

Dear editor and reviewers

Thanks very much for your effort and precious comments on our manuscript. The following list is the responses to the reviewers comments point to point, and we hope sincerely our response can make you satisfactory.

Reviewer #1: The authors have tried to make advances in gastrointestinal tumors imaging by investigating intravoxel incoherent motion diffusion-weighted MRI (IVIM) which is supposed to bring more detailed information regarding the assessment of response to chemotherapy. In addition, they specifically focused on the hypothesis that important IVIM derived biomarkers could reflect the microenvironment, microcirculation in the capillary network and diffusion in tumor tissues, without any contrast agent intravenous administration. Although this work is of significant interest to the field, and, obviously, further research on this topic should be encouraged, there are important concerns that could be addressed in the next version. These are outlined below. Major concerns: In Abstract- the phrase- In the previous studies, the sensitivity and specificity of these parameters used in the evaluation of GTs is different and the role of the IVIM in the GTs is discrepant. Some studies even negate IVIM's important role in GTs.- is ambiguous and should be detailed in the manuscript and supported by specific references. Other phrases are also ambiguous (E.g. page no 10- But in a report by Kim et al[44], in patients with liver metastasis...) and should be reconsidered in order to have a logical flow. Page 7-8- In the paragraph- In a report including 25 consecutive patients with advanced rectal carcinoma... the language is unclear, making it difficult to follow as well as the reference is not evident. The same for page 10- But in a report by Kim et al[44], in patients with liver metastasis from(CRC treated with... for metastasis from CRC. In general, the manuscript needs significant editing for language and writing quality, therefore, I advise the authors work with a writing coach or copyeditor to improve the flow and readability of the text. The Conclusion does not offer entirely a concise summary of the hypotheses and of main results from the manuscript. Authors should

also reflect upon and address possible limitations of the techniques in the debated area. Regarding Figure no 1- HE staining image should be explained in conjunction with disease characteristics and IVIM findings. Image of calculated MVD and its value in correlation with IRM parameters should be added to emphasize that f and D^* correlated positively with MVD, as stated in the text. (The same regarding HE staining image in Figure no 2). Finally, to me it seems that vascular enhancement is not evident in Figure no 2- image E, as pointed previously by the white arrows, but I must admit that I am not confident about this, as this part of the work is out of my area of expertise. Minor concerns Moreover, the paragraph- Encouragingly, based on the IVIM technique, more precise and effective parameters emerged in GTs, such as αpCR after CRT- seems more suitable to the Colorectal related part.

RE: Thanks for the reviewer's great efforts and precious comments.

1) In Abstract- the phrase- In the previous studies, the sensitivity and specificity of these parameters used in the evaluation of GTs is different and the role of the IVIM in the GTs is discrepant. Some studies even negate IVIM's important role in GTs.- is ambiguous and should be detailed in the manuscript and supported by specific references.

RE: As for the concerns, we replaced these sentences with “Currently, the sensitivity and specificity of these parameters used in the evaluation of GTs are different and the results of the IVIM in the GTs are discrepant, and the variability of IVIM measurements in response to chemotherapy and/or radiotherapy in these studies remains controversial. So, the question that could intravoxel incoherent motion diffusion-weighted MRI be feasible and helpful in the evaluation of gastrointestinal tumors is worthwhile to be expounded?” All the changes were marked with red letters.

2) In page no 10- But in a report by Kim et al[44], in patients with liver metastasis...) and should be reconsidered in order to have a logical flow.

RE: Yes, it is ambiguous, so we made some changes with “In patients with liver metastasis from CRC treated with cytotoxic chemotherapy reported by Kim et al^[44], after first cycle of chemotherapy, ADC(1191.9 ± 232.2 vs $1263.5 \pm 266.4 \times 10^{-3} \text{ mm}^2/\text{s}$; p

= 0.012) and $D(1085.9 \pm 232.9$ vs $1173.5 \pm 248.9 \times 10^{-3} \text{mm}^2/\text{s}$; $p = 0.012$) values increased, while f values decreased ($173.7\% \pm 39.8\%$ vs $133.5\% \pm 28.3\%$; $p = 0.017$) in eight responding patients.” This paragraph focused on the IVIM role on the metastasis, so we think it is feasible with this order, would you please give us your understanding?

3) In Page 7-8- In the paragraph- In a report including 25 consecutive patients with advanced rectal carcinoma... the language is unclear, making it difficult to follow as well as the reference is not evident.

RE: We have edited our manuscript by AJE to make our paper to understand easily. As for the reference, the content were cited with Ref 11 listed in the text.

4) The same for page 10- But in a report by Kim et al[44], in patients with liver metastasis from(CRC treated with... for metastasis from CRC.

RE: We have edited our manuscripts by AJE.

5) The Conclusion does not offer entirely a concise summary of the hypotheses and of main results from the manuscript. Authors should also reflect upon and address possible limitations of the techniques in the debated area.

RE: According to the reviewers comments, we made some changes in the conclusion. As for the limitations, because this manuscript is Editorial, so our focus is the useful application of IVIM in GTs, we contemplate it it inappropriate and no useful to address the specific limitations. Thanks for you understanding.

6) Regarding Figure no 1- HE staining image should be explained in conjunction with disease characteristics and IVIM findings.

RE: We must admit the lack of immunohistochemical staining images is our limitation. HE staining can not fully reflect the disease characteristics and IVIM findings.

7) Image of calculated MVD and its value in correlation with IRM parameters should be added to emphasize that f and D^* correlated positively with MVD, as stated in the text. (The same regarding HE staining image in Figure no 2). Finally, to me it seems

that vascular enhancement is not evident in Figure no 2- image E, as pointed previously by the white arrows, but I must admit that I am not confident about this, as this part of the work is out of my area of expertise. Minor concerns Moreover, the paragraph- Encouragingly, based on the IVIM technique, more precise and effective parameters emerged in GTs, such as αpCR after CRT- seems more suitable to the Colorectal related part.

RE: The MVD are not performed and calculated in this manuscript. This is the main limitation. In Fig 2, the vascular enhancement is evident by our measurement. And the last sentence, we also made some changes in the manuscript.

Reviewer #2: This manuscript by Zuo, et al updates the new functional MRI technique, intravoxel incoherent motion (IVIM), in gastroenterological tumors. This is an important imaging technique that benefits patients and this mini review would have broad interest to basic and clinical cancer works.

RE: Thanks for the reviewer's great efforts and precious comments.

Reviewer #3: This is a very interesting article with regard to pre-operative evaluation of tumors of GI tract. Nevertheless, the structure of the article is not well provided. The Abstract is totally without structure and the aim of the study is not clear. The Introduction section should be reduced. Information included in manuscripts should be removed to the Discussion section. Please clarify the aim of the survey. Specific analysis of the Imaging technique is warranted. Since the study is a narrative review results provided by newly published investigations should be summarized. Comparative analysis of relevant comments is implemented instead of results' description. Newly published references should be added. Grammatical errors should be corrected.

RE: Thanks for the reviewer's great efforts and precious comments.

RE: Because this manuscript type is editorial, so the abstract is written without the special structure(Aim, Materials and methods, Results and Conclusion). The abstract is also reduced according to the comments. And the aim of this manuscript is “could intravoxel incoherent motion diffusion-weighted MRI be feasible and helpful in the evaluation of gastrointestinal tumors is worthwhile to be expounded? In this text, we cited the latest published papers and the related data, the data is the potent evidence for the support of the IVIM in GTs. The brief analysis of the imaging technique is to elicit the role of IVIM. And the manuscript are edited by AJE.

Reviewer #4: This paper is well written. However, there are a lot of lousy typing (e.g., 'a'). English language should be checked by English consultant.

RE: Thanks for the reviewer's great efforts and precious comments. And the manuscript are edited by AJE.

Although we revised our manuscript carefully according to the comments, but it's also too difficult to make every reviewer satisfactory. We sincerely hope our revision can be accepted by WJR.