Author’s response to reviews

Title: Salivary Gland Function in Nasopharyngeal Carcinoma Before and Late After Intensity-Modulated Radiotherapy Evaluated by Dynamic Diffusion-Weighted MR Imaging with Gustatory Stimulation

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Author’s response to reviews:

Dear Dr Omar Kujan,

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate editor and reviewers very much for their positive and constructive comments and suggestions on our manuscript entitled “Salivary Gland Function in Nasopharyngeal Carcinoma Before and Late After Intensity-Modulated Radiotherapy Evaluated by Dynamic Diffusion-Weighted MR Imaging with Gustatory Stimulation”. (ID: OHEA-D-19-00496).

We have studied reviewer’s comments carefully and have made revision which marked in red in the paper. We have tried our best to revise our manuscript according to the comments. Attached please find the revised version, which we would like to submit for your kind consideration.

Below are our specific responses to the reviewers’ comments.

Amanda Phoon Nguyen (Reviewer 1):

Comment 1: The patient characteristics need to be reported. In table form, each patient's age, the dose of the IMRT, chemo details, and factors relevant to salivary gland hypofunction should be included.

Response 1: We thank reviewer for the helpful suggestion. Patient basic information is supplemented in table form, in page 7 line 17, see supplementary material. Exclusion criteria for enrolled patients have ruled out the factors that may reduce the function of the salivary glands.
Comment 2: Instead of lemon juice, have you considered the use of a saliva test kit? Why or why not?
Response 2: We thank reviewer for the helpful suggestion. In this study, lemon juice was used as a taste stimulator to stimulate the salivary glands to secrete saliva, and then to obtain salivary flow rate. However, the saliva test kit is a reagent for detecting saliva components. The roles of the lemon juice and the saliva test kit are different, and the detection of saliva components is not part of this study.

Comment 3: I have difficulty understanding the clinical utility and the aim of the paper. I don't think the conclusion is supported, which is that DW-MRI with transient gustatory stimulation could be used to evaluate salivary gland hypofunction. Could you please expand on how this may be used clinically?
Response 3: We thank reviewer for the helpful suggestion. In this study, DW-MRI was used to evaluate the function changes of salivary glands in patients with nasopharyngeal carcinoma before and after radiotherapy. The results showed that some parameters of DW-MRI were significantly different before and after radiotherapy, and these parameters have a certain correlation with salivary flow rate and xerostomia scores, which indicating that DW-MRI can be used for non-invasive evaluation of function changes of the salivary glands after radiotherapy. However, due to the limitation of sample size, this study is still a preliminary study. This study is not yet possible to obtain a certain DW-MRI parameter threshold for judging salivary glands dysfunction directly, which needs to be completed by large sample size and multi-center study in the future. It is also possible to establish a predictive model of salivary glands dysfunction after radiotherapy in patients with nasopharyngeal carcinoma based on DW-MRI. And this method can also be used for clinical or experimental research on the prevention and treatment of radiation damage in the salivary glands.

Comment 4: A distinction should be drawn between xerostomia and salivary gland hypofunction; these words are not interchangeable
Response 4: We thank reviewer for the helpful suggestion. Although many related documents also use xerostomia and salivary gland hypofunction at the same time, indeed, the two are not the same. Xerostomia is the subjective feeling of dry mouth, while the salivary gland hypofunction is an objective measure of reduced salivary secretion. Xerostomia and salivary gland hypofunction may represent the same condition of the patient, and the two are related. In the present study, radioactive damage to the salivary gland resulted in a salivary gland hypofunction, reduced salivary secretion, which in turn caused xerostomia in patients. We think that it is inevitable that both of xerostomia and salivary gland hypofunction appear in the article at the same time.

Comment 5: Images may be useful for the readers to follow what is being described.
Response 5: We thank reviewer for the helpful suggestion. This study mainly studied the changes of salivary gland function through parameter changes, so there is no picture added in the text.

Comment 6: Appropriate controls should be used.
Response 6: We thank reviewer for the helpful suggestion. In this study, because all patients had no xerostomia before RT and all of them occurred to xerostomia after RT, so we recorded the patients as non-xerostomia group before RT and xerostomia group after RT, which has been stated in the last paragraph of methods section in page 7 line 18 and 19.

Comment 7: Could you please comment on the reproducibility of these tests?
Response 7: We thank reviewer for the helpful suggestion. The MRI method, saliva measurement method and xerostomia scoring method used in this study are all conventional methods, which are simple and easy, and do not require special equipment or preparation. Therefore, similar studies can be carried out in different research centers, and we believe that they have good repeatability.
Comment 1: In the abstract, the background should include the research question and include the objectives separately after this.
Response 1: We thank reviewer for the helpful suggestion. Research question and the objectives have been modified in background section of the abstract in page 2 line 2-6. “Xerostomia caused by radiation-induced salivary glands injury has a considerable impact on patients’ quality of life. Nowadays, the existed different methods of evaluating xerostomia in clinical practice there are still some disadvantages and limitations. This study used diffusion-weighted magnetic resonance imaging (DW-MRI) with gustatory stimulation to assess salivary glands function after intensity-modulated radiotherapy (IMRT) in patients with nasopharyngeal carcinoma (NPC).”

Comment 2: There are a couple of spelling mistakes of medical conditions. Otherwise the paper is very informative and well written.
Response 2: We thank reviewer for the helpful suggestion. The spelling mistake has been corrected, in page 7 line 10, in page 9 line 18 and 19, in page 30 line 8.