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To
Lian-Sheng Ma, Science Editor,
Company Editor-in-Chief, Editorial Office

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Köln, den 10.07.2021

Dear Prof. Lian-Sheng Ma,

Thank you very much for your precious time and the fast review of our manuscript "Clinical use of augmented reality, mixed reality, 3D-navigation and artificial intelligence in liver surgery". We are grateful to have the chance to resubmit a revised version of our manuscript to "Artificial Intelligence in Gastroenterology". With the comments of the reviewer we were able to improve the quality of our manuscript and hope it is now suitable for publication.

Below you could find our point-by-point response to the reviewers' comments:

Reviewer #1

There is however a lack of discussion concerning the problem of real-time acquisition of images during the surgical procedure and real-time reconstruction. In fact, the issue of the image registration caused by deformation may be solved by real-time acquisition and computer reconstruction. Many works are evaluating this specific aspect and should be discussed in this paper.

We added the passage "Organ deformation may reduce the precision of the registration and the navigation process during the surgical procedure. Updating the navigation information by intraoperative real-time CT image acquisition using injected fiducials could further minimize the registration error and increase precision in a pre-clinical setting." to the section "Augmented

and mixed reality for 3D Navigation” and the passage “Deformation of the liver tissue is still a major issue for precise registration and the substantial use of navigation and image superimposition during surgery. Convolutional neural networks are able to learn soft tissue behavior, which could be transferred to surgical navigation. Elastic surface based-matching registration algorithms may reduce registration errors” to the section “Artificial intelligence”. We included also the relevant references.

The authors discuss the navigation based on intra-operative ultrasound, and determination of landmark definition. Nevertheless, there are other systems that can be used which include GPS localisation of reconstructed biliary ducts, arteries or veins.

After extensive literature research we could not find a paper describing the use of a “Global positing system” in liver surgery for navigation.

The authors do not discuss the specificity of real-time fluorescence which is significant part of the development in this field. In the same way, the review should take into account the recent application of fluorescence imaging during robotic surgery. In fact, the principle of robotic surgery represents significant data acquisition that can be mixed with image reconstruction to give integrated images which is a key development of robotic companies.

We added the new section “Fluorescence guided navigation technology and robotic platforms” to our review. Another relevant article about robotic liver surgery and navigation was cited in the section “Augmented and mixed reality in laparoscopic liver surgery”

Fluorescence and robotic liver surgery are very important topics, but represent a large scientific field, which should be discussed in detail in a separate review article.