

Dear Editor Ma:

Please find enclosed the edited manuscript in the Word format (file name: 25141-Revised manuscript.docx).

Title: Intravoxel incoherent motion diffusion-weighted imaging for monitoring chemotherapeutic efficacy in gastric cancer

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We appreciate editor and reviewers very much for their valuable and very helpful comments on previous draft. We revised the manuscript in accordance with the reviewers' comments, and carefully proof-read the manuscript to minimize typographical, grammatical, and bibliographical errors.

Here below is our description on revision according to the reviewers' comments.

Response to Reviewer's (02977366) comments:

Thanks for your comments on our paper. We have revised our paper according to your comments:

1) The authors reported the results about 5-FU in treating gastric cancer, why they choose 5-FU? Could these results be repeated in the other

chemotherapeutic agents?

Answers: We believe that 5-FU-based chemotherapy has been widely used for treating gastric cancer as a standard chemotherapy regimen. IVIM-DWI can be potentially used to predict the early stage of treatment response of gastric cancer. The diffusion and perfusion related parameters including ADC, D, f and D* values are be used to predict the efficacy of the chemotherapeutic responses from the tumors necrosis, apoptosis and angiogenic activity because of these merits of IVIM-DWI. We assume this technique can be utilized to other chemotherapeutic agents for early monitoring the necrosis, apoptosis and angiogenic activity changes of tumor.

2) To help the readers easily understand the meaning of this study, the language of this manuscript need be polished.

Answers: We got help from a native speaker to polish the paper. Please, refer to the letter attached.

Response to Reviewer's (00225291) comments:

Thanks for your comments on our paper. We appreciate the positive comments about the manuscript. We have revised our paper according to your valuable comments:

1) Interesting study that, however, as also pointed out by the authors, has a serious flaw in the short period time of the experiment.

Answers: We agree with your opinion and consider it is also necessary to state this limitation. In this study, the short-term of 7 days 5-FU treatment was performed, because this study was designed to investigate the potential of IVIM-DWI for monitoring the early chemotherapeutic efficacy in cancer model in connection with diffusion and perfusion parametric in response to treatment. In the future studies, we need a long-term observation with a large

sample sizes to investigate the usefulness of IVIM-DWI in cancer therapy. We appended a sentence clarifying this tissue to the limitation paragraph in the discussion section on page 17.

2) Abbreviations should be avoided in the title or, if present, explained in full.

Answers: We followed your suggestions. The title of "IVIM-DWI for Monitoring Chemotherapeutic Efficacy in a Mouse Gastric Cancer Model" was changed to "Intravoxel Incoherent Motion Diffusion-weighted Imaging for Monitoring Chemotherapeutic Efficacy in Gastric Cancer".

3) In the Material and Methods section it should be clearly stated that the cell lines used are of human origin, a human gastric cancer-derived cell line.

Answers: According to your suggestion, we have clearly stated the origin of cell line in the material and methods section on page 9.

4) There are some grammar corrections in the text, which I point out below.

Answer: All of the grammar errors that you pointed out were corrected.

Response to Reviewer's (00535896) comments:

Thanks for your comments on our paper. We have revised our paper according to your comments:

1) A more precise Introduction including a more comprehensive explanation of the problematic of IVIM-DWI for Monitoring would be useful.

Answers: Thank you for the invaluable suggestion. Additional information was added to the introduction section on page 7-8.

2) Spelling has to be checked. (e.g. nasopharyngeal carcinoma in the discussion part) and the language of this manuscript needs to be polished.

Answers: We are sorry for this mistake. We followed your suggestions and

this manuscript has been polished by a native speaker. Please see the letter attached

3) As described by the author, the limitation of this study is the short observation endpoint. In addition there is no need for a small sample sizes in a mice model.

Answers: We agree with your opinion and consider it is also necessary to state this limitation. In this study, the short-term of 7 days 5-FU treatment was performed, because this study was designed to investigate the potential of IVIM-DWI for monitoring the early chemotherapeutic efficacy in cancer model in connection with diffusion and perfusion parametric in response to treatment. In the future studies, we need a long-term observation with a large sample sizes to investigate the usefulness of IVIM-DWI in cancer therapy. We appended a sentence clarifying this tissue to the limitation paragraph in the discussion section on page 17.

For the reviewers' convenience, all the changes are highlighted in yellow in the manuscript.

We hope that the correction will meet with approval.

Thank you again for considering our manuscript for publication at *World Journal of Gastroenterology*

Best regards.

Sincerely yours,

Dr. Heoung Keun kang.

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