Peer Review File

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<mark>Reviewer A</mark>

Comment: This study tried to build a 3D simulation framework of normal liver anatomy derived from contrasted CT images (336 healthy people), classify them and validate their effectiveness in aiding liver resection (either open or laparoscopic approach) by 6 HCC cases. The major issue is that the so-called "validation" is actually not a validation by comparing cases using this system and those not using this system. In experienced hands, liver resection can be performed safely without using the 3D simulation. Therefore, the study results are not valid scientifically.

Reply: We are deeply thankful for these critiques. We acknowledge that the validation in this study by applying the proposed conceptual framework to assist anatomic liver resection in 6 cases with tumor in the right posterior section was not rigorous enough. The number of the clinical samples in our single-center exploratory cohort was too small to scientifically verify the effectiveness of the proposed framework by comparing cases using this system and those not using this system. We will focus on expanding the sample size and conducting multicenter clinical controlled study to validate the feasibility of the framework in further study. We have discussed the limitations above of the present study in the text (Page 11, line16 to Page 12, line 2). Besides, we firmly believe that the anatomic liver resection can be performed safely in experienced hands without preoperative 3D simulation. Several studies have proved the application value of preoperative 3D reconstruction in assisting hepatectomy especially complex liver resection (Tian et al., World J Gastroenterol 2015; Hallet et al., J Hepatobiliary Pancreat Sci. 2015; Mise et al., Ann Surg. 2018 and so on), which allows stereoscopic identification of the spatial relationships between physiologic and pathologic structures and offers quantifiable liver resection proposals based on individualized liver anatomy. We believe that a full preoperative understanding of anatomic structures with 3D reconstruction would facilitate safer hepatectomy and nurture more young surgeons. We would like to thank the reviewer again for taking the time to review our manuscript.

Changes in the text: We have discussed the limitations of the present study in the revised manuscript (Page 11, line16 to Page 12, line 2).

Reviewer B

Major comments

Comment 1: The authors developed a framework for anatomical right posterior section ectomy and proposed 4 types of anatomy for the right posterior section. They compared what would be the transection line following anatomy of the right hepatic vein and what would be the transection line based on glissonian anatomy of the right posterior section. The paper is well written and the video highlights the interest of pre-operative identification of anatomical variations. The paper is very interesting.

The main message is that glissonian anatomy of the posterior section does not necessarily follow the root the right hepatic vein, which is not new.

Reply 1: We have found that the right posterior lobe is not exclusively dominated by the right posterior portal pedicle (RPP) in surgery. Several studies have reported that the demarcation of the right posterior portal pedicle was dissociated with the course of the right hepatic vein after clamping the RPP. However, little is known about the detailed relationship between portal vein variations and the aberrant intersegmental plane. It has been revealed by Cho et al. that the aberrant right cranial part was associated with the dorsal branch of segment 8 portal pedicle(P8c) crossing over to the right hepatic vein. However, we have found that the aberrant right cranial part can be related to the P8c crossing over to the RHV or a portal pedicle of segment 7 originated from the right portal vein in clinical practice. Besides, we have also found that the aberrant left caudal part was associated with specific portal vein variants. Therefore, we aimed to reveal the relationship between the aberrant demarcation of the right posterior portal territory and the portal venous variation, then develop a comprehensive framework of the right posterior section as guidance for surgical planning.

Changes in the text: We briefly describe the findings of previous studies and the purpose of this study in the section 'Introduction' (see Page 4, line 5-10).

Comment 2: I disagree with the authors about 2 naming:1) Type IIa with S5d originating near the hilum is not a variation of the posterior section. The corresponding figure (3A) shows a S5d branch originating far from the division between S6 and S7. We can't name that "S5d originating from the right posterior portal pedicle", as the right posterior pedicle, by definition, is after the origin of S5d. **Reply 2:** We do agree with the reviewer's comment that the right posterior pedicle is after the origin of P5. We appreciate our error in naming the variation of the right posterior pedicle in type IIa as the S5d branch. In order to describe the variable portal branches of the right posterior portal pedicle across the ventral side of RHV in Type II, we named the variants in Type IIa as ventral-P6, defined by Yamamoto Y et al (J Gastrointest Surg 2017), and the ventral distal branch of P6 in Type IIb.

Changes in the text: We have renamed the variants in Type II in the section 'Abstract' (Page 2, line 12-13), in the section 'Results' (Page 7, line 4-6), in the new paragraph on tailored surgical strategies (Page 8, line 14), and in the section 'Discussion' (Page 10, line 1-11).

Comment 3: I disagree with the authors about 2 naming: 2) Fig 3D: the right cranial part is from a so-called "aberrant S7 branch from S8". I consider this part as vascularized by S8d, with terminal branches across the right hepatic vein. This had been described several years ago by Torzilli et al. in their paper about extended posterior sectionectomy (Ann Surg 2008).

If the authors disagree with that, please show a true aberrant S7 distinct from S8d and give the proportion between S7 aberrant and "extended" S8d.

Reply 3: Actually, Cho et al. revealed that the aberrant right cranial part in type IIIb was fed by the dorsal branch of segment 8 portal pedicle(P8c), defined by Takayasu et al. (Radiology 1985), across the right hepatic vein. It is a controversial issue whether this aberrant area belongs to segment 7 or 8. Thanks to the reviewer's insightful remark, we decided to mark the right cranial proportion in type IIIb as the S8d across the right hepatic vein. And we modified the tailored surgical strategy as 'RPS + S8d' for eligible cases with poor cut margin.

Changes in the text: We have renamed the variant branch in type III in the abstract (Page 2, line 17-18), in the section 'Results' (Page 7, line 17-21), and in the section 'Discussion' (Page 11, line 2-8). And we modified the surgical strategy in patients with respective type III cases in the new paragraph on tailored surgical strategies (Page 8, line 11-13).

Comment 4: The video needs some commentaries: 1) Why did the author not conserve the second S5d. On 3D reconstruction, it seems that the right posterior pedicle can be controlled just after this second S5d branch.

Reply 3: Two ventral-P6s were observed emitting at 10.23mm and 24.55mm from the boot of the right posterior portal pedicle, estimated by the preoperative 3D simulation system. Though the second ventral-P6 emitted near the first ventral-P6, it was far away from the Rouviere's sulcus. The liver parenchyma needed to be dissected further to control the second ventral P6, which would increase the incidence of intraoperative bleeding and postoperative ischemia. So that we just preserved the first ventral-P6 for sparing more parenchyma and preventing postoperative ischemia. And we added a subtitle that the second ventral-P6 was dissected for fear of postoperative ischemia in the supplementary video.

Changes in the text: We have renamed the variable portal branches of type IIa as ventral-P6 in the video and added some subtitles to the video that the second ventral-P6 was dissected for fear of postoperative ischemia. We have added some comments to the figure legend of Fig.6 (see Page 19, line 13).

Comment 5: The video needs some commentaries: 2) From an oncologic point of view, the tumor is located between S7 and S8d. The tumor is far from the origin of S7 pedicle. Why not performing a resection of S7-S8d only? If the reason is an anterior approach to facilitate the resection, why not (especially as the patient had previous liver surgery). Anyway, all S5d could have been preserved.

Reply 4: The recurrent tumor was located in segment 7, with poor cut margin not only between segment 7 and segment 8, but also between segment 6 and segment 7. So that, we performed an anatomical right posterior sectionectomy combined with dorsal subsegment 8 hepatectomy to obtain R0 resection. Besides, the second 'ventral-P6' was deeply located in the liver and far away from the Rouviere's sulcus to be dissected. So that, we could only preserve the first 'ventral-P6' on the level of Rouviere's sulcus.

Changes in the text: We have added a subtitle to the video on the tailored ARPS combined with S8d resection. We have added some comments to the figure legend

of Fig.6 on the reason why we failed to preserve the second Ventral-P6 <mark>(Page 19, line 13).</mark>

Minor comments

Comment 1: Table 1: please add the percentages. Reply 1: We have added the frequencies with percentages in the revised Table 1. **Changes in the text:** Table 1 (Page 16).

Comment 2: Text: please add aberrant volumes in cc (or mL), rather than percentages only.

Reply 2: We have added aberrant volumes in ml in the text.

Changes in the text: We have added aberrant volumes in ml in the revised manuscript (see Page 2, line 14-15, 18-20, and Page 7, line 10-11, 20-22).

Comment 3: Figure 3: please add the percentages of anatomical variations. Reply 3: We have added the percentages of anatomical variations in the revised Figure 2, Figure 3, and Figure 4.

Changes in the text: We have added the percentages of anatomical variations in Fig. 2, Fig. 3, and Fig. 4.

<mark>Reviewer C</mark>

Comment 1: This review was very interesting but it will be not easy to understand to general leaders. It is very informative to the experts for liver resection. Some more details and validation will be needed to be widely accepted for clinical application. **Reply 1:** Thanks for your valuable and constructive comments. We have made some meticulous modifications to our manuscript and improved the English writing in the revised manuscript. We have added some details and overall

descriptions of the key outcomes of our study. The readers may understand our

work more clearly. **Changes in the text:** We have carefully checked the whole article and improved the English writing in the revised manuscript. We have added some details and descriptions of the key outcomes in the section 'Results' (see Page 7, line 9-10, and line 20-21) and the section "Discussion" (see Page 10, line 6-8, and Page 11, line 2-4, and line 5-6).

Comment 2: In figure 2, please add proportion of each type which is described in the results for leaders.

Reply 2: We have added the proportion of each type in the revised Figure 2, Figure 3, and Figure 4.

Changes in the text: We have added the proportion of each type in Fig. 2, Fig. 3, and Fig.4.

Comment 3: If you think every right posterior sectionectomy should be tailored,

please add some recommendations for safe right posterior sectionectomy according to the type.

Reply 3: Thanks to the reviewer's valuable advice, some surgical strategies for tailored and safe anatomical right posterior sectionectomy(ARPS) according to the type have been depicted in the new Figure 5 and a new paragraph on the tailored surgical strategies (see Page 8, line 8-17). Since we have renamed the aberrant part fed by the dorsal branch of segment 8 portal pedicle (P8c) crossing over to the right hepatic vein (RHV) as "S8d" (see Page 7, line 18-19), and the aberrant portal branch of the right posterior portal pedicle across the RHV as "Ventral-P6" (see Page 7, line 4-5) as advised. Respective surgical strategies according to the morphological framework of the right posterior section were modified as follows. ARPS oriented by the right posterior portal territory (RPPT) ought to be performed in cases with enough lesion margin and functional liver remnant, no matter the morphological types. ARPS combined with S8d resection oriented by the RPPT in the caudal part and the course of RHV in the cranial part is recommended for cases with poor lesion margin in type III and type IV to achieve R0 resection. Parenchyma-sparing ARPS by reserving the variable Ventral-P6 is suitable for cases with poor liver function in type II and type IV to maximize the functional liver remnant. Parenchyma-sparing ARPS combined with S8d resection instead of ARPS is recommended for type IV cases with poor cut margin and poor liver function.

Changes in the text: We displayed the tailored surgical strategies according to the framework in a new Fig.5 and described the tailored surgical strategies for RPS in a new paragraph (see Page 8, line 8-17).