Journal of Endocrinological Investigation https://doi.org/10.1007/s40618-018-0935-8

ORIGINAL ARTICLE

1



- ² Thyroid ultrasonography reporting: consensus of Italian Thyroid
- ³ Association (AIT), Italian Society of Endocrinology (SIE), Italian Society
- 4 of Ultrasonography in Medicine and Biology (SIUMB) and Ultrasound
- ⁵ Chapter of Italian Society of Medical Radiology (SIRM)

T. Rago¹ · V. Cantisani² · F. Ianni³ · L. Chiovato⁴ · R. Garberoglio⁵ · C. Durante⁶ · A. Frasoldati⁷ · S. Spiezia⁸ · R. Farina⁹ ·
 G. Vallone⁹ · A. Pontecorvi³ · P. Vitti¹

⁸ Received: 5 June 2018 / Accepted: 3 August 2018

⁹ © Italian Society of Endocrinology (SIE) 2018

¹⁰ Abstract

11

12

13

14

15

16

17

18

19

Thyroid ultrasonography (US) is the gold standard for thyroid imaging and its widespread use is due to an optimal spatial resolution for superficial anatomic structures, a low cost and the lack of health risks. Thyroid US is a pivotal tool for the diagnosis and follow-up of autoimmune thyroid diseases, for assessing nodule size and echostructure and defining the risk of malignancy in thyroid nodules. The main limitation of US is the poor reproducibility, due to the variable experience of the operators and the different performance and settings of the equipments. Aim of this consensus statement is to standardize the report of thyroid US through the definition of common minimum requirements and a correct terminology. US patterns of autoimmune thyroid diseases are defined. US signs of malignancy in thyroid nodules are classified and scored in each nodule. We also propose a simplified nodule risk stratification, based on the predictive value of each US sign, classified and scored according to the strength of association with malignancy, but also to the estimated reproducibility among different operators.

Keywords Thyroid · Thyroid nodules · Thyroid ultrasonography · Autoimmune thyroiditis · Graves' disease · Thyroid cancer

²² Introduction

Thyroid ultrasonography (US) is the gold standard for thy roid imaging and its widespread use is due to an optimal
 spatial resolution for superficial anatomic structures, a low
 cost and the lack of health risks. Thyroid US is currently

	_	
A1 A2		T. Rago rago@endoc.med.unipi.it
A3 A4 A5	1	Endocrinology Unit, Dept. Clinical and Experimental Medicine, University of Pisa, Via Paradisa, 2, 56124 Pisa, Italy
A6 A7 A8	2	Dept. of Radiological Science, Policlinico Umberto I, University Sapienza, Viale del Policlinico, 155, Rome 00161, Italy
A9 A10	3	Endocrinology Unit, University Cattolica del Sacro Cuore, Largo Agostino Gemelli, 8, Rome 00168, Italy
A11 A12 A13	4	Internal Medicine and Endocrinology Unit - ICS Maugeri, IRCCS, University of Pavia, Via S. Maugeri, 4, Pavia 27100, Italy

used for the diagnosis and follow-up of diffuse or focal thyroid illnesses such as Hashimoto's thyroiditis [1, 2], Graves' disease [3, 4], goiter and thyroid nodules [5–9].

Thyroid hypoechogenicity has been shown to be indicative of thyroid autoimmunity, due to a diffuse lymphocytic infiltration that disrupts the normal array of thyroid

5 Endocrinology, Diabetology and Metabolism Unit, A14 Dept. Medical Science, University of Torino, Via Magellano, A15 1, Turin 10128, Italy A16 Dept. of Internal Medicine and Medical Specialties, A17 University Sapienza, Viale del Policlinico, 155, Rome 00161, A18 Italy A19 Endocrinology Unit, Arcispedale S. Maria Nuova, IRCCS, A20 Viale Risorgimento, 80, Reggio Emilia 42123, Italy A21 Endocrine Surgery, Ospedale del Mare, Via Enrico Russo, A22 Naples 80147, Italy A23 9 Dept. of Advanced Biomedical Science, University of Naples A24 Federico II, Corso Umberto I, 40, Naples 80128, Italy A25

28

29

30

31

Deringer

of risk [26, 27].

Thyroid US methodology

parenchyma in Hashimoto's thyroiditis or to the microfol-

licular pattern and increased vascularity in Graves' disease

[3–10]. Thyroid hypoechogenicity at ultrasound helps to

identify patients who have a diffuse Hashimoto's thyroiditis

among a larger group of patients with goiter and circulating

thyroid autoantibodies [3]. The pattern of thyroid hypoecho-

genicity at ultrasound was shown to have a higher sensitiv-

ity than thyroid autoantibody positivity for diagnosing or

information regarding the size of nodules and defines pat-

terns correlated with the risk of cancer. Several studies have

been conducted to establish the usefulness of thyroid US in

the diagnosis of benign versus malignant thyroid nodules

[5–8, 13–15]. The US features more frequently associated

with thyroid carcinoma are hypoechogenicity, absence of

a halo sign, the presence of microcalcifications, a "taller

than wide" shape [13–18]. However, the sensitivity, speci-

ficity, and accuracy of these US signs are extremely vari-

able in the literature. It is widely recognized that any single

ultrasound pattern cannot be considered specific for malig-

nancy. Rago et al. demonstrated that one single parameter is

weakly predictive of malignancy, while the combination of

US features has a higher specificity than any single pattern,

but this gain of specificity is achieved at the expense of a

lower sensitivity [13]. Most scientific societies agree that

US feature should support the indication to perform fine

needle aspiration (FNA). To this purpose, several classifica-

tion systems have been proposed with the aim to stratify the

risk of cancer in thyroid nodules [7, 19–25]. Some of these

systems were termed TI-RADS (Thyroid Imaging, Report-

ing and Data System) because they were modeled according

to the American Committee of Radiology BI-RADS, which

has been widely accepted in breast imaging. Some socie-

ties, such as the American Thyroid Association (ATA), have

taken a slightly different, pattern-oriented approach [6]. The

plethora, complexity, and lack of congruence of these sys-

tems have limited their adoption in the clinical practice. Fur-

thermore, the comparison of the scoring systems currently

proposed has shown relevant differences in the stratification

drawbacks such as the poor reproducibility, due to differences in the equipments used, and a lack of a standardized

US reporting. To fully capitalize the diagnostic capabilities

of an ultrasound examination in the context of thyroid disease, the purpose of this consensus statement is to stand-

ardize the report of thyroid US through the definition of

common minimum requirements and a correct terminology.

Aside the well-recognized advantage, thyroid US has also

In nodular thyroid disease, conventional US provides

predicting hypothyroidism and hyperthyroidism [11, 12].

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

61

62

63

64

65

66

67

68

69

70

71

72

73

74

75

76

77

78

79

80

81

Thyroid US is performed with the patient lying in the 83 supine position and having his/her neck extended. A high-84 frequency (7.5-14 MHz) linear transducer, along with 85 color flow or power Doppler examination, is used. Limi-86 tations exist for large thyroid glands, such as multinodular 87 sub-sternal goiters, and for the upper mediastinum explo-88 ration, which may benefit from additional scans using a 89 6-MHz linear transducer or a 3-5-MHz convex transducer. 90 Elastosonography, a tool nowadays available in a grow-91 ing fraction of modern US equipments, may add useful 92 information in the evaluation of thyroid nodules (Fig. 2).

- (a) Perform a thorough transverse US scanning from the sub-lingual position to the subclavicular region, starting with a global assessment of the thyroid gland and obtaining an anatomical overview of its relation with the central neck structures.
- (b) Using transverse and longitudinal US scanning, focus on the location, size, shape, margins and echostructure of the right and left lobe and isthmus. Detect the presence of focal lesions, their precise location, size, morphology, vascularization and elasticity by elastosonography, if available.
- (c) Using transverse US scanning, perform a global assess-105 ment of the central and cervical lymph nodes. Start 106 from the sub-mental group (level Ia) to the central 107 compartment (level VI) until the subclavicular region. 108 Then move to the sub-mandibular group (level Ib) 109 and, maintaining as anatomical reference the jugular 110 carotid short axis, explore II-III-IV levels (respec-111 tively, upper-medium-lower jugular groups). There-112 after, scan transversely from the sternocleidomastoid 113 muscle to the supraclavicular region to explore the V 114 level (posterior triangle group), on both sides. Focus 115 on clinically relevant lymph nodes obtaining transverse 116 and longitudinal scanning parallel to the long axis to 117 evaluate size, morphology and vascularization. 118
- (d) Evaluate any accessory pathological findings in the thyroid nearby space (e.g. parathyroid glands, salivary glands, vessels).
 121

Rules for US reporting

- (a) Images should be labeled stating the patient's name and facility identification, the examination date, the anatomic site and side.
 123
 124
 125
- (b) Describe thyroid position and shape when abnormal.
 Report the size of the thyroid gland (through estimation of the thyroid volume or the maximum diameter 128

Dispatch : 11-10-2018

122

,

82

93

94

95

96

97

98

99

100

101

102

103

129		of depth, width and length, the parenchymal echostruc-
130		ture, echogenicity and vascularization (Table 1).
131	(c)	Focus on the presence of focal lesions within the thy-
132		roid, which should be defined as thyroid nodules or
133		pseudo-nodules and report their precise location, mor-
134		phology and vascularization (Table 2). Report the pre-
135		cise location of thyroid nodules when more than one
136		is detected. It will allow avoiding mistakes in guiding
137		fine needle aspiration (FNA) and will guarantee inter-
138		observer agreement in the US follow-up. In multinodu-
139		lar goiter report dominant and/or suspicious nodule(s).
140		Describe them following a predetermined order, e.g.
141		from the top to the bottom of the right lobe, the left
142		lobe and then the isthmus (the thyroid nodules can be
143		numbered to help their identification). Optionally, add
144		a schematic representation of thyroid lesions along with
145		the US report. Most importantly, add for each thyroid
146		nodule an estimation of the US risk of malignancy (see
147		below).
148	(d)	Report position, size and features of clinically relevant
		1 max 1 max 1 max 1 1 2 max max 1 max

lymph nodes (Table 3), pointing out the suspicious 149 one(s). 150

(e) Report accessory pathological findings in the thyroid 151 nearby space (e.g. hyperplastic/adenomatous, parathy-152 roid glands, abnormal salivary glands, vessels). 153

154

155

156

US report in autoimmune thyroid diseases (ATD) (Figs. 1, 2, 3, 4, 5)

The echographic pattern of ATD is due to the pathologi-157 cal changes typical of these conditions. Hashimoto's thy-158 roiditis is characterized by lymphocytic infiltration of the 159 gland with lymphoid follicles replacing thyroid follicles 160 and reducing the follicular cell/colloid interface, the main 161 factor of the peculiar echogenicity of a normal thyroid 162 parenchyma [1, 2]. The degree of lymphocytic infiltration 163 and fibrosis is the main determinant of the different echo-164 genic patterns observed in Hashimoto's patients. Graves' 165 disease is characterized by hypercellularity, scanty col-166 loid and hypervascularization resulting in a similar hypo-167 echoic pattern [3, 4]. The hypoechoic pattern is a useful 168 sign both for diagnosis in patients with Hashimoto's thy-169 roiditis and negative serum thyroid autoantibodies and 170

1. Position	Normal location Mediastinal extension
2. Shape	Normal shape Presence of lobe asymmetry Presence of thyroid anatomic variants (lobe agenesis, ectopic thyroid, pyramidal lobe, thyroglos- sal duct nodule or cyst, Zuckerkandl's tubercle)
3. Size	Report the three diameters for each lobe in mm ^a Report thyroid volume in ml ^b
4. Echotexture (echoes distribution)	Homogeneous: uniform appearance of the thyroid parenchyma Heterogeneous: non-uniform appearance of the parenchyma, due to an irregular echo pattern showing numerous micro-nodules or echogenic septa
5. Echogenicity (echoes brightness)	Normal echogenicity: higher echogenicity compared to pre-thyroid (neck strap) muscles, similar/ slightly higher echogenicity compared to salivary glands [1, 2] Hypoechogenicity: diffusely reduced echogenicity of thyroid parenchyma Mild: thyroid parenchyma slightly darker than normal Moderate: thyroid parenchyma clearly darker, but less dark than neck strap muscles Marked: thyroid parenchyma clearly darker, similar or higher than neck strap muscles
6. Vascular pattern (color and power Doppler)	 Pattern 0 (reduced): parenchymal flow is absent or limited to few sub-capsular vessels Pattern 1 (normal): prevalent blood flow in main peripheral thyroid arteries and sub-capsular vessels, with scarce parenchymal blood flow with patchy, uneven distribution Pattern 2 (moderately increased): clearly increased parenchymal blood flow with patchy distribution Pattern 3 ("thyroid inferno"): markedly increased blood flow with diffuse homogeneous distribu-

^aA standardized order of the diameters should be used: antero-posterior (AP), transverse (T), longitudinal (L) diameter. This will likely avoid ambiguity, as well as ensure that subsequent measurements of the same structure are recorded in a similar fashion, even though in different settings

^bThyroid volume is estimated summing the volume of each lobe calculated by the ellipsoid formula (AP \times T \times L \times 0.52). Report isthmus size if AP diameter is > 0.5 cm. The normal thyroid volume varies with age, sex and geographic area. In Italy (borderline iodine sufficient area) the mean estimated thyroid volume was 12.9±3.6 and 9.2±2.9 ml in males and females, respectively [10]. Goiter is defined when thyroid volume is greater than the mean + 2 SD in each sex [males: > 20.1 (12.9 ± 7.2) ml; females: > 15 (9.2 ± 5.8) ml]

Journal : Large 40618	Article No : 935	Pages : 9	MS Code : JENI-D-18-00315	Dispatch : 11-10-2018	

Table 1	US	report	of the	thyroid	gland
---------	----	--------	--------	---------	-------

 Table 2
 US report in nodular thyroid disease

1. Position	Superior/medium/inferior, anterior/posterior, paraisthmic/isthmic, define if close to the thyroid capsule (sub- capsular)
2. Size	Report the three diameters for each nodule (depth or AP, width or T, length or L)
3. Shape	Round: equal length of the three diameters Oval: depth less than width and depth less than length Irregular: neither oval nor round, including 'taller than wide' (depth > width) and 'taller than long' (depth > length) shape
4. Composition	Solid: composed almost entirely of solid tissue with < 10% liquid Mixed predominantly solid: liquid component > 10% but < 50% Mixed predominantly cystic: liquid component > 50% but < 90% Cystic: composed entirely or nearly entirely of liquid (> 90%) Spongiform appearance: tiny cystic spaces separated by thin septa
5. Echotexture	Homogeneous: uniform appearance of parenchyma Heterogeneous: non-uniform appearance of parenchyma
6. Echogenicity of solid nodule	 Isoechoic: brightness similar to the surrounding thyroid parenchyma. When the echogenicity of the surrounding thyroid tissue is decreased, such as in Hashimoto's thyroiditis, the echogenicity can be compared to that of the sub-mandibular salivary glands Hyperechoic: brighter appearance in comparison with the surrounding thyroid parenchyma Mildly hypoechoic: darker appearance in comparison with the surrounding thyroid parenchyma, but less dark than neck strap muscles Markedly hypoechoic: dark appearance, similar or higher than that of the neck strap muscles
7. Margins	 Smooth margins: clear demarcation with respect to the surrounding thyroid parenchyma Ill-defined margins: lack of clear demarcation with respect to the surrounding thyroid parenchyma. Ill-defined margins are distinct from irregular margins and do not alter the nodule risk category Irregular margins: presence of one or more sharp angles of the margins (spiculated) or presence of one or more smooth focal round protrusions of the margins (lobulated) Halo/rim: describe as thin or thick, partial or complete
8. Calcifications	Macrocalcification: > 1 mm coarse calcifications with posterior acoustic shadowing Egg shell calcifications: echogenic line surrounding the nodule giving an appearance of discrete calcified wall, along with marked posterior acoustic shadowing Microcalcifications: < 1 mm most often round calcifications, without acoustic shadowing
9. Accessory features	Comet tail: reverberation artifacts within cystic component Extracapsular invasion: interruption of thyroid capsule
10. Elastosonography	Score 1: nodules with high elasticity Score 2: nodules with inhomogeneous distribution Score 3: nodules with high stiffness Report strain ratio or Kpa-M/s (if shear wave available)>cut-off values, depending on the equipment used and more recent literature [30–35]
11. Vascularity	Type I: absence of intranodular or perinodular flow Type II: presence of perinodular and/or slight intranodular flow Type III: presence of marked intranodular flow [36]

Table 3 US report in lymph- nodes	1. Size	Report the 3 diameters for each lymph-node (depth or AP, width or T, length or L)
	2. Position	Superior, medium, inferior, in lateral-cervical position, lateral or medial to carotid artery/jugular vein, in central compartment or latero-cervical levels (from I to VI) [38]
	3. Features	Typical shape/echostructure: oval shape, presence of the hilum Atypical shape/echostructure Indeterminate: round shape, absence of hilum Suspicious: solid pattern with echogenicity similar to the thyroid nodule; presence of micro-macrocalcifications; cystic or mixed appearance; irregular (chaotic) vascularization

🖄 Springer

Journal : Large 40618	Article No : 935	Pages : 9	MS Code : JENI-D-18-00315	Dispatch : 11-10-2018
-----------------------	------------------	-----------	---------------------------	-----------------------

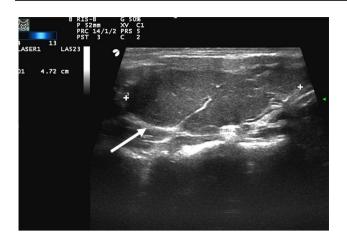


Fig. 1 Autoimmune thyroiditis. Longitudinal section: enlarged thyroid lobe with diffuse, homogeneous and moderate hypoechogenicity

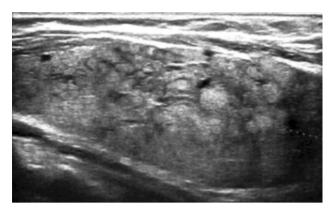


Fig. 4 Autoimmune thyroiditis. Longitudinal section: enlarged thyroid lobe with diffuse, mild hypoechogenicity with pseudo-nodular appearance



Fig. 2 Autoimmune thyroiditis. Longitudinal section: enlarged thyroid lobe with diffuse, mild hypoechogenicity

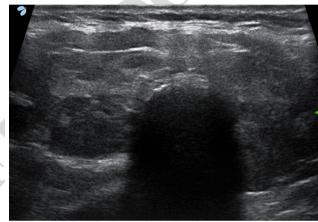


Fig. 5 Autoimune thyroiditis. Transverse section: enlarged thyroid lobe with diffuse, moderate hypoechogenicity, marked inhomogeneity, with hypoechoic nodular area in the right lobe

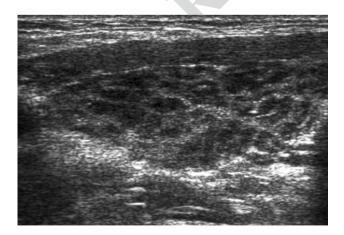


Fig.3 Autoimmune thyroiditis. Longitudinal section: enlarged thyroid lobe with diffuse moderate hypoechogenicity, marked inhomogeneity with honeycomb appearance

for predicting the risk of developing hypothyroidism in patients with goiter and circulating thyroid autoantibodies [1, 12].

The typical US pattern of Hashimoto's thyroiditis is a 174 hypoechoic thyroid gland with hyperechoic fibrous septa 175 crossing the parenchyma. Lymphocytic infiltration may 176 also cause a pseudo-nodular pattern with multiple discrete 177 hypoechoic areas. On the other hand, solid hyperechoic 178 areas can also be detected in a diffusely hypoechoic paren-179 chyma representing areas spared from lymphocytic infil-180 tration. These also are often referred to as pseudo-nodules. 181 We recommend reporting the above findings as hypoechoic 182 or hyperechoic areas, respectively, rather than nodules. 183 These areas should receive a thorough examination to keep 184 them distinguished from "true" thyroid nodules. 185



Table 4 US features and patterns associated with benignity

Completely anechoic texture (cystic nodules) Mixed/spongiform texture Oval shape Iso/hyper echogenicity Regular margins Complete halo Coarse macrocalcifications Hyperechoic pseudo-nodular areas in thyroid autoimmune diseases Coalescent iso/hyperechoic nodule in the context of goiter High elasticity at elastosonography

186 US report in subacute thyroiditis

The diagnosis of subacute or De Quervain thyroiditis is usu-187 ally made on the basis of clinical symptoms of neck pain and 188 189 fever, together with laboratory findings of thyrotoxicosis and inflammation. The typical appearance of subacute thyroiditis 190 is a diffuse heterogeneity with the presence of patchy, poorly 191 defined hypoechoic areas that can affect a portion of one or 192 both lobes, an entire lobe, or the entire gland [28]. These 193 ill-defined hypoechoic areas typically change and migrate 194 during the active phase of the disease and disappear on 195 remission. The affected part of the gland has a decreased 196 blood flow at color and power Doppler examination (Fig. 4). 197

198 US report in nodular thyroid disease

Thyroid US is a mainstay in the clinical assessment of
nodular thyroid disease [29]. Indeed, US is essential in
monitoring nodule size and echostructure and US features
help defining the risk of malignancy in thyroid nodules.

acute thyroiditis of patchy, poorly ortion of one or and [28]. These The US report in nodular thyroid disease should be structured as described in Table 2.

US report in lymph nodes

Typical lymph node is characterized by a hypoechoic pattern, oval shape and the presence of a central hyperechoic206stroma corresponding to the hilum. Pathological lymph208nodes have a cystic or solid pattern, iso- or hyperechoic with209round or irregular shape, without hilum [37]. The position of210lymph nodes that for their pattern deserve description must211be precisely localized following the scheme of Robbins [38].212

Table 5 Risk category	1. Low risk N	lodules with at least 2 US features associated w nity (Table 4) and no feature associated with r (Table 6)	
	2. Intermediate risk N	lodules with risk score 1–3	
	3. High risk N	lodules with risk score ≥ 4	
Table 6 US features associated with malignancy	Low specificity, high reproducibility	Hypoechogenicity Thick halo	Risk score 1
	High specificity, poor reproducibility	Microcalcifications Irregular, disrupted, spiculated or lobulated margins High stiffness at elastosonography	Risk score 2
	High specificity, high reproducibility	Marked hypoechogenicity Irregular shape, including "taller than wide"	Risk score 3
	Very high specificity, high reproducibility, accorsory features	es- Extra capsular extension Suspicious lymph nodes	Risk score 4

Deringer

Journal : Large 40618	Article No : 935	Pages : 9	MS Code : JENI-D-18-00315	Dispatch : 11-10-2018



Fig. 6 Thyroid nodule with low risk: longitudinal section of right

lobe. Isoechoic nodule with halo sign and cystic area

205

203

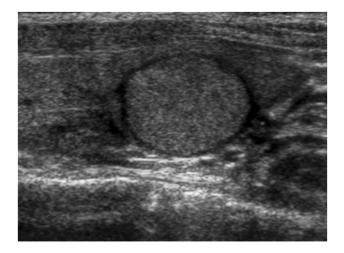


Fig. 7 Thyroid nodule with intermediate risk (risk score 2): longitudinal section of right lobe. Isoechoic nodule with thick halo and spiculated margins



Fig. 8 Thyroid nodule with high risk (risk score>4): transverse section of right lobe. Inhomogeneous hypoechoic nodule with irregular margins, taller than wide shape and extracapsular extension

Risk stratification of thyroid nodules (Figs. 6, 7, 8, 9, 10, 11)

Indications for fine needle aspiration are based on the US
evaluation of risk of malignancy that should be scored
in each nodule. As several risk stratification systems for
thyroid nodules are published, the report should include
the reference of the system used.

US features and patterns suggestive of benignity are summarized in Table 4. In this consensus, we propose a simplified nodule risk stratification (Table 5), based on the predictive value of each US sign, classified and scored according to the strength of association with malignancy,



Fig.9 Thyroid nodule with high risk (risk score>4): longitudinal section of right lobe. Hypoechoic nodule with irregular shape and spiculated margins



Fig. 10 Thyroid nodule with high risk (risk score >4): Longitudinal section of right lobe. Inhomogeneous hypoechoic nodule with irregular margins and anechoic area

but also to the estimated reproducibility among different 225 operators (Table 6). 226

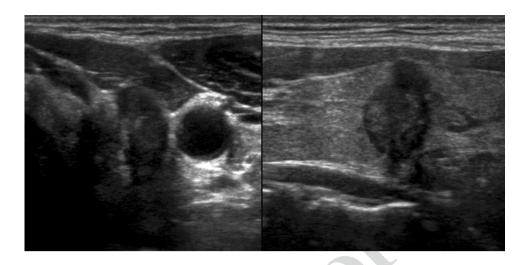
Conclusive remarks

Autoimmune and nodular thyroid diseases, especially in 228 subclinical forms, are extremely frequent. Thyroid US is 229 nowadays widely used as first diagnostic approach in such 230 patients. The peculiar pattern of thyroid US of patients 231 with Hashimoto's thyroiditis and Graves' disease is easily 232 recognizable by most operators, but the terminology used 233 to describe these patterns is not uniform, possibly causing 234 misunderstandings in the interpretation of the reports. In the 235 last years, several papers were focused on the possibility to 236

🖄 Springer

Journal : Large 40618	Article No : 935	Pages : 9	MS Code : JENI-D-18-00315	Dispatch : 11-10-2018

Fig. 11 Thyroid nodule with high risk (risk score > 4): transverse and longitudinal section of left lobe. Inhomogeneous hypoechoic nodule with irregular margins, taller than wide shape and extracapsular extension



stratify the risk of cancer in thyroid nodules, based on US
features. Accordingly, scientific societies of endocrinologists
and radiologists have drawn up guidelines and consensus
statements inspired by the TIRADS system used for breast
cancer. The plethora of these systems and in some cases their
complexity have hampered their use in the clinical practice.

We propose here a consensus agreed by Italian scientific societies that collect specialists who deal with the diagnostic management of thyroid patients. At difference with previous publications, autoimmune thyroid diseases and subacute thyroiditis are included together with nodular thyroid diseases in the suggestion of a standardized reporting.

The hope of participating societies is that the indications contained in this consensus will be adopted by most specialists who deal with thyroid diseases, with the result of decreasing the ambiguity and inhomogeneity of thyroid US reporting.

- 254 Compliance with ethical standards
- 255 Conflict of interest The authors have nothing to disclose.

Ethical approval This article does not contain any studies with humanparticipants or animals performed by any of the authors.

258 Informed consent No informed consent.

259 References

- Marcocci C, Vitti P, Cetani F, Catalano F, Concetti R, Pinchera A (1991) Thyroid ultrasonography helps to identify patients with diffuse lymphocytic thyroiditis who are prone to develop hypothyroidism. J Clin Endocrinol Metab 72:209–213. https://doi. org/10.1210/jcem-72-1-209
- Vitti P, Lampis M, Piga M, Loviselli A, Brogioni S, Rago T, Pinchera A, Martino E (1999) Diagnostic usefulness of thyroid ultrasonography in atrophic thyroiditis. J Clin Ultrasound 22:375–379
 - Description Springer

- Vitti P, Rago T, Mancusi F, Pallini S, Tonacchera M, Santini F, Chiovato L, Marcocci C, Pinchera A (1992) Thyroid hypoechogenic pattern at ultrasonography as a tool for predicting recurrence of hyperthyroidism after medical treatment in patients with Graves' disease. Acta Endocrinol 126:128–131 PMID: 1543017
- Vitti P, Rago T, Chiovato L, Pallini S, Santini F, Fiore E, Rocchi R, Martino E, Pinchera A (1997) Clinical features of patients with Graves' disease undergoing remission after antithyroid drug treatment. Thyroid. 7:369–375. https://doi.org/10.1089/thy.1997.7.369
- 5. Haugen BR, Alexander EK, Bible KC et al (2016) 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American thyroid association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 26:1–133. https://doi. org/10.1089/thy.2015.0020
- Gharib H, Papini E, Garber JR, Duick DS, Harrell RM, Hegedüs L, Paschke R, Valcavi R, Vitti P, on behalf of the AACE/ACE/ AME Task Force on Thyroid Nodules (2016) American association of Clinical endocrinologists, American college of Endocrinology and Associarione medici endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules 2016 update. Endocr Pract. https://doi.org/10.4158/EP161 208.GL
- Russ G, Bonnema SJ, Erdogan MF, Durante C, Ngu R, Leenhardt L (2017) European thyroid association guidelines for ultrasound malignancy risk stratification of thyroid nodules in adults: the EU-TIRADS. Eur Thyroid J 6:225–237. https://doi.org/10.1159/00047 8927
- Knobel M (2016) Etiopathology, clinical features and treatment of diffuse and multinodular goiters. J Endocrinol Investig 39:357– 373. https://doi.org/10.1007/s40618-015-0391-7
- Vitti P, Rago T, Mazzeo S, Brogioni S, Lampis M, De Liperi A, Bartolozzi C, Pinchera A, Martino E (1995) Thyroid blood flow evaluation by color-flow Doppler sonography distinguishes Graves' disease from Hashimoto's thyroiditis. J Endocrinol Investig 18:857–861. https://doi.org/10.1007/BF03349833
- Rago T, Chiovato L, Aghini-Lombardi F, Grasso L, Pinchera A, Vitti P (2001) Non-palpable thyroid nodules in a borderline iodine-sufficient area: detection by ultrasonography and follow-up. J Endocrinol Investig 24:770–776. https://doi.org/10.1007/BF033 43926
- Pedersen OM, Aardal NP, Larssen TB, Varhaug JE, Myking O, Vik-Mo H (2000) The value of ultrasonography in predicting autoimmune thyroid disease. Thyroid 10(3):251–259. https://doi. org/10.1089/thy.2000.10.251

269

270

271

272

273

274

275

276

277

278

279

280

281

282

Journal : Large 40618 Article No : 935 Pages : 9 MS Code : JENI-D-18-00315 Dispatch : 11-10-2018		Journal : Large 40618	Article No : 935	Pages : 9	MS Code : JENI-D-18-00315	
--	--	-----------------------	------------------	-----------	---------------------------	--

- Rago T, Chiovato L, Grasso L, Pinchera A, Vitti P (2001) Thyroid ultrasonography as a tool for detecting thyroid autoimmune diseases and predicting thyroid disfunction in apparently healthy subjects. J Endocrinol Investig 24:763–769 (PMID: 11765045)
- Frates MC, Benson CB, Charboneau JW, Cibas ES, Clark OH, Coleman BG et al (2005) Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. Radiology 237:794–800. https://doi.org/10.1148/ radiol.2373050220
- Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccagna S, Nardi F, Panunzi C, Rinaldi R, Toscano V, Pacella CM (2002) Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. J Clin Endocrinol Metab 87:1941–1944. https://doi.org/10.1210/jcem.87.5.8504
- 15. Mandel SJ (2004) Diagnostic use of ultrasonography in patients
 with nodular thyroid disease. Endocr Pract 10:246–252. https://
 doi.org/10.4158/EP.10.3.246
- 16. Khoo ML, Asa SL, Witterick IJ, Freeman JL (2002) Thyroid calcification and its association with thyroid carcinoma. Head Neck 24:651–655. https://doi.org/10.1002/hed.10115
- 17. Kim EK, Park CS, Chung WY et al (2002) New sonographic criteria for recommending fine-needle aspiration biopsy of non palpable solid nodules of the thyroid. Am J Roentgenol 178:687–691. https://doi.org/10.2214/ajr.178.3.1780687
- 18. Peccin S, de Castro JA, Furlanetto TW, Furtado AP, Brasil BA,
 Czepielewski MA (2002) Ultrasonography: is it useful in the
 diagnosis of cancer in thyroid nodules? J Endocrinol Investig
 25:39–43 (PMID:11885575)
- Tessler FN, Middleton WD, Grant EG, Hoang JK, Berland LL,
 Teefey SA, Cronan JJ, Beland MD, Desser TS, Frates MC, Hammers LW, Hamper UM, Langer JE, Reading CC, Scoutt LM, Stavros AT (2017) ACR thyroid imaging, reporting and data system (TI-RADS): white paper of the ACR TI-RADS committee. J Am
 Coll Radiol 14:587–595
- 20. Horvath E, Majlis S, Rossi R et al (2009) An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management. J Clin Endocrinol Metab 94:1748–1751. https://doi.org/10.1210/jc.2008-1724
- 21. Kwak JY, Han KH, Yoon JH et al (2011) Thyroid imaging reporting and data system for US features of nodules: a step in establishing better stratification of cancer risk, Radiology 260:892–899. https://doi.org/10.1148/radiol.11110206
- Na DG, Baek JH, Sung JY et al (2016) Thyroid imaging reporting and data system risk stratification of thyroid nodules: categorization based on solidity and echogenicity. Thyroid 26:562–572. https://doi.org/10.1089/thy.2015.0460
- 23. Park JY, Lee HJ, Jang HW et al (2009) A proposal for a thyroid imaging reporting and data system for ultrasound features of thyroid carcinoma. Thyroid 19:1257–1264. https://doi.org/10.1089/thy.2008.0021
- Seo H, Na DG, Kim JH, Kim KW, Yoon JW (2015) Ultrasound-based risk stratification for malignancy in thyroid nodules: a four-tier categorization system. Eur Radiol 25:2153–2162
- Shin JH, Baek JH, Chung J, Ha EJ, Kim JH, Lee YH, Lim HK, 25. 368 Moon WJ, Na DG, Park JS, Choi YJ, Hahn SY, Jeon SJ, Jung SL, 369 Kim DW, Kim EK, Kwak JY, Lee CY, Lee HJ, Lee JH, Lee JH, 370 Lee KH, Park SW, Sung JY, Korean Society of Thyroid Radiology 371 (KSThR) and Korean Society of Radiology (2016) Ultrasonogra-372 phy diagnosis and imaging-based management of thyroid nodules: 373 revised Korean society of thyroid radiology consensus statement 374 and recommendations. Korean J Radiol 17(3):370-395. https:// 375 doi.org/10.3348/kjr.2016 376
- 26. Persichetti A, Di Stasio E, Guglielmi R, Bizzarri G, Taccogna S,
 Misischi I, Graziano F, Petrucci L, Bianchini A, Papini E (2018)

Predictive value of malignancy of thyroid nodule ultrasound classification systems: a prospective study. J Clin Endocrinol Metab 103:1359–1368. https://doi.org/10.1210/jc.2017-01708

- 27. Maino F, Forleo R, Martinelli M, Fralassi N, Barbato F, Pilli T, Capezzone M, Brilli L, Ciuoli C, G Cairano G, Nigi L, Pacini F, Castagna MG (2018) Prospective validation of ATA and ETA sonographic pattern risk of thyroid nodules selected for FNAC. J Clin Endocrinol Metab 103:2362–2368. https://doi.org/10.1210/ jc.2018-00274
- Bogazzi F, Dell'Unto E, Tanda ML, Tomisti L, Cosci C, Aghini-Lombardi F, Sardella C, Pinchera A, Bartalena L, Martino E (2006) Long-term outcome of thyroid function after amiodarone-induced thyrotoxicosis, as compared to subacute thyroiditis. J Endocrinol Investig 29:694–699. https://doi.org/10.1007/bf033 44178
- Campanella P, Ianni F, Rota CA, Corsello SM, Pontecorvi A (2014) Quantification of cancer risk of each clinical and ultrasonographic suspicious feature of thyroid nodules: a systematic review and meta-analysis. Eur J Endocrinol 170:203–211. https ://doi.org/10.1530/EJE-13-0995
- Rago T, Santini F, Scutari M, Pinchera A, Vitti P (2007) Elastography: new developments in ultrasound for predicting malignancy in thyroid nodules. J Clin Endocrinol Metab 92:2917–2922. https ://doi.org/10.1210/jc.2007-0641
- Magri F, Chytiris S, Capelli V, Gaiti M, Zerbini F, Carrara R, Malovini A, Rotondi M, Bellazzi R, Chiovato L (2013) Comparison of elastographic strain index and thyroid fine-needle aspiration cytology in 631 thyroid nodules. J Clin Endocrinol Metab 12:4790–4797. https://doi.org/10.1210/jc.2013-2672
- Cantisani V, Consorti F, Guerrisi A, Guerrisi I, Ricci P, Di Segni M, Mancuso E, Scardella L, Milazzo F, D'Ambrosio F, Antonaci A (2013) Prospective comparative evaluation of quantitative-elastosonography (Q-elastography) and contrast-enhanced ultrasound for the evaluation of thyroid nodules: preliminary experience. Eur J Radiol 82(11):1892–1898. https://doi.org/10.1016/j.ejrad .2013.07.005
- Hegedus L (2010) Can elastography stretch our understanding of thyroid histomorphology? J Clin Endocrinol Metab 95:5213– 5215. https://doi.org/10.1210/jc.2010-2411
- 34. Chandramohan A, Therese M, Abhraham D, Paul TV, Mazhuvanchary PJ (2018) Can ARFI elastography be used to differentiate parathyroid from thyroid lesions? J Endocrinol Investig 41:111– 119. https://doi.org/10.1007/s40618-017-0694-y
- Cosgrove D, Barr R, Bojunga J, Cantisani V, Chammas MC, Dighe M, Vinayak S, Xu JM, Dietrich CF (2017) WFUMB guidelines and recommendations on the clinical use of ultrasound elastography. Ultrasound Med Biol 43:4–26. https://doi.org/10.1016/j. ultrasmedbio.2016.06.022
- 36. Rago T, Vitti P, Chiovato L, Mazzeo S, De Liperi A, Miccoli P, Viacava P, Bogazzi F, Martino E, Pinchera A (1998) Role of conventional ultrasonography and color flow-doppler sonography in predicting malignancy in 'cold' thyroid nodules. Eur J Endocrinol 38:41–46 (PMID: 9461314)
- Leenhardt L, Erdogan MF, Hegedus L, Mandel SJ, Paschke R, Rago T, Russ G (2013) 2013 European thyroid association guidelines for cervical ultrasound scan and ultrasound-guided techniques in the postoperative management of patients with thyroid cancer. Eur Thyroid J 2:147–159. https://doi.org/10.1159/00035 4537
- Robbins KT, Shaha AR, Medina JE, Califano JA, Wolf GT, Ferlito A, Som PM, Day TA (2008) Consensus statement on the classification and terminology of neck dissection. Arch Otolaryngol Head Neck Surg 134:536–538. https://doi.org/10.1001/archo tol.134.5.536

379

380

381

382

383

384

385

386

387

388

389

390

391

392

393

394

395

396

397

398

399

400

401

402

403

404

405

406

407

408

409

410

411

412

413

414

415

416

417

418

419

420

421

422

423

424

425

426

427

428

429

430

431

432

433

434

435

436

437

438

439

440

441

Journal : Large 40618 Article No : 935 Pages : 9	MS Code : JENI-D-18-00315	Dispatch : 11-10-2018
--	---------------------------	-----------------------