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Dear Professor Ma, Professor Ahmed, Professor Rodriguez and Professor Kasi:

22 June, 2019

Thank you very much for your favorable consideration of our paper entitled "**Hypofractionated particle beam therapy for hepatocellular carcinoma–a brief review of clinical effectiveness**" (Manuscript NO.**:** 47264) for publication in **World Journal of Gastrointestinal Oncology**. We very much appreciate the comments of the reviewers and have improved our paper based on their suggestions. A point-by-point list of our responses and amendments is attached.

We appreciate your tremendous patience and generous help in editing our manuscript.

Respectfully yours

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Response to Reviewer's Comments

It is a good minireview. Authors have given a concise summary of particle radiotherapy for hepatocellular carcinoma. It is proposed to add the following two items:

1. Explain Bragg Peaks with diagrams.

Authors' response

We thank you for this pertinent suggestion. Accordingly, we have provided a new Figure 1 to explain Bragg Peaks with diagram. The figure legend of Figure 1 is "The illustration of Bragg peak and spread-out Bragg peak (SOBP)".

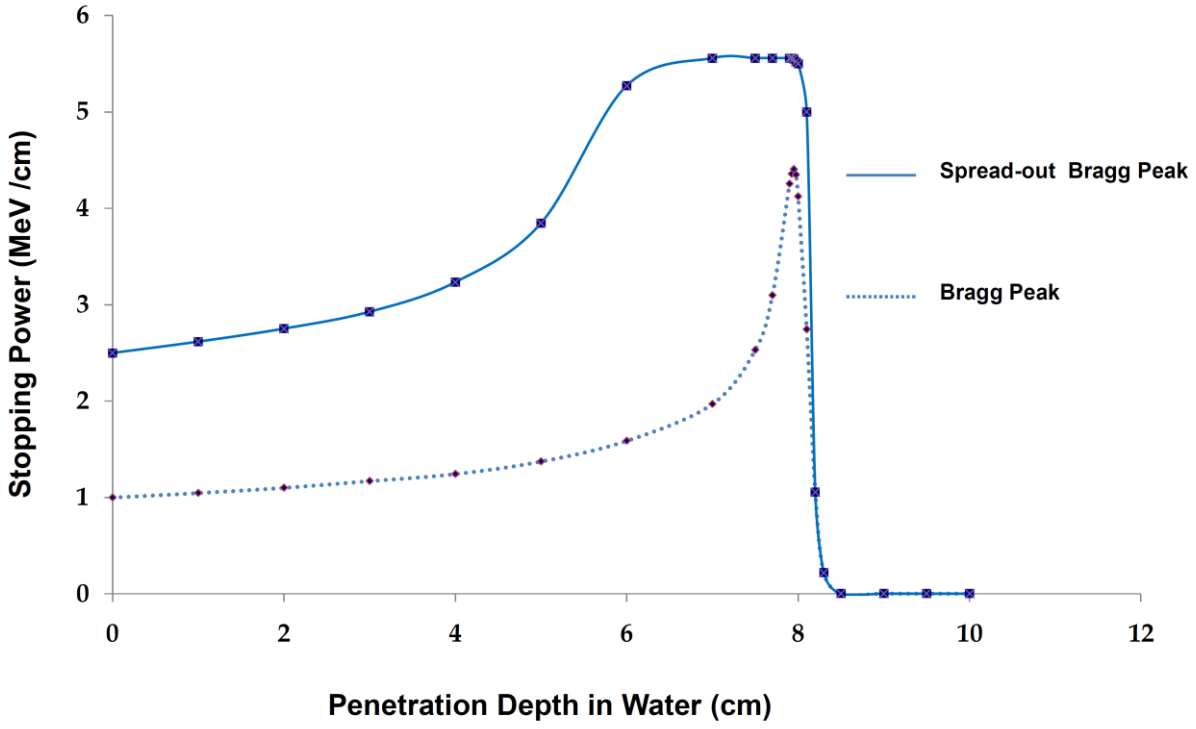

Figure 1. The illustration of Bragg peak and spread-out Bragg peak (SOBP)

2. Please elaborate on another radiobiological advantage of particle beams-OER(Oxygen Enhancement Ratio).

Authors' response

We greatly appreciate your comment, and as per your suggestion, we have provide the advantage of particle beams-OER (Oxygen Enhancement Ratio) in the text (Page 6, Lines 10-15).

Moreover, the direct DNA damage effect produced via the CPT beam also had another radiobiological advantage in terms of the oxygen enhancement ratio (OER), which is defined as the ratio of radiation dose required to produce the same tumoricidal effect under hypoxic and normoxic conditions. The OER can be reduced to 1 by using the CPT beam, with a linear energy transfer more than 100 keV/μm for oxygen concentrations between 0% and 20% [31].

Ref. **31**. Tinganelli W, Durante M, Hirayama R, et al. Kill-painting of hypoxic tumours in charged particle therapy. Scientific reports 2015; 5: 17016