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Full title: Comments on "The tubarial salivary glands: first description of a potential new organ at risk for head-neck radiotherapy"

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Letter to the Editor

Comments on "The tubarial salivary glands: first description of a potential new organ at risk for head-neck radiotherapy".

To the Editor,

We read with interest the recent article by *Valstar et al.* reporting on the tubarial glands: a previously unreported new organ at risk for radiotherapy [1]. There are several aspects that should be considered before these glands are to be called a new organ. What gives a group of tissues in a given part of the body the features to be considered as an organ? When it comes to glands, what distinguishes minor from major glands as adnexal organs from essential organs? The evolution of a new organ was already studied in detail via a placenta model recently [2], with organs such as major salivary glands presenting their own innervation and vascularization including a higher branching as opposed to minor salivary glands, and it remains clear that the three major salivary glands account for 90% of saliva production [3].

The mucous membrane of the aerodigestive tract is characterized by a continuous lining that encompasses the larynx, pharynx, oral cavity, nasal cavities and auditory tubes. Underneath this mucous membrane a high number of racemose mucous glands can be seen, which are especially numerous at the upper part of the pharynx around the orifices of the auditory tubes, in which case they are obviously not called salivary glands [4]. Therefore, from an anatomical point of view, the presence of seromucous glands in the adjacent connective tissue is very common even in the respiratory submucosa, which would be the case with the tubarial glands, when they should not be called salivary glands [5].

Furthermore, heterotopic salivary gland disease - the presence of salivary gland tissue arising outside the normal distribution of the minor and major salivary glands tissue has been documented in the middle ear, larynx, lower neck, chest wall, sternoclavicular joint and brain [4]. The exact mechanism of salivary gland heterotopia is uncertain but as this is a known feature it seems plausible that the findings of "tubarial glands may not be as unique as suggested [6]. Also, from a microscopic standpoint, the authors failed to demonstrate genuine lobular structures and ductal differentiation, which are necessary to support the theory of a "previously unnoticed pair of salivary glands in the nasopharynx" [3].

Last but not least, it comes to our attention that when the same research group published the PET/CT physiologic distribution of PSMA-ligand in salivary

glands and seromucous glands of the head and neck, the tubarial seromucous glands did not seem to present a significant uptake [7]. Accordingly, it seems too early to state that this area may lead to significant clinical toxicity based on imaging findings from two patients [1].

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