October 10, 2018

Bing Wu, Ph.D.

Review Editor

Editorial Department

JoVE

1 Alewife Center, Suite 200

Cambridge, MA 02140 USA

RE: Proton Therapy Delivery and its Clinical Application in Select Solid Tumor Malignancies

Dear Dr. Wu,

Thank you again for your consideration of this manuscript for publication in which we have examined the practical nuances of cancer treatment using proton based external beam radiation techniques.

We have addressed the editorial comments provided by your staff, which we believe have further enhanced the paper. A point-by-point summary of the changes is attached to this letter.

We hope that these additional revisions are well received, and look forward to your review.

Thank you again for your consideration.

Sincerely,

Adeel Kaiser, MD

Responses to Editorial Comments for 58372\_R1 – REVISED 10-10-18:

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.

**Completed**

1. For in-text referencing, please put the reference number before a period or comma.

**Completed**

1. All protocol steps have been renumbered, please ensure that all steps are referenced correctly throughout the manuscript. For example, in step 1.4, step 12 is referenced. However, it’s now numbered as step 1.12.

**Completed**

1. The highlight protocol steps are over 2.75 page limit (including the headings and spacing). Please reduce the amount of highlighted steps.

**Since there are 43 lines per page, I calculated 118 lines of highlighting as 2.75 pages. The highlighted portion has been reduced to 99 lines to stay within this number.**

1. For steps that are done using software, a step-wise description of software usage must be included in the step. Please mention what button is clicked on in the software, or which menu items need to be selected to perform the step.

**We would request the steps utilizing software be left as is. There is tremendous variability in the software interfaces of various radiation planning systems. Our goal was to write a protocol providing sufficient detail that could be adapted and utilized by any proton center regardless of their specific software package.**

1. Please use h, min, s for time units.

**Completed**

1. Step 1.24: Please write this step in imperative tense.

**Completed**

1. 2.13.5.1-2.13.5.8: Please write these steps in complete sentences and imperative tense.

**Completed**

1. 2.15.2.1-2.15.2.4: Please write these steps in complete sentences and imperative tense.

**Completed**

1. 2.17: Please split this step into two or more steps.

**Language was simplified to limit it to one step.**

11. 2.17.1-2.71.4: Please write these steps in complete sentences and imperative tense.

**Completed**

12. 2.21: Please write this step in imperative tense.

**Completed**

13. 3.11.1-3.11.4: Please write these steps in complete sentences and imperative tense

**Completed: Step 3.11 was split into 2 steps. Substeps 3.11.1 to 3.11.4 were eliminated and instead replaced by a reference steps 2.17.1 to 2.17.4.**

14. 3.15: Please write this step in imperative tense.

**Completed**

15. 4.17.1: Please write this step in imperative tense.

**Completed**

16. Please remove all headers from Representative Results (line 532, 580, 635).

**Completed**

17. For each figure, please provide a title and a short description of the figure in the figure legend.

**Completed**