

Dear Editor,

Thank you very much for considering our manuscript entitled “Improving the accuracy and consistency of clinical target volume delineation for rectal cancer by an education program” (Manuscript NO.: 73855) and providing us with the opportunity to resubmit the revised version to your esteemed journal. We also greatly appreciate your efforts and those of the four reviewers, whose specific comments and suggestions provided valuable feedback, helping us improve our manuscript. All comments have been seriously considered, and modifications have been made in the revised manuscript. We also have revised the format according to the author’s guidelines of your esteemed journal. The formal ethics approval document and a new language certificate have been provided. We hope the revised manuscript will meet your journal’s standards. Because of the extensive attention on accurate target volume delineation, while no study regarding the current situation of rectal cancer target delineation in China and the impact of educational interventions on rectal cancer target delineation is available, we believe that this study, which provided a strategy to improve the accuracy and consistency of CTV delineation, would be of great interest to readers of *World Journal of Gastrointestinal Oncology*.

Our point-by-point responses to the Editorial Office and the four reviewers’ comments were attached as follows. If there are any additional questions, please inform us, so we can further try to resolve them. Thank you for your consideration.

With best regards,

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Response to Reviewer #1:

Comments:

1. Comments: First, the manuscript has limited original findings. No new phenomena were found in this study. Wide variations in CTV delineation for rectal cancer are observed among radiation oncologists in mainland China.

Response: Thank you for your thoughtful comment. To our knowledge, this is the first study that examined the interobserver variation in CTV delineation for rectal cancer among radiation oncologists from mainland China and the first study that evaluated the impact of an education program on CTV delineation for rectal cancer. The results validated the presence of large variations in CTV delineation and confirmed the effectiveness of education interventions which are relatively easy to implement and have important implications for improving the accuracy of treatment delivery. The results of qualitative analysis first pointed out that inappropriate inclusion of the external iliac region and ischiorectal fossa were the two main issues in the CTV contouring, which are notable and instructive for the clinical practice of radiation oncologists.

2. Comments: Second, this paper does not contain new concepts or methods. The present study is based on the usual methods and it does not unfortunately solve the problems under discussion.

Response: Thank you for your valuable comment. Indeed, our study adopted indices and methods that have been reported in previous studies. But in our studies, all the methods are organically integrated to verify the conclusions. Besides, the four issues in the qualitative analysis were proposed and investigated for the first time in our study. Although the study had some limitations, including the small sample size, a single case for contouring, and the short follow-up time. The results are still meaningful, which validated the presence of large variations in CTV delineation and confirmed the effectiveness of a well-structured education program.

3. Comments: Third, this publication does not have an impact on the basic science, but it can produce some improvements in current clinical practice.

Response: Thank you for your valuable comment. As a clinical study, our results do not really have an impact on basic science. However, our study can remind radiation oncologists to pay attention to the existence of target delineation variations, which are associated with poorer outcomes and more toxicities, and provide an effective strategy to improve the accuracy and consistency of CTV delineation.

Response to Reviewer #2:

Comments: Thank you very much for the opportunity to review this excellent paper. This is an original paper: Improving the accuracy and consistency of clinical target volume delineation for rectal cancer by an education program with the aim of examine whether an education program could improve the accuracy and consistency of preoperative radiotherapy CTV delineation for rectal cancer. And the conclusion of the wide variations in the delineation of CTV for rectal cancer were present among radiation oncologists. Inappropriate inclusion of the external iliac region and ischiorectal fossa were the two main issues in the CTV contouring. A well-structured education program could improve delineation accuracy and reduce interobserver variations. It is feasible to incorporate such a program into the continuing education programs for radiation oncologists. Excellent quality of the study. The limitations including a small sample size and only a single case for contouring. Furthermore, the long-term outcomes were not assessed; thus, it is unclear whether the education program is associated with lasting effects. Further studies need to include more participants and rule out possible selection biases resulting from a single patient and anatomic differences by tumor locations.

Response: Thank you very much for your valuable comment. Your recognition of our work is deeply appreciated. And your suggestion is very important for

further improvements. Our study first validated the presence of large variations in rectal cancer CTV delineation among Chinese radiation oncologists and confirmed the effectiveness of a well-structured education program. In further studies, we would recruit more participants and include more cases for target volume delineation. Besides, we will prolong the follow-up time to investigate the long-term effects of the education program.

Response to Reviewer #3:

Comments: This is a well written article but has some concerns to be addressed.

#Major comments In this study, a case of stage IIIC (T3N2bM0) rectal adenocarcinoma was selected, and participants completed a CTV delineation prior to the educational program. Real-time feedback on the deficiencies in each participant's delineation was then provided, and a question-and-answer period was provided for further clarification. The participants then delineated the CTV again using the same case, and the parameters were compared before and after the program. However, it is natural that the parameters would improve when examined in this way, and furthermore, the sample size is small. Therefore, I don't agree with the conclusion that this educational program is effective based on these results. I think it is necessary to prove that the CTV delineation variation and interobserver variation (IOV) can decrease using another one or several cases after the educational intervention.

Response: We are appreciative of your valuable suggestion. Indeed, it will be more convincing if more participants are recruited and more cases for contouring are included. One reason for the relatively small number of participants is that we adopted the form of interactive teaching and real-time feedback to ensure the teaching effects. If the number of participants is too large, sufficient communication is impossible. Besides, we did not use another case for contouring after the program because only the parameters of the same case are comparable. Although the same case was used, all the participants delineated target volumes independently, and the images of other participants

and the standard CTV were invisible to them. The only condition affecting the parameters was the education intervention. Thus, the improvement of accuracy and consistency of delineation is meaningful. However, more cases can be included to rule out possible biases resulting from a single patient and anatomic differences by tumor locations. Your concern is of great importance for our further studies, and we will try to make improvements according to your kind suggestion.

Response to Reviewer #4:

1. Comments: This study tested the potential usability of an educational program and found that the program could improve the accuracy of and consistency of preoperative radiotherapy CTV delineation for rectal cancer. Despite the limitations mentioned in the manuscript, this study showed the possibility of the educational program. This study was well conducted and the manuscript was well written.

Response: Thank you very much for your valuable comment. Your recognition of our work is deeply appreciated.

2. Comments: there are some minor faults: - (page7) Hu --> HU (Hounsfield units).

Response: Thank you for your kind reminder, and the appropriate abbreviation for Hounsfield units should be HU. We have corrected it according to your suggestion.

3. Comments: - (page9) Wilcoxon signed-rank test is used in a set of matched samples, NOT Wilcoxon rank sum test. The authors should check whether proper statistical methods were used.

Response: Thank you for your valuable suggestion. Actually, the Wilcoxon signed-rank test is used in this study. We have corrected the name of the statistical method. Besides, the statistical review was performed again by a

biomedical statistician, and some minor clerical errors have been corrected in the revised manuscript.

Response to Re-reviewer:

Comments: The authors have carefully revised the manuscript according to the reviewer's comments. I have no additional comments on this manuscript.

Response: Thanks for your comments.