CME ARTICLE

A method in the madness in ultrasound evaluation of thyroid nodules

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ABSTRACT Around 50% of the population harbour thyroid nodules on ultrasonography, up to 7% of which may be malignant irrespective of size. While fine-needle aspiration biopsy is reliable, subjecting every thyroid nodule to this procedure is not cost-effective. Hence, ultrasonography is used primarily to characterise thyroid nodules, whereas nodules that have suspicious features are subject to a fine-needle aspiration biopsy. The presence of microcalcifications, macrocalcifications, irregular margins, 'taller-than-wide' shape, marked hypoechogenicity and intrinsic vascularity are features that render a thyroid nodule suspicious for malignancy. Spongiform appearance and the presence of colloid plugs or purely cystic nodules are considered features of benignity. In this article, these aforementioned sonographic features of malignancy and benignity are pictorially illustrated and a basic approach to dealing with solitary and multiple thyroid nodules is highlighted.

Keywords: follicular adenoma, intrinsic hypervascularity, microcalcifications, papillary thyroid carcinoma, thyroid nodule
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INTRODUCTION

A thyroid nodule is a discrete lesion within the gland that is radiologically distinct from the surrounding parenchyma. Up to 50% of the population harbour thyroid nodules on ultrasonography (US).[1] These nodules may be large enough to be palpable in 3%–7% of asymptomatic adults. The incidence of malignancy stands at 9.2%–13% for thyroid nodules irrespective of whether they are palpable or incidentally discovered on other imaging studies.[1] Thyroid nodules have been conventionally evaluated on real-time US and fine-needle aspiration biopsy (FNAB). FNAB increases the rate of detection of thyroid cancer and reduces the number of unnecessary surgical procedures and the overall cost of medical care.[2,3] However, performing FNAB on every thyroid nodule detected on imaging is not cost-effective due to the high prevalence of such nodules. Newer non-invasive techniques such as US elastography and contrast-enhanced US are being proposed for evaluating these lesions. Shear wave elastography provides objective assessment of the stiffness of the nodule and is based on the presumption that malignant nodules are stiffer than benign lesions.[4] Contrast-enhanced US has demonstrated differences in the enhancement pattern of benign and malignant nodules. However, further validation of data in this regard is essential in order to validate the use of these non-invasive techniques to replace FNAB in routine clinical practice.[5] Hence, US itself forms the primary modality for evaluating these nodules. This paper illustrates pictorially some US signs to characterise thyroid nodules as a method of triage for FNAB. Characteristic features of benign and malignant thyroid nodules are illustrated, and a basic approach to dealing with multiple nodules is highlighted in this article.

APPROACH

Ideally, the diagnosis of thyroid nodule should be made with knowledge of the patient's history, physical examination and thyroid function tests. Previous FNAB reports, if any, should be sought lest the nodule in question has already been cytologically tested. Patients at high risk of thyroid cancer are generally those with childhood exposure to radiation, family history of cancer, multiple endocrine neoplasia (MEN) syndrome and a history of thyroid cancer. The index of suspicion for these patients is higher.

Studies have noted that a smaller nodule size does not equate to a lower risk of malignancy and that the mean maximal diameter of malignant nodules is significantly smaller than that of benign ones.[6,7] However, in general, smaller malignancies have a more favourable prognosis than larger lesions.[8-10] Based on the guidelines of the American Thyroid Association, only nodules > 1 cm are evaluated in the authors' institutions, since they have a greater potential to be clinically significant cancers, unless there are smaller nodules with highly suspicious features.[8]

As the risk of malignancy in a multinodular thyroid gland is comparable to that of a solitary nodule, each nodule must be individually assessed on US.[11] One or more of these nodules may be selected for biopsy on the basis of the clinical assessment, the presence of suspicious US features and the patient's risk factors. FNAB is not likely to be necessary in a diffusely enlarged gland with multiple nodules of similar and benign US appearances, without intervening normal parenchyma.[11] Extracapsular spread and vascular invasion are definitive signs of malignancy. No thyroid US examination is complete without the assessment of cervical lymph nodes for enlargement or suspicious features such as microcalcifications or cystic changes (Fig. 1). However,

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Table I. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of some important ultrasonographic features of thyroid nodules.*

Ultrasonographic feature	Sensitivity	Specificity	PPV	NPV
Microcalcification[10-14]	26.1–59.1	85.8–90.0	24.3–70.7	41.8–94.2
Macrocalcification[5,15]	9.7–28.4	79.2–96.1	64.8	59.1
Tall than wide shape[5,11]	32.7–40.0	91.4–92.5	66.7–77.4	67.4–74.8
Irregular margins[11-14]	17.4–77.5	38.9–85.0	9.3–60.0	38.9–97.8
Hypoechogenicity[11-14]	26.5–87.1	43.4–94.3	11.4–68.4	75.3–93.8
Marked hypoechogencity[5,11]	26.5–41.4	92.2–94.3	68.4–79.7	68.1–73.5
Solid[13,14]	69.0–75.0	52.5–55.9	15.6–27.0	88.0–92.1
Vascularity[4,12]	54.3–74.2	78.6–80.0	24.0–41.9	85.4–97.4

*Adapted from Frates et al.[1]

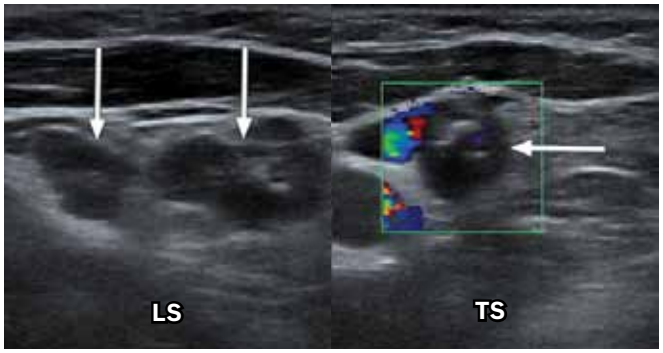

Fig. 1 A 47-year-old woman with metastatic cervical adenopathy from papillary thyroid carcinoma. Longitudinal (LS) and transverse (TS) sections show enlarged cervical lymph nodes (arrows) with internal calcifications.

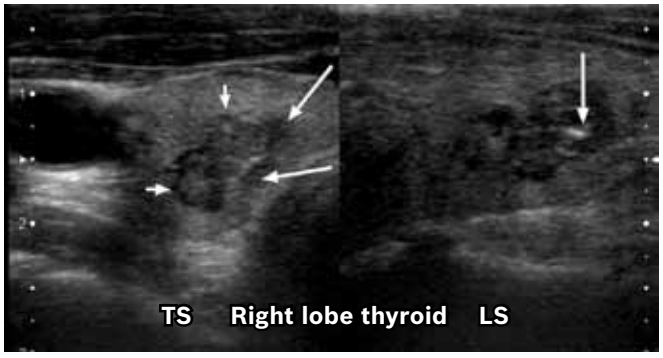

Fig. 3 A 32-year-old woman with papillary thyroid carcinoma. Transverse (TS) and longitudinal (LS) sections show a hypoechoic nodule with partly irregular (arrowheads in TS) and ill-defined margins (arrows in TS) and microcalcifications (arrow in LS).

the two aforementioned signs have not been elaborated in this paper, as they do not pose a dilemma for the radiologist. This paper specifically deals with the evaluation of thyroid nodules. The sensitivity, specificity, and positive and negative predictive values of some important US features are provided in Table I.[6,12-17]

US CHARACTERISATION OF THYROID NODULES

Microcalcifications

Microcalcifications correspond to clusters of psammoma bodies on pathology and are considered the hallmark of papillary thyroid carcinoma. On US, they appear as tiny hyperechoic foci

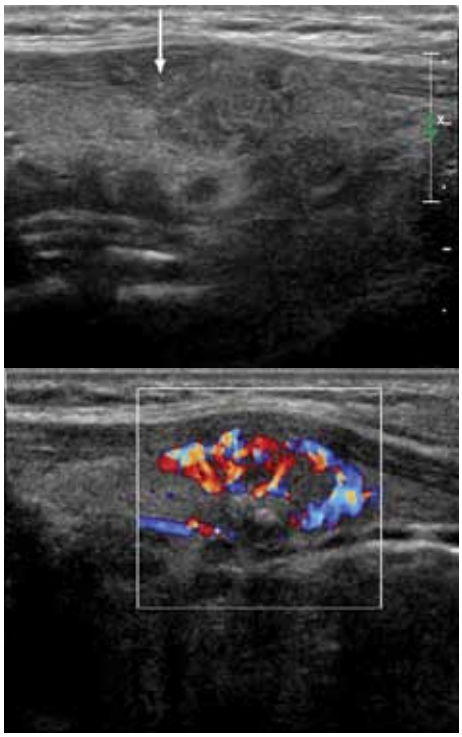

Fig. 2 A 54-year-old woman with papillary thyroid carcinoma. Longitudinal sections show a hypoechoic nodule with irregular margins, fine punctate microcalcifications (arrow) and increased internal vascularity.

of around 1 mm, with or without acoustic shadowing (Figs. 2 & 3).[13] Although fairly reliable, microcalcifications are not easily deciphered by inexperienced operators and tend to have poor sensitivity.[7,13] Specificity is high, but rare occurrence of microcalcifications in other thyroid malignancies, and even in some benign nodules, should be borne in mind.[7,13] A practical problem often faced by an inexperienced operator is the differentiation between microcalcification and inspissated colloid in benign thyroid. By identifying the comet-tail or reverberation artifact that often accompanies colloid, unnecessary FNAB may be avoided in these lesions (Fig. 4).

Macrocalcifications

Coarse calcifications represent dystrophic amorphous deposits of calcium in fibrous tissue or necrotic material. They are more frequently seen in the benign nodules of multinodular goitre

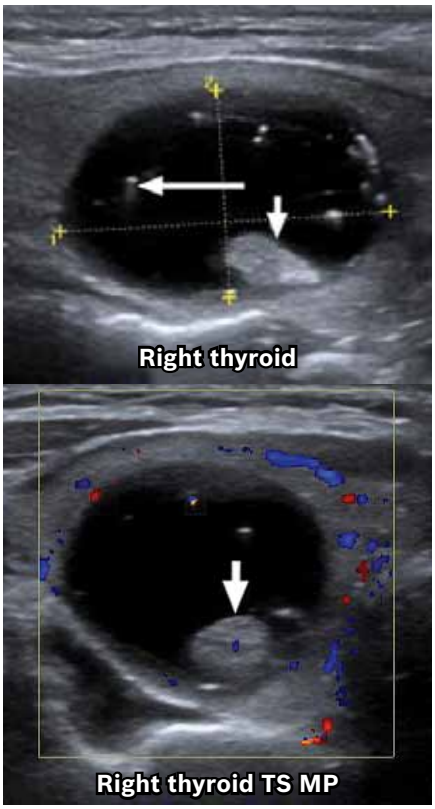

Fig. 4 US images show colloid particles with reverberation artifacts (arrow) and colloid plugs (arrowheads).

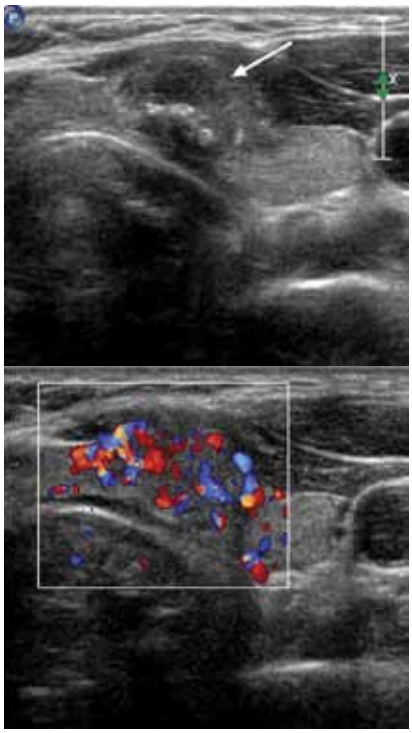

Fig. 6 A 43-year-old woman with papillary thyroid carcinoma. A 'taller-than-wide' hypoechoic nodule is seen (arrow) with coarse central macrocalcifications and high intrinsic vascularity on colour Doppler [Reprinted with permission from the International Cancer Imaging Society].[5]

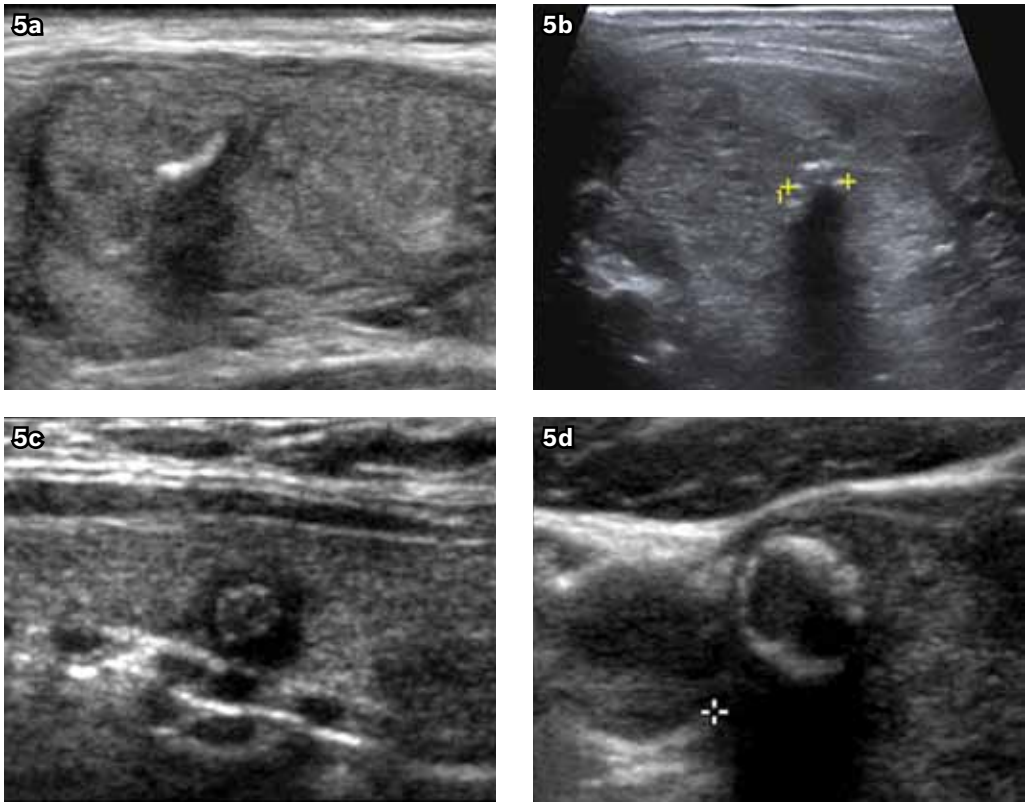

Fig. 5 Spectrum of macrocalcifications on US in four different histopathologically proven benign thyroid nodules. (a) Coarse central macrocalcification; (b) granular macrocalcification; (c) nodular macrocalcification; and (d) peripheral 'eggshell' calcification.

than in malignancy, and may be granular, nodular, or irregularly or 'eggshell' shaped (Fig. 5). However, when found in solitary nodules, they may be associated with as high as 75% malignancy rates.[11,18] Coarse calcification manifests as an irregular or fragmented echogenic focus with posterior shadowing (Fig. 6). They are the most common type of calcification in medullary

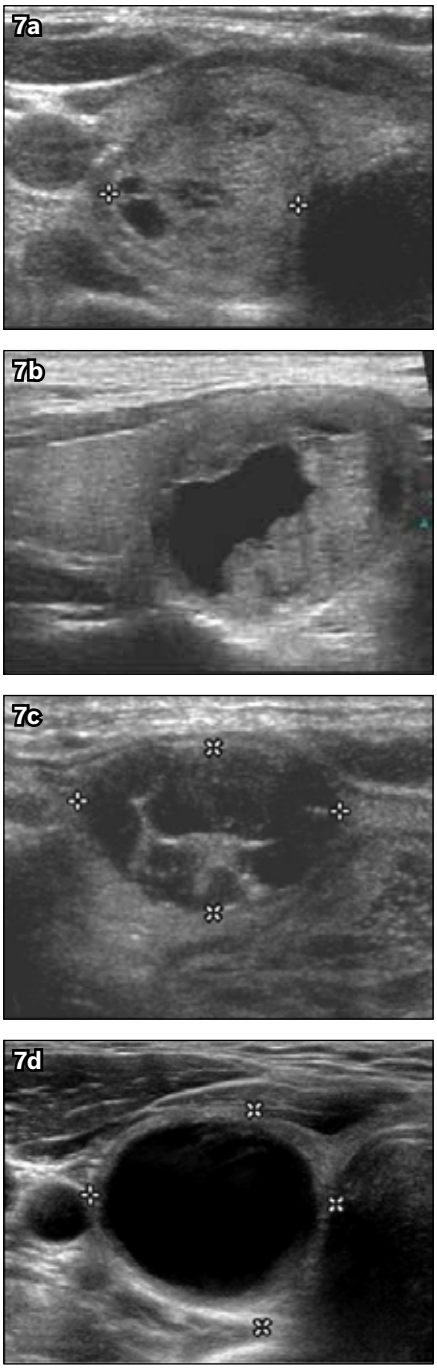

Fig. 7 A 57-year-old woman with colloid nodules. (a) Nodule 1 is almost completely solid; (b) nodule 2 is around 60% solid; (c) nodule 3 is less than 30% solid; and (d) nodule 4 is purely cystic.

thyroid carcinomas.[11] Peripheral 'eggshell' calcifications (Fig. 5d) are also a form of macrocalcification that is generally considered to be benign, although rare exceptions do exist.[19]

Internal content and echogenicity

The internal content of a thyroid nodule may be predominantly solid (> 50%–100% solid) or predominantly cystic (0%–49% solid) (Fig. 7). A predominantly solid nodule should raise suspicion of malignancy. In practice, however, most benign and malignant nodules are predominantly solid, making it difficult to use this criterion for differentiating the two.[7] Hence, the internal content cannot be relied on as a single criterion to

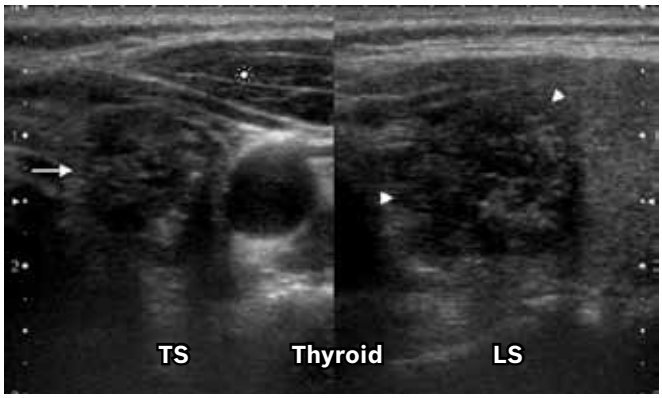

Fig. 8 A 53-year-old woman with papillary thyroid carcinoma. Transverse (TS) and longitudinal (LS) sections show a 'taller-than-wide' nodule (arrow in TS), echogenicity of which is lower than that of the overlying strap muscle (asterix in TS). The nodule has irregular margins (arrowheads in LS) [Reprinted with permission from the International Cancer Imaging Society].[5]

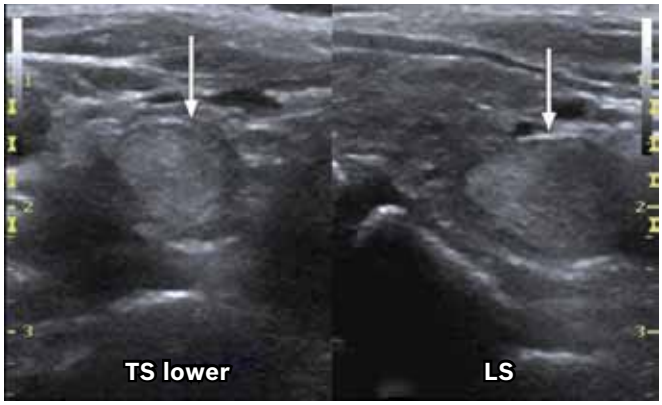

Fig. 9 A 42-year-old man with a colloid nodule. Transverse (TS) and longitudinal (LS) sections show a nodule (arrows) that is hyperechoic to the adjacent thyroid parenchyma.

characterise thyroid nodules, and thus, the nodule must be further assessed.

The solid component of the nodule may be hypoechoic, isoechoic or hyperechoic to the surrounding normal-appearing thyroid parenchyma. The nodule is termed as 'markedly hypoechoic' if it is of lower echogenicity than the overlying strap muscles, and is thus highly suspicious for malignancy (Fig. 8).[7,13] This sign has been found to be highly specific (92%–94%). The incidence of malignancy is relatively uncommon in lesions and almost unlikely among hyperechoic nodules. The incidence of malignancy is also relatively uncommon in isoechoic lesions (Fig. 9).[20]

Some solid nodules may have a spongiform appearance, identified as an aggregation of multiple microcystic components in more than 50% of the volume of the nodule.[7] Bonavita et al[20] likened this appearance to a 'puff pastry' pattern (similar to the ultra-thin layers of flaky pastry in desserts such as napoleons), which is found to be characteristic of colloid nodules or goitre (Fig. 10). These nodules are generally avascular or occasionally isovascular in relation to the rest of the gland and are considered benign.[6,7,20]

A cystic nodule containing a central plug of avascular colloid is also the sign of a colloid nodule (Fig. 11). Evaluation of the solid

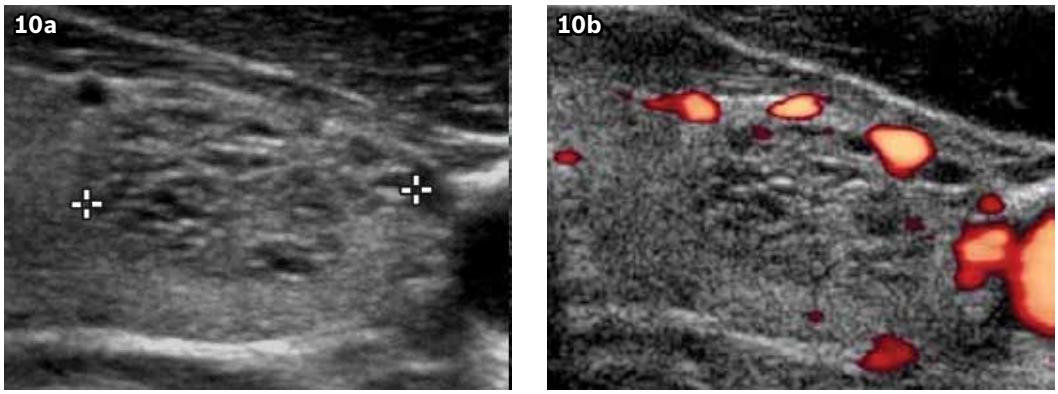

Fig. 10 A 51-year-old man with a colloid nodule. (a) Gray-scale image shows a nodule with a typical spongiform appearance. (b) No hypervascularity is demonstrated within the nodule on the colour Doppler image.

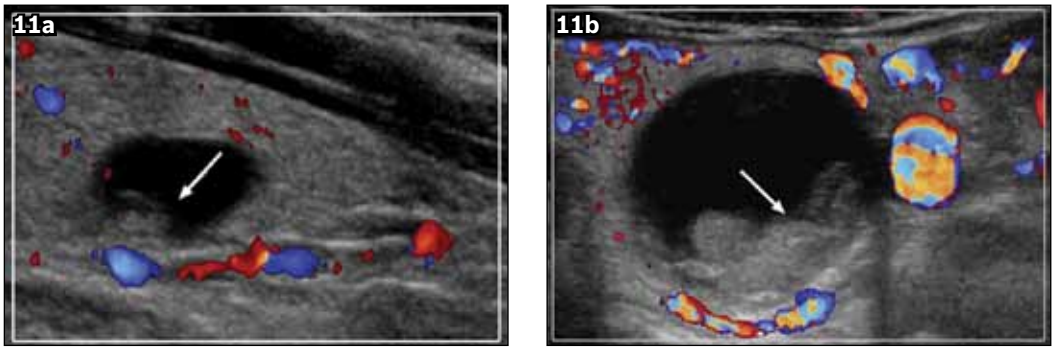

Fig. 11 A 54-year-old woman with colloid nodules. Colloid plugs (arrows) in two different nodules (a & b) are demonstrated on colour Doppler. No internal vascularity is demonstrated within these solid-looking colloid plugs.

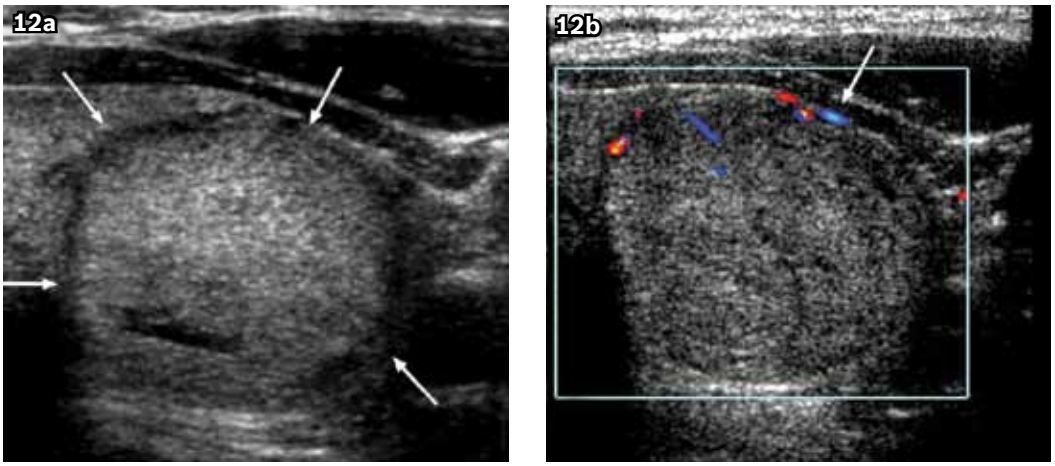

Fig. 12 A 40-year-old woman with a colloid nodule. (a) Gray-scale image depicts a solid isoechoic nodule with a halo (arrows) around it. (b) Minimal perinodular vascularity (< 25% of nodule circumference) is demonstrated on the colour Doppler image (arrow).

component of the nodule may reveal a spongiform pattern or the presence of colloid particles within. Doppler interrogation should be performed to confirm that the solid component is indeed avascular.[20] A pure cystic nodule is highly unlikely to be malignant (Fig. 7d).[1,6] These are usually benign nodules that have undergone cystic or haemorrhagic degeneration. A cystic component occurs in 13%–26% of all thyroid malignancies, but a predominant cystic appearance is uncommon, although not unknown.[21,22] Nodules with predominant cystic appearance generally represent cystic change in a hyperplastic nodule. However, a careful US assessment of the solid components for hypervascularity and microcalcifications is advisable.[20,21,23]

Shape of the nodule

Thyroid nodules that have a 'taller-than-wide' shape (when the anteroposterior diameter of a nodule is longer than its transverse diameter on a transverse or longitudinal plane) are considered to be at a higher risk of malignancy (Figs. 6 & 8).[7,13] This appearance is thought to be due to a centrifugal tendency in tumour growth, which does not necessarily occur at a uniform rate in all dimensions. This is a highly specific (91.4%–92.5%) but poorly sensitive (32.7%–40.0%) finding.[7,13]

Margins

This criterion has the highest interobserver variability of the

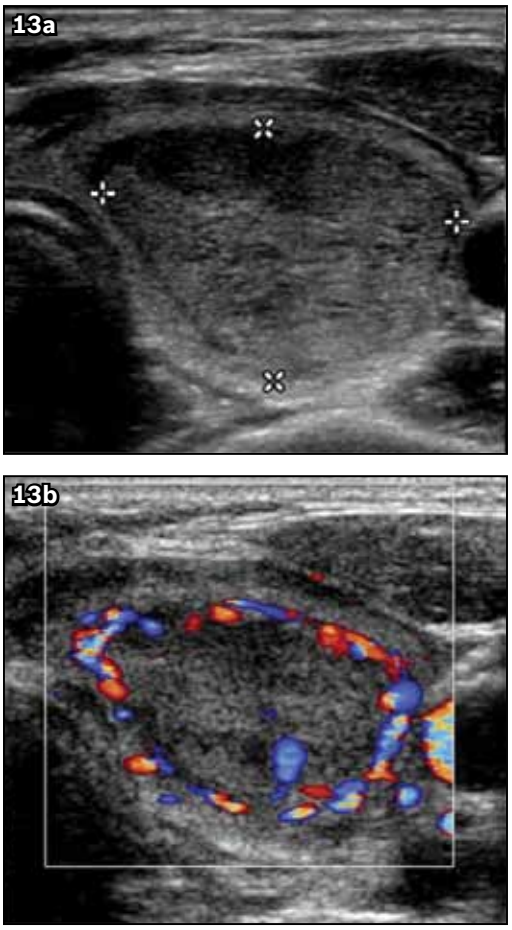

Fig. 13 A-38-year-old woman with a follicular adenoma. (a) Gray-scale image shows a solid hypoechoic nodule. (b) Florid perinodular vascularity is demonstrated on the colour Doppler image.

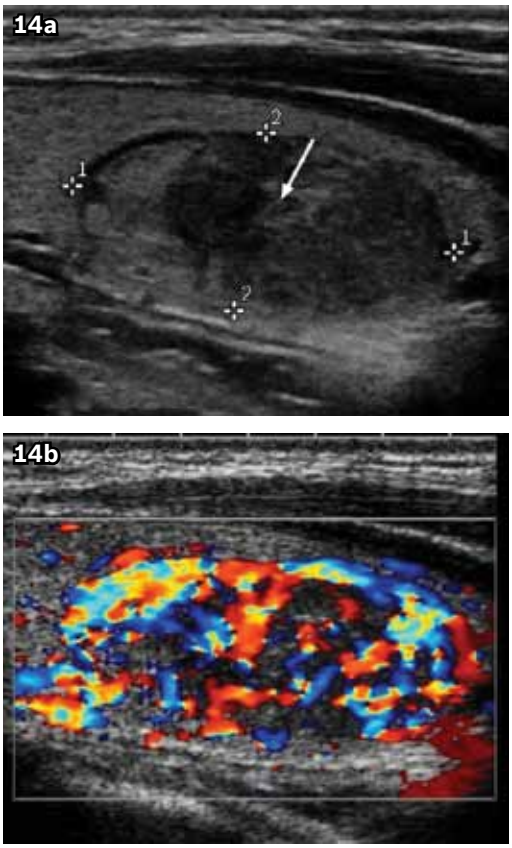

Fig. 14 A 49-year-old woman with papillary thyroid carcinoma. (a) Gray-scale image shows a heterogeneous nodule with central microcalcifications (arrow). (b) Chaotic intrinsic vascularity is demonstrated on the colour Doppler image.

sonographic features.[14] Characterisation may be even more difficult on static images. The margin of a nodule may be well-defined smooth, well-defined spiculated or ill-defined.[7] Generally, nodules with spiculated or ill-defined margins are considered suspicious (Figs. 2, 3 & 8).[7,9] However, many malignant nodules are also associated with well-defined or regular margins, while some benign lesions may have ill-defined or spiculated margins.[21,24] The finding is fairly specific (83%–91.8%) but poorly sensitive (48.3%–55.1%).[7,13] A completely uniform halo around a nodule is considered highly suggestive of benignity (Fig. 12).[21,25] However, a halo is absent at US in more than half of all benign thyroid nodules, and a complete or incomplete halo has been associated with thyroid malignancies and follicular neoplasms.[20-22]

Vascularity

Sparse perinodular vascularity (vascularity in 25% of the nodule circumference) is generally not associated with malignancy (Fig. 12), although there are exceptions to this.[2,21,26] Florid peripheral flow pattern may be seen in follicular neoplasms (Fig. 13),[24] and these nodules should be subject to FNAB. Intrinsic hypervascularity is defined as a flow in the central part of the tumour that is greater than that in the surrounding thyroid parenchyma, and it is suspicious for malignancy.[11] It must be kept in mind that the current generation of US machines tends to show some degree of internal vascularity in most of the solid thyroid nodules, fading away the initial enthusiasm with Doppler interrogation of thyroid. Malignant nodules tend to have chaotic flow in the central part of the tumour (Figs. 2, 6 & 14).

CONCLUSION

To summarise, US may be useful for the preliminary characterisation of thyroid nodules and may help to avoid FNAB in these nodules. The presence of microcalcifications, macrocalcifications, intrinsic hypervascularity, marked hypoechogenicity, 'taller-than-wide' shape and irregular/ill-defined margins are the US features of a nodule that requires further evaluation by FNAB. Spongiform appearance, a purely cystic nodule or a cystic nodule with a colloid plug may be considered benign on US.

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

(Code SMJ 201211B)

	True	False
Question 1. The following sonographic criteria are suspicious for malignancy in a thyroid nodule:		
(a) Microcalcification.	☐	☐
(b) Spongiform appearance.	☐	☐
(c) 'Wider-than-tall' orientation.	☐	☐
(d) Perinodular halo.	☐	☐
Question 2. The following sonographic criteria are reassuring of benignity in a thyroid nodule:		
(a) Irregular margins.	☐	☐
(b) Extreme hypoechogenicity.	☐	☐
(c) Hyperechoic foci with reverberation artifacts.	☐	☐
(d) Macrocalcifications.	☐	☐
Question 3. The following pattern of vascularity associated with a thyroid nodule on colour Doppler is not considered suspicious:		
(a) Peripheral sparse vascularity.	☐	☐
(b) No vascularity.	☐	☐
(c) Central vascularity.	☐	☐
(d) Florid peripheral vascularity.	☐	☐
Question 4. The following type of calcification is associated with papillary thyroid carcinoma:		
(a) 'Eggshell' calcification.	☐	☐
(b) Granular calcification.	☐	☐
(c) Microcalcification.	☐	☐
(d) Nodular calcification.	☐	☐
Question 5. The following thyroid nodule may not be subject to FNAB or surgical excision:		
(a) Completely cystic nodule.	☐	☐
(b) Solid isoechoic nodule.	☐	☐
(c) Solitary solid nodule with central macrocalcification.	☐	☐
(d) Nodule with florid peripheral vascularity.	☐	☐

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