Author’s response to reviews

Title: Outcomes of Orbital Malignancies Treated with Eye-Sparing Surgery and Adjuvant Particle Radiotherapy: a retrospective study

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Author’s response to reviews:

Dear Dr. Rades,

Thank you very much reviewing our manuscript titled “Outcomes of Orbital Malignancies Treated with Eye-Sparing Surgery and Adjuvant Particle Radiotherapy: a retrospective study”. We appreciate your time and efforts. Based on the reviewers’ comments, we have revised the manuscript and have addressed all the comments and suggestions. The point-by-point responses to the reviewers’ comments are presented below.

If you have any questions about our work, please do not hesitate to contact us. We are looking forward to hearing from you soon.

Best wishes,

Drs. Lin Kong and Jiade J. Lu

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Replies to Reviewer 1:

This is a retrospective case series of patients with primarily adnexal tumors treated with eye sparing surgery and adjuvant particle beam (primarily carbon beam) radiotherapy. Excellent local control and a low rate of severe delayed side effects are noted among this population of 22 patients followed for about 2 years on average. This case series is well described, potential predictive factors are examined in univariate and multivariate analysis and relevant case series in the literature are compared to the authors experience. The manuscript is well written and organized. A suggestion would be to consider including a figure of a carbon ion distribution (perhaps with a comparison dose distribution with an IMRT plan or Proton plan) for a typical case as most readers will not be familiar with the physical distributions of CIRT.

Response: We thank the reviewer for encouraging us with a very positive review. We totally agree that a figure of dose distribution of carbon ion radiation will be helpful for the readers to understand the concept better. We have added a typical CIRT treatment plan of a lacrimal gland tumor (Fig.1) in the section of “Particle Radiotherapy”.

Replies to Reviewer 2:

I read with interest the work by Hu et al, which aims at confirming the recent positive experience with eye-sparing surgery plus radiotherapy in the treatment of orbital malignancies. Unfortunately, as correctly pointed out by the Authors, these are rare and heterogeneous tumors, thus definitive conclusions are difficult to draw. However, I think that the Authors have exhaustively analyzed their data and adequately reviewed the literature context.

My requests are:

- ophthalmologic outcome should be defined in detail, if possible. I mean, it would be interesting to know the status of visual acuity and ocular movements of patients before and after radiotherapy. The Authors have reported only one case of reduced visual acuity, but I think that this topic is very important and should be better analyzed.

- follow-up is quite short. This must be recognized as a limitation of the study.

Response: We would like to thank the reviewer for his/her careful review and constructive advice. We are very much encouraged by the comments of the reviewer praising our exhaustive efforts for the analyses and literature review. The point-by-point responses to the 2 comments from the reviewer are as follow:

Comment: Ophthalmologic outcome should be defined in detail, if possible. I mean, it would be interesting to know the status of visual acuity and ocular movements of patients before and after radiotherapy. The Authors have reported only one case of reduced visual acuity, but I think that this topic is very important and should be better analyzed.
Response:

All patients’ visual acuity and ocular movement of affected eye were normal before particle radiotherapy, except for one patient who has eyeball fixation and amblyopia of the affected side due to eye-sparing surgery (twice) and photon-based radiotherapy for locally recurrent lacrimal gland malignancy. However, there was no further decline of affected side visual acuity, and movement of eyeball did not improve after CIRT of this patient with recurrent tumor.

There were two patients developed vision impairment after CIRT, and no visual changes in the remaining patients. One experienced vision acuity reduction from normal to 20/200-40/200 at 6 months with MRI confirmed optic atrophy, and another patient developed blindness at 3 months without MRI changes (but the patient refused to have further ophthalmologic examination). No ocular movement disorder was observed in all patients who received particle radiotherapy (except the patient with recurrent tumor). We have provided the details in the “Acute and chronic toxicities” section as the reviewer suggested in the revision.

Longer follow-up is necessary to further examine the impact of CIRT on visual acuity and ocular movements. Further study on this topic may be conducted in the future.

Comment: Follow-up is quite short. This must be recognized as a limitation of the study.

Response: Indeed, in less than 3 years, we treated 23 ESS patients, owing to the limited follow up time, these results must be considered with caution, we will continue to follow these patients and report clinical outcomes with longer period. In the discussion section, we have recognized that the short follow-up time is a limitation of the study as requested by the reviewer.