

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: WJG 78385 revision.docx).

Title: Ultrasound-based Artificial Intelligence in Gastroenterology and Hepatology

Author: Ji-Qiao Liu, Jia-Yu Ren, Xiao-Lan Xu, Li-Yan Xiong, Yue-Xiang Peng, Xiao-Fang Pan, Christoph F. Dietrich, Xin-Wu Cui

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 78385

We are very grateful about the reviewers' valuable comments. We believe that these comments have made our manuscript more comprehensible. We have made all the changes as required. We have made the required changes in the main text, tables, references, legends and figures. We tracked the changes in the text.

Reviewer 02446627:

The author has addressed the emerging modality very nicely. The table summation of the studies is excellent. Minor language polishing is needed. Seems AI is the future.

[Reply: Thank you very much. Our review has been given a linguistic polish.](#)

Reviewer 02461627:

The manuscript entitled "Ultrasound-based Artificial Intelligence in Gastroenterology and Hepatology" and authored by Liu et al reviewed the basic technical knowledge about AI and its clinical application in the ultrasound of liver and gastroenterology. Authors then discussed the challenges and future perspectives of AI. More detailed insights into the molecular mechanisms of gastroenterological lesions especially of liver, colon & pancreas are lacking. This notion should be thoroughly covered where data from the following studies should be integrated: PMID: 33338743,

<https://thescipub.com/abstract/ajptsp.2006.21.25>, PMID: 32837538, PMID: 21258076, PMID: 33782460, PMID: 32460808, PMID: 17151316, PMID: 17151319, <https://www.scirp.org/journal/paperinformation.aspx?paperid=7085>, PMID: 34202689, PMID: 33255507, <https://doi.org/10.1186/s41936-020-00177-9>, PMID: 34639131, PMID: 26034352, <https://doi.org/10.4236/ajps.2018.96091>, <https://doi.org/10.3390/antiox11061125>, PMID: 22812448.

Reply: Thank you very much for giving us valuable suggestions, which would make my manuscript better. We have added some detailed insights into the molecular mechanisms of gastroenterological lesions and it was shown as follows: Liver fibrogenesis involves the activation of the quiescent hepatic stellate cell into an activated myofibroblast that is characterized by α -smooth muscle actin expression and the production of collagens (types I and III). (Page 8, line 12)

Pathways involved in essential cancer related events including angiogenesis, cell proliferation, and apoptosis are main targets for HCC drug development. In addition, transcription factors like nuclear factor-kappa B and cell cycle regulators such as cyclins and cyclin-dependent kinases serve as attractive anti-HCC drug targets. (Page 15, line 1)

Pancreatic cancer results from hereditary germline or somatic acquired mutations in cancer-related genes (oncogenes, tumor suppressor genes, cell cycle genes, apoptosis and genome maintenance genes), and mutations also cause cancer progression and metastasis. In addition, cell turnover, shortened telomerase and genomic instability have significant roles in progression of pancreatic epithelial cells to pancreatic cancer. (Page 18, line 5)

Colorectal cancer arises from mutations in the colonic and rectal epithelial tissues that target oncogenes, tumor suppressor genes and genes related to DNA repair mechanisms. The pathogenic mechanisms implicated in this type of cancer may involve one of three different molecular pathways: chromosomal instability, microsatellite instability and cytosine preceding guanine island

methylator phenotype. (Page 21, line 24)

It'd be useful to enrich the discussion with GI patents. For example, the following patents (and/or others) may prove useful: US Patent 20210015835, US patent 20200276133.

Reply: Thank you very much for your suggestion. The two patents are not related to ultrasound and they focus on the drug treatment of liver cancer. Our review focuses on the application of ultrasound in liver cancer, so we didn't use the suggested patents.

One main issue is the lack of details like the time range of publication this review article covered, what keywords did the search for literature include, what were the inclusion criteria, how many studies did the search find and how many were primary research vs review articles, of those how many were selected for evaluation in this study, and finally what criteria were used for selecting the articles that were reviewed (was it the subject of the study, its novelty or both). Other than that, this is a well-thought through review that would make an interesting read if fully revised. Other comments • Proofreading is required. • References need updating, the studies suggested earlier in this report will also help with that serious issue.

Reply: Thank you very much for giving us valuable suggestions. Our review includes 40 primary articles and the time range of publication our review covered was from 2001 to 2021. The key words of the search of literature were ultrasound, artificial Intelligence, gastroenterology and hepatology. We found 453 studies and 98 were review articles. But many studies were not related to ultrasound. Our review is not a systematic review so we chose the recent application of artificial intelligence ultrasound in liver and gastrointestinal diseases.

We would like to thank the reviewer again for taking the time to review our manuscript.

Thank you again for publishing our manuscript in the World Journal of Gastroenterology.

Sincerely yours,

A handwritten signature in black ink that reads "Xinwu Cui". The signature is written in a cursive style and is positioned above a thin horizontal line.

Prof. Dr. med. Xin-Wu Cui

Email: cuixinwu@live.cn