
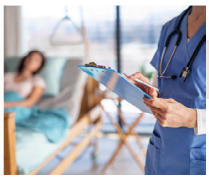

CASE REPORT

Received: 13 December 2025
Last revision: 11 January 2026
Accepted: 12 January 2026
Published: 18 September 2026

Diagnostic Challenges in Detecting Thyroid Microcarcinoma Using [^{99m}Tc]Tc-Sestamibi WashOut Index (WO_{IND}) in Toxic Intrathoracic Multinodular Goiter: A Case Report

Nitami Oktavia Indiarti*, Basuki Hidayat, Trias Nugrahadi, Achmad Hussein Sundawa Kartamihardja
Department of Nuclear Medicine and Theranostic Molecular, School of Medicine, Universitas Padjadjaran,
Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia.

ABSTRACT

Introduction: Intrathoracic multinodular goiter is a type of goiter that extends partially or completely into the thoracic cavity. Hyperthyroidism is uncommon in this condition, and the incidence of malignancy is also low (approximately 5.9%). [^{99m}Tc]Tc-Sestamibi washout index (WOind), with a cutoff of –19%, is used as an additional modality to assess the malignancy risk of hypofunction thyroid nodules, with a high negative predictive value of 100%. However, cancer detection is decreased in microcarcinomas, resulting in false-negative results. **Case:** A 54-year-old female with hyperthyroidism and intrathoracic multinodular goiter complained of a goiter and palpitations for one year. Fine-needle aspiration (FNA) cytology showed bilateral adenomatous goiter (Bethesda II). The patient was treated with propylthiouracil for one month, resulting in subclinical hyperthyroidism. A [^{99m}Tc]Tc-Pertechnetate uptake test was normal and showed predominant cold and warm nodules in multinodular goiter. The [^{99m}Tc]Tc-Sestamibi WOind ranged from -30% to -52% in all nodules (indicating benign). SPECT/CT showed tracheal deviation due to the large goiter, with a recommendation for resection. Postoperative histopathological results showed a focus of micropapillary thyroid carcinoma follicular variant in ƒthe left lobe, and adenomatous goiter in the right lobe and isthmus. The small size of the microcarcinoma in large adenomatous goiters makes it difficult to detect with FNA cytology and [^{99m}Tc] Tc-Sestamibi WOind. A focus of microcarcinoma is very unlikely to show malignant imaging characteristics, including on [^{99m}Tc] Tc-Sestamibi WOind. **Discussion:** Despite benign FNAB findings and a negative [99mTc]Tc-Sestamibi WOind scan, postoperative histopathology revealed micropapillary thyroid carcinoma, representing a false-negative result likely related to the small tumor size and limited detectability within a large, heterogeneous goiter. **Conclusion:** The [^{99m}Tc]Tc-Sestamibi WOind is a useful adjunct in diagnosing malignancy in thyroid nodules. However, clinicians must be aware of the possibility of false negatives, especially in cases of microcarcinoma within large adenomatous goiters.

Keywords: [^{99m}Tc]Tc-Sestamibi, case report, false-negative, intrathoracic multinodular goiter, thyroid microcarcinoma, washout index (WOind).

https://doi.org/10.55175/cdk.v53i09.2299
e-ISSN: 2503-2720

INTRODUCTION

Intrathoracic multinodular goiter (IMNG) is a challenging clinical entity because the thyroid gland extends into the thoracic cavity,[1,2] potentially causing significant compressive symptoms.[3,4] IMNG with coexisting hyperthyroidism is rare,[5] and the incidence of occult malignancy within large goiters is similarly low, reported at approximately 5.9%.[3,6] [^{99m}Tc]Tc-Sestamibi scintigraphy is a valuable modality for risk stratification of hypofunctioning thyroid nodules, with semi-quantitative analysis using the Wash-Out Index (WOind) demonstrating a sensitivity and Negative Predictive Value (NPV) of 100% for ruling out malignancy.[7,8] However, a significant limitation persists, as [^{99m}Tc]Tc-Sestamibi detection capability decreases in microcarcinomas (< 1 cm), which are often too small to demonstrate malignant imaging characteristics and can result in false-negative findings.[7] This diagnostic pitfall underscores the necessity of a cautious, multidisciplinary approach, as histopathology may be discordant with functional imaging findings in patients with large goiters harboring microscopic foci of carcinoma.[9]

CASE

A 54-year-old female was referred from the endocrinology department with the chief complaint of a progressively enlarging lump in her neck over the past year, accompanied by palpitations. A significant family history includes a relative who had died from thyroid cancer. **Figure 1** shows clinical images.

Initial laboratory workup on March 5, 2025 confirmed overt hyperthyroidism with a

***Correspondence Author** nitami.oktavia@gmail.com


free thyroxine (fT4) level of 46.07 pmol/L (reference range: 9–22 pmol/L) and a thyroid-stimulating hormone (TSH) level of < 0.09 mIU/L (reference range: 0.4–4.0 mIU/L). The patient was treated with propylthiouracil (PTU) 100 mg twice daily for one month. Follow-up laboratory tests after approximately one month of therapy showed a transition to subclinical hyperthyroidism with an fT4 level of 1.6 ng/dL (reference range: 0.7–1.8 ng/dL) and a TSH level of < 0.02 µIU/mL (reference range: 0.3–5.0 µIU/mL).

*Photo documentation by Nitami Oktavia Indiarti.

Figure 1. Clinical images of the 54-year-old female patient with hyperthyroidism and intrathoracic multinodular goiter, image from front (A), right side (B), and left side (C).

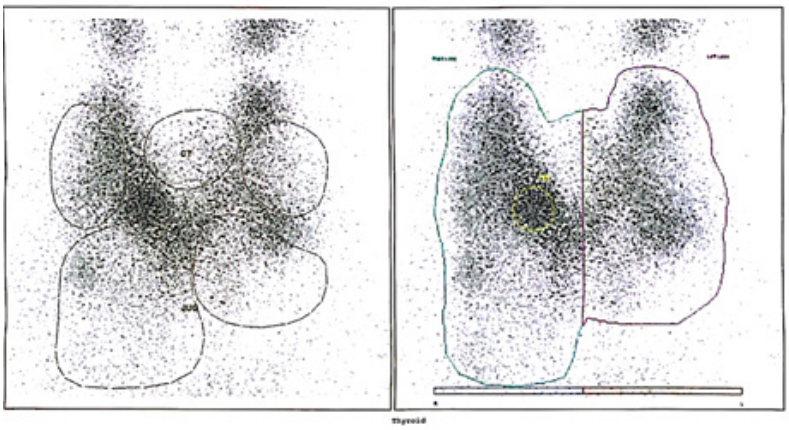

*Photo documentation by Nitami Oktavia Indiarti.

Figure 2. [^{99m}Tc]^{99m}Tc-Pertechnetate thyroid scintigraphy. The image shows enlarged lobes with heterogeneous uptake (mixed cold and warm nodules). The global thyroid uptake value was in the normal range at 1.9% (N: 0.5%–5%).

*Photo documentation by Nitami Oktavia Indiarti.

Figure 3. The thyroid SPECT/CT showed multiple mixed cold and warm nodules with intrathoracic extension. It also visualized the tracheal deviation and compression caused by the goiter (arrows).

Diagnostic and Imaging Findings

- CT scan (February 8, 2025): Showed large, heterogeneous masses with calcifications originating from both thyroid lobes and extending into the superior thoracic aperture. The masses measured approximately 4.9 x 3.7 x 10.8 cm on the right and 4.8 x 4.2 x 6.8 cm on the left, causing significant narrowing and deviation of the trachea. Total mass weighs 262.4 grams.
- Fine-Needle Aspiration Biopsy (FNAB) (March 10, 2025): Showed Fine-Needle Aspiration Biopsy of both right and left thyroid lobes yielded a conclusion of "Adenomatous goiter bilateral (Bethesda category II)".
- Thyroid Scintigraphy ^{99m}Tc-Pertechnetate (April 16, 2025): Showed enlarged lobes with uneven radiotracer uptake, consistent with a multinodular goiter (mixed cold and warm nodules). The thyroid uptake value was in the normal range at 1.9% (N: 0.5%–5%) **(Figure 2).**
- SPECT/CT (April 16, 2025): Confirmed the large, lobulated, heterogeneous nodules with calcifications extending intrathoracically. It clearly visualized the tracheal deviation and compression caused by the goiter **(Figure 3)**.
- [^{99m}Tc]Tc-Sestamibi WOind: Semi-quantitative analysis was performed on six dominant nodules. All six nodules demonstrated a high-washout (negative) result, with WO*ind* values ranging from -30.4% to -52% (benign cutoff: < 19%). This result strongly indicated a benign nature for all analyzed nodules **(Figure 4)**.

Surgical Outcome and Final Diagnosis

Despite the benign FNAB and [^{99m}Tc]Tc-Sestamibi WOind results, a total thyroidectomy and sternotomy were performed on May 15, 2025, due to the goiter's large size and the significant compressive symptoms (tracheal narrowing).

Postoperative histopathological examination established the final diagnosis as follows: Adenomatous goiter with micropapillary thyroid carcinoma, follicular variant (in the left thyroid lobe).

1. Adenomatous goiter (in the right lobe and isthmus) (**Figure 5**).
   The finding of microcarcinoma in the left lobe was in direct contrast to the false-negative [^{99m}Tc]Tc-Sestamibi WOind.

DISSCUSION

Intrathoracic multinodular goiter (IMNG) is a well-documented clinical entity that presents significant diagnostic and therapeutic challenges.[1] Our patient presented with a rare clinical triad: a large IMNG, hyperthyroidism, and an occult malignancy. The incidence of these factors occurring together is low. Hyperthyroidism in this condition is rare, reported in approximately 9.3% of cases,[5] and the prevalence of concurrent malignancy in large goiters is similarly low, at about 5.9%.[3] Despite the patient's initial overt hyperthyroidism, thyroid scintigraphy with [99mTc]Tc-Pertechnetate demonstrated normal thyroid uptake (1.9%; reference range: 0.5%–5.0%). This apparent contradiction is well explained by the patient's one-month course of propylthiouracil (PTU) before the scan. PTU is a thionamide that primarily inhibits thyroid peroxidase (TPO), blocking iodine organification and the synthesis of new thyroid hormones.[10–12] Studies have long shown that PTU administration markedly depresses the thyroid's accumulation of radioiodine, reducing overall uptake to euthyroid or low levels.[13] Therefore, the "normo-uptake" seen in our patient is a direct pharmacological effect of the recent PTU therapy and does not reflect the underlying autonomous, hyperfunctioning nature of the goiter.

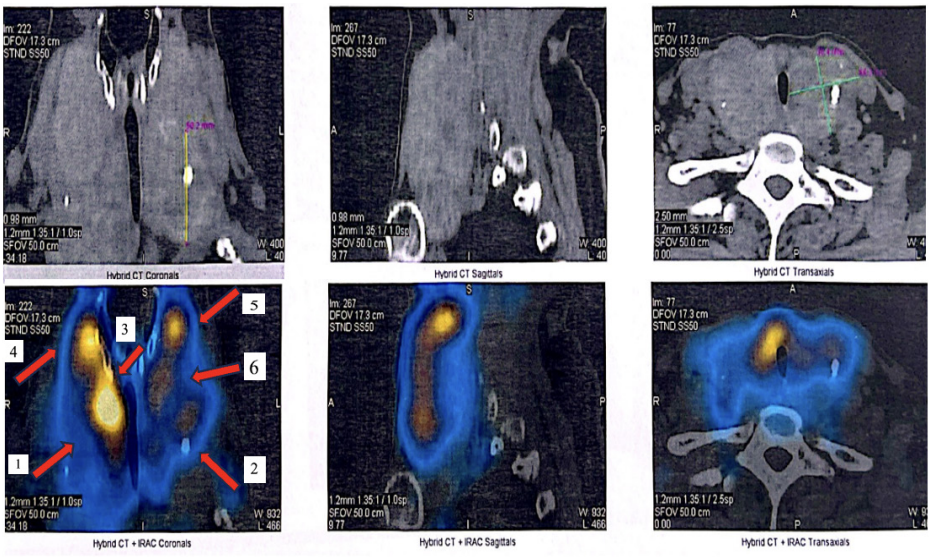

*Photo documentation by Nitami Oktavia Indiarti.

Figure 4. Semi-quantitative [99mTc]Tc-Sestamibi WOind analysis. Images show anterior views at 10 minutes (left) and 60 minutes (right) with regions of interest (ROIs) drawn over the dominant nodules. [^{99m}Tc]Tc-Sestamibi WOind. examination Procedure: (A) Early uptake result (ER) = mean nodular [^{99m}Tc]Tc-Sestamibi uptake – mean background [^{99m}Tc]Tc-Sestamibi uptake (early scans, 10–15 minutes post-injection). (B)Late uptake result (LR) = mean nodular [^{99m}Tc]Tc-Sestamibi uptake – mean background [^{99m}Tc]Tc-Sestamibi uptake (late scans, 60 minutes post-injection). [^{99m}Tc]Tc-Sestamibi Wash Out Index (WOind) = [(LR/ER) X100)-100 %] Patient's WOind results**:** Nodule 1: -45 % Nodule 2: -52 % Nodule 3: -46.4 % Nodule 4: -34.6 % Nodule 5: -30.4 % Nodule 6: -46.6 %. All nodules are high-washout (< 19%), [^{99m}Tc]Tc-Sestamibi WOind. negative, likely benign (arrows).

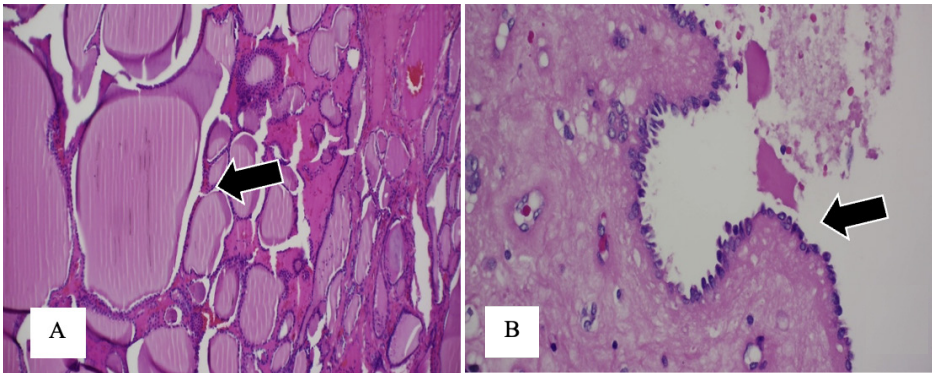

*Photo documentation by Nitami Oktavia Indiarti.

Figure 5. Postoperative histopathology. (A) Adenomatous goiter (in the right lobe and isthmus/*dextra et isthmus*). (B) Adenomatous goiter with micropapillary thyroid carcinoma, follicular variant (in the left thyroid lobe/*thyroid sinistra*) (arrows).

The central diagnostic challenge was the significant discordance between preoperative and postoperative findings. The patient's initial FNAC was benign (Bethesda II). Consequently, [^{99m}Tc]Tc-Sestamibi scintigraphy was performed as an additional modality to rule out malignancy definitively, a recommended step for risk stratification in nodules with indeterminate or inconclusive cytology.[14–16] Our patient's scan showed a strongly negative result with high washout (WOind values -30.4% to -52%), which, based on the established -19% cutoff,[7] indicated a benign lesion. This result was considered highly reliable, as the [^{99m}Tc] Tc-Sestamibi WOind method is cited in a European multicenter study as having a high sensitivity and a Negative Predictive Value (NPV) of 100%.[7,8,17]

Despite the benign FNAB and the 100% NPV associated with a negative [^{99m}Tc]Tc-Sestamibi WOind scan,[6,7] the postoperative histopathology revealed a micropapillary thyroid carcinoma (follicular variant). This finding represents a clear false-negative result, which highlights a critical, well-documented limitation of this imaging modality.[15,18,19] [^{99m}Tc] Tc-Sestamibi accumulation is dependent on high cellular density and, most importantly, mitochondrial richness.[9,18,20] Malignant cells, which are often metabolically active, typically retain the tracer, resulting in low or no washout


(a positive scan).[8,21]

The primary cause of false-negative [^{99m}Tc]Tc-Sestamibi scintigraphy is the small tumor size.[14,18] A microscopic focus of cancer (< 1 cm), such as in our patient, possesses an insufficient metabolic volume to be adequately resolved by the gamma camera, especially when masked within a large, heterogeneous, and partially cystic goiter.[18] It is also important to note the opposite diagnostic challenge: [^{99m}Tc]Tc-Sestamibi scintigraphy is known to produce false-positive results in benign, mitochondrially-rich oncocytic (Hürthle cell) adenomas, which can mimic the uptake pattern of a carcinoma.[7,20]

Although the preoperative workup was reassuringly benign, surgical intervention was strongly indicated. The decision for a total thyroidectomy and sternotomy was based on established guidelines for the management of IMNG.[1,3] The patient's CT scan demonstrated a massive goiter (total weight 262.4 g) with significant intrathoracic extension, causing severe tracheal deviation and narrowing. Such compressive symptoms pose a risk of acute airway obstruction and are a primary indication for surgery, regardless of benign cytology, to alleviate respiratory distress.[1,2,4,7]

Ultimately, this case underscores the vital importance of an integrated, multidisciplinary approach to managing complex thyroid nodules.[9] Diagnosis cannot rely on a single modality. While [^{99m}Tc]Tc-Sestamibi WOind is a powerful tool for ruling out cancer, clinicians must be aware of its limitations, particularly the potential for false-negatives in the setting of microcarcinoma.[7,18] This diagnostic pitfall, when functional imaging was discordant with histopathology, highlights the need for a cautious, multidisciplinary approach, as the final pathology report can contradict the functional scans in patients with large goiters that may harbor microscopic foci of carcinoma.[9]

CONCLUSION

This case underscores the diagnostic limitations of [^{99m}Tc]Tc-Sestamibi WOind in the setting of a large intrathoracic multinodular goiter. While the [^{99m}Tc]Tc-Sestamibi WOind is a useful adjunct with a high Negative Predictive Value, its efficacy is reduced in detecting microcarcinoma, which can lead to false-negative results as seen in this patient. This finding reinforces the need for a comprehensive diagnostic approach, recognizing that histopathological evaluation remains the definitive standard, especially when surgical intervention is already indicated for compressive symptoms.

Consent for Publication

Informed consent for publication of this case report was obtained from the patient.

Funding

This case report received no financial support or funding.

Author Contributions

Nitami Oktavia Indiarti: conceptualization, investigation, data curation, visualization, and writing—original draft. Basuki Hidayat: supervision, methodology, and writing—review and editing. Trias Nugrahadi: supervision, validation, and writing—review and editing. Achmad Hussein Sundawa. Kartamihardja: supervision, validation, and writing—review and editing. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Conflict of Interest

None declared.

Declaration on the Use of Artificial Intelligence (AI)

The authors declare that no artificial intelligence tools were used in the conduct of this study or preparation of this manuscript.

Acknowledgments

The authors would like to thank the Indonesia Endowment Fund for Education (LPDP) from the Ministry of Finance, Republic of Indonesia, for the scholarship granted to the first author [Scholarship Number: LOG-20759/LPDP.3/2024]. The authors also wish to express their deepest gratitude to the academic advisors for their invaluable contributions to this work.

REFERENCES

1. Unlu MT, Aygun N, Kostek M, Isgor A, Uludag M. Substernal goiter: from definitions to treatment 2022;56(2):167–76. doi: 10.14744/SEMB.2022.30806.
2. Iriarte MB, Morales EI, Velasquez M, Zuniga V, Sua LF, Fernndez-Trujillo L. Giant intrathoracicgoiter of atypical presentation: a case report. Clin Pathol. 2020;13:2632010X20916741. doi: 10.1177/2632010X20916741.
3. Chen Q, Su A, Zou X, Liu F, Gong R, Zhu J, et al. Clinicopathologic characteristics and outcomes of massive multinodular goiter: a retrospective cohort study. Front Endocrinol (Lausanne). 2022;13:850235. doi: 10.3389/fendo.2022.850235.
4. Linhares SM, Scola WH, Remer LF, Farra JC, Lew JI. Morbidity associated with surgical removal of substernal thyroid goiters. J Surg Res. 2022;277:254–60. doi: 10.1016/j.jss.2022.04.018.
5. Coskun A, Yildirim M, Erkan N. Substernal goiter: when is a sternotomy required? Int Surg. 2014;99(4):419–25. doi: 10.9738/INTSURG-D-14-00041.1.
6. Cappellacci F, Canu GL, Rossi L, De Palma A, Mavromati M, Kuczma P, et al. Differences in surgical outcomes between cervical goiter and retrosternal goiter: an international, multicentric evaluation. Front Surg. 2024;11:1341683. doi: 10.3389/fsurg.2024.1341683.
7. Schenke SA, Campenni A, Tuncel M, Bottoni G, Sager S, Bogovic Crncic T, et al. Diagnostic performance of 99mTc-methoxy-isobuty-isonitrile (MIBI) for risk stratification of hypofunctioning thyroid nodules: a European multicenter study. Diagnostics (Basel). 2022;12(6):1358. doi: 10.3390/diagnostics12061358.

8. Campenni A, Siracusa M, Ruggeri RM, Laudicella R, Pignata SA, Baldari S, et al. Differentiating malignant from benign thyroid nodules with indeterminate cytology by 99mTc-MIBI scan: a new quantitative method for improving diagnostic accuracy. Sci Rep. 2017;7(1):6147. doi: 10.1038/s41598-017-06603-3.

9. Giovanella L, Campenni A, Tuncel M, Petranovi Ovaricek P. Integrated diagnostics thyroid nodules. Cancers (Basel). 2024;16(2):311. doi: 10.3390/cancers16020311.

10. Abdi H, Amouzegar A, Azizi F. Antithyroid drugs. Iran J Pharm Res. 2019;18(Special Issue):1–12. doi: 10.22037/ijpr.2019.1100516.

11. Amisha F, Rehman A. Propylthiouracil (PTU) [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549828/. PMID: 31751018.

12. Wang Z, Haange SB, Haake V, Huisinga M, Kamp H, Buesen R, et al. Assessing the influence of propylthiouracil and phenytoin on the metabolomes of the thyroid, liver, and plasma in rats. Metabolites. 2023;13(7):847. doi:10.3390/metabo13070847.

13. Iqbal A, Rehman A. Thyroid uptake and scan. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026. Available from: https://pubmed.ncbi.nlm.nih.gov/32310438/. PMID: 32310438.

14. Mostafa M, Rezk Kh, Khalifa W, Ali W, Sherif M, Mohamadien N. Utility of 99mTc-MIBI single photon-emission computed tomography/computed tomography in pre-surgical characterization of thyroid follicular neoplasm. Egypt J Nucl Med. 2021;23(2):23–43. doi:10.21608/egyjnm.2021.217687.

15. Riazi A, Kalantarhormozi M, Nabipour I, Eghbali SS, Farzaneh M, Javadi H, et al. Technetium-99m methoxyisobutylisonitrile scintigraphy in the assessment of cold thyroid nodules: is it time to change the approach to the management of cold thyroid nodules? Nucl Med Commun. 2014;35(1):51–7. doi: 10.1097/MNM.0000000000000013.

16. Benderradji H, Beron A, Wemeau JL, Carnaille B, Delcroix L, Do Cao C, et al. Quantitative dual isotope 123iodine/99mTc-MIBI scintigraphy: a new approach to rule out malignancy in thyroid nodules. Ann Endocrinol (Paris). 2021;82(2):83–91. doi: 10.1016/j.ando.2021.03.003.

17. Fischer L, Girotto N, Ili Toma M, Mavrinac M, Leki A, Antoni D, et al. Enhanced differentiation of amiodarone-induced thyrotoxicosistypes using semi-quantitative 99mTc-MIBI uptake analysis: a pilot study. Med Sci Monit. 2024;30:e945444. doi: 10.12659/MSM.945444.

18. Yordanova A, Mahjoob S, Lingohr P, Kalff J, Trler A, Palmedo H, et al. Diagnostic accuracy of [99mTc]Tc-Sestamibi in the assessment of thyroid nodules. Oncotarget. 2017;8(55):94681–91. doi: 10.18632/oncotarget.21866.

19. Hurtado-Lopez LM, Martnez-Duncker C. The role of Tc-99 m-MIBI can in the assessment of the cystic thyroid nodule. Nucl Med Mol Imaging. 2021;55(4):181–5. doi: 10.1007/s13139-021-00708-4.

20. Kreissl MC, Ovcaricek PP, Campenni A, Vrachimis A, Tuncel M, Giovanella L. The European Association of Nuclear Medicine (EANM)'s response to the 2023 European Thyroid Association (ETA) clinical practice guidelines for thyroid nodule management and nuclear medicine: a deliberate oversight? Eur J Nucl Med Mol Imaging. 2024;51(6):1678–81. doi: 10.1007/s00259-023-06571-z.

21. Schenke S, Klett R, Acker P, Rink T, Kreissl MC, Zimny M. Interobserver agreement of planar and SPECT Tc99m-MIBI scintigraphy for the assessment of hypofunctioning thyroid nodules. Nuklearmedizin. 2019;58(4):258–64. doi: 10.1055/a-0894-4843.