

Subject: Response to Reviewers' Comments - Manuscript ID 86565

Dear Editor-in-Chief Jin-Lei Wang,

We express our sincere gratitude for considering our manuscript, for publication as a Mini-Review in the esteemed World Journal of Transplantation. We greatly appreciate the constructive feedback provided by the reviewers, which has undoubtedly enriched the quality and depth of our work.

In response to the reviewers' comments, we have meticulously addressed each point raised. We believe that our revised manuscript is now well-aligned with the journal's standards and objectives. Below, we present a comprehensive point-by-point response to the reviewers' feedback:

#### **Reviewer #1**

1. Liver volume measurement is important in both living donor liver transplantation and liver resection for liver cancer, so it is maybe more appropriate to change the title to liver surgery. There is no mention of the research progress of liver anatomy, only liver volume. **Answer: We appreciate your valuable feedback. We have taken your suggestion into consideration and have subsequently revised the title to "Assessing Liver Volume and Anatomy in Living Donor Liver Transplantation: Exploring Contemporary Imaging Techniques and Artificial Intelligence Integration."** Furthermore, we have included an in-depth evaluation of liver anatomy specifically pertaining to live donors within the manuscript. It is important to note that the primary objective of our article is to concentrate on liver transplantation. While we acknowledge the significance of pre-liver resection evaluation for various pathologies, addressing this aspect within the confines of this review would extend beyond the scope of our intended focus. As such, we have deliberately limited our discussion to the context of liver transplantation. We trust that this approach will provide a more comprehensive exploration of the chosen subject matter. Thank you once again for your thoughtful comments, which have contributed to enhancing the clarity and precision of our work.

2. The volume or weight of the liver in vitro is less than the assessed liver volume due to the supply of liver blood flow to the hepatic arteries. When the graft restores the arterial blood supply, the volume increases appropriately to match the estimated liver volume. **Answer: Thank you for your insightful comment. Indeed, you've raised a pertinent observation. Our measurements are indeed predicated upon the weighted liver. This approach stems from the practicality that post-reperfusion, an immediate assessment of liver volume becomes unfeasible due to the inability to weigh or evaluate the liver accurately.**

**Post-reperfusion, an array of recipient-related factors comes into play, exerting an influence on the newly transplanted liver's volume, which notably includes portal pressure dynamics. In recognition of this complexity, our presentation encompasses the factors underlying potential inaccuracies. Notably, our discourse highlights the significance of excluding blood vessels and bile ducts during imaging volumetric assessment to prevent potential overestimations.**

**This point is underscored within the Manual Volumetry section, specifically within the third paragraph. We draw attention to a noteworthy observation wherein a 9% volume reduction was attributed to the intrahepatic blood that gets flushed out of the liver during back-table preparation, facilitated by the preservation solution. This aspect has been previously discussed in references [9, 31, 37]. Your valuable comment enriches the depth of our discussion, allowing us to offer a more comprehensive and nuanced examination of the intricacies involved. Thank you once again for your contribution to enhancing the precision and thoroughness of our manuscript.**

3. FLR of the donor original liver volume graft volume to the standard liver volume (SLV) is the important reference index obtained by imaging before surgery. Graft recipient weight ratio is the important reference index obtained after surgery. Liver volume is related to graft weight, Therefore, the timing of the application of these two parameters is different and should not be confused. **Answer: Thank you for your comment, before the surgery we can have an estimation of the graft to recipient weight ratio. These terms were corrected in the manuscript.**

4. Liver volume measurement requires the involvement of an experienced liver surgeon, as only the surgeon can conclusively determine the plane of separation of the liver and remove the effects of the middle hepatic veins and caudate lobes. **Answer: Thank you for your comment, this will be highlighted in the text.**

#### **Reviewer #2**

This study is aimed to provide a comprehensive review of the literature, presenting both traditional and emerging methods of LV, while discussing their respective strengths and weaknesses. By examining the current state of LV techniques. The topic of this review is somehow of importance, but some revisions are still needed.

1. Why did the author focus on the Volumetric calculations in liver donors? It is also important in many patients with liver diseases? Please provide more backgrounds to support your review only focus on this relatively small population. **Answer: We express our gratitude for**

your valuable comment on our research paper. Indeed, the significance of the topic you have raised regarding liver resection for tumors is undeniable; however, we must clarify that our study primarily focuses on living donor liver transplantation. The practice of living donor liver transplantation is currently witnessing substantial expansion, especially in Asian countries. Consequently, ensuring the safety of the donors and optimizing recipient outcomes become paramount considerations. These factors are greatly influenced by the accurate pre-operative anatomical and volume calculations. Across the globe, there is an increasing trend of employing imaging and artificial intelligence in the pre-operative evaluation of donors. As such, the population under study should not be perceived as small, given the growing emphasis on pre-operative assessment in the context of living donor liver transplantation. Once again, we appreciate your input and assure you that we have duly considered the broader implications of our research.

2. Are the “semi-automated image processing, automated liver volumetry techniques, and machine learning-based approaches” parallel concepts? The semi-automatic and automatic techniques may use the machine learning approaches. Please consider to re-organize the three parts – maybe manual, semi-automatic and automatic; or manual, traditional machine learning, and deep learning? **Answer: We appreciate your thoughtful comment. Indeed, the concepts you’ve highlighted are intricately intertwined. In the realm of clinical practice, many computer-aided diagnostic systems rely on conventional machine learning techniques. The effectiveness of these approaches hinges on the expertise of their human developers. Therefore, the limitations inherent in conventional learning are inherently tied to the limitations of the human developer’s understanding and insight.**

In our context, both manual and semi-automated volumetry operations are contingent upon conventional machine learning methodologies. On the other hand, deep learning represents a distinct paradigm within representation learning. Operating through intricate multi-layer neural network architectures, deep learning has the unique capability of autonomously learning intricate data representations. This is achieved by progressively transforming input data into multiple levels of abstraction. An integral advantage of deep learning lies in its automated learning process, enabling the analysis of vast datasets comprising thousands or even millions of cases. Such a scale of analysis surpasses the capacities of even the most proficient human experts, whose cognitive abilities may be limited by the constraints of memorization.

It’s noteworthy that automated liver volumetry leverages deep learning techniques. However, it’s important to acknowledge that, even within this framework, the process isn’t fully automated. Certain software solutions still necessitate the surgeon’s input for segmentation tasks. Notably, the exclusion of blood vessels and bile ducts can be executed automatically. As the trajectory of progress advances, the industry is moving towards the aspiration of achieving fully automated liver segmentation and volumetry. This evolution is underway, although it warrants thorough validation to ensure its reliability and clinical applicability. Your insightful comment adds to the richness of our discussion, allowing us to offer a more comprehensive understanding of the intricate landscape within which these developments are taking place. Your input is greatly appreciated in furthering the depth and accuracy of our manuscript.

In order to make these concepts more clear for the reader, this part was restructured.

3. Why did the author put the deep learning approach separately in the “Future direction”? Deep learning approaches are currently used by many papers. Actually, it is not the future, but the current hotspot. **Answer: Thank you for your comment, the topic was included in the automated liver volumetry.**

4. This paper is aimed to discuss the volume measurement of liver. Is radiomics a technique for volume measurement? I don’t think it is appropriate to put the radiomics in this review. **Answer: Thank you for your comment. The paragraphs regarding radiomics was removed to avoid confusion.**

#### OTHER QUESTIONS

5. Language polishing requirements for revised manuscripts submitted by authors who are non-native speakers of English.

**Answer: Indeed, we have taken steps to ensure the linguistic refinement of our manuscript. We initially engaged a native English-speaking expert to review our work, and subsequently, we incorporated your feedback to make necessary revisions. Following these updates, we have once again submitted the manuscript, this time specifically requesting a thorough language polishing.**

**We believe that these efforts collectively enhance the clarity and coherence of the manuscript, aligning it more closely with the standards and requirements of the journal. Your discerning attention to detail is greatly appreciated, and we are optimistic that these measures will render our manuscript suitable for consideration within your esteemed journal. We extend our gratitude for your kind observation and guidance throughout this process.**

6 EDITORIAL OFFICE’S COMMENTS: Authors must revise the manuscript according to the Editorial Office’s comments and suggestions, which are listed below:

**Answer: Thank you for your comments. We changed the figures labels as your suggestions. Please, let us know if any further modifications are needed.**

We believe that the alterations and clarifications we have implemented successfully address the reviewers' concerns while enhancing the manuscript's overall quality. We are confident that our revised version, accompanied by this detailed response, meets the journal's standards for publication.

Once again, we extend our gratitude to the reviewers and the editorial team for their time, expertise, and valuable feedback. We eagerly await your final decision regarding the publication of our manuscript. Thank you for the opportunity to contribute to the World Journal of Transplantation.

Sincerely,

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