Real-time Thyroid Ultrasonography – an essential diagnostic tool for the thyroid specialist with an emerging role in the treatment of thyroid nodules

Introduction

Thyroid ultrasonography has become a routine tool for the endocrinologist in the diagnosis and management of thyroid disorders However, it is now clear that the thyroid specialist ("thyroidologist") with a portable ultrasound machine is in the best position to correlate the features of thyroid nodules and other thyroid disorders with the clinical findings and blood test results. In addition, the thyroid specialist can provide "one stop shopping" for their patients as they also perform their own fine needle aspiration biopsies (FNAB) of suspicious nodules. The focus of this review is to provide an understanding of the utility of real time thyroid, parathyroid and neck ultrasound and how can it help in the patient's management especially those with thyroid nodules.

Normal thyroid gland

Critical to being able to recognize ultrasonographic abnormalities in patients with various thyroid disorders, it is necessary to understand the sonographic characteristics The normal thyroid of the normal thyroid gland. The texture, or echogenicity, of the normal thyroid gland is determined using the ultrasound "grey scale" is characterized as "isoechoic" and has an off-white or whitish-grey colour (fig 1). Features of an abnormal gland, such as cysts or nodules, that are less white than normal, namely grey through black, are described as being variably hypoechoic. Some nodules and areas of inflammation that are whiter than normal are described as mildly, moderately or severely hyperechoic. Thyroid cysts, which are fluid containing sacs, and the 'black holes" of end stage Hashimoto thyroiditis, are uniformly black, benign colloid nodules are usually isoechoic or slightly hypoechoic whilst more cellular follicular nodules may be slightly hyperechoic. The ability to recognize variations in the overall echogenicity of the thyroid tissue and that of specific lesions including nodules, cysts or inflammatory infiltrations can only be obtained by extensive, long-term experience.

The overall size of the thyroid gland is determined by measuring the width, depth and length of the isthmus and both lobes. With experience, the user can develop their own reference ranges for adult males and adult females, and for pregnancy (the volume of the thyroid gland increases by approx. 30% during pregnancy). While there is a big variation in the size of the normal gland which reflects both genetic and environmental factors such as local iodine availability and the effect of pregnancy, each lobe of the normal gland measures approx. 50 x 30 x 10 mm with a thin isthmus connecting the two. lobes. Some subjects have an enlarged gland that looks with normal echoicity and is presumed to be a normal variation although rare abnormalities of thyroid hormone metabolism or iodine deficiency. An extra small lobe arising from the top of the left lobe, called the pyramidal lobe, which can be misdiagnosed as a nodule, is found in 20% of people.

Another feature of the thyroid gland to be assessed is its vascularity. Or blood supply the normal vascularity of the thyroid reflects the distribution through the gland of the thyroid arteries and veins which will vary from subject to subject and include several anatomical variations, all of which are described as "normal".

In Graves hyperthyroidism, the overall blood supply is greatly increased due to the diffuse and intense inflammatory reaction, whereas in Hashimoto thyroiditis, the blood supply to the thyroid is initially increased when the inflammatory reaction is active then decreases as the gland is progressively destroyed over time and replaced by fibrosis and scarring.

Fig. 1. Right lobe of the thyroid gland of a 28-year-old female with no personal or family history of thyroid disease. The gland is of "normal size" and the texture throughout is described as "isoechoic".

Thyroid nodules

Benign thyroid nodules are very common, increasing to a prevalence of about 60% in adult women aged 60 or more. Most benign nodules are "colloid" according to the dominant presence of fluid and few cells, i.e., the nodule comprises scattered normal thyroid follicular cells in a background of thick, viscous fluid, the colloid Although the prevalence of cancer is only about 5% in patients with one or more nodules, the risk of cancer is greater in patients with a single cold (does not take up isotope on thyroid scan) nodule since multi nodular, or colloid, goitre is , by definition, a benign disease and all of the nodules are expected to be the same, differing only in size. On ultrasound benign colloid nodules typically have a sharp edge, halo (a black ring thought to represent compressed blood vessels) and are isogenic. They are usually big (> 3 cm diameter) texture and wider than tall, as shown in fig. 2. A micro cancer incidentally found in a multi nodular gland can be considered to be an incidentaloma that would not have harmed the patient if left alone.

Figure 2. Thyroid ultrasound from a patient with a nodule that was shown to be benign on biopsy. The nodule is isogenic, wider than tall, with a sharp edge and halo.

Some intra nodular "micro-calcifications" are actually colloid, which may be lined up like a comet tail or dispersed around the inner edge of the nodule (fig. 3). Others, brighter and sharper, are probably colloid crystals. Many nodules have a single bright spot at one side of the nodule, like the nucleus of a cell, that might be the source of the colloid fluid, that could be called "colloidoma". Although some radiologists describe these as "calcifications" - implying suspicion for papillary thyroid cancer, they are actually quite different from the micro calcifications of papillary thyroid cancer, as will be seen later.

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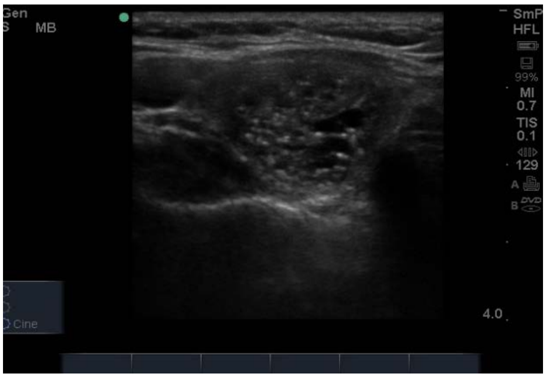
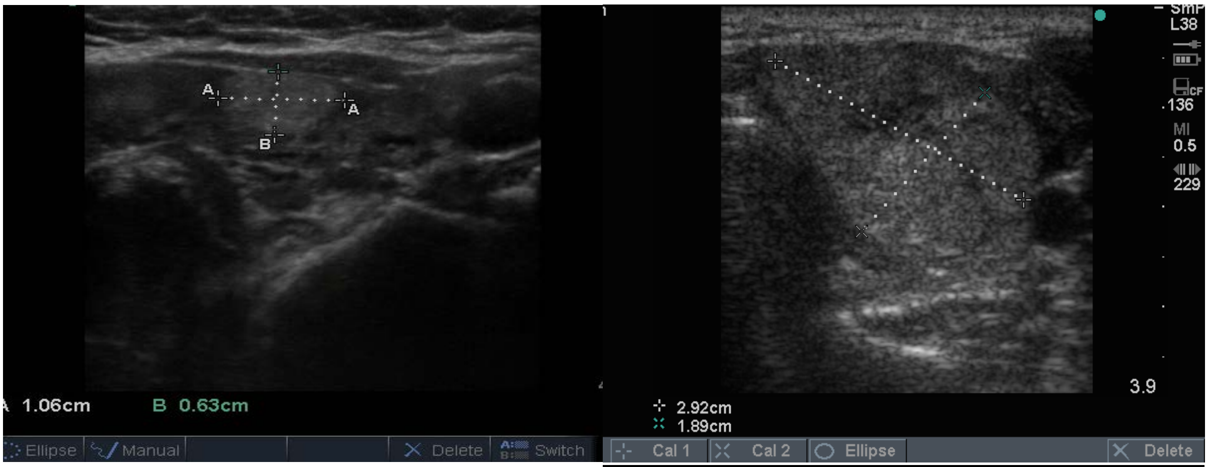


Figure 3. A benign nodule with a series of bright micro-calcifications inside the cell membrane. These spots need to be differentiated from the larger softer (less bright) micro calcifications which are often found in papillary thyroid cancer cells.

Follicular nodules

Follicular nodules are much less common than colloid nodules with a different appearance on ultrasound. They are more cellular, giving a solid appearance, with a whitish colour, and described as milady hyperechoic (Fig. 4). They also have a sharp edge and halo and grow slowly over time. The problem with these lesions is that FNAB is unable to differentiate between a benign follicular adenoma and follicular cancer and if the latter is suspected thyroid surgery, is the final arbitrator. About 10% of benign thyroid nodules are follicular and most of them end up being removed. Examples of follicular nodules that were finally proven to be benign are shown in fig.4 A and 4 B, below. On follow-up US, 6 – 12 months later, repeat biopsy might be indicated if a nodule has grown by 20% or more in two or more dimensions; benign nodules also grow, but less quickly.



A. B.

Figure 4. Two examples of follicular nodules that were shown at surgery to be benign. The nodules are roughly oval shaped, slightly hyper echoic and have sharp edges and, particularly the bigger of the two, thick halos

Hot nodules

Nodules shown to be "hot" or "toxic" on technetium scan are "never" cancerous as they are at least partially differentiated, in other words produce thyroid hormones. It is however sometimes appropriate to carry out FNAB in order to relieve the patient and confirm the benign nature of the nodule. The appearance of toxic nodules varies but they are usually similar to the colloid nodules. Occasionally they are markedly hypoechoic, or cystic, as in this case (fig. 5)

Figure 5. Thyroid nodule in a patient with hyperthyroidism shown, from technetium uptake and scan, to be "hot" or "toxic".

Thyroid cysts

Thyroid cysts are important because it may be possible to relieve the patient's neck symptoms by removing the fluid. However, a cyst tends to refill, which can be a sign that it has a solid component which, in about 10% of cases, is cancerous (fig. 5) Sometimes it is difficult to differentiate a cyst from a hyperechoic colloid or "toxic" nodule, even after biopsy, since fluid may be drawn off from both lesions. Both may look hypoechoic (black) but a cyst is usually larger and more round, somewhat blacker and has a thin, sharp edge, as shown here in fig. 6. The cyst has a specific feel on palpation (whereas a colloid nodule where palpable, feels firm, even hard) and if, tested for, is translucent. Cysts may have a solid component whose echogenicity may be hypo or hyper echoic, sometimes only seen after removal of the fluid

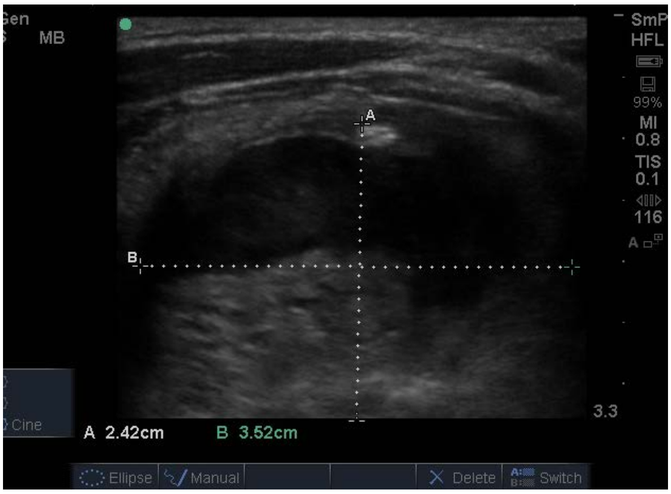
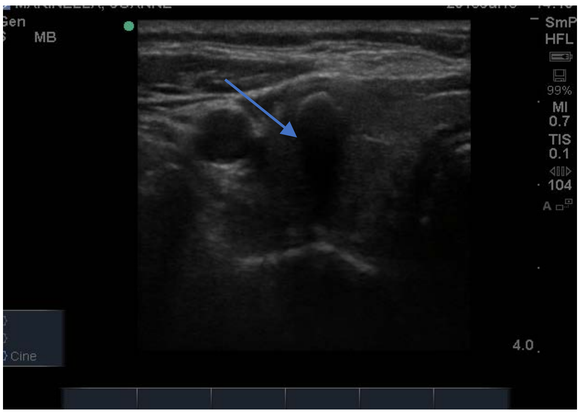


Figure 6. Large thyroid nodule of mixed appearance, i.e., comprising both solid (lower half) and cystic (upper half) components. FNAB of the solid component showed that the lesion was benign whereas biopsy of the upper region obtained a large amount of chocolate coloured fluid.

Calcification

The normal gland does not contain any calcification. The presence of calcification is association with nodules generally indicates chronicity of any associated disease, such as nodules or Hashimoto thyroiditis, and therefore that the nodules are benign. However, breaks in the wall of a calcified nodule suggests that the nodule is a cancer which has invaded into the surrounding thyroid tissue and is considered a suspicious feature of a nodule Calcification surrounding a thyroid nodule, giving it the appearance of a "bone ball", can be felt as a hard, mobile lump on neck palpation that is crunchy on FNAB. Chronic linear or egg shell calcification is associated with shadowing because the ultrasound waves are unable to pass through calcified tissue (fig. 7A,7 B). Sometimes calcification is seen as scattered spots or sheets scattered throughout the thyroid

A.



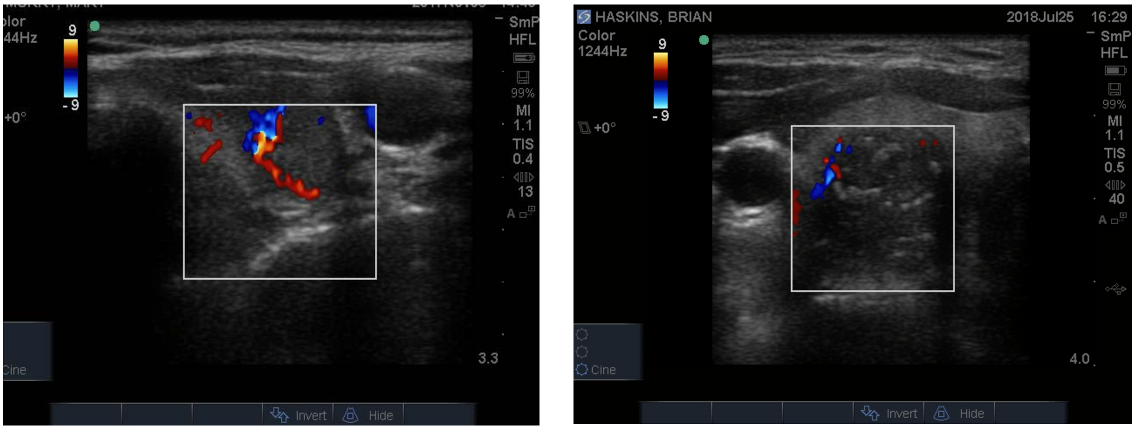
B.

Figure 7. In (A) is seen linear calcification in the anterior aspect of a benign 15 mm nodule is seen as a curved bright hypoechoic shelf (arrow) that blocks the transmission of the ultrasound waves, so the nodule behind appears to be hypoechoic, as in a cyst. In (B) is seen a small calcified nodule (upper arrow) and linear calcification in the lower part of the nodule

<u>Vascularity</u>

The blood supply to thyroid nodules is an important feature to be documented in the course of real time ultrasonography. There are three types of vascularity to be discussed. Firstly, the so-called hypoechoic halo surrounding a benign nodule is caused by compressed blood vessels which can be seen when the "colour" button is engaged. An example of this is seen in fig. 8A. Secondly, the degree of vascularity around the outside of a nodule is reflective of its activity and prominent blood supply around a nodule maybe a sign of thyroid cancer (fig. 8B) but can also be present around nodules shown by biopsy to be benign. It has recently been shown that blood vessels within a nodule, especially if it has other suspicious features (fig 8 B). may be a reliable sign of cancer

Figure 8. Examples of vascularity around the edge of a benign nodule and (A) and associated with blotchy macro calcifications in a hard, irregular edged, nodule that is suspicious for papillary cancer (B)



A B

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Below (fig. 9) is shown matching images of a benign nodule without (A) and with (B) blood flow in the halo around the nodule

A, B.

Fig.9 A small 8 mm benign nodule in the left thyroid lobe shown as an ultrasound image in (A) and with surrounding vascularity in (B)

Thyroid cancer

The thyroid specialist using his own portable US machine will, with experience, learn to recognize those characteristics of nodules which are suspicious for malignancy. These include; taller than wide indicating that the tumour is growing through, rather than along, the tissue planes, absence of a peripheral halo (compressed blood vessels in a benign nodule), the 3-4 mm "fluffy" intra nodular micro calcifications (actually psamoma bodies rather than true calcification) which are 90% specific for papillary cancer, intra nodular hypervascularity which is presumed to be feeding the cancer and size > 3 cm.

` Three examples of papillary thyroid cancer are shown here; Firstly, a large typical papillary cancer with the characteristic micro calcifications) is seen in fig. 10.

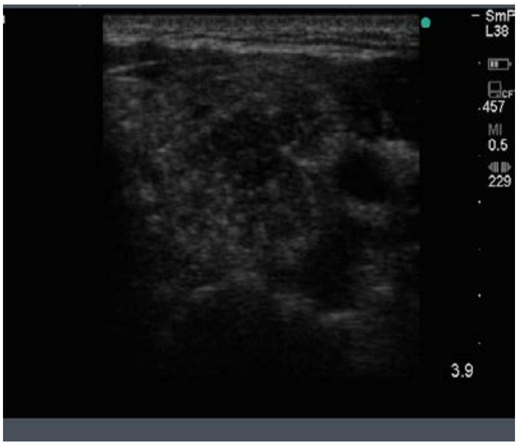


Figure 10. Thyroid ultrasound from a patient with confirmed papillary thyroid cancer. The nodule is large (3 cm) and hypoechoic with an indistinct irregular edge and central micro calcifications. The calcifications are softer (less white) that seen above in some benign nodules and larger, around 2-3 mm (arrow). There is no halo. Not seen here, the blood supply was increased in the lesion and there was a feeding vessel on one side of the lesion.

Secondly, a smaller but more hypoechoic lesion with obvious and larger soft micro calcifications and an irregular edge is shown in fig. 11. These two nodules are typical for papillary cancer and are reported from FNAB as "suspicious for papillary thyroid cancer". In both cases this was confirmed at thyroidectomy

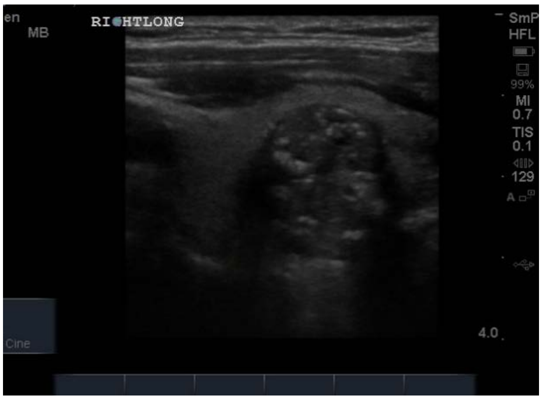


Figure 11. Papillary cancer lesion with large fluffy micro calcifications an irregular edge and overall hypoechoic texture.

Thirdly, an example of a much smaller lesion that turned out to be papillary cancer is shown in fig. 12. The nodule is only 10 – 12 mm in size, hypoechoic and has an unusual and irregular edge; Three years earlier the same lesion was seen on ultrasound and its size then was 8 x 9 mm with no other suspicious features and no micro calcifications nor feeding vessels, blood vessels, indicating that it has grown very little over the intervening 3 years. It was considered suspicious on ultrasound because of its shape and edge. The lesion was shown to be suspicious for papillary cancer at FNAB and confirmed at hemi thyroidectomy.

Figure. 12. Small 10 mm nodule with an overall blurry irregular edge that is taller than wide and hypoechoic, shown from FNAB to be papillary cancer

It is not possible to differentiate the more common papillary cancer from the very much less common follicular neoplasms by ultrasound, although follicular lesions are more cellular and less hypoechoic and do not usually contain micro calcifications, the diagnosis being made at open biopsy.

Recently, the emphasis has shifted to classifying nodules according to their degree of suspicion, regardless of their size. In the context of this changing approach to assessing thyroid nodules a sophisticated, if somewhat complicated, new scoring system, known as TI-RADS has been developed to allow everyone who carries out thyroid ultrasonography, whether technician, radiologist or endocrinologist, to be consistent in how they characterise and report features of thyroid nodules. As a result of the now almost universal use of TI-RADS, the tendency is to carry out more ultrasounds and fewer biopsies. This seems logical because we should remember that only about 5% of patients with one or more thyroid nodules turn out to have cancer.

Graves hyperthyroidism

In Graves hyperthyroidism, the gland is typically diffusely enlarged to a degree that reflects the severity of the hyperthyroidism. Its vascularity is increased, often dramatically, and is generalised. As the disease becomes chronic e.g., after one or more relapses post ant thyroid medication, the gland shrinks and become scarred and nodular, so called “nodular Graves disease”. However, it is not uncommon for patients with Graves disease to have incidental nodules, in which case the differential diagnosis is 1. Graves disease which has become thickened and nodular due to its chronicity 2. Graves disease with distinct nodules and 3. thyroid autoimmunity with a hot (toxic) nodule.

The blood supply in typical Graves disease is diffusely increased (and associated with a murmur) sometime up to 100 times normal, and the gland texture on ultrasound is usually heterogeneous (patchy) with a fine cystic appearance throughout which reflects the diffuse nature of the inflammatory process. Following radio iodine treatment, the normal gland architecture is disrupted because the follicles are destroyed, and scar tissue predominates.

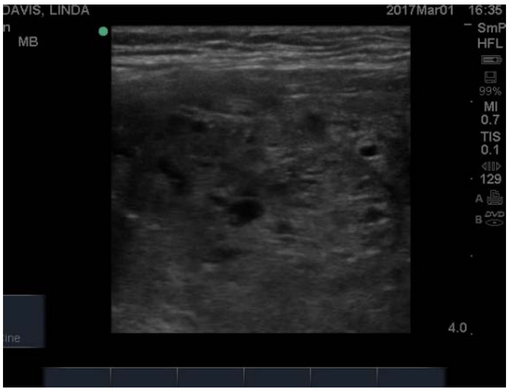
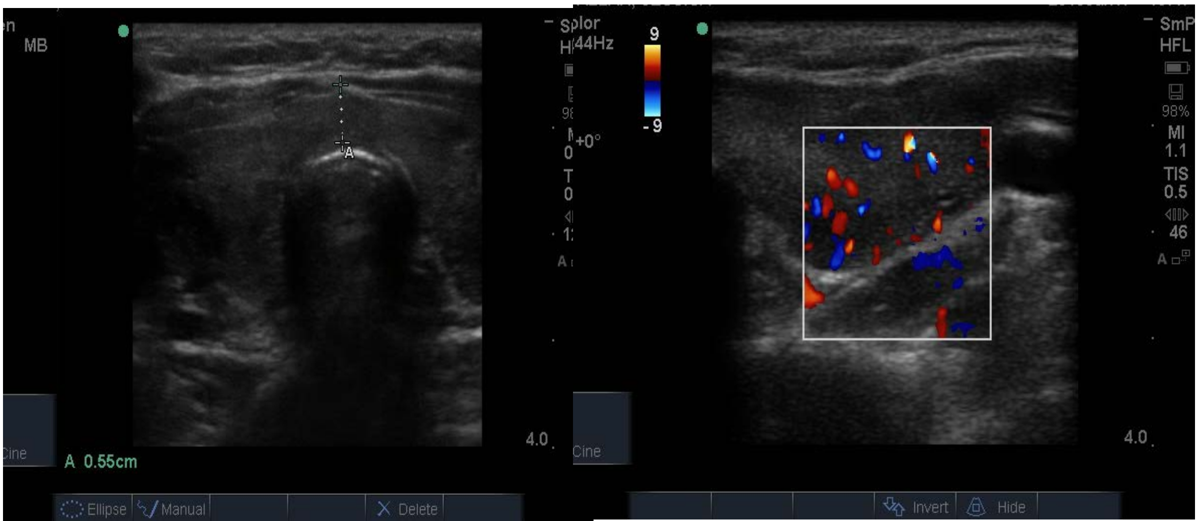


Figure 13. Thyroid ultrasound from two patients with Graves hyperthyroidism. In (A) is shown an example of early Graves hyperthyroidism manifest as multiple small inflammatory and lymphoid lesions, often described by the consultant radiologist as “nodules”. In (B)_is shown an enlarged thyroid, with a thick isthmus and a generalized patchy hypo echoicity due to the lymphocytic inflammation and thyroid cell proliferation. In (C) is shown the increased vascularity in the thyroid of the same patients as in (B)

A.

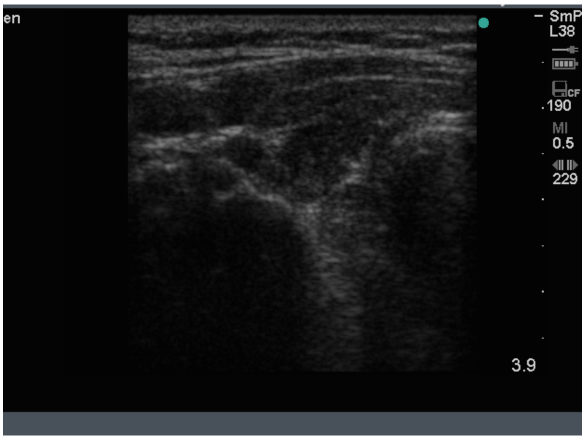


B C

Hashimoto thyroiditis

Hashimoto thyroiditis is common especially when diagnosed cytologically from biopsy of thyroid nodules, as an incidental finding, being demonstrated in 13.4% of one group of 811 patient, in one study. The disease is approximately 10 times more common in females than males. Ultrasonography should be performed in all patients with Hashimoto thyroiditis to identify any nodules. Although not clearly established, it seems likely that there is an increased prevalence of cancer in patients with this chronic inflammatory condition compared to patients without nodules Ultrasonography is also useful in following individual patients with Hashimoto thyroiditis as an aid to management with thyroxine replacement and to recognize the uncommon situation where hyperthyroidism changes ("flips") to Hashimoto thyroiditis

The author has developed a 5-stage classification of the inflammatory changes from early to end stage disease, as follows; Stage 1 is characterised by mild inflammatory changes manifest as small inflammatory lesions in a normal or slightly enlarged thyroid. In stage 2, the gland is enlarged and the cystic areas are better defined, more frequent and larger. The blood supply to the gland is increased in stages 1 and 2 but decreased in later stages. In stage 4 the gland is becoming avascular and the nodules are replaced by hypoechoic (black) spaces with scar tissue (fibrosis) with sheets of fibrosis, giving the appearance of pseudo nodules. In the final stage the gland is shrunken and scarred with absent blood supply and devoid of thyroid tissue. . Examples of the two types of end stage disease are seen in fig 14 below



A B

Fig, 14. Thyroid ultrasound findings in 2 patients with different features of late-stage Hashimoto Thyroiditis. In (A) the dominant feature is diffuse hypo echoicity, seen as black "holes" indicating the absence of thyroid tissue, some scarring, decreased vascularity and architectural damage in an overall enlarged gland. In (B), the thyroid gland is now shrunken, scarred, and shrivelled with pseudo nodules and scattered fibrous bands in a small gland; this is the final stage and the patient has no thyroid function.

Vocal cord assessment

Recently, the thyroid specialist has found a new use for his portable ultrasound machine. Although thyroid surgeons generally send their patients to an ENT specialist for direct laryngoscopic assessment of the vocal cords to identify any problem that was present before surgery, the thyroid specialist can learn to recognize and quantify normal abduction and adduction of the true vocal cord, especially in female patients. They do this by placing the small parts probe in a transverse plane across the anterior wall of the larynx just below the thyroid notch, with the patient speaking and humming (preferably in tune).

The future

New approaches to the use of ultrasound to assess thyroid nodules including shear wave elastography which measures tissue stiffness, are being developed in order to help identify those nodules that need to be biopsied. Thyroid specialists in Europe often treat thyroid cysts by injecting 90% alcohol to replace the fluid removed and some solid nodules are treated by laser ablation. These procedures are rarely used in Canada and Australia, countries where author has worked, and it is unlikely that this approach will ever become mainstream outside of Europe.

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