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A review of the current state of 3D printing and 3D computer simulation in the field of hepatic cancer hepatectomy and treatment

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Co-ordinator

BRIAN LORANGER

Student

B.M. LATHAM

MSc

MEDICAL VISUALISATION & HUMAN ANATOMY

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SCHOOL OF SIMULATION AND VISUALISATION
THE GLASGOW SCHOOL OF ART

University of Glasgow

A review of the current state of 3D printing and 3D computer simulation in the field of hepatic cancer hepatectomy and treatment

B.M. Latham

1. INTRODUCTION

1.1 Common cancers of the liver

Cancer is a formidable cause of death worldwide and any technology that offers a means of helping control it is welcome. One of the biggest cancer-related killers is hepatocellular carcinoma (HCC) (Soon *et al*, 2016). HCC is the most common type of cancer that originates in the liver, and part of its lethalness is its tendency to develop metastatic disease. This means the patient forms secondary malignant growths at a distance from the site of origin in the liver. Pulmonary metastasis in the lungs is the commonest form of metastatic HCC (Hu *et al*, 2017). It is therefore imperative the original growth is removed from the liver before it spreads.

For other cancers the liver may be the site of secondary metastatic growth. Colorectal carcinoma (CRC) is the third commonest cancer globally. Of patients who suffer from CRC, 50 per cent will develop metastatic disease. Such growths are more difficult to remove and only 13 per cent of patients will survive to five years post diagnosis (Tabernero *et al*, 2015). The most common location of metastatic CRC tumours is the liver (Choi *et al*, 2017).

1.2 Introduction to hepatectomy

To remove such tumours a hepatectomy is performed. This is the surgical removal of part, or all, of the liver. In order to execute this operation it is important the surgeon has an accurate understanding of the unique patient-specific relationships among the anatomical structures surrounding the tumour. These relationships typically involve the hepatic veins, the branches of Glisson's sheath and the tumour itself (Oshiro & Ohkohchi, 2017). Such an understanding is the most important factor for safely performing a hepatectomy (Kuroda *et al*, 2017) as without it injury may be caused to the patient (Oshiro & Ohkohchi, 2017). Liver surgeries are dangerous, despite advances in medical technology and operative techniques (Madurska *et al*, 2017). Today, post hepatectomy complications range from 23 to 48 per cent, with significant mortality (Ma *et al*, 2017).

2. 3D PRINTING

2.1. Hepatectomy planning

The use of three-dimensional (3D) printing in medicine has rapidly increased in recent years. However, its application in treating liver tumours is still limited (Madurska *et al*, 2017). The use of 3D printed liver models of intrahepatic vessels and surrounding anatomical structures is highly beneficial for planning how to safely navigate during tumour removals.

As such, Madurska *et al* (2017) processed CT and MRI liver data that was collected retrospectively. These medical images were from a patient that had been diagnosed with an "operable hepatic malignancy". The visualisation software Amira 4.5.4 was used to segment this information. 3D digital models of the following segmented structures were then reconstructed: the tumour, hepatic and portal veins, the biliary tree and the gallbladder. These models were printed in 3D (figure 2.1.1.). The 3D printed models proved successful in accurately representing each anatomical structure. Moreover, they allowed for physical handling and viewing from any angle.

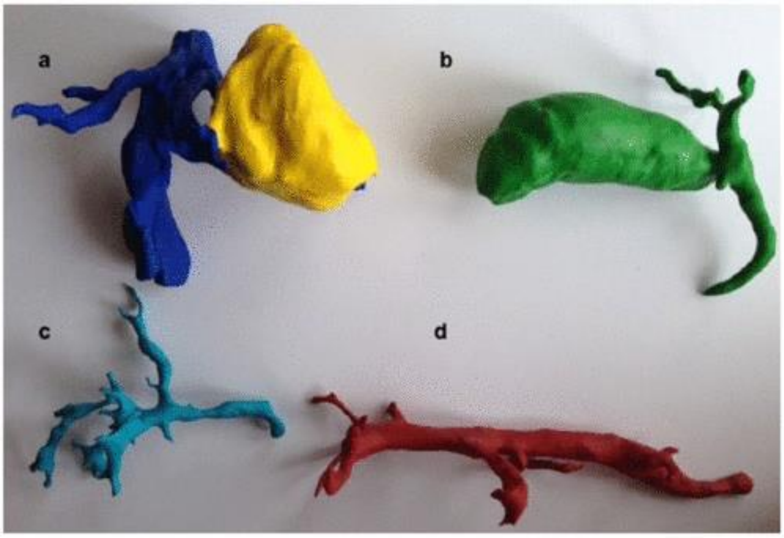

Figure 2.1.1. 3D printed hepatic models by Madurska *et al* (2017): (A) Portal veins with tumour. (B) Biliary tree and gallbladder. (C) Portal vein with branches. (D) Hepatic artery.

Similarly, Kuroda *et al* (2017) tested two 3D printed models corresponding to different case studies. Each case study was of a patient diagnosed with HCC. These tumours were CT-scanned and the data processed by the software Ziostation 2, to create 3D reconstructions of the patients' regional liver anatomy. From these digital reconstructions 3D models were then printed (figure 2.1.2.).

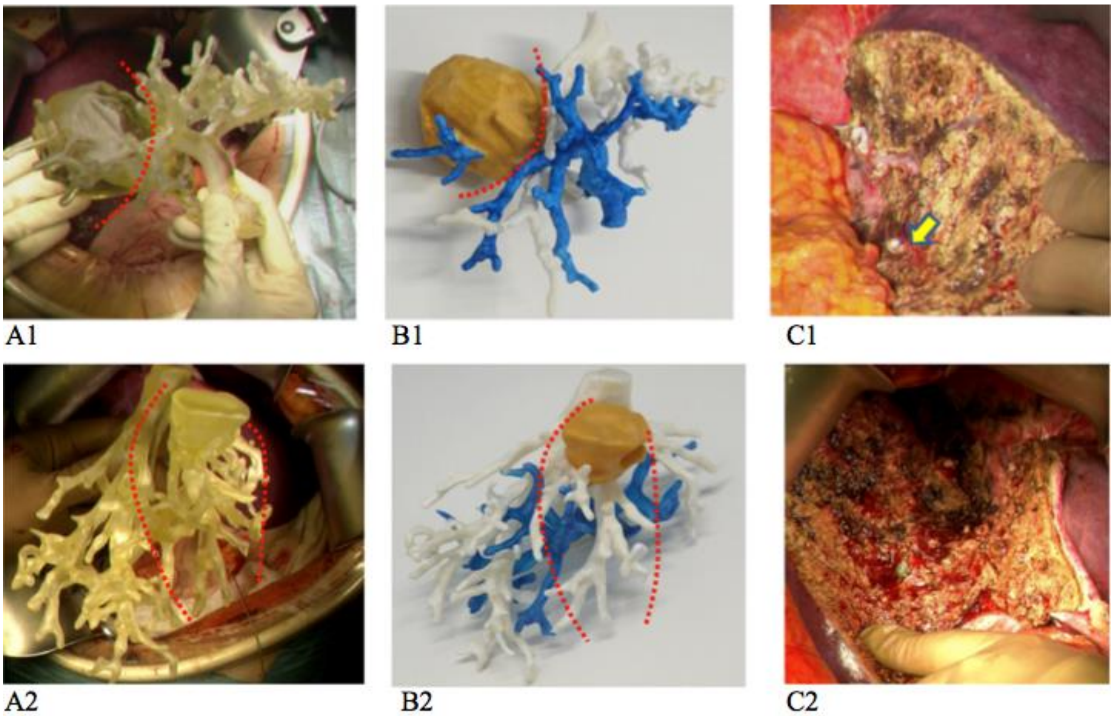

Figure 2.1.2. Kuroda *et al* (2017). (A) 3D printed model being used during hepatectomy. (B) 3D printed model after painting. (C) Liver post-cutting. (C1) Yellow arrow indicates the location of Glissonian pedicle in segment 7.

In the first case study a tumour with a diameter of 31 millimetres was successfully located in a particular segment of the liver, along with its nearest 'Glissonian pedicle'. Glissonian pedicles are tube-like liver structures that connect to the rest of the body. When removing a portion of the liver during a hepatectomy, severing one of these could cause severe complications to the patient. As such, accurately locating these structures before the operation is highly advantageous. In this case the corresponding 3D model helped reveal the relative position of the Glissonian pedicle within the segment containing the tumour. This allowed for the subsequent drawing of a demarcation line and the safe removal of this affected segment. In the second case study the tumour was positioned in segment 4/8 near to a structure called the middle hepatic vein. Using the

3D model for this case, a particularly challenging hepatectomy was planned and likewise safely executed.

2.2 Cost and efficiency of 3D printing

The cost of 3D printing can be prohibitively expensive (Oshiro & Ohkohchi, 2017). For their two case studies Kuroda *et al* (2017) converted their digital reconstructions into steriolithography (STL) file formats. STL is a form of 3D printing that creates models layer by layer. This is the preferred technology for printing liver models. In contrast, Fused Filament Fabrication (FFF) produces poorer quality prints. Yet according to Soon *et al* (2016) FFF is cheaper, less problematic and a potentially more suitable mechanism for 3D liver printing.

However, there is now a 3D printing method of combining the quality of STL with a reduction in cost, whilst also creating a clearer view of internal detail. Most 3D printed liver models for preoperative planning show only the tumour and surrounding anatomical structures (e.g. figures 2.1.1. & 2.1.2.). The challenge of such models is how to discern the exact position of these structures relative to the surface of the liver, so as to know where to make the incision. An established method for describing external and internal structures in the one model is to print the outside in a transparent material. However, printing more than one material increases the cost and the transparent substance itself is disproportionately expensive. According to Oshiro and Ohkohchi (2017) such models cost approximately 2000 US dollars. Instead, Oshiro *et al* (2017) printed a frame system around the surface of the liver to describe all necessary detail using significantly less material and of the one type (figure 2.2.1.).

Figure 2.2.1. A unique type of 3D printed hepatic model using a surrounding frame, by Oshiro *et al* (2017)

The clarity of this model was such that it was successfully utilised to perform a safe hepatectomy by determining the appropriate demarcation line on the liver surface.

2.3 3D printing for assessing post-chemotherapy tumour response

In severe cases it may be the tumour, or multiple metastatic tumours, cannot be safely resected from the liver. In such instances the patient is typically treated with chemotherapy. In order to guide future treatments and prolong the patient's survival it is important to monitor the response of the tumours to the treatment. To do this, the current mainstream method is to measure the greatest tumour diameter using two-dimensional (2D) MRI or CT slides and dosing the chemotherapy accordingly. However, there are a number of problems with this technique including the potential failure to accurately measure irregular shaped growths.

In contrast, 3D measurements of tumour volume provide considerably more accurate indications of tumour development. To do this, ultrasound (US) may be used directly on the patient to derive tumour shape and volume. However, this technique is also problematic due to the limited range of the US window, the effect of the patient's breathing movements during the US scanning process, and natural variability in patient anatomy. As such, for the first time, the potential of using patient-specific 3D printed tumour models was explored. Choi *et al* (2017) processed CT liver data from 20 patients diagnosed with metastatic CRC. This data was processed using in-house medical imaging software called MISSTA. From the segmented 3D reconstructions a total of 40 patient-specific models were printed in 3D. These 3D printed models were then individually scanned using US. Their results indicate this method is a statistically reliable and accurate technique for assessing post-chemotherapy hepatic tumour response.

3. 3D PRINTING VERSUS COMPUTER SIMULATION

The relative positions of intrahepatic structures are easier to understand from a 3D print compared to a 3D digital simulation on a 2D screen, due to the ability for a surgeon to physically handle a 3D printed model (Soon *et al*, 2016). However, detail and clarity can be distorted due to the concentration of complex anatomy in a small area and due to light-refraction (Oshiro & Ohkohchi, 2017). The monetary cost of 3D printing can also be significant.

In contrast, liver simulations using computer-assisted surgery (CAS) provide the means of transforming the model view - Including highlighting particular structures, removing layers or using multiple displays. Moreover, they are less costly than 3D printing. Such simulations have been shown to likewise be effective in hepatectomy planning. For example, Hai *et al* (2017) built and utilised a preoperative computer simulation, using the medical image processing software SYNAPSE VINCENT, of a liver from a patient diagnosed with cancer of the biliary tree (figure 3.1.). The simulation proved successful in establishing anatomical positions, planning the demarcation cutting line, and ultimately in the safe removal of 28.9 per cent of the patient's liver with thereafter no long-term complications.

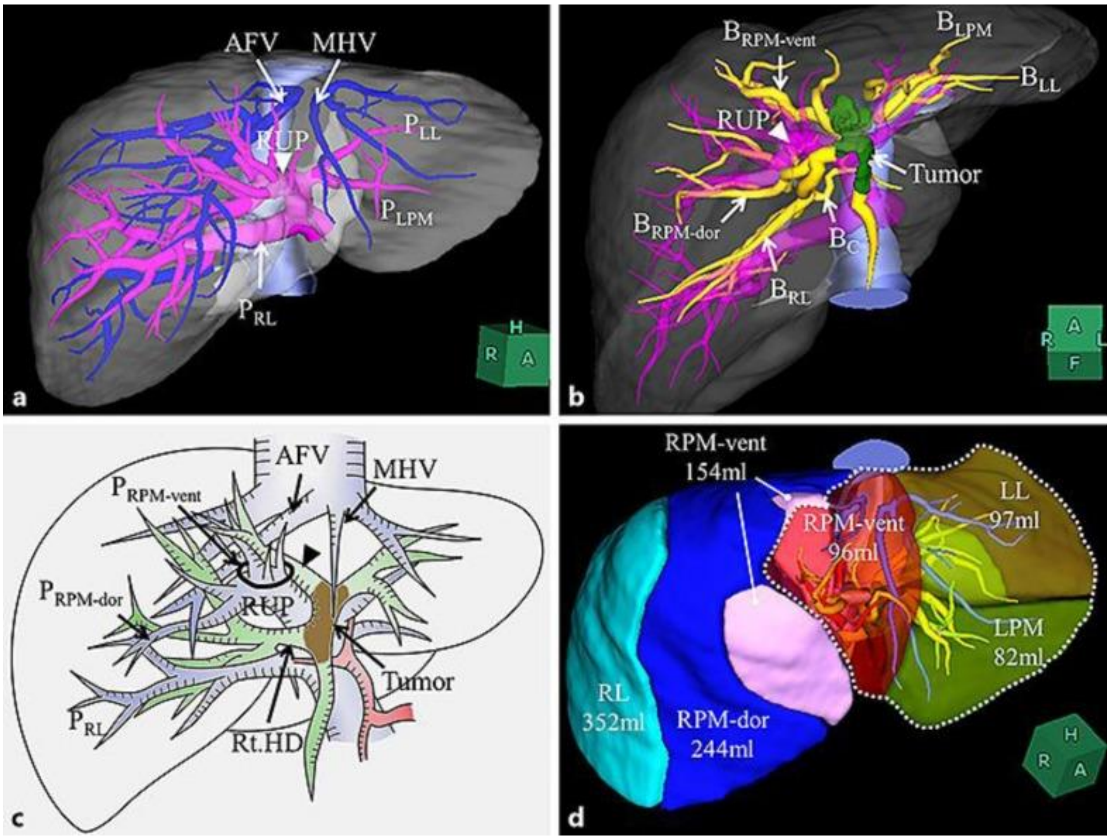

Figure 3.1. Hai *et al* (2017). (A & B) 3D reconstructions of key hepatic anatomy. (C) Illustration providing further anatomical detail. (D) Hepatectomy simulation, including dotted line indicating what to resect.

4. 3D COMPUTER SIMULATION

Using digital models to plan surgeries is becoming increasingly common. This is particularly true in Japan where 3D hepatectomy digital simulation is now covered by universal healthcare insurance. Since the year 2010, Oshiro and Ohkohchi (2017) have been researching the use of liver simulations. In their research they have developed a novel medical imaging technique called CT-MRI Fusion that enables surgeons to view additional structures such as the bile duct that can only be viewed via MRI, and vice versa. This novel system was successfully used in conjunction with SYNAPSE VINCENT to reconstruct in 3D the liver of a patient diagnosed with a tumour in the left hepatic vile duct (figure 4.1.). Additionally, this new imaging technique made it easier to share files among the surgical team.

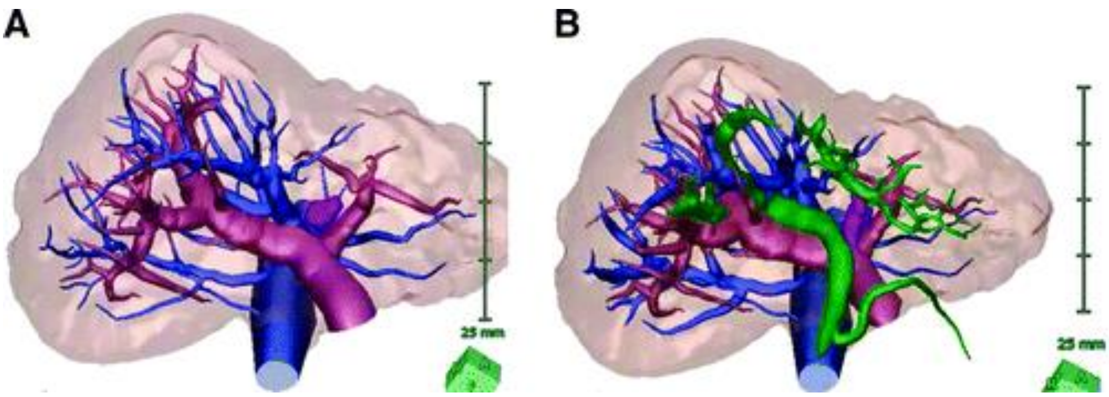

Figure 4.1. 3D hepatic computer simulations by Oshiro and Ohkohchi (2017). (A) Via SYNAPSE VINCENT. (B) Via SYNAPSE VINCENT and CT-MRI Fusion.

According to Madurska *et al* (2017), the potential of 3D printed hepatic models could be improved. They suggest the development of visualisation software specific to the liver as well as segmentation algorithms that can better pick out hepatic structures.

In fact, Oshiro and Ohkohchi (2017) designed the first such liver-specific software, in the year 2013, and named it Liversim. This unique application has several advantages to conventional software in the field. Others such as SYNAPSE VINCENT can only generate rigid hepatic models. However, during a real hepatectomy the liver changes shape. In Liversim the surgeon is able to cut into the digital model in real-time and observe not only physical transformation but also how the liver will appear once the target area has been resected. Liversim allows the surgeon a preview of what hepatic veins will be crossing the resection line, and plan the angle and depth of the resection. This simulation was successfully used to plan and predict a real hepatectomy. Both the simulation and the real hepatectomy agreed as to the location of the tumour in segment 7 and the crossing of the resection line by the hepatic vein responsible for draining segments 5 and 8 (figure 4.2.).

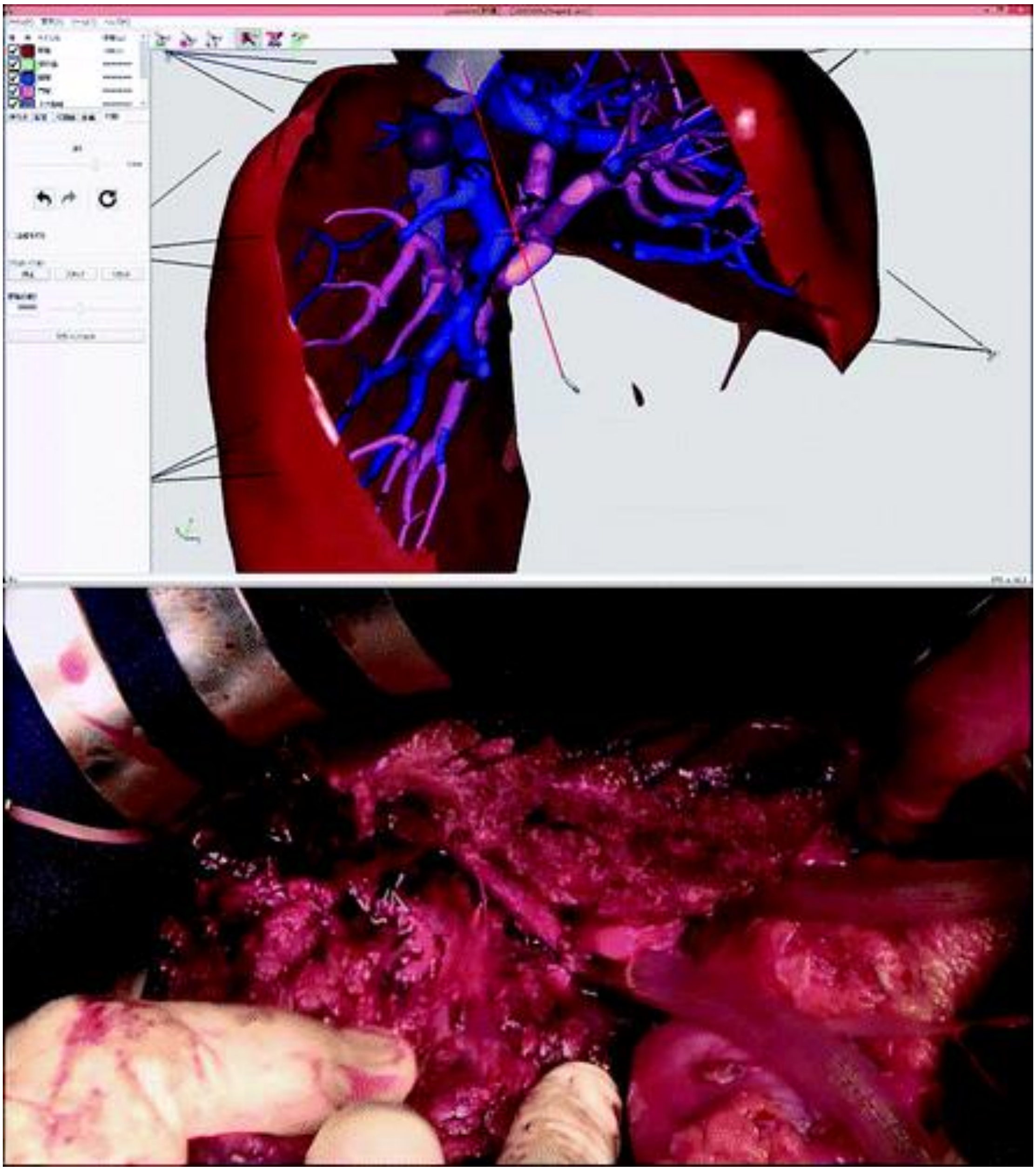

Figure 4.2. Simulated hepatectomy using Liversim and the real operation, by Oshiro and Ohkohchi (2017).

5. CONCLUSION

From this review it is clear there exists new technology and methods that can help control liver cancer. Both 3D printing and 3D computer simulation can accurately describe the positional relationships of structures surrounding a hepatic tumour. Furthermore, they have been shown to successfully aid surgeons in performing real hepatectomy operations.

However, there are advantages and disadvantages of both. 3D printed models should be the preferred option for understanding spatial relationships, particularly during surgery, and they even offer the potential for a post-chemotherapy application. In turn, computer simulations are better suited for planning the likes of the demarcation line.

It would be interesting to explore the potential of offering both techniques, in a synergistic capacity, to hepatectomy surgeons. If so, it is also clear there are a number of new developments that would improve the efficiency of the two tools. Printing the model using the frame system described and choosing FFF technology could reduce pecuniary cost even further. Regarding the simulation component, CT-MRI Fusion could be used in conjunction with liver-specific software such as Liversim to provide a more interactive application that shows more anatomical structures.

Lastly, despite this exciting prospect, digital simulations can be limited in terms of their interactive capabilities. Software such as SYNAPSE VINCENT can generate 3D-reconstructions that are too data-rich to be used in real-time applications. Moreover, due to the nature of the segmentation tools used, the model can have untidy and texturally unrealistic surfaces. To overcome this obstacle the modelling techniques of re-topology and texturing could be utilised. This would open greater opportunities for model interactions. New liver-specific and even client-specific computer programmes could be developed. These would not only help in hepatectomy planning but even provide clear and informative teaching aids for surgical education.

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