



January, 12th 2023

Dear Prof. Durante,

We read with interest the draft of the 2023 European Thyroid Association Clinical Practice Guidelines for Thyroid Nodule Management. As a society affiliated to ETA we would like to voice concerns against the guideline in its current version.

The Austrian Thyroid Association is a multidisciplinary society and our members are endocrinologists, nuclear medicine specialists, endocrine surgeons and thyroidologists from several other disciplines. In this context we are surprised that no nuclear medicine specialist was included in the panel of experts.

A European approach to the management of thyroid nodules is essential, as thyroidology in Europe is different to thyroidology in the United States.

1. In contrast to the US, wide parts of Europe have been previously **iodine deficient** or have still (or once again) a lack of iodine supply. The incidence of thyroid nodules is higher in Europe compared to the United States. Multinodular goiters are a common finding in Europe. Hyperfunctioning (hot) nodules can coexist with hypofunctioning (cold) nodules in euthyroid patients.

2. In many European countries, **nuclear medicine physicians serve as thyroidologists** and manage far more routine thyroid patients in their countries compared to the local endocrinologists. In many European countries, nuclear medicine physicians offer all the diagnostic procedures as Endocrinologists do.

This is the fact in Austria and Germany, and we think in the thyroid centers of Luxemburg, Belgium, Croatia, Bosnia and Herzegovina, Slovenia, and several other European countries, the majority of patients is also seen by nuclear medicine physicians.

3. In the US, 123-iodine scan is performed, which is expensive and has a challenging logistic. In contrast to the US, **in Europe, Tc99m is the isotope of choice** for the routine scintigraphy of the thyroid. Tc99m is very cheap, widely available, and has a very low radiation burden.

We suggest that the authors consider this special European situation when developing European guidelines on behalf of the European Thyroid Association and have the following comments:

1. There is no nuclear medicine physician among the authors. In addition to endocrinologists, representatives of various other medical specialists have contributed to the manuscript, but no nuclear medicine specialist was involved in the draft. At least one single thyroidologist, trained and certified as a nuclear medicine physician, should be added to the authors and should be involved in the discussion of the revised version of the manuscript.

2. Page 15. line 340: In contrast to other diagnostic methods, there are only nine lines of text on thyroid scintigraphy (line 341-349; "thyroid scintiscan"), with only one single reference which has been published 25 years ago by US-American surgeons. We do not agree that the only indication for thyroid scintigraphy is suppressed TSH or TSH at the lower normal limit. Several recent studies have shown that a substantial fraction of hyper- functioning nodules show a normal TSH value. More importantly, hyperfunctioning nodules often show a high TIRADS score, so without knowledge of the functional status (scintigraphy) they would undergo unnecessary biopsy or even surgery.

We suggest to revise this chapter together with nuclear medicine physicians. At least 5-10 references published during the last years on the role of scintigraphy in thyroid nodule management should be included in this chapter. The specific situation in Europe must be taken into account in a recommendation of the European Thyroid Association.

Suggested references:

Schenke S, Seifert P, Zimny M, Winkens T, Binse I, Görges R. Risk Stratification of Thyroid Nodules Using the Thyroid Imaging Reporting and Data System (TIRADS): The Omission of Thyroid Scintigraphy Increases the Rate of Falsely Suspected Lesions. J Nucl Med. 2019 Mar;60(3):342-347. doi: 10.2967/jnumed.118.211912. Epub 2018 Aug 10. PMID: 30097501.

- Noto B, Eveslage M, Pixberg M, Gonzalez Carvalho JM, Schäfers M, Riemann B, Kies P. Prevalence of hyperfunctioning thyroid nodules among those in need of fine needle aspiration cytology according to ATA 2015, EU-TIRADS, and ACR-TIRADS. *Eur J Nucl Med Mol Imaging*. 2020 Jun;47(6):1518-1526. doi: 10.1007/s00259-020-04740-y. Epub 2020 Mar 9. PMID: 32152666; PMCID: PMC7188716.
- Castellana M, Virili C, Paone G, Scappaticcio L, Piccardo A, Giovanella L, Trimboli P. Ultrasound systems for risk stratification of thyroid nodules prompt inappropriate biopsy in autonomously functioning thyroid nodules. *Clin Endocrinol (Oxf)*. 2020 Jul;93(1):67-75. doi: 10.1111/cen.14204. Epub 2020 May 5. PMID: 32319108.
- Schenke SA, Kreissl MC, Grunert M, Hach A, Haghghi S, Kandror T, Peppert E, Rosenbaum-Krumme S, Ruhlmann V, Stahl A, Wanjura D, Zaplatnikov K, Zimny M, Gilman E, Herrmann K, Görges R. Distribution of Functional Status of Thyroid Nodules and Malignancy Rates of Hyperfunctioning and Hypofunctioning Thyroid Nodules in Germany. *Nuklearmedizin*. 2022 Oct;61(5):376-384. English. doi: 10.1055/a-1856-4052. Epub 2022 Aug 2. PMID: 35917825.

3. The authors included several references of the Pierpaolo Trimboli group in the reference section. Why did they choose not a single manuscript of this group on the role of nuclear medicine in thyroid nodule management? What was the reason that the authors did not include a single manuscript of Simone Schenke and the German TIRADS Study group?

4. The evidence stated by the recent European publications on Tc99m-scintigraphy in thyroid nodule management should be included also in the rest of the revised manuscript, and tables and figures should be adapted, accordingly.

5. The European Thyroid Association should use the term "Thyroid Scintigraphy" instead of "Thyroid Scintiscan" and point out the importance of Tc99m thyroid scintigraphy according to the current level of evidence in their recommendations.

Further suggested references:

- Giovanella L, Avram AM, Iakovou I, Kwak J, Lawson SA, Lulaj E, Luster M, Piccardo A, Schmidt M, Tulchinsky M, Verburg FA, Wolin E. EANM practice guideline/SNMMI procedure standard for RAIU and thyroid scintigraphy. *Eur J Nucl Med Mol Imaging*. 2019 Nov;46(12):2514-2525. doi: 10.1007/s00259-019-04472-8. Epub 2019 Aug 7. PMID: 31392371.
- Felder GJ, Naeem M, Shady W, Shetty AS, Fraum TJ, Itani M. Risk Stratification of 18F-Fluorodeoxyglucose-Avid Thyroid Nodules Based on ACR Thyroid Imaging Reporting and Data System. *J Am Coll Radiol*. 2021 Mar;18(3 Pt A):388-394. doi: 10.1016/j.jacr.2020.08.021. Epub 2020 Oct 31. PMID: 33137296.
- Noto B, Eveslage M, Pixberg M, Gonzalez Carvalho JM, Schäfers M, Riemann B, Kies P. Prevalence of hyperfunctioning thyroid nodules among those in need of fine needle aspiration cytology according to ATA 2015, EU-TIRADS, and ACR-TIRADS. *Eur J Nucl Med Mol Imaging*. 2020 Jun;47(6):1518-1526. doi: 10.1007/s00259-020-04740-y. Epub 2020 Mar 9. PMID: 32152666; PMCID: PMC7188716.

Trimboli P, Piccardo A, Alevizaki M, Virili C, Naseri M, Sola S, Paone G, Russ G, Giovanella L. Dedicated neck 18 F-FDG PET/CT: An additional tool for risk assessment in thyroid nodules at ultrasound intermediate risk. *Clin Endocrinol (Oxf)*. 2019 May;90(5):737-743. doi: 10.1111/cen.13949. Epub 2019 Feb 27. PMID: 30740757.

Piccardo A, Puntoni M, Dezzana M, Bottoni G, Foppiani L, Marugo A, Catrambone U, Ugolini M, Sola S, Gatto M, Treglia G, Giovanella L, Trimboli P. Indeterminate thyroid nodules. The role of 18F-FDG PET/CT in the "era" of ultrasonography risk stratification systems and new thyroid cytology classifications. *Endocrine*. 2020 Sep;69(3):553-561. doi: 10.1007/s12020-020-02239-y. Epub 2020 Mar 2. PMID: 32124261.

Seifert P, Schenke S, Zimny M, Stahl A, Grunert M, Klemenz B, Freesmeyer M, Kreissl MC, Herrmann K, Görges R. Diagnostic Performance of Kwak, EU, ACR, and Korean TIRADS as Well as ATA Guidelines for the Ultrasound Risk Stratification of Non-Autonomously Functioning Thyroid Nodules in a Region with Long History of Iodine Deficiency: A German Multicenter Trial. *Cancers (Basel)*. 2021 Sep 4;13(17):4467. doi: 10.3390/cancers13174467. PMID: 34503277; PMCID: PMC8431215.

Verburg FA, Aktolun C, Chiti A, Frangos S, Giovanella L, Hoffmann M, Iakovou I, Mihailovic J, Krause BJ, Langsteiger W, Luster M; EANM and the EANM Thyroid Committee. Why the European Association of Nuclear Medicine has declined to endorse the 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer. *Eur J Nucl Med Mol Imaging*. 2016 Jun;43(6):1001-5. doi: 10.1007/s00259-016-3327-3. Epub 2016 Feb 17. PMID: 26883666.

Schenke SA, Campenni A, Tuncel M, Bottoni G, Sager S, Bogovic Crncic T, Rozic D, Görges R, Özcan PP, Groener D, Hautzel H, Klett R, Kreissl MC, Giovanella L. Diagnostic Performance of 99mTc-Methoxy-Isoobutyl-Isonitrile (MIBI) for Risk Stratification of Hypofunctioning Thyroid Nodules: A European Multicenter Study. *Diagnostics (Basel)*. 2022 May 31;12(6):1358. doi: 10.3390/diagnostics12061358. PMID: 35741167; PMCID: PMC9221758.

Schenke SA, Wuestemann J, Zimny M, Kreissl MC. Ultrasound Assessment of Autonomous Thyroid Nodules before and after Radioiodine Therapy Using Thyroid Imaging Reporting and Data System (TIRADS). *Diagnostics (Basel)*. 2020 Dec 2;10(12):1038. doi: 10.3390/diagnostics10121038. PMID: 33276695; PMCID: PMC7761536.

This statement is supported by the Austrian Thyroid Association, which is a multidisciplinary society: Nuclear medicine specialists, endocrinologists, endocrine surgeons and several other disciplines all work together for the benefit of their patients – according to evidence based thyroidology.

Sincerely yours

Georg Zettinig, Vienna

ETA member and pre-president of the Austrian Thyroid Association

This statement is supported by the Executive Committee of the Austrian Thyroid Association and by the following members of the European Thyroid Association from Austria, Germany, Switzerland, the Netherlands, and Croatia:

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