Reviewer’s report

Title: Prognostic value of the distance between the primary tumor and brainstem in the patients with locally advanced nasopharyngeal carcinoma

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Reviewer: Shaojun Lin

Reviewer’s report:

This is an article analyzed the prognostic value of the distance between the primary tumor and brainstem in locally advanced nasopharyngeal carcinoma, however, it cannot be published in its present form, as some important issues must be demonstrated clearly.

Major revision:

1. On the basis of geometry, the distribution of the isodose curves were correlated with both the distance between two objects and the contact area. The cutoff value of Dbs was 4.75mm, how the authors accurately detected Dbs to 0.05mm? The authors did not analyzed the PGTV data in different Dbs groups for those had a radiation dose lower than 66Gy.

2. In the Introduction part, the authors defined lower dose as less than ≤66.5Gy, however, 66Gy was demonstrated as the the prescription dose of PGTVnx in the Method part(2.4)

3. The chemotherapy given in this cohort irregular, was 21 patients did not received chemotherapy. It is not reasonable to decide the necessity of neoadjuvant chemotherapy according to the waiting time. In addition, the authors did not indicated clearly the chemotherapy details of the whole group and how many patients had not complete adequate chemotherapy. OS and DMFS should be analyzed after excluded other factors(i.e. chemotherapy).

4. Dbs could had great influence on the results of TPS, which could induce the underdose of GTV, then further influence the local control. Since different physicists may yield different radiation protocols in the same patient, false positive result results may be produced. The distance of Dbs was correlated to T category and the volume of tumor, both are factors of primary site, and may have more influence on local control. The difference of 3-year OS should be analyzed further, as local control of NPC patients in IMRT era was superior, distant metastasis was the main failure pattern.

5. It was not sufficiently rigorous that the authors analyzed the impact of Dbs on treatment outcomes without considering other factors, yield limited reference significance in clinic of this study.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
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No

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