Review Article

Planning the treatment: preoperative 3D reconstruction

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Abstract: Computed tomography and/or magnetic resonance imaging are commonly used for definite diagnosis of liver tumors, but they 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 (3D) aspect of the lesion to be removed or ablated and understand patients' hepatic features and vascular structures. The limitations of this imaging techniques mainly are 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.

Keywords: Hepatic surgery; thermoablation; laparoscopy; liver tumor; 3D models; 3D printing; virtual reality (VR)

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Introduction

The surgical treatments of liver tumors (hepatectomies or thermoablation procedures) are often a complicated procedure for the surgeon, above all if it was performed by a laparoscopic approach (1,2).

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(PET) (5), single photon emission computed tomography (SPECT) (6) and angiography, although direct angiography has been replaced by CT and magnetic resonance angiography, which are less invasive alternatives (7). These imaging modalities offer three-dimensional (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 3D aspect of the lesion to be removed or ablated and understand patients' hepatic features and vascular structures (8,9)

Furthermore, in recent years, laparoscopic surgery underwent rapid development, but it requires preoperative planning more accurately than open surgery (10,11). During the laparoscopy, the surgeon can use laparoscopic ultrasound (LUS) which is the only available tool for intraoperative tumor location, but an important limiting factor to its success is the learning curve (12). Furthermore, during the LUS evaluation, the visualization of the 3D spatial relationships of intra-hepatic structures to accomplish the surgical maneuvers is established on 2D images that lack depth information, so misleading or confusing our 3D comprehension (13).

The segmental anatomy of the liver is determined by the distribution of the blood vessels and bile ducts and they are different for a lot of patients: the presence of anatomical variations needs personalized surgical plans to guarantee that the operation is conducted safely (14,15). Expert surgeons can image a 3D representation in their minds supported by the preoperative 2D images such as either CT scan or MRI scan to accomplish the operation successfully, but it can be a significant challenge for surgeons if anatomical variants are present and they should be identified only by intraoperative ultrasound (16,17). 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 (18,19).

This review explains all the stages of the hepatic 3D modeling and printing procedure, produced by our multidisciplinary team (PRINTMED 3D), convenient for improving our preoperative surgical preparation for personalized surgery.

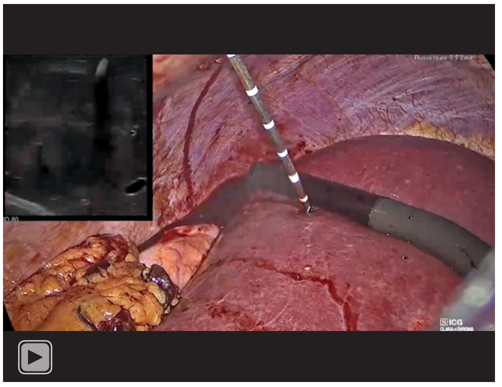
CT scan procedure

In the first phase of the protocol, an adequate triple-phase CT scan is made on the patient using a multislice CT scanner. MRI is a very important tool in the diagnosis of liver tumors (20), but 3D reconstruction can be made better with CT imaging. Cross-sections of very fine layers (1 mm) should be acquired with 50% coating and pitch 1, components essential for the subsequent reconstruction of the imaging details in 3D models. The scan is conducted in three distinct phases of perfusion of the liver: arterial, portal and late phase, for the appearance and subsequent segmentation of the arterial and venous system, but also for the demarcation of nodules which, determined by the kind of lesion, may demonstrate diverse enhancement in the course of time. 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 Hounsfield unit (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.

Open-source, free and commercial software tools for viewing Digital Imaging and Communications in Medicine (DICOM) images are available as well as 3D slicer, AW-Server, Image J and others (21). In our centre, CT scan imaging was initially examined using free, open-source medical image viewer (Horos software Version 3.3.6 or Osirix software version 4.1; Pixmeo, Geneva, Switzerland): it is an imaging handling software package designed for DICOM images (22,23). This software is specially dedicated for the navigation and the visualization of multimodality imaging. First at all, it is possible to obtain 3D rendering tools, such as multiplanar reconstructions: this simple operation permits the evaluation of the exact nodule position, and it can be useful to plan surgical procedures such as laparoscopic thermoablation or hepatic resections. The important thing is that the surgeon himself can execute all these maneuvers.

3D reconstruction

In the next step of the protocol, a 3D 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 HU, with



Video 1 Examples of virtual reality environment during laparoscopic treatments of liver tumors.

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, USA). 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 (*Video 1*).

Recent developments in the field of augmented reality (AR) have enabled the availability of AR 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 virtual reality (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 of personal computer (PC), so improving the pre-operative surgical planning and patient's understanding of the surgical treatment (31).

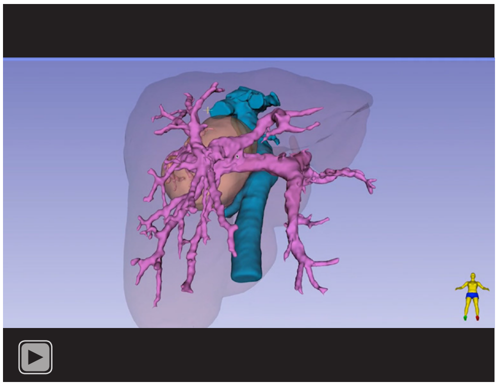
The 3D model obtained can be further manipulated and moved by the surgeon using the same software: in this way it is possible to exactly recognize eventually anatomical variations of the intrahepatic vasculature and its relationship with the lesion. So, the surgeon can provide the planning of the laparoscopic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

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



Video 2 3D technology and 3D-printed models for liver surgery.

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 VR 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).

3D printing

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.

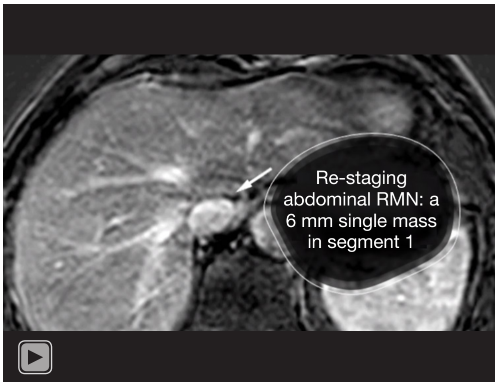
In the principal centers dedicated to hepatic surgery, above all through a laparoscopic approach, conventional imaging evaluation (with 3D reconstructions, eventually) can be sufficient to understand the exact position of the lesion and the hepatic anatomy. Therefore, 3D printing is not used regularly and is only implemented in complex cases (*Video 2*). The transparent 3D-printed model used for liver surgery permitted to obtain easier and more precise segmentation, better comprehension of spatial anatomy and higher confidence levels among surgical staff (40). Furthermore, 3D-printed models are very useful to provide novel educational tools.

3D imaging and 3D printing of the liver and tumoral nodule on a 1:1 scale is much more credible and explanatory than any knowledge a surgeon could give. Furthermore, the 3D imaging of the liver, its anatomy, and the lesion relationship, is useful to program the surgical strategy in anticipation with the rest of the surgical team, as well as to explain the surgical procedure and possible problems to students and surgeons. Furthermore, the competitive pressure, the decrease of the price of both consumables and the 3D printing devices, as well as the large accessibility of dedicated open-source software that is required for the creation of 3D printing have a positive impact on the diffusion of this technology in a customized medical setting based on patient-specific characteristics. In our experience, we used a hybrid fabrication approach to produce 3D liver models based on additive manufacturing and casting of tissue-mimicking materials into 3D models (33).

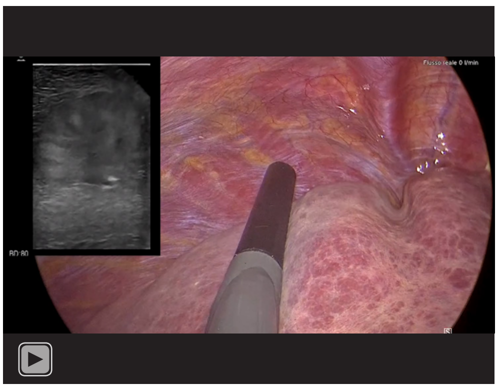
Moreover, providing a more accurate representation of the liver, 3D could play a key role also in liver transplantation (41). By this way, it is not surprisingly that most of the 3D printing cases were used in hepatic surgery to obtain individualized 3D models for preoperative strategy.

Laparoscopic resection of secondarism located in the 1st segment

A 65-year-old patient with a metastatic lesion of the first



Video 3 3D reconstruction procedures to aid the laparoscopic resection of colorectal metastasis located in the first segment.



Video 4 3D reconstruction procedures to aid the laparoscopic thermoablation of hepatocellular carcinoma located in the 8th segment associated to intra-hepatic vascular occlusion.

segment, previously submitted to anterior rectum resection, then undergoing adjuvant chemotherapy, with a good response, but not radical, has been proposed for surgical resection. Preoperative CT showed a single lesion of the first segment, reduced from 15 to 6 millimeters after 12 chemotherapy cycles. 3D reconstruction and VR have permitted us to exactly identify the location of the lesion and its relationship to the adjacent vessels.

Intraoperatively (*Video 3*), the use of fluorescence image confirmed the location of the lesion, located in the most cranial portion of the first segment. Intraoperative ultrasound showed a small hypoechogenic lesion, without vascular enhancement, after injection of contrast medium. The liberation of the caudate lobe started with the section of the venous ligament, proceeding from the most cranial portion, which joins the apex of the first segment to the area of origin of the left hepatic vein. Then, it continued in its most caudal portion, along with the remnant of the duct of Aranzio. Finally, the liberation finished with the section of the retro-hepatic ligament, so as to begin the detachment of the caudate lobe from the inferior vena cava. The posterior surface of the first segment is then separated from the inferior vena cava, with the section between clips of small accessory hepatic veins. At this point, the resection line of only the cranial portion of the first segment is well identified. Thus, the resection begins, starting from the average border to reach the section point of the venous ligament, always remaining, under the guidance of fluorescence vision, at an adequate distance from the lesion. At the end of the parenchymal resection, the caudate lobe remains attached to the inferior vena cava through a single accessory vein, particularly developed, that we had well identified with the preoperative 3D reconstructions. In view of its size, it was necessary to use hem-o-locks before cutting it.

The surgery lasted 165 minutes, with minimal blood loss, without hilum clamping. The patient was discharged on the fourth postoperative day, without any complication.

Laparoscopic microwave ablation of hepatocellular carcinoma (HCC) in the 8th segment with intra-hepatic vascular occlusion

An 80-year-old patient with severe comorbidities, previously operated on for peptic ulcer, has been evaluated for an HCC nodule in 8th segment. He has been already treated for HCC, with a percutaneous radiofrequency ablation. At a CT scan, he showed a new nodule of 33 millimeters of diameter, that was not visible by a percutaneous ultrasound. For this reason, a laparoscopic approach has been proposed. 3D reconstruction and VR have permitted us to exactly identify the location of the lesion and its relationship to the adjacent vessels. Particularly, we identify a portal branch for 8th segment which furnished the vascularization of the lesion. On the basis of the exact localization of the lesion, it is possible to plan the patient and trocar position for the LUS exploration and the most suitable percutaneous access of the antenna.

During the surgical exploration (*Video 4*), LUS confirmed the exact position of the lesion. The use of intravenous ultrasound contrast agents, during LUS evaluation, has been shown to improve nodule characterization in comparison with unenhanced ultrasound. Then, 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. Why is it important to identify tumor vascularization? Local recurrence is a problem of the ablation techniques, in some instances due to the local dissemination by the portal venous route. Systematic subsegmentectomy has been proposed to prevent this problem: a dye injection into the portal branch feeding tumor defined the stained area on the liver surface, which should be resected. Based on this principle, we used the microwave antenna to produce a devascularization area, centered on the lesion. For this reason, the microwave antenna was positioned near the tributary vessel of the lesion and we performed a thermoablation of this area for 3 minutes at 90 watts, to induce a selective thrombosis. Then, after the injection of indocyanine green, we can control the devascularization effect of the ablation of the tributary vessel at fluorescence imaging. Finally, after the confirmation of the complete intra-hepatic vascular occlusion, we positioned the microwave antenna into the lesion, and we performed a thermoablation with a duration of 7 minutes at 90 watts. After a few minutes, we repeated the ultrasound evaluation with contrast media: no enhancement has been visualized both into the lesion and on the surrounding liver parenchyma. The success of the procedure was further confirmed in the postoperative period: contrast-enhanced ultrasound was performed on the third postoperative day showing a complete necrosis area of ablation. CT scan at 1 month confirmed the complete necrosis of the lesion and showed the devascularized area post-ablation.

Conclusions

In conclusions, some considerations need to be underlined about the role of 3D reconstructions. 3D reconstruction models and 3D printing of liver anatomy (with the imaging of lesion and its vascular relationship), is an interdisciplinary and original process, which guarantees better pre-surgical planning and guidance during surgical procedures. The benefits of using both 3D virtual models could be exceedingly productive when they are combined with 3D-printed models using materials mimicking the haptic properties of liver tissue. Because 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 laparoscopic 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. It also encourages the students and young surgeons to perceive much better and with more reliable data the hepatic structure and the location and relationship of the lesion to get them ready for the actual procedures that will take place in the surgical operating room.

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.

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