



On the rational use of thyroid scintigraphy in thyrotoxic patients in the age of integrated diagnostics

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We read the Editorial recently published in the *European Journal of Nuclear Medicine Molecular Imaging* by Dizdarevic and Colleagues on the role of functional thyroid scintigraphy (TS) [i.e. with ^{99m}Tc-pertechnetate (Na^{99m}Tc) TcO₄) or iodine-123 (Na¹²³I)] in patients with thyrotoxicosis before a decision in favor of radioiodine therapy (RIT) is taken [1].

The authors suggest using TS in all patients with thyrotoxicosis regardless of the etiology (i.e. autoimmune or non-autoimmune hyperthyroidism) for early detection of the potentially malignant cold nodule(s), also among patients with non-palpable one(s) due to “*the possibility of coexisting thyroid cancer in thyrotoxic patients presenting for treatment*” [1].

As per consequence, TS should be performed in a significantly larger number of patients compared to those already indicated by the 2016 American Thyroid Association (ATA), 2018 European Thyroid Association (ETA), and 2023 National Institute for Health and Care Excellence (NICE) guidelines indications [2–4].

Accordingly, the authors required that “*future revisions of the guidelines for the treatment of thyrotoxicosis should reconsider the value of thyroid scintigraphy at the initial presentation in patients with no palpable nodules and not*

just in patients with nodular thyroid disease and TRAb negative disease.”

In our opinion some issues need to be addressed and clarified:

- First, the authors did not report on the recently published European Association of Nuclear Medicine guidelines [5] which clearly illustrated the possibility of having malignancy also in thyrotoxic patients and the role/usefulness of functional TS in the diagnostic algorithm of thyrotoxic patients. However, it should be clear that the current role of TS consists in functional mapping of thyroid parenchyma while the thyroid US and FNAC are demanded to identify and characterize lesion(s) suspicious for malignancy. It is well known, in fact, that the sensitivity of US for small lesions is largely superior to that of TS. Additionally, neck US allows the complementary evaluation of cervical lymph nodes. Accordingly, EANM guidelines suggested TS for:
 1. Patients with (multi)nodular goiter and low-normal to suppressed TSH in order to (i) confirm/exclude hyperfunctioning nodule(s) and (ii) assess the degree of extra-nodular thyroid parenchyma suppression. Both information have an important impact on the decision-making process and appropriate selection of patients for iodine-131 therapy excluding cases with cold nodule(s) suspicious at thyroid ultrasound (US) and suspicious/malignant at FNAC.
 2. Patients with autoimmune hyperthyroidism with negative TRAb and/or in cases with unclear diagnosis of Graves' disease (i.e. DD painless thyroiditis). Noteworthy, TS cannot be used either to detect non-palpable nodule(s) or to indicate FNAC since it is limited by a low yield in detecting small cold lesions (≤ 10 mm) [6]. In addition, US rather than scintigraphy is pivotal to detect and differentiate suspicious from non-suspicious nodules. Basing on US results

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a TS should be required (i.e. to further characterize nodules > 10 mm) but the additional value in a diffuse hyperthyroidism with no nodules at US is negligible. All in all, the limited indications for TS reported by ATA, ETA, and NICE guidelines were overtaken by the EANM guideline: for more details, our readers are addressed to previous papers from our group [7, 8].

- Second, to support the use of TS to detect non-palpable nodule(s), the authors referred to two papers published in 2009 and 2001, respectively. The paper published by Sundaraiya and colleagues [9] reported a single case with a literature review. In the reported case, nodular lesions in both lobes (size not specified) were detected in a computed tomography scan performed after TS while US was not performed. In addition, the reviewed literature ranged from 1946 to 2005 and, as per consequence, in most of such patients TS represented the only available imaging study while the thyroid US couldn't be performed for most of them. Strictly speaking in terms of methodology, using a case report and an old literature review to support a change of practice is questionable at the very least. The second paper was published by Lacey et al. [10] aiming to highlight the role of TS to better diagnose the origin of thyrotoxicosis (i.e. autoimmune hyperthyroidism vs non-autoimmune hyperthyroidism vs viral thyroiditis) while thyroid US confirmed cold lesions in all patients. Thus, Lacey did not support the use of TS to detect non-palpable nodule(s) but, rather, pointed on the importance of integrating morphological-structural US and functional imaging information in the diagnostic algorithm of hyperthyroid patients.
- Third, TS is certainly the only diagnostic study able to assess “in vivo” the functional status of the thyroid parenchyma and must be included in an updated diagnostic algorithm in which information regarding the presence of nodule(s) can be easily obtained by thyroid US. This is consistently proved in patients with thyroid nodules at intermediate to high suspicious of malignancy by TI-RADS score where TS is able to exclude from FNAC patients with euthyroid autonomously functioning thyroid nodules. This is another indication supported by EANM guidelines but widely neglected in nuclear medicine practice [10].
- Fourth, a rationale and integrated use of different diagnostic (and therapeutic) methods and the diffusion of a more clinically oriented culture in nuclear thyroidology is the main aim of the EANM Thyroid Committee and we invite all nuclear medicine colleagues to enlarge their horizons and increase their knowledge (and ideally practice) in clinical management, laboratory medicine, ultrasound and FNAC in addition to nuclear medicine

techniques. Insisting on old and not supported indications is not, in our opinion, the best way to enhance our role in thyroid patients management.

In conclusion, we thank the authors for sponsoring the role of TS in thyrotoxic patients. However, according to robust literature data and consolidated clinical practice, using TS aiming to detect non-palpable thyroid nodule(s) seems to be anachronistic in the era of integrated thyroid diagnostics.

Declarations

Ethics approval Institutional Review Board approval is not required this paper being an Editorial.

Conflict of interest The authors declare no competing interests.

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