Author’s response to reviews

Title: Cervical Spine Osteoradionecrosis or Bone Metastasis after Radiotherapy for Nasopharyngeal Carcinoma? The MRI-Based Radiomics for Characterization

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Version: 2 Date: 24 Jul 2020

Author’s response to reviews:

Dear editor,

Thank you for your kind letter regarding our manuscript entitled, “Cervical Spine Osteoradionecrosis or Bone Metastasis after Radiotherapy for Nasopharyngeal Carcinoma? The MRI-Based Radiomics for Characterization” (BMIM-D-20-00212), and the referee’s remarks. We have revised and modified the manuscript in accordance with the reviewer’s comments. At this time, we have re-submitted the revised manuscript through the Author Center, and we hope to have the opportunity to publish this paper in BMC Med Imaging.

We have used the tracked changes function of Word’s when revising the paper for easier review purposes. All changes were marked in red text. We hope the revised manuscript will meet your standard. Below you will find out point-by-point responses to the reviewers’ comments/questions.
Responses to Reviewers:

Reviewer 1: Needs some language corrections before being published. Check citation, source of data, etc., properly.
Answer: Thank you very much for your meaningful comments. To address the reviewer’s concern, we have corrected language, checked citation and source of data in our revised manuscript.

Reviewer 2: The authors have fully addressed the concerns and suggestions of this reviewer. The revised version just has a couple of editing errors to correct, as listed below.

1. Page 5, Abstract/Method, lines 17-25. "279 radiomics features were …, a radiomics signature was …, and a nomogram was …". These three sentences should be separated by period mark ".", rather than by comma ",".
Answer: Thank you very much for your meaningful comments. The three sentences have been separated by period mark "." in our revised manuscript (Page 2, Abstract/Method, lines 7-9).

2. Page 9, line 4. The two sentences "MR images were … (…; Philips), the MRI protocol included …" should be separated by a period ".".
Answer: Thank you very much for your meaningful comments. The two sentences have been separated by period mark "." in our revised manuscript (Page 6, Paragraph 1, lines 2-3).

Reviewer 3: I have not seen my comments being addresses in the revised version. I am repeating my comments:

1. Pathological assessment was performed for only one ORN patients. Correct "s" at the end of the sentence and please explain why only one patient pathology was used. Are the authors confident the one patient was enough?
Answer: Thank you very much for your meaningful comments. We have corrected "s" at the end of the sentence. Pathologic confirmation for cervical spine ORN is unpractical attributed to the relatively high risks related to biopsy of cervical spine (eg, injury to the vertebral artery or the cervical spinal cord). As described in previous studies, the reference standard for ORN was based on the MRI and clinical follow-up [1, 2]. In fact, this is a retrospective study, we found that only one patient had undergone lesion resection due to the lesion protruded into the spinal canal and induced severe neurological symptoms.

2. Could the authors explain a possible relation of this paper to the other one by the same authors: 10.3389/fonc.2020.00015. Were the same patients used in both studies?
Answer: Thank you very much for your meaningful questions. In our previous study (10.3389/fonc.2020.00015), we have assessed the value of qualitative MRI in the differentiation of cervical spine ORN from bone metastasis detected by BS, all patients showed cervical spine increased radiotracer uptake on a bone scan. In the previous study, we found qualitative MRI showed potential value in the differentiation of ORN and bone metastasis. Thus, in this study, we preliminarily explored the value of MRI-based radiomics for distinguishing ORN from bone metastasis. The sample size in present study is significantly larger than that of our previous study (76 vs 35). Firstly, we reviewed consecutive NPC patients from January 2008 in this study (from 2013 in previous study). Secondly, compared with our previous study, patients without bone scan examination or bone scan negative findings were also included in this study.

3. Could the authors address possible application of other MRI pulse sequences in the studies, such as T2-w or DW?
Answer: Thank you very much for your meaningful questions. Both ORN and bone metastasis showed obvious enhancement on contrast-enhanced T1-weighted image (CE-T1WI), and the boundary of lesions is clear on CE-T1WI. Thus, regions of interest (ROIs) were delineated on CE-T1WI. Indeed, radiomics based on T2-w or DW may also show potential value in the differentiation of ORN and bone metastasis. However, ORN usually shows equisignal on DW, and reactive bone marrow edema associated with ORN also shows hyperintensity on T2w. In this case, the boundary of lesions may be indiscernible on T2-w or DW, placement of ROI accurately is difficult on T2-w or DW images.