SHIP
Leben und Gesundheit in Vorpommern

EUthyroid

EUthyroid recommendation on conducting thyroid ultrasound in population studies

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EUthyroid

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1 Introduction

1.1 Aims

This guidance is indented as a practical tool for study nurses and ultrasound readers conducting population based studies to monitor iodine deficiency disorders (IDD). The guidance may be useful when writing a study manual and may be used for educational as well as training purposes. In addition to this guidance, training efforts can be supplemented with the EUthyroid ultrasound training video (https://vimeo.com/168037156) and the EUthyroid training application ARCUS (https://arcus.euthyroid.medizin.uni-greifswald.de), a web-based ultrasound reader certification tool (registration required).

The guidance was written within the EUthyroid project, which aims to harmonize iodine and thyroid-related population based studies in Europe. This can be realized by ensuring comparability of results therefore, improving the overall quality of studies. The objective of thyroid ultrasound in epidemiological studies is to track the prevalence and incidence of thyroid disorder (e.g. goitre, thyroid nodules) in a study population. In particular, changes of the thyroid gland due to improved iodine supply can be of interest in prevalence trend analyses. In addition, knowledge of risk factors and correlations with other organ systems can be obtained.

1.2 General Information

The ultrasound enables three-dimensional morphological structure analysis of the thyroid gland free from superposition. Sonographic volumetric is the gold standard for determining the organ size. The sonographic method currently used in clinical practice is based on the principle that ultrasound is radiated into the tissue and, once reflected from tissue structures; its sound components are captured and processed electronically (pulse-echo method, B-mode sonography).
The transmission frequencies used for this purpose are usually between 7.5-10MHz, the choice of the respective frequency represents a compromise between resolution and penetration depth. Although a higher frequency improves the resolution of the image displayed, it allows for a smaller penetration depth into the tissue.

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2 Anatomy of the thyroid gland

The thyroid gland is shaped like the letter 'H', with an oval lobe on each side of the trachea connected by the isthmus (Figure 1). The pyramidal process, originating from the isthmus and developing in the midline upwards, is a rare inborn variant. Abnormalities, such as the sublingual thyroid or a unilateral gland, are also very rare. The two lower arteries (inferior thyroid artery) enter the capsule of the thyroid on the dorsal side of the lower poles.

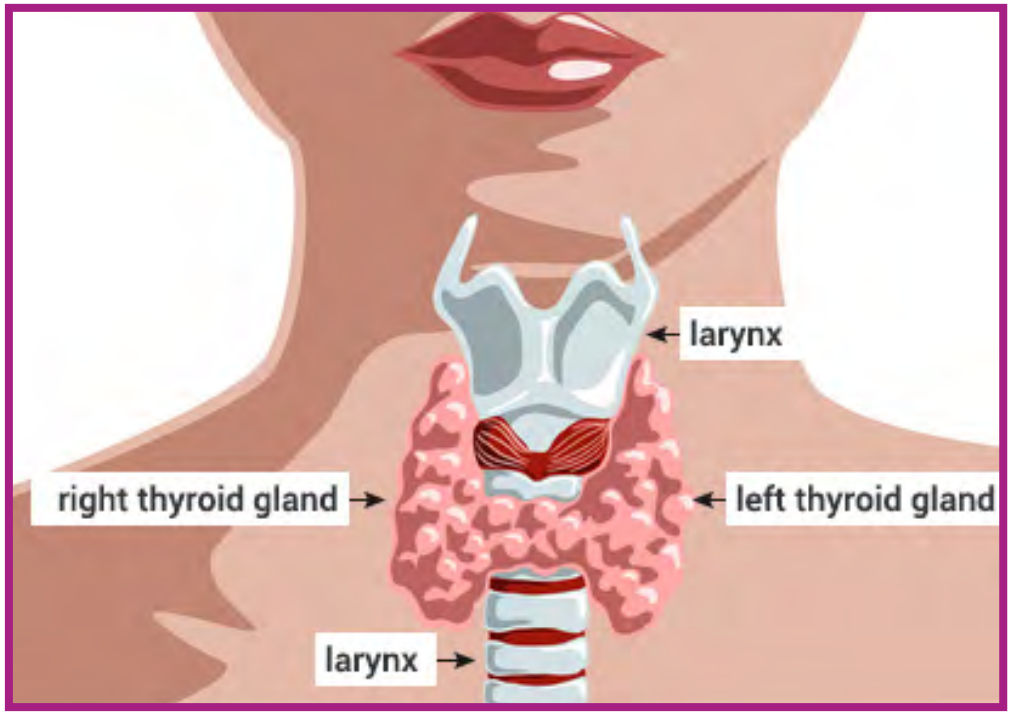

Figure 1: Thyroid Gland

The two upper arteries (superior thyroid artery) originating from the external carotid artery enter the upper poles. The thyroid gland consists of small lobules, each containing around 25 follicles. The content of the follicles depends on their function. It also determines the echo pattern (Table 1).

The echo pattern of the thyroid gland is homogeneous and hyperechoic, at normofollicular stage, giving a strong contrast to the hypoechoic pattern of the surrounding muscles, which can serve as a reference. The outline of the gland is regular and smooth. The bright echoes behind the isthmus are caused by air within the trachea. The section of the lobes is round or triangular in transverse planes and oval in longitudinal planes. The size of each lobe is 5–6 cm (length (a)) * 2–4 cm (width (b)) * 1–2.5 cm (thickness (c)). The volume of the whole gland is up to 18 ml in females and 25 ml in males according to Gutekunst et. al., 1993. Please refer to the Section 4 – Endemic goitre and Zimmermann et al., 2004 on specific reference values for children. The gland volume is determined by adding the volumes (V) of both lobes, each calculated from the formula:

V = 0.479 x length x width x depth (Brunn et al., 1981)

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Please note that the cut-off to determine goitre is only useful for epidemiological studies. Reference values for thyroid volumes vary depending on the iodine status under investigation. Therefore, cut-off shall not be used in a clinical setting. By experience, slightly enlarged thyroid glands are rarely accompanied with symptoms. By using the definition of goitre established by Gutekunst results of current studies can be compared with findings of population surveys and of monitoring studies performed in the last decades.

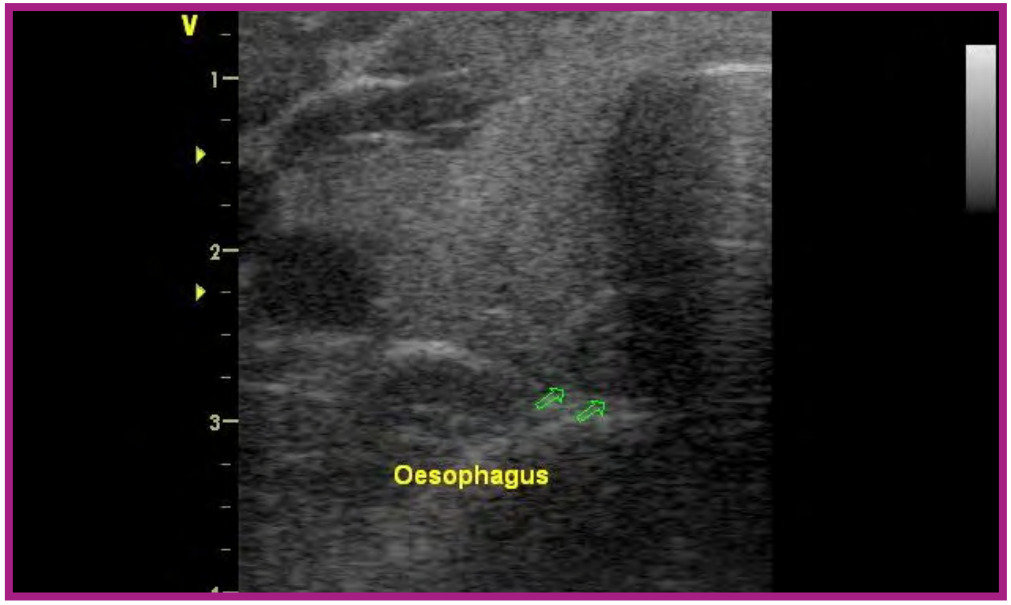

Figure 2: Oesophagus

Oesophagus

The cervical oesophagus (Figure 2) can be seen in the transversal plane behind the thyroid as a tubular or target-like structure if this area is scanned with the probe moved to the left-hand side to avoid the shadow of air within the trachea.

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Vessels

The large vessels (the carotid artery and the jugular vein) are behind the sternocleidomastoid muscles and lateral to the thyroid gland. The jugular vein shows as an oval shape and may collapse in certain phases of respiration or from the pressure of the probe. The carotid artery is round and shows stronger wall echoes than the vein.

Lymph nodes

The number of lymph nodes is especially high in the neck. High-frequency ultrasound frequently demonstrates normal lymph nodes, which are usually oval, with a maximum short axis diameter of 8 mm. The pattern is hypoechoic with a hyperechoic central hilum. In older people, the pattern becomes increasingly hyperechoic due to fatty degeneration, mostly starting from the hilum.

Muscles

The muscles are hypoechoic with a striated structure. They are important as anatomical landmarks and serve as a reference point for evaluating the echo pattern of the thyroid.

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3 Examination

3.1. Examination preparation

Figure 3: Example of examination room

SPECIFICATION FOR EXAMINATION ROOM

- Temperature: approx. 26°C ± 2°C
- Sufficient space for equipment (10m^2 recommended)
- Room has to be shaded by blinds

EQUIPMENT

- Treatment table
- Height adjustable sonographer chair
- Ultrasound system, 5-12 MHz linear array (most frequently 7.5 MHz)
- Knee pillow for support
- Neck roll to hyper-extend the neck

SUPPLIES

- Probe gel
- Sheet for treatment table
- Disinfectant

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3.2 Thyroid gland echo pattern

Number and size of the thyroid follicles and its colloidal content influence the echo pattern. The assessment of nodule echo patterns follows the echo pattern guidelines of the thyroid gland.

Table 1: Differentiation of thyroid echo patterns

Echo-normal	**normofollicular, normally functioning thyroid gland**
Hypoechoic	**micro-follicular, the image appears dark**
Hyperechoic	**macro-follicular, the image appears bright**
Echo-complex	**concurrent echo-normal/hypoechoic/hyperechoic patterns in one structure with blurred margins**
Echo-free	**dark areas, possible fluid (cyst)**
Echo-dense	**Possible calcifications**

3.3 Performing the thyroid ultrasound examination

3.3.1 Participant set-up

After the participant has entered in the ultrasound room, the sonographer reviews the examination with the participant to make sure he/she understands the procedure and to gain his/her cooperation. The participant will also be asked about any thyroid surgery and radioiodine therapy. The year of the last operation and the operated side and the year of the last radio-iodine therapy should be documented.

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Figure 4: Position of neck roll room

The participant will be asked to undress the neck and remove necklaces and large earrings. The thyroid ultrasound is performed in the supine position with slightly overstretched cervical spine. In support of the cervical spine a neck roll placed underneath (Figure 4). The head portion of the examination table is not to be raised. In exceptional cases, breaks during the ultrasound examination can be offered. The neck area will be covered with a cloth and ultrasound gel is applied to the throat. Scars should be documented.

3.3.2 Examination

Please use the following image sequence when examining the thyroid gland.

Examination	Documentation//labelling
Evaluation of the echo pattern right Transverse and longitudinal scan right	Split image // Right lobe
Volume measurement right Transverse scan right, longitudinal scan right	Transverse and longitudinal image with measurements // Volume right
Evaluation of the echo pattern left Transverse and longitudinal scan left	Split image // Left lobe
Volume measurement left Transverse scan left, longitudinal scan left	Transverse and longitudinal image with measurements // Volume left
Nodules Transverse and longitudinal scan right Transverse and longitudinal scan left	Split Image // Right lobe, nodule 1...5 Split Image // Left lobe, nodule 1...5

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Please note, when thyroid ultrasound is performed in a clinical setting, cervical lymph nodes should be assessed. Locating the thyroid gland Locating the thyroid gland Locating the thyroid gland

Locating the thyroid gland

After a brief orientation the probe is applied in a coronal plane above the cricoid without any additional pressure. It is then moved slowly and continuously towards the sternum. The trachea is clearly visible in the image centre. Thus, the transverse axis of both thyroid lobes can be followed.
The echo pattern of the thyroid gland is homogeneous and hyperechoic giving a strong contrast to the hypoechoic pattern of the surrounding muscles, which can serve as a reference. The outline of the gland is regular and smooth.

Evaluation of the thyroid echo pattern

The trachea, the accompanying vessels (carotid artery, jugular vein) and the echo pattern of the surrounding muscle groups (Smm (sternocleidomastoid muscle)) serve as a reference point for assessing the thyroid tissue echo pattern.

The examination starts in the coronal plane and the transverse scan image is captured first. Then the probe is rotated at the point of the largest expansion in width of the thyroid gland by 90 ° and the lobe is examined in a longitudinal scan. The longitudinal scan image is added to the already recorded transverse image (split).

In a hypoechoic pattern, the coloration of the thyroid tissue is identical to the muscle tissue. Muscle and thyroid tissue can only be visibly separated by the connective tissue of the thyroid capsule.

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Documentation/labelling: A split image of the transverse and longitudinal scan should be saved for each lobe. In case of enlarged thyroid glands, a non-complete longitudinal scan image is sufficient. The image is labelled either "right lobe" or "left lobe" in the bottom right corner.

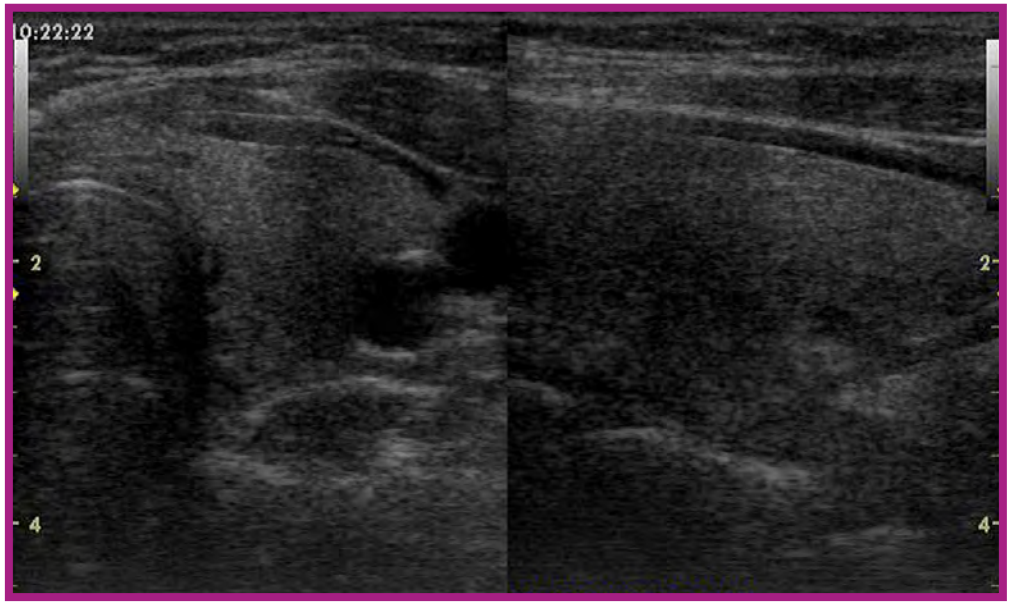

Figure 5: Documenting echo pattern, split image of left lobe; transverse scan left, longitudinal scan right

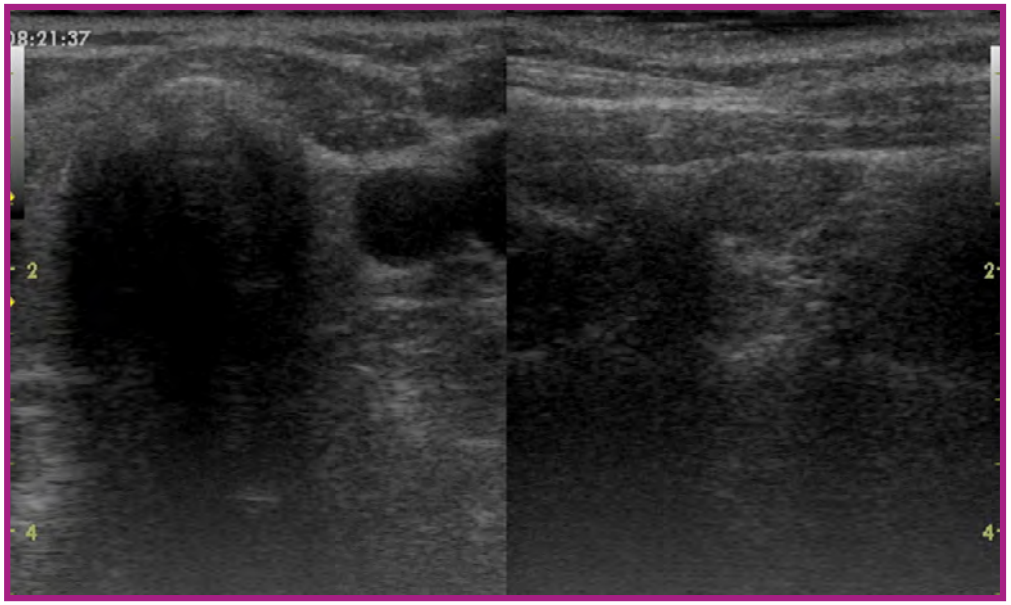

Figure 6: Documenting echo pattern, split image of left lobe after subtotal resection

After subtotal resection, small thyroid tissue remnants may be hard to identify, especially if they are not hyperechoic. Lack of the isthmus is typical example of a post-operative situation.

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Volume measurement

To determine the volume of each lobe, the width and depth are measured first in the transverse image. The width is measured at the lobe largest expansion. The depth is measured axial from the top edge to the bottom edge of the lobe.

Documentation/labelling: The transverse image with measurements is saved labelled either "volume right" or "volume left" in the bottom right corner of the image. The transverse image should be saved even if the participant has an operated thyroid gland.

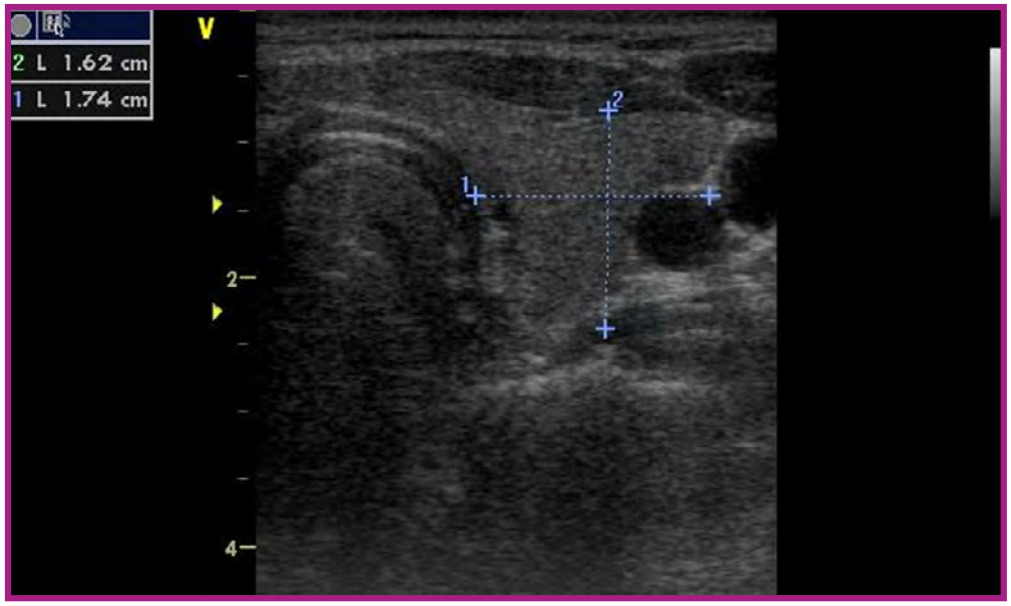

Figure 7: Diameter measurements of left lobe; 1) width, 2) depth

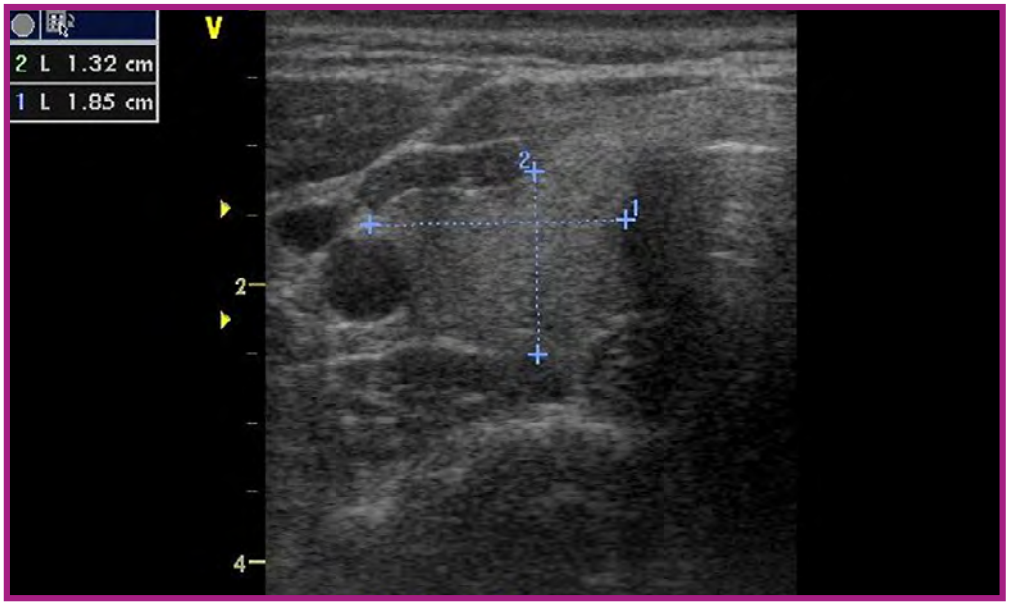

Figure 8: Diameter measurement of right lobe; 1) width, 2) depth

To capture the largest expansion in length, the lobe needs to be measured in a slight angle extending towards the cranium.
For accuracy, a complete image of the longitudinal scan is preferred. The volume for each lobe is calculated according to the formula:

V = 0.479 x length x width x depth (Brunn et al., 1981)

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Between the volume measurements of both thyroid lobes the depth of the isthmus is measured and recorded as well. The isthmus thickness should always be examined. If the isthmus measures > 1cm, it should be examined for nodules.

Documentation/labelling: The longitudinal image with measurements is saved labelled either "volume right" or "volume left" in the bottom right corner of the image. The longitudinal image should be saved even if the participant has an operated thyroid gland.

Table 2: Plausible measurements for each dimension of a thyroid lobe and the isthmus

Dimension	Minimum (in cm)	Maximum (in cm)
Width	0.2	4.8
Depth	0.5	4.4
Length	1.2	10.3
Isthmus	0.1	1.5

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In rare occasions the gland is enlarged so that it cannot be shown in one longitudinal scan or the probe used is insufficient in size to depict the full length of lobe. The following procedure is a recommendation on how to estimate the length if not despicable in one ultrasound image:

- a. The caudal tip of the lobe is adjusted in the longitudinal scan, so that it is exactly on the right hand side of the screen.
- b. The sonographer remembers the structures on the left hand side of the screen.
- c. The probe is moved slowly along the longitudinal axis of the thyroid gland in cranial direction until the memorized structure from the left hand side is just visible on the right hand side of the screen.
- d. Freeze the image.
- e. In case the thyroid extension exceeds the length of the probe, the sonographer measures the length from the right hand side of the screen to the cranial tip of the lobe, and adds 4 cm to this measurement to estimate the complete length of the lobe.

The length measurement must be performed at least twice. If the two measurements differ substantially, a third assessment is required. The length measurements are averaged and used to calculate the volume for each lobe according to formula listed previously.

Documentation/labelling: Since the longitudinal scan cannot be depicted within the screen, no image will be saved.

Nodules

Thyroid nodule is a structure, which can be differentiated from thyroid parenchyma by an imaging method. Each nodular structure (up to five) with a diameter larger than 1 cm in at least one dimension should be documented in a split image. Width, depth and length are measured. Based on the nodule's contour, the distinction between well definable margin or blurred margin and the echo pattern should be documented with the measurements. In comparison, cysts and cystic lesions have a hypoechoic pattern. All three dimensions should always be measured and documented as well.

Documentation/labelling: A split image of the transverse and longitudinal scan with measurements should be saved for each nodule. The image is labelled in the bottom right corner with the following information: either "right lobe" or "left lobe" and nodule number (1 through 5).

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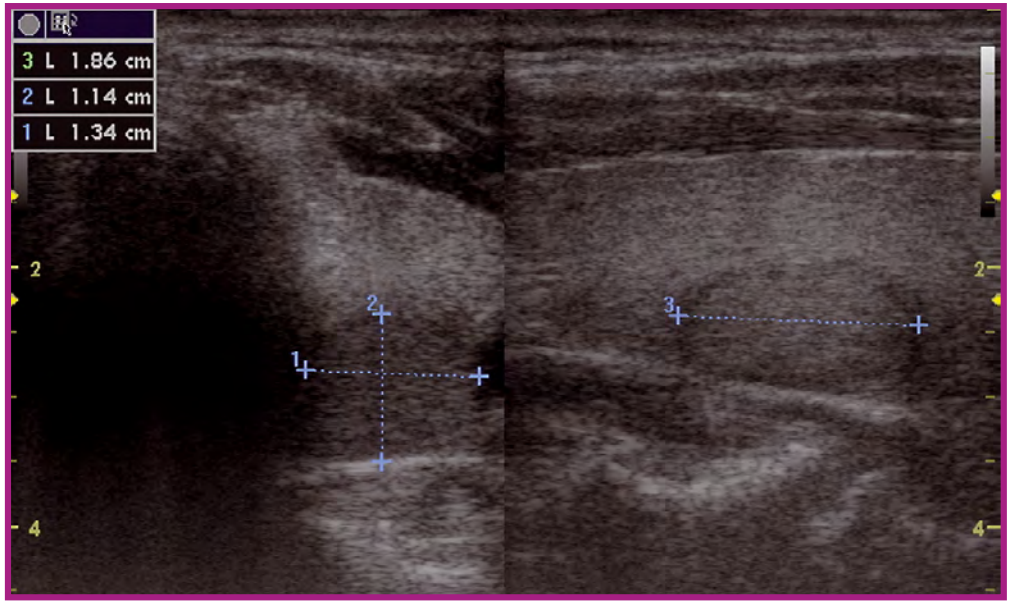

Figure 9: Left lobe; Nodule; 1) width; 2) depth; 3) length

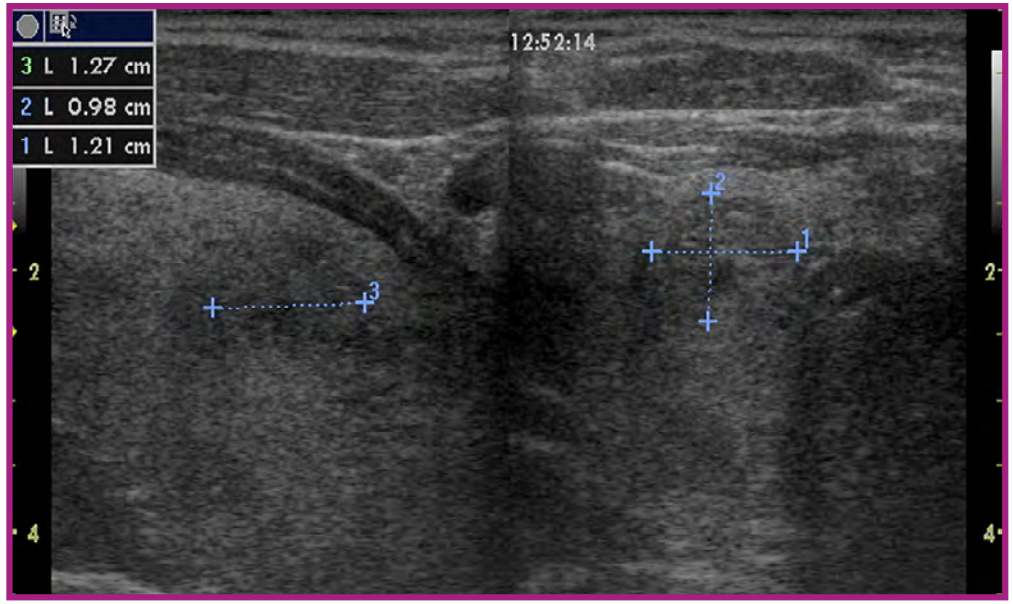

Figure 10: Right lobe; Nodule; 1) width; 2) depth; 3) length

3.3.3 Examination Wrap-Up

After removing the ultrasound gel and the cloth from the participant's upper body, the participant gets up and dressed. The sonographer can briefly review the examination results pointing out goitre, noticeable echo patterns and nodules.

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3.4 Flow-Chart

Participant set-up **(Duration: 5min)**	• Checking on all supplies • Verbally preparing the participant • Inquire about any thyroid surgery and radioiodine therapy • Ask participant to undress neck area and remove necklaces and earrings • Dimming lights or closing blinds • Preferred position for examining a patient is supine • Look for scars in the thyroid area
Examination **(Duration: 6-12 min; depending on indications and quality of images)**	• Assessment of each lobe's echo pattern and homogeneity • Volume measurement of each lobe • Monitoring and recording of pathological findings
Examination wrap-up **(Duration: 5 min)**	• Ask participant to get dressed • Review examination results and findings

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4 Diagnostic Findings

Endemic goitre (iodine-deficiency induced goitre)

Endemic goitre is very common in areas of iodine deficiency and is defined by an enlarged thyroid volume (>18 ml in women, >25 ml in men). In children aged 6 to 12 years, a thyroid volume above 97th percentile from international reference distributions (age-, sex-, and body surface-area- specific) is defined as goitre (Zimmermann et al., 2004). A moderate thyroid enlargement is rarely accompanied by symptoms.
Endemic goitre shows a homogeneous, hyperechoic pattern in the early stage of the disorder.

At this stage, goitre may regress if iodine deficiency is corrected. The pattern becomes inhomogeneous (nodular goitre), mainly in middle-aged patients, because of inhomogeneous growth of the thyroid follicles and the development of macro-follicular hyperechoic nodules. Degenerative alterations, such as cystic degeneration of the nodules and calcification, may also occur. Liquid parts of the nodules are echo-free and may imitate cysts. Calcifications cause strong echoes, sometimes with acoustic shadows.

Autoimmune disorders of the thyroid

A common sonographic finding in autoimmune disorders of the thyroid is a hypoechoic pattern.

Graves' disease

In this disease, autoantibodies against the thyroid-stimulating hormone receptor stimulate the thyroid in similar way as TSH. The disease occurs more often in young female adults, but can be seen at any age and also in men. Ultrasound can be used to visualize a moderately enlarged thyroid with a characteristic hypoechoic homogeneous or slightly inhomogeneous pattern corresponding histologically to hyperplastic but empty follicles. Colour and power Doppler examinations demonstrate striking hypervascularity. Focal lesions (nodules) within the hypoechoic thyroid gland in Graves-Basedow's disease are independent of the basic disease and should be considered separately.

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Autoimmune thyroiditis (Hashimotos' thyroiditis)

In this disease, lymphocytic infiltration slowly destroys the gland. This infiltration causes a hypoechoic or heterogeneous pattern of the thyroid, which develops over a long time.

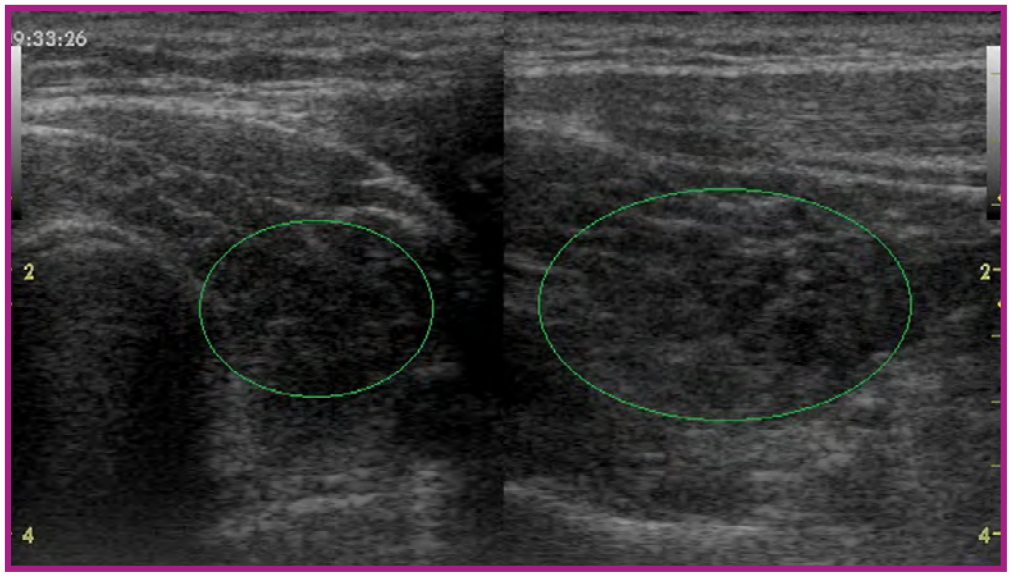

Figure 11: Hypoechoic pattern typical for Hashimotos' thyroiditis

In the initial stage, the gland might be slightly enlarged; in the later (atrophic) stage, however, the thyroid gland becomes small, with a volume of less than 10 ml, and blood flow can remain normal or decrease.
In some patients, though, the thyroid gland remains enlarged, with heterogeneous structures. Typical focal lesions should be considered for biopsy. Ultrasound imaging alone cannot confirm Hashimoto's thyroiditis. Additional blood analysis is required to confirm the diagnosis.

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Focal lesions

Cysts and cystic lesions

True cysts of the thyroid are very rare, and most cystic echo-free lesions are cystic-degenerated nodules (Figure 12). In these cases, ultrasound demonstrates a cloud of echoes floating in the fluid. The puncture shows brownish fluid ('chocolate cyst').

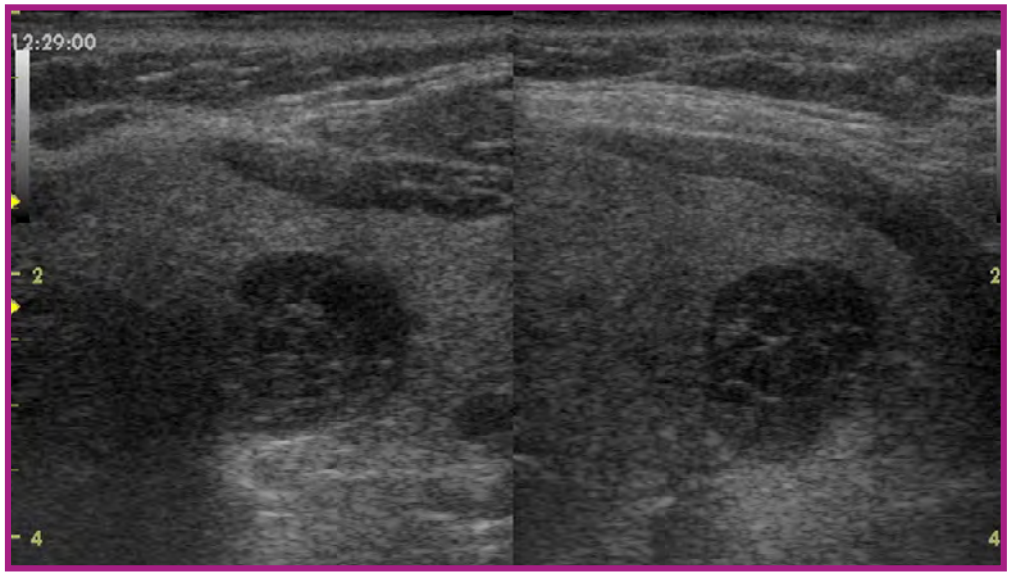

Figure 12: Cyst in the right lobe (transverse scan left, longitudinal scan right)

Solid nodules

Nodules in the thyroid are common findings and are often asymptomatic. Malignant tumours of the thyroid are relatively rare. The differentiation of benign and malignant nodules is a challenge in the ultrasound diagnosis of the thyroid gland.

Benign lesions

Adenomas are encapsulated, grow slowly and are mainly micro-follicular. Adenomas vary in their function. Toxic adenomas are highly differentiated and can accumulate iodine independently of thyroid-stimulating hormone regulation. Depending on the follicular structure, adenomas are mostly hypoechoic (micro-follicular) or more hyperechoic and rather homogeneous. Their contour is smooth. A hypoechoic halo (B-scan) with vessels around the nodule is characteristic of a benign adenoma and is, therefore, best demonstrated with colour Doppler. Toxic adenomas often show hypervascularity. Hyperplastic nodules develop over several years in cases of endemic goitre, and are caused by the differential growth ability of the thyroid cells. These lesions are not true neoplasms. Owing to their normofollicular or macro-follicular structure, they are often hyperechoic with a hypoechoic halo. Degenerative alterations, such as cystic parts or calcifications, are common, causing a complex sonographic pattern with echo-free areas and strong echoes.

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Malignant tumours

Papillary and follicular carcinomas are the commonest thyroid carcinomas, with prevalence of 75% and 16%, respectively. They are highly differentiated and grow slowly. Anaplastic carcinoma is rare, especially in iodine-sufficient areas (ca. 1–2%), and is a carcinoma of older patients (> 65 years). Medullary carcinoma arises from the C cells. It occurs either sporadically, in a hereditary form (RET mutation; isolated familial MTC), or as part of multiple endocrine neoplasia type 2 (2A or 2B). Metastases, mainly from lung cancer and malignant lymphomas, may involve the thyroid gland. The malignant tumours are hypoechoic and slightly inhomogeneous, although an inhomogeneous pattern is difficult to recognize in smaller lesions. An extremely hypoechoic pattern is found in malignant lymphomas and anaplastic carcinomas. Lack of a halo is typical. The contour is irregular and may show pseudopods or spicules. Interruption of the thyroid capsule and infiltration of the surrounding tissue can be visualized. When the sagittal diameter is greater than the transverse diameter, the finding is usually suspect. Dispersed strong echoes arising from micro-calcifications are characteristic in papillary carcinoma. Spotted calcifications also occur in medullary and anaplastic carcinomas. Occasionally, small echo-free or cystic parts are seen in papillary carcinomas.
The Doppler technique shows hypervascularity in highly differentiated carcinomas, but without a vascular halo. Anaplastic carcinomas, most of the metastases and the lymphomas are hypovascular when compared to the thyroid.

Post-treatment thyroid

Providing the patient with information about the treatment (disease and method) is a prerequisite for post-treatment check-ups. This is especially important after surgery. During the preparation of the patient's neck for thyroid ultrasound, the examiner should look for scars. After subtotal/non-radical resection of an endemic goitre, relatively large nodular relapses with inhomogeneous echo patterns on both sides of the trachea may be seen. Lack of the isthmus is typical in the post-operative situation. After subtotal resection, it is sometimes difficult to identify small thyroid remnants, especially if they are not hyperechoic (echo-rich). Examination of the lymph nodes and identification of the local recurrence are the main objectives of follow-up checks after surgical treatment of carcinomas. Enlarged, rounded lymph nodes are suspicious. It is interesting that lymph node metastases from highly differentiated carcinomas show a hypervascularity similar to that of the primary tumours. In Graves' disease, the typical hypoechoic pattern disappears with functional remission after/during treatment whereas after radioactive iodine treatment the thyroid remains hypoechoic. A reduction in the elevated flow velocity in the feeding arteries appears to be an early sign of successful treatment. In contrast, the hypoechoic pattern of Hashimoto thyroiditis is seen in all phases, independent of function. Radioiodine ablation of the thyroid or radiation of the neck (lymphomas) causes a reduction of thyroid tissue and ultimately leads to a small thyroid. Warm or toxic adenomas treated successfully with alcohol instillation not only become smaller and more hyperechoic, but their hypervascularity disappears.

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5 Literature

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