

## Letter to the Editor

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# Tubarial or not to be – a potential new organ in the pharynx

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In an elegantly presented and thought-provoking manuscript published by the journal *Radiotherapy and Oncology*, Valstar et al. characterize previously unreported structures comprising salivary gland tissue near the torus tubarius [1]. The authors present their findings in three stages. First, they identify these entities in patients with prostate or urethral gland cancer who underwent positron emission tomography / computed tomography with prostate-specific membrane antigen ligands (PSMA PET/CT), which technique—despite its name—demonstrates avidity for salivary glands. The investigators then evaluate these glands using human cadavers, and finally assess the effect of radiation therapy involving this region in head & neck cancer (HNC) patients.

Ultimately, the authors proffer two conclusions from their findings. First, they propose recognition of this region as newly identified paired organs, suggesting the designation of “tubarial glands.” Second, they underscore the importance of sparing this area from the toxic effects of radiation therapy, to whatever extent feasible. Whereas the second of these points seems more resonant and straightforward, the authors appear to emphasize the first, in terms of coverage and explication. The dichotomy between these claims, and the relative prominence of the purported anatomic contribution within the manuscript, potentially detract from study’s significant clinical impact.

The anatomic issue—whether these glands more closely resemble major or minor salivary glands—is an interesting question. In terms of features shared in common with major glands, the authors discuss several analogies between the tubarial glands and sublingual glands. For instance, the tubarial glands lack a capsule, and the sublingual glands show only partial encapsulation. The authors also demonstrate the tubarial glands’

“multiple macroscopically visible draining duct openings in the dorsolateral pharyngeal wall” in Figure 4. The sublingual gland secretes its products through multiple ducts as well. However, these features (absence of a fibrous capsule, and presence of multiple ducts) pertain to minor salivary glands as well as the sublingual gland, and therefore may not distinguish the tubarial glands as major versus minor.

Conversely, the tubarial glands exhibit several aspects analogous to the minor salivary glands of the palate, potentially suggesting a designation as minor rather than major glands for the region in question. The authors concede these resemblances, stating “the tubarial glands have many similarities with the palatal conglomerate of microscopic glands.” From the perspective of a pathologist, anyway (and based on the text), the relationship between the radiologic features of the tubarial and palatal glands is difficult to discern. The authors alternately describe the PET avidity of the tubarial glands as “consistently more than the uptake in the palate,” and/or as “comparable to the mucous aspect and PSMA-ligand uptake of minor salivary glands in the palate.” Whether these statements represent contradictory assessments is perhaps beyond my purview. Anatomically and histologically, however, commonalities between the tubarial glands and the palatal glands are evident. The photomicrograph in Figure 3, for instance, appears to show arrangement of acini more reminiscent of minor salivary glands. The authors also invoke distribution of minor rather than major glands when discussing the historical omission of / inability to previously recognize these glands. Their explanation that “the newly detected tubarial glands involve flat submucosal glandular structures” seems to describe the configuration of minor salivary units, not major glandular structures.

In some ways (and, perhaps, correctly), the authors undermine the significance of labeling these glands as major versus minor. By writing “we think these qualification systems may not be suited and relevant to interpret and appreciate this finding,” they contradict their emphasis on appropriate designation of the tubarial glands throughout much of the manuscript. Alternatively, they propose “all salivary glands together could be interpreted

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as a continuum, formed by smaller and larger collections of acini that together form a salivary gland system.” This apt and valid statement certainly warrants consideration. This stance, however, seems at odds with recognition of the tubarial glands as newly identified organs, which they advocate repeatedly, including in the manuscript’s title.

Most significantly, the authors endorse inclusion of this anatomic region within the category of organs-at-risk (OAR), warranting careful consideration for protection from radiation therapy. With this proposal, they once again establish an analogy between the tubarial glands and major salivary glands, since “the major salivary glands are [also] regarded as organs-at-risk (OAR) and need to be spared when possible.” This principle applies to the anatomic region they painstakingly characterize, regardless of whether these newly identified structures receive recognition as distinct organs. Their correct and noteworthy conclusion “it does suggest an opportunity for sparing in RT for patients treated for HNC to avoid toxicity” does not depend upon the designation of the tubarial glands as major or minor salivary glands. By devoting a significant proportion of their manuscript to the latter anatomic prospect rather than the former clinical imperative, the authors may dilute the impact of their important and valuable contribution.

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## References

- [1] Valstar MH, de Bakker BS, Steenbakkens RJHM, de Jong KH, Smit LA, Klein Nulent TJW, et al. The tubarial salivary glands: A potential new organ at risk for radiotherapy. *Radiother Oncol*. In Press. doi: 10.1016/j.radonc.2020.09.034.