LS LAPAROSCOPIC SURGERY
AN OPEN ACCESS JOURNAL COVERING NEW FINDINGS IN LAPAROSCOPIC SURGERY

Peer Review File

Article information: https://dx.doi.org/10.21037/ls-22-6

Reviewer A:

This is a review article about using 3D reconstructions and 3D printing in preoperative planning of liver lesions. 3D visualisation and reconstruction (including VR) as well as 3D printing are increasingly used in liver tumours, both preoperative planning and simulation. Unfortunately, authors did not do well in this general literature review. CT and MRI are commonly used imaging modalities, while ultrasound and SPECT, PET, PET/CT are also used, in particular, ultrasound is a common modality used. This is one of the limitations.

Reply: I enclosed further comments on the use of ultrasound and SPECT, PET, PET/CT, but this review is centered on the development of 3D evaluation and reconstruction and for this only CT or MRI are useful for this

Changes in the text: see point 2 of the specific comments

Another limitation of the review lies in lack of details on how 3D printed models assist preoperative planning and simulation of surgical resection of liver tumours. Increasing studies reported the clinical value or usefulness, while authors only cited some of them but failed to provide good review on it.

Reply: I prefer to show the videos as example of 3D printed model during operation. In the alternative (a new video has been included) the use of hologram in the operative room could be used instead of 3D printed model

Changes in the text: new video shows the use of holograms during operation

This review needs to undergo a major revision to improve it before it is considered for publication. The 3 videos are really nice showing how the 3D reconstruction and VR including 3D printing in liver lesion resection.

Specific comments:

1. Abstract: CT and MRI can provide not only 2D views but also 3D reconstructions. I think their limitation mainly lies in the lack of providing realistic 3D perception of complex structures, and this can be overcome with use of VR or 3D printing technologies. Authors need to highlight it.

Reply: We agree with your suggestions and we have rewritten the abstract

Changes in the text: The limitations of this imaging techniques mainly is due to the absence to furnish a realistic 3D perception of the anatomical intra-hepatic structures as the relationship of the lesion and the vasculo-biliary anatomy. Furthermore, in recent years, laparoscopic surgery underwent rapid development, but it requires preoperative planning more accurately than open surgery: laparoscopic ultrasound should help the surgeon to identify the position of the lesion, its relationship with glissonian pedicles and the best resection lines. 3D reconstruction view and 3D printing technologies can clearly demonstrate the precise spatial anatomy of a nodule and can help the surgeons improve their surgical preparations, which can be used for either liver resection or thermoablation. The use of 3D printed models or holograms in the operative room during the operation increases the surgical accuracy. This article describes all the phases of the hepatic 3D modeling and printing procedure, convenient for improving our preoperative surgical preparation for personalized surgery.

2. Introduction: authors stated that a variety of imaging modalities are used in diagnosing liver tumors, but they only cited CT and MRI which is insuffiicient. Ultrasound, SPECT, PET, SPECT/PET/CT, or even PET/MRI are also used. This should be included in your review. Further, they provide not just 2D views, as they also offer 3D visualisations, perhaps limited to 2D flat screen lacking realistic 3D perception.

Reply: We agree with your suggestions and we have rewritten the following sentence:

Changes in the text: *The tumor's diagnosis is obtained by a variety of imaging techniques as Computed Tomography (CT) and/or Magnetic Resonance Imaging (MRI) [2]. These imaging techniques furnish only two-dimensional data to the surgeon, which in many cases is difficult to use during surgical treatments because the surgeon must evaluate the three-dimensional aspect of the lesion to be removed or ablated and understand patients' hepatic features and vascular structures.*

In:

Liver tumors diagnosis is obtained by several imaging modalities including ultrasonography (US) [3], contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI) [4], positron emission tomography (PET) [5], single photon emission computed tomography (SPECT) [6] and angiography, although direct angiography has been replaced by CT and MR angiography, which are less invasive alternatives [7]. These imaging modalities offer 3D visualizations that, however, are limited by traditional display devices that can show only two-dimensional (2D) flat images that lack depth information, so misleading or confusing our 3D comprehension. In many cases they are difficult to use during surgical treatments because the surgeon must evaluate the three-dimensional aspect of the lesion to be removed or ablated and understand patients' hepatic features and vascular structures.

line 77 the sentence: "but it could be serious trouble for the surgeons". what do you authors mean of serious trouble? This is unclear or confusing. Consider revising it.

Reply: We have rewritten the sentence:

Changes in the text: Furthermore, in LUS the visualization of the three-dimensional (3D) spatial relationships of intra-hepatic structures in order to accomplish the surgical maneuvers is established on two-dimensional (2D) images that lack depth information, so misleading or confusing our 3D comprehension.

Same page, last para, 3D printing has been used in many areas, such as education, preoperative planning and simulation, doctor-patient communication, etc. Authors need to include them then focus on the liver tumour planning.

They also need to emphasise why this review focuses on 3D reconstruction and 3D printing in liver tumour preoperative treatment. Is this because of the challenging area that cannot be resolved by 2D views? please clarify it.

We have reworded the paragraph:

3D printing technology allows the conversion of digital model into a tangible replica of the original. 3D printing has started being utilized in other various surgical specialties and most of the 3D printing cases were used in hepatic surgery to obtain individualized 3D models for preoperative strategy.

Changes in the text: 3D printing technology allows the conversion of digital model into a tangible replica of the original. 3D printing has been used in many areas, such as surgical simulation and training and in a variety of surgical specialties [34-36]. Moreover, 3D printing has also been considered to positively affect doctor–patient communication [37]. Recently, the Radiology Society of North America (RSNA) has developed the 3D printing clinical data registry to collect 3D printing data from medical imaging data, to characterize the different approach to obtain the 3D printed model (segmentation procedures, 3D printing techniques, software and hardware requirements) and to evaluate the impact of this new technology (https://www.acr.org/Practice-Management-Quality-Informatics/Registries/3D-Printing-Registry). In this context, RSNA has considered suitable the use of 3D printed models for the accurate assessment of liver anatomy in the approach to liver neoplasms, as liver surgery for hepatic lesions can be challenging due to the complexity of the relationships between the vascular-biliary structures and the site of the lesion [38, 39]. The 3D printed or virtual model (in both cases, the 3D reconstruction organ from medical imaging is the "core" of these new technologies) a more detailed visualization of liver mass with respect to the intra-parenchymal arterial, portal and outflow venous branching. …..

Moreover, providing a more accurate representation of the liver, 3D could play a key role also in liver transplantation [41]. By this way, it is not surprisingly that most of the 3D printing cases were used in hepatic surgery to obtain individualized 3D models for preoperative strategy.

3. CT scan procedure. Authors stated in previous paragraphs that CT and MRI are commonly used while from this paragraph onwards, they focused on CT data. Please explain it. Multi-phase or tri-phasic CT of liver scan is a common procedure. Authors need to provide the scan delay time for each phase.

Reply: I enclosed the suggested information

Changes in the text: Patients are referred to our Centre from other medical departments and they are evaluated based on imaging examens already performed in other Hospitals: only Ct scan imaging examens with adequate characteristics are used for 3D reconstructions. On the contrary, an imaging technique is repeated in our Radiology department according to standardized protocols: for triphasic acquisitions, scanning was started with a 10 seconds scan delay (about 25–30 seconds after injection of the contrast agent) for the hepatic arterial phase after the attenuation value of the aorta reached 120 HU. Fifteen seconds after the end of the hepatic arterial phase (about 50–55 seconds after injection of the contrast agent), the scans for the portal phase were acquired. Late-phase images were acquired 120 seconds (about 180–200 seconds after injection of the contrast agent) after the end of the acquisition of the portal phase.

Horos software is just one of the open source tools as there are many others, such as 3D Slicer, Radiant, Image J, etc. They are used for viewing DICOM images.

Reply: I enclosed the suggested information

Changes in the text: Open-source, free and commercial software tools for viewing DICOM images are available as well as 3D slicer, AW-Server, Image J and others [21].

4. 3D reconstruction: 3D Slicer is a useful open source tool, so authors may need to emphasise as there are other commercial tools such as Analyze, Mimics, etc.

The key part or important component in 3D reconstruction is about the process or steps involved in segmenting the anatomical structures including liver tumours on CT datasets. Authors did not provide details of how they achieved segmentation of the volume data. Was it done manually or semi-automatically? how long it usually take to segment these structures, such as hepatic arteries, portal veins, liver parenchyma, etc? Please provide details here as readers are more interested in it, especially for those who have not done it before or not very familiar with it. They briefly mentioned that they applied semi-automatic techniques, but insufficient.

Contents or reviews on 3D VR are weak, and I suggest that authors enhance it in their review. Any similar works done before? what techniques are involved in generating 3D views using VR? Hololens-generated augmented reality is another approach that shows advantages, so perhaps briefly mention it.

Reply: We have rewritten the following paragraph: (3D RECONSTRUCTION)

Changes in the text: In the next step of the protocol, a three-dimensional reconstruction of the different liver structures (parenchyma, lesions, vascular branches of the hepatic artery, portal, and hepatic vein) from DICOM datasets of CT scans has been accomplished using segmentation procedure. Different methods of liver segmentation have been proposed [24, 25]. In this context, manual segmentation could be considered the “gold standard” but is tedious and time-consuming. The DICOM dataset of CT images of the patient was uploaded into 3D Slicer, a free open-source software for advanced analysis and processing of medical imaging [26]. The anatomical structures of surgical interest (i.e., liver parenchyma and its vascular pedicles, major intrahepatic arteries and veins and inferior cava vein) have been segmented using semiautomatic algorithms based on thresholds in Hounsfield units, with manual adjustment of the boundary to refine little branches of vessels. The bile ducts were not reproduced due to the absence of intravenous. hepatobiliary contrast. Other 3D image-based engineering software, such as Analyze (https://analyzedirect.com) and Mimics (https://www.materialise.com/en/medical/mimics-innovation-suite/mimics) are available. We have chosen 3D Slicer because it is fully open source and can be readily extended and redistributed. In addition, 3D Slicer is designed to facilitate the development of new functionality in the form of 3D Slicer extensions and/or plugins.

Once validated by expert radiologists, the generated 3D reconstruction can be exported in STL file format and then adjusted and converted in Blender v.2.80 (Blender Foundation, Amsterdam, Netherlands), a 3D computer graphics open-source software, to a format file to be used in the game engine Unity (Unity Technologies, San Francisco, CA). Lastly, the converted file is uploaded in a Virtual Reality Environment (VRE) developed by our team using Unity [27]. The VRE could be visualized through a mobile head-mounted display (i.e., Oculus Quest). In the VRE, the user can navigate and interact with the scene adapting the focus, changing the level of transparency of the different structures (vessels, organs), rotating the 3D scene in any direction and zooming in and out.

Recent developments in the field of augmented reality have enabled the availability of augmented reality devices (i.e., Microsoft HoloLens), that overlays digital information on real elements. HoloLens have been evaluated to play a useful role in surgical education and as a surgical visual aid in alternative to conventional monitors in endoscopic surgery [28]. These findings contribute towards the role that VR and AR could play to improve understanding of patient-specific anatomy and surgical planning.

3D analysis is particularly advantageous to visualize the relationships among the different structures of the liver, that has an anatomically complex vasculo-biliary structure [29, 30]. Such essays, providing an awesome visualization of the intrahepatic vessels and lesions, allow the accurate volumes of vascular territories to be computed.

In our VRE, the 3D model can be moved, rotated, zoomed and the different structures could be made transparent. Moreover, the mirroring option included in the VRE allows to share the 3D scene of the VRE to a screen PC, so improving the pre-operative surgical planning and patient's understanding of the surgical treatment [31].

The 3D model obtained can be further manipulated and moved by the surgeon using the same software: in this way it is possible to exactly recognize eventually anatomical variations of the intrahepatic vasculature and its relationship with the lesion. So, the surgeon can provide the planning of the laparoscopic surgical resection or thermoablation:

- Patient placement in the operative room is dependent on the place of the hepatic lesions to be treated;
- The site for introducing the LUS probe is limited by the position of the trocars: first, the umbilical port can be done for laparoscopic examination, and the second trocar position for LUS probe can be chosen based on both the preoperative imaging reconstruction and the intraoperative circumstances as visualized by laparoscopy [32].

3D models offered resections with parenchyma sparing more frequently, above all for a laparoscopic approach, reducing the risk of submillimeter surgical margins [13, 17]. 3D models can help to maintain the quality of radical resection strategy for liver tumors playing a crucial role in rendering mass image information and favoring safe hepatectomies, above all during the laparoscopic approach. On the other hand, the limits of usual "freehand" LUS-guided thermoablation (tumor size, tumor location, or number of nodules) can be overcome by 3D simulation process: three-dimensional planning allows for precise needle placement, above all if it is necessary to perform multiple needle insertions, improving ablation performance [19].

Furthermore, 3D reconstruction software allows surgeons to achieve a preoperative workout of the hepatic resection operation or laparoscopic ablation procedure in virtual reality.

The virtual manipulation of the liver could overcome some laparoscopic limitations such as

the limited maneuverability, the use of rigid instruments, and a restricted field or the quality of vision. In this context, the surgeon, even if using LUS, could have difficulties to identify the lesion and its relationship with vessels and biliary ducts [19, 32].
However, it is necessary to outline that the process to obtain virtual reality models is a time-consuming process, not only for preoperative strategy and hepatic rendering, but also for the intraoperative setup. The required time to obtain 3D virtual models from DICOM and to transfer them in the VRE was about 2 hours that is consistent with clinical practice. However, it must be underline that the time depends also on the complexity of the anatomical structures to reconstruct. The situation is different regarding to 3D printing, where times are more dilated, although different printers could be used in parallel, to minimize fabrication times [33].

4. 3D printing: this section needs improvement too. 3D printing has been increasingly used in liver tumours, such as surgical planning and simulation, liver transplants, etc. Please enhance it by citing more relevant studies.

We have already answered this question in the previous section.

5. Laparoscopic treatment of two cases: this needs to be explained as an example of showing authors' work on utilising 3D views and 3D printing techniques in selected cases.

In our experience, a 3D liver model was built, based on preoperative liver CT scans. This allowed the identification of the main structures of the liver, i.e. hepatic parenchyma, main arterial and venous vessels, main vascular regions, lesions. Int first case 3D reconstruction permitted to identify the exact position of a huge hepatic vein while in the second case we used LUS to identify the type of vascularization of the lesion or the presence of perilesional vessels: based on the preoperative 3D reconstruction, I can identify the vessels furnishing the tumor.

6. Conclusions: see above comments as future research should be included.

Reply: We have rewritten the following paragraph

In conclusions, some considerations need to be underlined about the role of 3D reconstructions. As a consequence of the reduction in 'hands-on' experience limiting the opportunities for trainees to receive surgical training, VR technology allows to acquire technical skills and intuition and to face learning curve that is a critical point in videolaparoscopic surgery.
Virtual reconstructions and 3D printing models have the advantage to provide a better comprehension of the patient's specific anatomy and could represent a useful training tool for trainees and surgeons in a safe environment.
Future research should analyze a more standardized use of these technologies to evaluate its impact on the learning curve, its incorporation into surgical training curricula operation planning to identify the most optimal surgical operative strategy, intraoperative simulation and image-guided surgery, improve the material behavior of the 3D printed and virtual organs, and lastly perform a cost-benefit analysis.

7. Images: these two images of multiphase liver tumours are very general and are seen routinely in clinical practice, so suggest deleting them. Consider replacing them with something meaningful.

Reply: We agree with your suggestions and the figures have been removed

9. The manuscript will benefit from language editing.

Reply: We agree

Reviewer B:

In this study, the authors were able to find out the relationship between intrahepatic vessels and tumor as well as anatomical variations through 3D reconstruction using a CT scan. In addition, the authors created a virtual reality model and a 3D printing model, which was helpful in preoperative planning and guiding during surgery, especially in laparoscopic surgery. The authors showed how 3D technology can be used through video and showed the surgery and procedure scenes through two real cases.

I think 3D reconstruction and 3D printing will be educational and of practical help for young surgeons and students. Also, these models will be helpful even for experienced surgeons in establishing pre-operative planning in complex cases such as patients with anatomical variations. In our center, 3D reconstruction and 3D printing of complex cases in laparoscopic liver resection are performed, but it takes quite some time and money even with professional manpower. I wonder how much time and cost it took for each case from 3D reconstruction to 3D printing for the authors.

Reply: your suggestions have been accepted (see above points)