REPLY

Response to Letter to the Editor: Thyroid nodules with indeterminate cytology: is it safe to say ‘thyroidectomy can be excluded if ^{18}F -FDG-PET suggests benignity’?

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(2021) **28**, L3–L4**Dear Editor,**

We thank Qichang and Bin for the comments regarding our review ‘Usefulness of accessible imaging methods in thyroid nodules with indeterminate cytology’ ([Rosário et al. 2021](#)), published in this issue of *Endocrine-Related Cancer* pages L1–L2.

Regarding the preference for ^{18}F FDG-PET/CT, we do not disagree. We do not provide details on this imaging method because its protocol should follow that recommended in the EANM/SNMMI guideline ([Giovannella et al. 2019](#)).

Qichang and Bin cite two sentences with which they disagree. Although we do not disagree, the statement that ‘A nodule characterized by low or absent ^{18}F FDG uptake is considered at a very low RoM’ was mentioned by us as the conclusion reached by the EANM/SNMMI guideline. The sentence ‘thyroidectomy can be excluded if these tests suggest benignity’ in fact refers to molecular tests that could still be obtained in some nodules with ^{18}F FDG uptake; let us see the full sentence: ‘Depending on the clinical context (considering pre-test RoM and maximum SUV) and availability of molecular tests, a positive ^{18}F FDG-PET scan does not necessarily represent an indication for surgery. The patient can still be submitted to molecular tests and thyroidectomy can be excluded if these tests suggest benignity’.

Our conclusion regarding ^{18}F FDG-PET in thyroid nodules with indeterminate cytology seems to be clear: ‘In the case of nodules that are not very suspicious on US, ^{18}F FDG-PET can be obtained and, if it does not reveal nodular uptake, the risk of the nodule corresponding to

a macrocarcinoma is sufficiently low to allow follow-up’. First, we recommend this imaging method for nodules without a high RoM. Second, we consider ^{18}F FDG-PET to be negative in the absence of uptake; thus, the sensitivity is higher, 84–88% according to the meta-analysis cited by Qichang and Bin ([Qichang et al. 2020](#)). Within this context, the meta-analysis estimated a negative predictive value (NPV) of 92–97%. Third, we consider it important that the method detects malignant and clinically relevant (>1 cm) tumors since nodules <1 cm would not have an indication for FNA ([Haugen et al. 2016](#)). Since some false-negative cases of ^{18}F FDG-PET were microcarcinomas and tumors of uncertain malignant potential or borderline, its sensitivity and NPV would be even higher when only macrocarcinomas were considered.

Even assuming the NPV of 92–97% estimated by the meta-analysis, we do not think that the difference between this value and the NPV considered acceptable for a molecular test ruling out the need for surgery ($\geq 94\%$) ([Vargas-Salas et al. 2018](#)) is clinically significant. In addition, we do not agree that any nodule with a RoM above this percentage of approximately 5% does necessarily have an indication for surgery and cannot be followed up.

Declaration of interest

The author declares that there is no conflict of interest that could be perceived as prejudicing the impartiality of this article.

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