G.N., E.P., J.A.S., J.H.B., A.F., G.G., E.G., J.K.H., S.J.M., W.D.M., R.N., L.A.O., J.H.S., P.T., J.H.Y., F.N.T.**

Disclosures of conflicts of interest: **C.D.** Advisory board member for Eisai, Lilly, and Roche. **L.H.** No relevant relationships. **D.G.N.** No relevant relationships. **E.P.** No relevant relationships. **J.A.S.** Member of the American Thyroid Association Board of Directors. **J.H.B.** No relevant relationships. **A.F.** Member of the directorship of the Italian Association of Clinical Endocrinologists (AME). **G.G.** No relevant relationships. **E.G.** Grants from Siemens Healthineers and Canon; member of the *Radiology* editorial board. **E.H.** No relevant relationships. **J.K.H.** No relevant relationships. **S.J.M.** Honoraria from the Taiwan Endocrine Society, Indonesian Thyroid Association, and Mayo Clinic; support for attending meetings or travel from the Serbian Endocrine Society, Taiwan Endocrine Society, Indian Thyroid Society, and International Society of Endocrinology; co-chair of the American Thyroid Association task force for guidelines of the management of thyroid nodules in adult patients, member of the board of directors for the International Society of Endocrinology, and chair of the Endocrine Society Laureate Awards Committee. **W.D.M.** No relevant relationships. **R.N.** No relevant relationships. **L.A.O.** No relevant relationships. **J.H.S.** No relevant relationships. **P.T.** No relevant relationships. **J.H.Y.** No relevant relationships. **F.N.T.** Consulting fees from DeepSight Technology; payment for hotel from the World Congress on Thyroid Cancer; chair of the American College of Radiology (ACR) TI-RADS Committee and member of the ACR RADS Committee; advisor for AIBx.

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