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Relation	

Article type: HOW TO DO IT

Title: Simulation and navigation of living donor hepatectomy using a unique three-dimensional printed liver model with soft and transparent parenchyma

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Key words: 3D printing model, transparent liver parenchyma, living donor hepatectomy

Abstract

Three-dimensional printed liver models have been used for preoperative simulation. Unlike the standard three-dimensional system on a monitor, the three-dimensional printed model can be observed from any angle manually; therefore, surgeons can obtain a clear image directly from the model. Here, we report the use of a unique three-dimensional liver model with a soft and transparent liver parenchyma. Through the parenchyma, the surgeons can observe the intrahepatic vessels and can also perform incision in the model as a preoperative simulation. In this work, we apply this model for donor hepatectomy, which under most circumstances, requires meticulous attention to detail. Actual processes and uses of a 3D liver model in clinical surgeries for liver transplantation were presented.

Introduction

Living donor liver transplantation (LDLT) is established as a standard treatment for end-stage liver diseases, particularly in countries with a shortage of cadaveric grafts. Living donor hepatectomy for LDLT requires meticulous attention to detail to determine donor vessels' cut line in order to avoid the lack of length in graft vessels, stenosis of the donor's vessels, and biliary complication of the donor. Furthermore, because the anatomical structure of intrahepatic liver vessels varies significantly, preoperative planning and simulation of vessel reconstruction is necessary in each case.

Currently, preoperative planning using a three-dimensional (3D) imaging system is commonly performed in hepatic resection [1]. Additionally, with the increasing availability of the 3D printing technology, 3D printed liver models are utilized for various purposes, including preoperative simulation of hepatectomy [2]. We also reported the preoperative and intraoperative uses of 3D models of liver vessels and tumors [3]. Although our previous models well expressed the relationship between the vessels and tumors, they were not suitable for donor hepatectomy because of the lack of a liver parenchyma. In this study, we report a unique 3D liver model with a soft and transparent parenchyma for use in daily planning and simulation of LDLT.

Methods

Patients

From 2004 to 2019, a total of 212 LDLTs were performed in our institute. We divided these cases into three groups: without 3D system (Feb. 2004-Dec.2011, N = 145), with 3D system (Jan. 2012-Feb. 2019, N = 62), and with 3D model (Sep.2016-Nov.2018, N = 5). Preoperative factors and postoperative results were retrospectively compared among the three groups.

Surgeon's opinions

We collected the opinions of 10 transplant surgeons in our institute about how the 3D system and 3D model contribute toward the liver transplantation through seven questions. The responses were rated from 1 to 5, with 1 being useless and 5 being very helpful.

Preparation of the 3D model

We processed the data regarding 3D printing models of the liver reported in a previous study. [3] In addition to the dataset of dynamic computed tomography (CT), drip infusion cholangiography CT (DIC-CT) was prepared. The regional anatomy of the liver was converted from a reconstructed 3D image to a stereolithography (STL) file by using the 3D image analysis system Mimics Research version 17.0 (Materialise, Leuven, Belgium). We also used the 3D date of the hepatic surface to create a template of liver parenchyma.

After exporting the STL files, we designed the template of the liver parenchyma tracing the STL data on the liver surface using a 3D processor application FreeForm (SensAble Technologies, Woburn, MA). The template was designed such that three parts can be prepared separately, which can be combined later after setting the 3D printed vessels. This template was fabricated by a plaster-type 3D printer ZPrinter 450 (3D Systems Co., Rock Hill, SC) with a 1:1 scaling between the 3D reconstructed image and the model. One part of the template, an inlet to pour polyurethane was mounted. (Fig. 1A, B)

We also adjusted the thickness and positional relation of each vessel, and deleted the unnecessary structures using FreeForm. (Fig. 1C) After the processing, the vessel system was fabricated by a resin-type 3D printer, Bellulo 200 (Systemcreate, Higashi Osaka, Japan), also with 1:1 scaling. A thermoplastic elastomers (TPE) filament, PolyFlex (Polymaker., Shanghai, China), was also used in this system. After printing, the model was colored by a technician. (Fig. 1D)

After coating the surface preparation agent SP-12-PL (Polysis, Hamamatsu, Japan) on the inside of the liver template, the three parts of the template were combined using the prepared vessel system model. This vessel system model was adjusted as per the liver template to partially form the vessel's shape, and the locational relationship between the vessel and the liver parenchyma was correctly defined. (Fig. 2A) From the inlet mounted on top of the template, polyurethane Policrystal PC-00 (Polysis, Hamamatsu, Japan) was poured slowly. The compounding ratio of the main agent to the curative agent of Policrystal PC-00 was 1:0.45, whose softness and elasticity were almost similar to that of a normal human liver parenchyma. On standing overnight at room temperature, approximately 20°C, polyurethane was completely coagulated. The plaster template was cautiously broken and removed (Fig. 2C), and a surface preparation agent, SP-12-PL, was coated several times on the adhesive surface of the coagulated polyurethane liver parenchyma.

(Fig. 2D)

How to use the 3D model

The completed 3D liver model had several unique characteristics. One is the softness and elasticity of the parenchyma. The feel of the material was similar to that of a real liver, thereby providing the surgeons with a vivid imagination. Furthermore, the weight of this 3D model was approximately 1,300 g, which is also close to that of the real liver. Next, the transparent parenchyma could observe the vessels even in deep parenchyma. Therefore, using this model, the surgeons could image the positional relationship between the vessels and the surface of the liver even after mobilization and rotation of the liver during the surgery. (Fig. 3A, B)

Preoperative simulation of hepatectomy for procedure is also possible. We actually performed donor right-lobe hepatectomy using this 3D model. The soft liver parenchyma could be cut by scissors easily (Fig. 3C), as shown in the movie. (Online Resource 1) The cutting point of the vessels was well understood by the surgeons compared with standard 3D systems on the monitor. Further, we discussed the surgical procedure in detail with the members of the operation team. Members of the transplant team performed actual simulations (hepatic resection) by using a 3D model, which had a near identical feel in terms of size, weight, and correct present of each vessel. Furthermore, we discussed the operative and reconstructive procedure in detail by using the 3D model of the liver of a donor and the hilar vascular model of a recipient, which were created separately. As these models were life-sized, the members of the operation team could obtain representative images before performing the operation. After the re-coating of SP-12-PL on the adhesive cutting surface of the liver parenchyma, the 3D model was sterilized by ethylene oxide gas and used as a navigation model intraoperatively. (Fig. 3D)

We present a case-based application for the proposed 3D model; the observation of the cutting surface and the preoperative planning and simulation of vessel reconstruction. The vessel orifice and intrahepatic running pattern could be easily confirmed. For example, in a case that required complicated reconstruction of the hepatic vein as a right-lobe graft in the LDLT, the inferior right hepatic vein (IRHV), branch of the middle hepatic vein in segment 8 (MHV-V8), and right hepatic vein (RHV) should be anastomosed to the recipient's IVC to avoid segmental congestion in the transplanted graft. (Fig. 4A) Distance from MHV tributaries to IVC was as follows: MHV-V8 to IVC; 25 mm, IRHV to RHV; 28 mm. Although the positional relationship of each orifice is usually difficult to understand, this 3D model aids in planning the method of hepatic vein reconstruction using a saphenous vein graft. During the actual LDLT, we performed a sutured saphenous vein graft patch for each venous orifice on the back table. After placing the graft in the recipient, we could anastomos patch graft to the IVC through a large orifice in short time. (Fig. 4B) Furthermore, we recognized the distance between two orifices of bile duct; B5+6+8 and B7, which was 15 mm, in the right-lobe graft. (Fig. 4A) Therefore, we performed anastomosis of B5+6+8 and B7 of the right-lobe graft to one large orifice of the recipient's common bile duct (CBD), as the preoperative plan. (Fig. 4C)

Statistical analysis

For continuous variables, parametric analyses were performed using Student's t test. Mann–Whitney U test, and the Kruskal–Wallis test was used for nonparametric analyses. Categorical variables were compared using the chi square test or Cochran–Armitage test. The Kaplan–Meier method was used for analyzing the overall survival rate, whereas comparisons between different groups were performed using the log-rank test. A difference was considered to be significant if the P value was less than 0.05. Statistical analyses were performed using BellCurve for Excel (SSRI Co., Ltd., Tokyo, Japan).

Results

Table 1 shows a comparison among the three groups regarding the general characteristics and operative results of the donors and recipients. In the background, right lobe graft tended to be selected in Without 3D system group, that is to say in old era. ($P < 0.01$) With respect to donor surgery, blood loss in the with 3D system group tended to be large. ($P<0.01$) The morbidity rate of donor in each group was as follows: without 3D system group: 7/145 (4.8%), with 3D system group: 4/62 (6.4%), with 3D model group: 1/5 (20.0%). ($P = 0.37$) A case of morbidity in with 3D model group was delayed onset bile leakage which was required readmission and drainage. No mortality of donor was observed in any of the groups. The age of recipients tended to be high in the with 3D system group. ($P<0.01$) Preoperative MELD score and overall survival rate of recipients in each group was almost similar. ($P = 0.28, 0.92$)

The opinions of surgeons regarding the 3D system and 3D model are summarized in Table 2. The responses to questions 1 to 4 indicated that surgeons felt the 3D model was more useful for understanding anatomical positional relationship of the donor's liver compared with the 3D system. Regarding the assessment of vessels' area, surgeons believed that the 3D system was superior to the 3D mode. On the other hand, surgeons felt that 3D model was suitable for actual preoperative simulation.

Discussion

Surgeons can never directly observe complicated liver vessels through liver parenchyma. Moreover, because of the anatomical anomaly of the vessels or influence of liver diseases such as cirrhosis, understanding intrahepatic anatomy is often difficult even for experienced surgeons. Simulation using 3D imaging systems is one of the answers, which has improved the quality of hepatic surgery. However, as Wang et al. described, 3D images lack a sense of reality for surgeons.[4] The 3D images are displayed on a two-dimensional computer screen, and objects can occlude each other, which makes it hard for a spatial comprehension of depth or complex structures. Thus, the objective was to create a realistic 3D model of the liver. In particular, the feel of the liver parenchyma and visible vessels provided significant information directly. The 3D model can faithfully reproduce the patient- or donor-specific anatomical characteristics. Through observation or by actually cutting this model, the surgeons and surgical assistants can improve their understanding and confirm the operative plan and image. The 3D model can also be manipulated during the operation to confirm the positional relationships or the cut line of the vessels. Therefore, our 3D model has merits in improving the quality of the donor hepatectomy. The opinions of surgeons regarding the 3D system and 3D model also confirmed this impression.

We compared the background and operative results of the donor among the three groups: without 3D system, with 3D system, and with 3D model. The comparison results could not demonstrate statistically the superiority of using the 3D model in donor surgery. (refer Table 1). Though we only considered 5 unique cases of the 3D model, further cases are necessary to discuss the usefulness of the 3D model.

Previously, several 3D printed liver models made of various materials, as well as clear liver parenchyma, have been reported. A simple and effective model reported by Oshiro et al. explained the liver surface using several flames [5]. Baimakhanov et al. reported a case of 1-step reconstruction of multiple hepatic veins during LDLT facilitated by a simple 3D models.[6] Wang et al. reported the usefulness of 3D models for pediatric LDLT in terms of the operative time and cost. [4] The 3D model in those report was created as simple and separate models of graft and remnant liver. Furthermore, the size of the model was half size. The size of our 3D model was the same as that of the donor with soft and transparent parenchyma, detailed hilar anatomy, and branch of vessels near the liver surface. We can also determine the transection line by using the 3D model and a member of the transplant team can actually perform preoperative simulations. Zein et al. and Soejima et al. also reported preoperative simulations for donor hepatectomy by using 3D liver models with transparent parenchyma; however, the parenchyma in these models was either hard or flexible, and its feel was far from that of an actual liver [7, 8]. Furthermore, their printers, Connex serials (Stratasys, Inc., MN), and printing materials were expensive.

Finally, our developed model has two limitations. One, because our model involves many complicated processes, the technicians are to possess skills for processing 3D data and understanding the liver anatomy, to maintain the high quality of this model. In this study, a dental technician unit in our university, which is special group for handling 3D printing, collaborated with our project. Second is the high cost of materials and long process time. The liver template, which was made of plaster, needed 3 days to prepare and incurred a cost of approximately $600 for the materials. The process of vessel model also needed 3 days and $40, and the process of liver parenchyma needed 4 days and $40. Therefore, a total 10 days or more and an approximate cost of $700 or more is required. Because these cost and time constraints do limit the use of the 3D printed models in all cases of hepatectomy, donor hepatectomy for LDLT might be feasible, which only requires deep understanding and preoperative planning.

In conclusion, a 3D liver model in LDLT donor surgery has higher costs and the processes are time-consuming, and there are no significant donor and recipient outcomes. We have just presented the in-house processing of 3D liver images and pilot clinical uses in LDLT.

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Compliance with ethical standards

Conflict of interest All the authors declare that they have no conflict of interest.

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Figure legends

Fig. 1 a: Designed template of liver parenchyma using 3D reconstruction application. **b:** Printed plaster template of the liver parenchyma, which was separated into three parts. One part was mounted as inlet to pour polyurethane (arrow). **c:** Designed 3D data of vessels; white: venous system, light blue: portal system, red: arterial system, yellow: biliary system. **d:** Printed vessel system using TPE filament.

Fig. 2 a: Combined part of liver template and vessel system. **b:** All parts of the template were combined, and polyurethane was poured from the inlet (arrow). **c:** The plaster template was cautiously broken and removed. **d:** The surface preparation agent coated on the adhesive surface.

Fig. 3 a: Front View. **b:** Bottom view. **c:** Preoperative simulation of the right-lobe donor hepatectomy using the 3D model. **d:** Intraoperative navigation using the sterilized 3D model.

Fig. 4 a: View of the cutting surface of the 3D model. The vessel's orifice and extending branch into the parenchyma is observed. The 3D model provided an actual image of operation for vessel reconstruction. (right hepatic artery; RHA, right branch of portal vein; RPV, branch of the bile duct of segment 6+5+8; B6+5+8. that of segment 7; B7, inferior right hepatic vein; IRHV, branch of middle hepatic vein in segment 8; MHV-V8, right hepatic vein; RHV) **b:** IRHV, MHV-V8, and RHV were sutured to saphenous vein graft on the back table. A large orifice of the reconstructed hepatic vein was anastomosed to IVC. **c:** Intraoperative image of anastomosis of the graft at B6+5+8 and B7 to the recipient

Legend of electronic supplementary material:

Online Resource 1: As shown in the movie, we performed the preoperative simulation of the right-lobe graft in the LDLT using the 3D model. The elasticity of model's parenchyma was almost similar that of an actual normal liver. Additionally, the see-through parenchyma enabled the observation of the vessels situated at a deep level. First, we cut the branch of the middle hepatic vein (MHV). Next, we cut the right hepatic artery (RHA), right portal vein (RPV), B6+5+8, and B7. Finally, we cut the IRHV, MHV-V8, and RHV. Therefore, the donor's right hemihepatectomy was completed.

Legend of supplementary Table:

Table 1: General characteristics and operative results of the donors and recipients

We compared the background and operative outcomes among 3 groups; Without 3D system group (N = 145), and With 3D system group (N = 62), and With 3d model group (N = 5). Each factor among 3 groups was statistically compared. A difference was considered significant if the P value was less than 0.05. *Median (Range)

Table 2: Seven questions to the 10 transplant surgeons about impression of 3D system and 3D model.

Data are given as Mean±SD. All questions are answered from 1 to 5 point; Very helpful as 5 point, useless as 1 point

Fig. 1

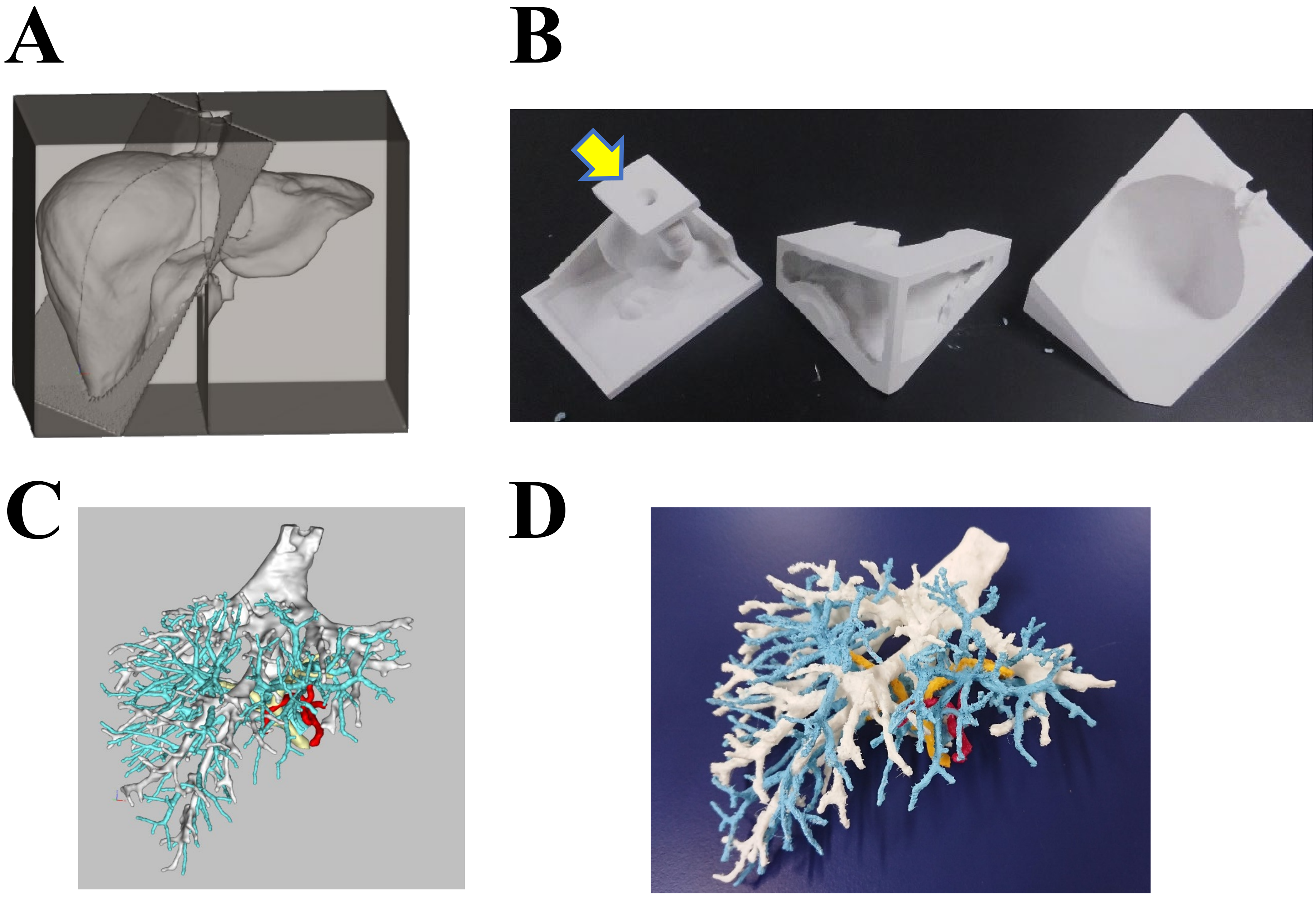

Fig. 2

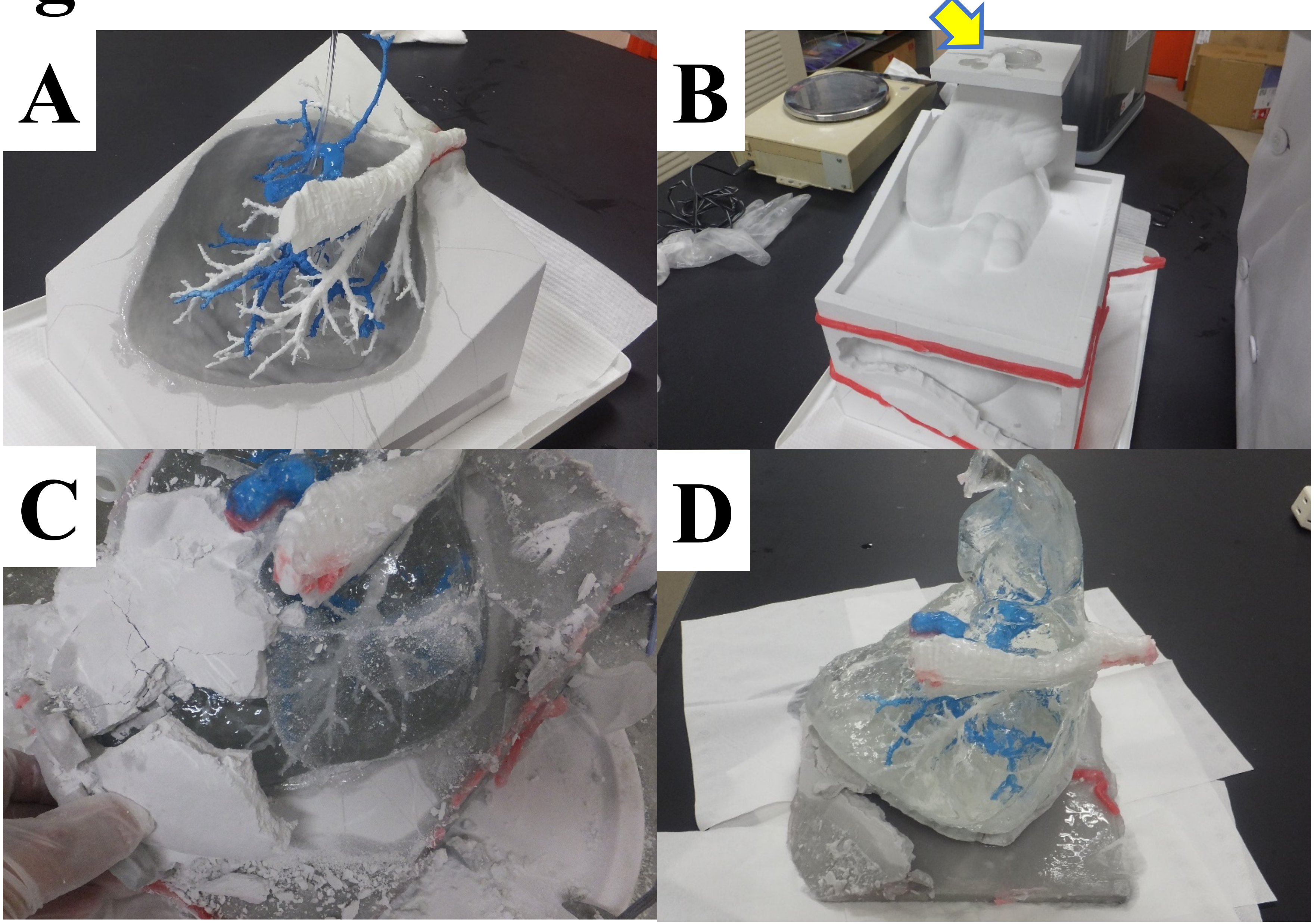

Fig. 3

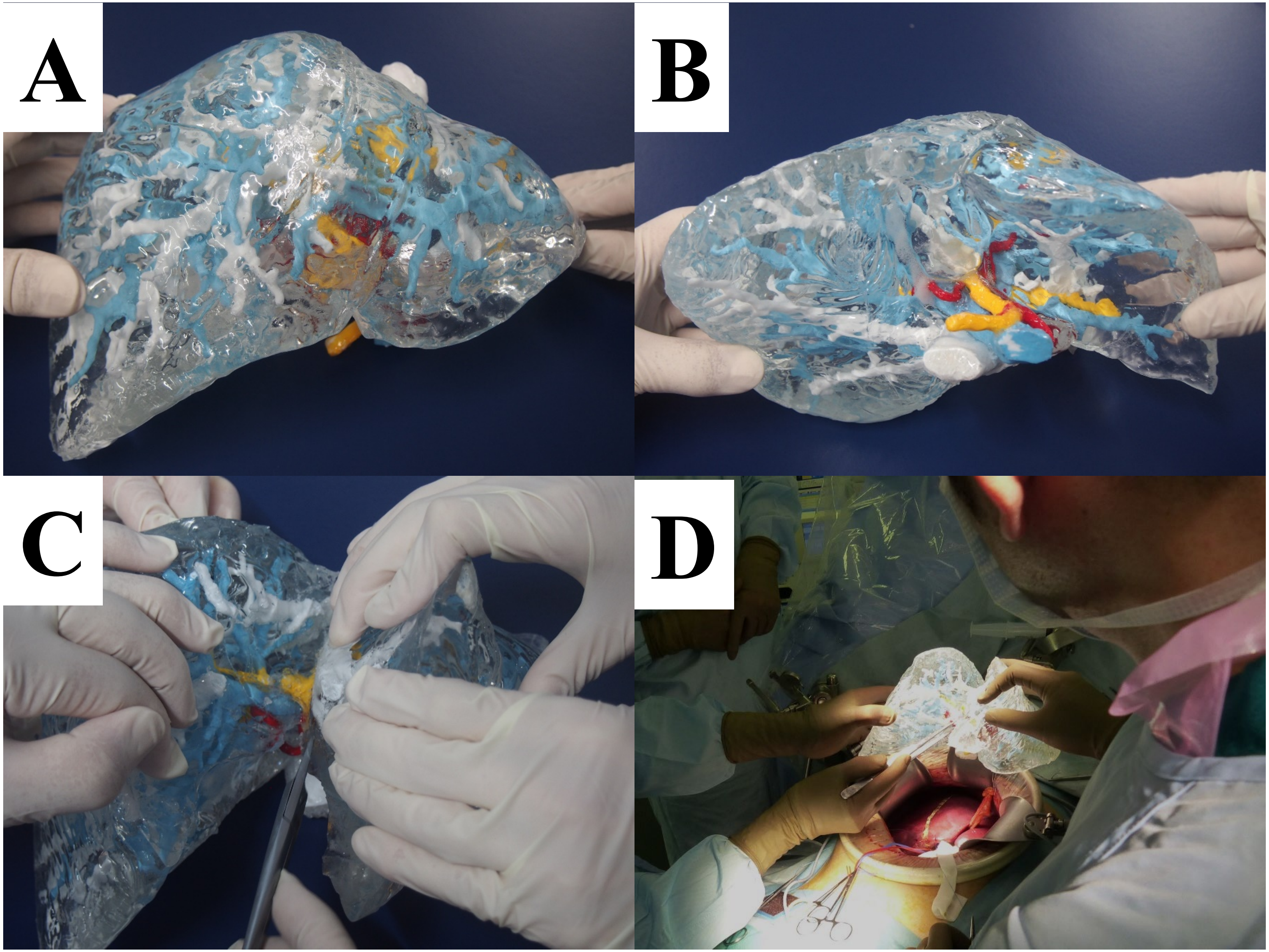

Fig. 4

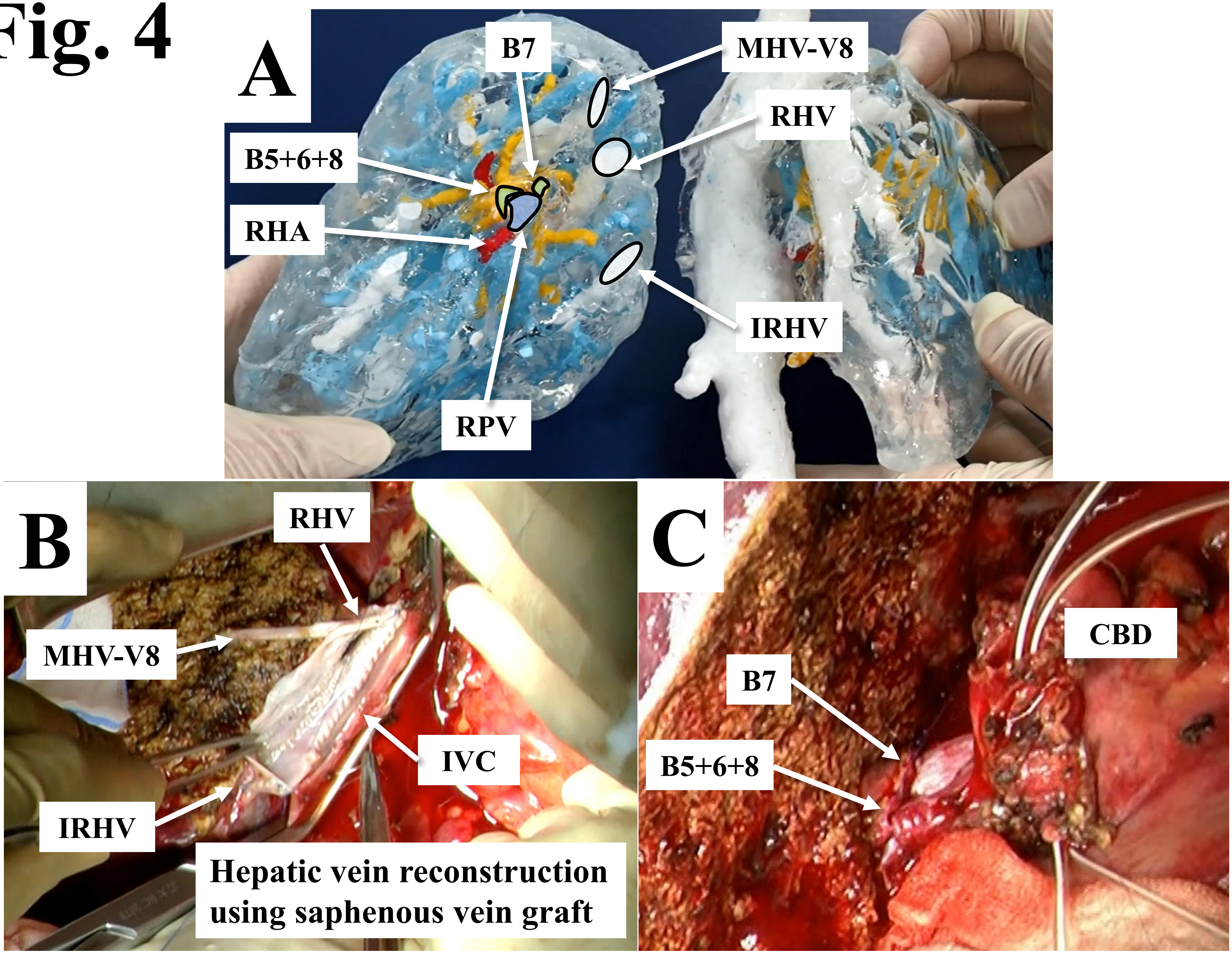
A
B7
MHV-V8
RHV
B5+6+8
RHA
IRHV
RPV
B
RHV
MHV-V8
IVC
IRHV
Hepatic vein reconstruction
using saphenous vein graft
C
CBD
B7
B5+6+8

Table 1.

	Without 3D system (N = 145) Feb.2004-Dec.2011	With 3D system (N = 62) Jan.2012-Feb.2019	With 3D model (N = 5) Sep.2016-Nov.2018	P value
Donor				
Age*	36 (17-67)	38 (21-67)	55 (37-64)	0.05
Gender Male/Female	91/54	43/19	3/2	0.43
Graft type Right lobe/Left lobe/Posterior segment	103/39/3	23/38/1	1/4/0	<0.01
Differences in actual and planned graft volumes (ml)*	-	-31(-98-+44)	-87 (-148-+11)	0.19
Operative time (min) *	406 (270-649)	436 (247-700)	394 (279-490)	0.07
Blood loss (g)*	200 (30-1340)	479 (129-1223)	350 (244-804)	<0.01
Blood transfusion cases (%) (All cases were used autologous blood transfusion)	14/145 (9.7%)	8/62 (12.9%)	1/5 (20.0%)	0.39
Morbidity rate (%)	7/145 (4.8%) Bile leakage; 4 Abscess; 3	4/62 (6.4%) Bile leakage; 3 Respiratory failure; 1	1/5 (20.0%) Bile leakage; 1	0.37
Postoperative hospital stays (day)*	12 (7-24)	12 (7-49)	11 (10-18)	0.97
Recipient				
Age*	55 (19-69)	61 (26-69)	56 (19-66)	<0.01
MELD score*	15 (6-44)	17 (8-39)	17 (11-29)	0.28
Overall survival rate 1, 2, 5 year (%)	81.4%, 77.2%, 66.1%	79.1%, 76.9%, 74.4%	80.0%, -, -	0.92

Table 2

	3D system	3D model	P value
Q1. Can you look at it from various angles?	4.0±0.6	4.9±0.3	<0.05
Q2. Can you determine the change in the vessel's position with the deformation of the liver?	2.4±1.1	4.7±0.5	<0.01
Q3. Can you determine the cutting line of the liver?	4.0±0.6	5.0±0.0	<0.01
Q4. Can you perform preoperative simulation?	3.5±1.1	4.9±0.3	<0.01
Q5. Can you determine the area of each vessel?	4.5±0.7	3.6±0.9	<0.05
Q6. Can you determine the cutting point of the vessel?	3.4±0.8	4.9±0.3	<0.01
Q7. Can you determine the distance between vessels during reconstruction?	3.5±0.8	4.8±0.6	<0.01