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Review Article

Three-dimensional modeling in complex liver surgery and liver transplantation

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Liver resection and transplantation are the most effective therapies for many hepatobiliary tumors and diseases. However, these surgical procedures are challenging due to the anatomic complexity and many anatomical variations of the vascular and biliary structures. Three-dimensional (3D) printing models can clearly locate and describe blood vessels, bile ducts and tumors, calculate both liver and residual liver volumes, and finally predict the functional status of the liver after resection surgery. The 3D printing models may be particularly helpful in the preoperative evaluation and surgical planning of especially complex liver resection and transplantation, allowing to possibly increase resectability rates and reduce postoperative complications. With the continuous developments of imaging techniques, such models are expected to become widely applied in clinical practice.

Introduction

Hepatobiliary cancer and chronic liver failure are diagnosed more and more frequently. For these diseases, liver resection and liver transplantation (LT) are the most effective treatments [1,2]. Although well standardized, postoperative complications and deaths still occur after such procedures [3,4]. Especially advanced hepatobiliary surgery is challenging because surgeons have to deal with the complexity and variability of the Glissonean pedicles, the hepatic venous anatomy and the relationship between these intrahepatic structures and the lesions [5]. Accurate preoperative assessment and preparation are of utmost importance both to obtain an R0 resection and to reduce postoperative complications.

Presently computed tomography (CT) and magnetic resonance imaging (MRI) are the main tools used to evaluate the extent, spread, resectability and transplantability of hepatobiliary tumors [6]. These two-dimensional (2D) imaging techniques allow to visualize the hepatic arterial (HA) and portal vein (PV) blood supply, the accompanying biliary structures, the draining hepatic veins and their frequently present anatomic variations [7–10]. Moreover, angio-CT and MRI can determine, through identification of the "feeding and draining" vascular structures rather precisely, both anatomic and functional, total and residual liver volumes (RLV) [11–14]. Some shortcomings in relation to a detailed view of the liver anatomy and lesion can be resolved by 3D modeling and printing [15]. 3D printing is the process in which an excavated model is transformed into a 3D morphology. Such models have already been widely used in the fields of stomatology, neurosurgery and nephrology. More recently their use has been introduced in complex liver resection and (living donor) LT procedures [16–21]. These models help in the preoperative surgical planning by providing precise anatomical details and spatial intrahepatic relationships. This information is crucial especially in the accurate planning of complex surgical procedures including vascular reconstructions [22–24].

Methods

A systematic literature published in English was searched in PubMed and EMBASE using the search terms: "3D print", OR "3D model", OR "Three-dimensional print", OR "Three-dimensional model", AND "liver surgery", OR "liver transplantation", OR "liver", and the search date was defined 1990/01/01-2021/12/31. Finally, 18 (3.2%) of 566 papers were retained for the analysis (Table 1, Fig. 1)

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Table 1
Selected review of the literature in relation to 3D printing models and advanced liver surgery and transplantation.

Studies	Year	*n*	Disease	Aim	Imaging method	Significant findings made by the authors in relation to 3D printing
Liver resection						
Madurska et al. [25]	2017	1	HCC	Preoperative planning	CT/MRI	Providing good anatomical details of the relationship between liver tumors and adjacent structures.
Kuroda et al. [26]	2017	2	HCC	Preoperative planning	CT	The simplified 3D models of intrahepatic vessels without liver parenchyma are sufficient to effectively guide intraoperative operations and is suitable for all HCC surgeries.
Perica et al. [27]	2017	1	HCC	Preoperative planning	CT	3D printing models are of limited value in diagnostic radiology. However, it still has guiding significance in the surgical planning and intraoperative guidance of hepatocellular carcinoma treatment.
Souzaki et al. [28]	2015	1	Hepatoblastoma	Preoperative planning	CT	3D printed models help in surgical planning of pediatric liver malignancies.
Takagi et al. [29]	2014	1	PHCCA	Preoperative planning	CT	The reproducibility of 3D modeling by the latest imaging has been clarified and future preoperative simulation should be dramatically changed.
Larghi Laureiro et al. [30]	2020	1	PHCCA	Preoperative planning	CT	The application of 3D models in liver surgery helps clarify some useful preoperative questions and the accuracy of the model is high.
Igami et al. [31]	2014	2	CRLM	Preoperative planning	CT	It is a simple and feasible method to use 3D printing liver to perform hepatectomy for small tumors that cannot be seen by intraoperative ultrasound examination.
Oshiro et al. [32]	2017	1	CRLM	Preoperative planning	CT	This model can clearly simulate the resection line and help safely perform the surgery; and it is cost effective, and has a shorter production time.
Witowski et al. [33]	2017	1	CRLM	Preoperative planning	CT	A cost-effective technique for the preparation of 3D-printed liver models is proposed that can reduce operative time and improve surgical outcomes.
LDLT						
Zein et al. [34]	2013	6	Liver cirrhosis	Preoperative planning LDLT	CT/MRI	These models are proved to be very accurate, and this was the first time that a human liver has been replicated and validated at the time of surgery with an actual local liver.
Baimakhanov et al. [35]	2015	1	HCC	Preoperative planning LDLT	CT	3D printing models are recommended for LDLT with complex vascular or biliary tract anatomy that require multiple or complex anastomoses.
Soejima et al. [36]	2016	1	Secondary biliary cirrhosis post Kasai	Preoperative planning LDLT	CT	Preoperative simulation using 3D-printed liver models is a technological innovation in pediatric LDLT, especially for small infants.
Ishii et al. [37]	2020	1	Secondary biliary cirrhosis post Kasai	Preoperative planning LDLT	CT	Patient-specific 3D liver model facilitated the identification of vessels during living donor liver transplantation in situs inversus totalis.
Wang et al. [38]	2019	10	Biliary atresia (6), congenital cholangiectasis (1), biliary cirrhosis (1), Wilson's disease (1), autoimmune hepatitis (1)	Preoperative simulation LDLT	CT/MRI	In small infants and complex cases of pediatric LDLT, 3D printing models can help minimize the risk of large-size syndrome and graft reduction.
Rhu et al. [39]	2021	90	HCC (59); others (31)	Preoperative simulation LDLT	CT/MRI	3D printing models can improve clinical outcomes, especially in bile-duct division.
Raichurkar et al. [40]	2021	1	Wilson disease	Preoperative simulation LDLT	CT	Three-dimensional printing of liver models can help predict the actual size of the graft after donor hepatectomy, in patients undergoing LDLT.
Others						
Lopez-Lopez et al. [41]	2021	35	CRLM (12), ICC (7), Klatskin tumor (5), hemangioma (1), adenoma (1), focal nodular hyperplasia (1), HCC (3), gallbladder (1), primary sarcoma (2), sarcoma metastases (1), adrenal metastases (1).	Preoperative planning	CT/MRI	The 3D printing liver models has a good correlation with CT/MRI, which is helpful for preoperative simulation, but does not affect postoperative outcomes.
Chen et al. [42]	2021	291	N/A	Preoperative simulation	CT/MRI	It is possible to take medial segment graft as a donor liver with the help of 3D printing technology.

CT: computed tomography; MRI: magnetic resonance imaging; LDLT: living donor liver transplantation; HCC: hepatocellular carcinoma; ped tumors: pediatric tumors; CRLM: colorectal liver metastases; PHCCA: perihilar cholangiocarcinoma; ICC: intrahepatic cholangiocarcinoma; N/A: not available.

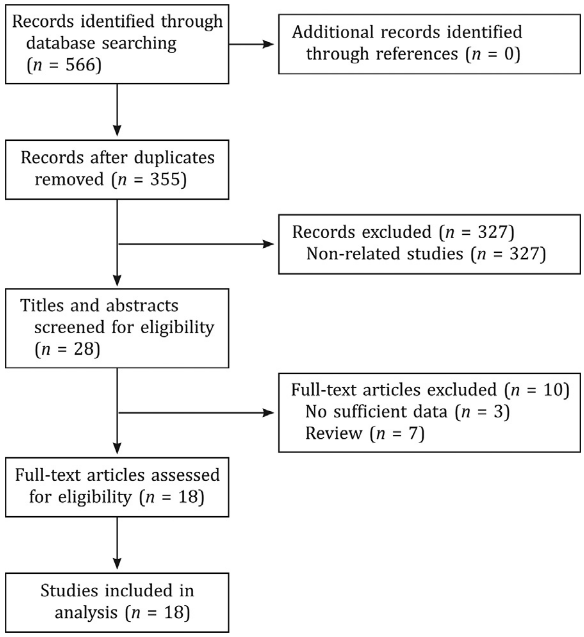

Fig. 1. Flow diagram related to the systematic review of the English literature related to 3D printing models and liver resection and transplantation.

[25–42]. The specific process of the 3D printing models in liver surgery is shown in Fig. 2.

3D printing models in advanced liver surgery

The complexity and variability of the hepatic vessels and their corresponding biliary tracts represent a main technical difficulty in complex liver resections. To enhance safety and efficacy, one must fully understand the location and the spatial relationship between the lesion(s) and the biliary and vascular structures. 3D printing models can precisely visualize the shape and location of the HA, the PV and the biliary tract, the size and location of tumors and finally the inter-relationship between all those structures. A detailed cartography helps the liver surgeon preserve or resect these structures and calculate the functional RLV, both of which enhance the safety of the planned procedure [25].

3D printing models and primary hepatobiliary tumors

In children, hepatoblastoma and undifferentiated embryonal sarcoma are the most frequent liver tumors [43–45]. As these tumors are often extended and therefore intermingled with the blood vessels, resection may compromise the residual liver function. Moreover, in these patients the fragility of the vasculartture increases the risk for intra- and postoperative complications [46–48]. The exact preoperative evaluation of tumor size, the relationship with the adjacent blood vessels and the determination of RLV are all of particular importance in these pediatric patients.

Souzaki et al. reported a liver resection in a 3-year-old girl with hepatoblastoma after chemotherapy located between the left and right PV branches. Intraoperative findings correlated well with the 3D printing liver models, allowing to perform an extended left hepatectomy. The pathology of the resected specimen confirmed a negative surgical margin [28].

In adults, large HCC are common and are often accompanied by invasion of the portal and/or hepatic veins and impairment of liver function because they mostly develop in a fibrotic/cirrhotic liver [49,50]. This frequently present underlying liver disease implies the necessity for a detailed preoperative evaluation of both the liver function and the functional reserve of the RLV [51–53]. Xiang et al. [54] reported the application of 3D printing technology in the resection of a complex large HCC in the presence of a PV variation that a segment 4 vein branch coming from the right anterior PV. 3D printing models can clearly visualize this anomaly. A right hepatectomy would have reduced RLV to only 21.37%; adaptation of the surgical technique based on the 3D printing models can preserve the S4 PV branch and thereby increase the RLV from 21.37% to 57.25%.

The anatomic resection of an HCC, including its draining PV branch, can reduce intraoperative bleeding and improve tumor-free survival [55,56]. Such approach requires a thorough understanding of the segmental liver anatomy [57–59]. Kuroda et al. [26] performed 3D printing models guided anatomic R0 resections of segment 7, segment 4 and right anterior ventral segment. Based on their experience the authors concluded that 3D printing models guided surgery make these procedures safer.

When liver tumors invade large blood vessels, vascular reconstructions are often required to ensure an R0 resection [60]. Huber et al. [61] summarized a series of 10 complex liver resections guided by 3D printing models. Seven required a vascular reconstruction. Again, the authors believed that 3D printing models are of great help not only assess the relationship between a tumor and the blood vessels but also give useful information in relation to vascular reconstruction. Based on this experience they proposed to set up prospective studies to evaluate the real clinical impact of 3D imaging and printing in advanced liver surgery. Similarly, a multicenter study [41] involving 35 patients from 8 centers confirmed the strong correlation between 3D printing models and the analysis of the hepatectomy specimen. The obtained information, however, did not affect the results of surgery. More studies are needed to demonstrate the impact of 3D printing models on complications and prognosis of liver resection.

Perihilar cholangiocarcinoma (PHCCA) is featured by an insidious onset, a difficult early diagnosis, a rapid disease progression and, consequently, a poor prognosis [62–65]. Due to the complex relationship with the accompanying HA and PV as well as the high anatomical variability of these Glissonean structures, R0 surgical resection is difficult to achieve. Enhancing the accuracy of preoperative evaluation in relation to local and environmental tumor extension is very important to optimize the surgical planning [66]. 3D printing models may be an effective tool [29].

Larghi Laureiro et al. [30] reported a 29-year-old woman with PHCCA invading the right PV in which an R0 right trisectionectomy with removal of the entire englobed thrombosed PV followed by a complex vascular reconstruction was successfully performed based on 3D printing models. 3D printing models were highly accurate to identify the anatomical relationship between the tumorous bile duct and the invaded accompanying vessels. Zeng et al. [67] combined 3D visualization and 3D printing models in the individualized precision surgical treatment of 10 patients presenting Bismuth-Corlette III and IV PHCCA. Despite several vascular variations, all complex surgical procedures could be performed safely based on the preoperative 3D visualization and printing models which fit the different encountered intraoperative findings very closely.

3D printing models and secondary liver tumors

Colorectal cancer is one of the most common cancers and the liver is the most common site of metastasis [68,69]. Unlike primary liver cancer, metastatic liver cancer is usually diagnosed in an advanced stage and therefore usually requires neoadjuvant therapy to improve resectability and outcome [70]. 3D printing models can help assess the efficacy of this complementary medical therapy and reevaluate the initial preoperative imaging following their

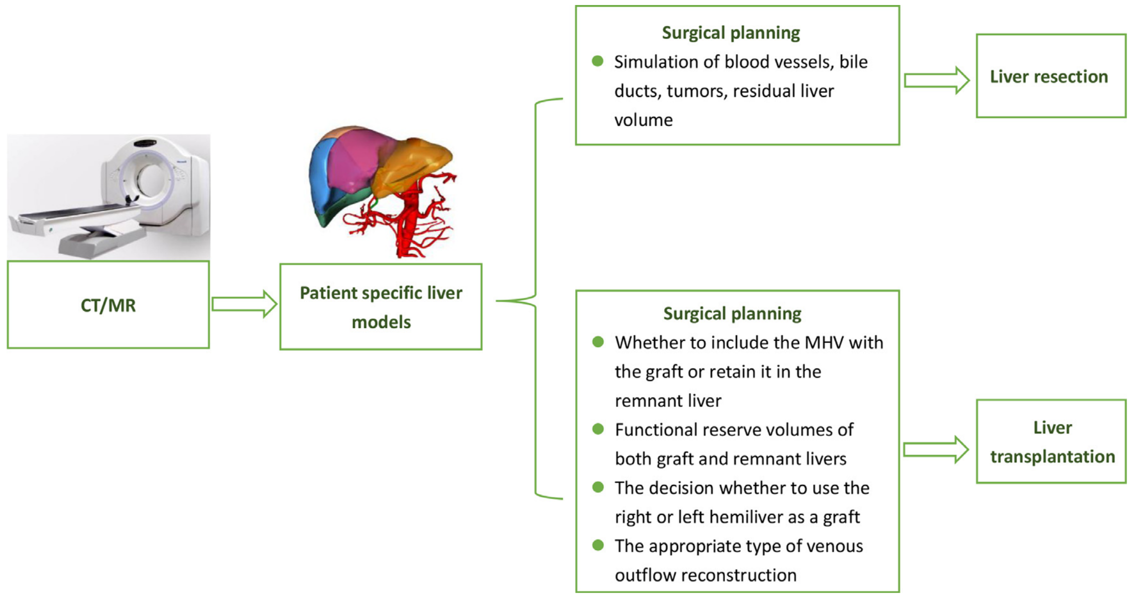

Fig. 2. Operating processes using 3D printing models in liver surgery and transplantation. CT: computed tomography; MRI: magnetic resonance imaging; 3D: three-dimensional; MHV: middle hepatic vein.

shrinking process [71]. Igami et al. [31] performed hepatectomy in two patients evaluated for multiple colorectal metastases using 3D printing models. Following chemotherapy 3D printing models can identify small “missing” tumors by preoperative ultrasound and adapt the resection lines, facilitating an appropriate hepatectomy.

3D printing models in LT

LT is the most effective therapy for end-stage liver disease [72,73]. Living donor liver transplantation (LDLT) and split-LT are two means to enlarge the liver allograft pool [74–76]. Comprehensive accurate imaging of all vascular structures of these allografts is vital in the application of the precision LDLT and split-LT surgery allowing to increase the safety both in donor and recipient [77–79]. 3D printing models are means to identify better the anatomical structures and to accurately determine both donor and recipient standard liver volumes (SLVs) and graft volumes. By simulating the perfusion of all segmental territories the corresponding LV can be measured to precisely calculate the respective graft body weight ratios, which are necessary for an optimal function of the liver graft and for the safety of the donor [34].

3D printing models and LDLT in adults

Adult to adult LDLT is a complex and risky undertaking, the surgical difficulty of adult being related not only to the various vascular and biliary constellations but also to the risk for liver insufficiency both in donor and recipient [80–82]. In 2013 Zein et al. [34] first printed translucent 3D liver models of three donors and three recipients. Their models were highly accurate in relation to the diameters of the vascular structures (with an average size error of less than 4 mm for the main portal and hepatic veins and of less than 1.3 mm for the HA). Table 2 shows that the errors of the 3D printing models group in cases are 3.3%, 3.3% and 16.6%, while the errors of the CT group are 4.3%, 28.8% and 30.1%. In relation to the volume measurements 3D printing models outperformed 3D imaging model [83]. Based on this small experience, the authors concluded that physical 3D printing models give very precise information and that they may also allow to improve the tactile and spatial relationships of blood vessels compared to those generated from computerized 3D graphic models. Baimakhanov et al. [35] transplanted a right liver including the middle hepatic vein guided by 3D printing models. This donor had a middle hepatic vein (MHV) larger than the right hepatic vein (RHV), and this MHV partially drained a vast area, including segment 6. 3D printing models measured a liver volume corresponding to 47.5% of the recipient SLV. Hence, they decided to use an extended right lobe graft and an autologous portal vein Y-graft interposition for the hepatic vein anastomosis. The solid 3D printing models made it easier to imagine the reconstructed shape and angulation of the anastomosis based on a better spatial perception. Finally, the Y-type shaped hepatic vein reconstruction was performed by connecting the right portal branch to the MHV and the left portal branch to the RHV.

Table 2
Differences between liver volume measured using 3D printing models and 3D imaging compared to CT evaluation (Zein et al. [34])

Patient	Native LV (mL)	3D printing LV (mL)	CT LV (mL)
Case 1	1215	1175 (3.3%*)	1267 (4.3%*)
Case 2	1195	1235 (3.3%*)	851 (28.8%*)
Case 3	1250	1458 (16.6%*)	1626 (30.1%*)

*: errors presented in percentage. CT:computed tomography; LV: liver volume.

Rhu et al. [39] analyzed 200 adult LDLTs. Compared with the non-image guided group, 90 LDLTs completed with image guidance did not reveal differences in relation to the type of bile duct anatomy (P = 0.144), but 3D printing models obtained a significantly higher number of single bile duct orifices (80.0% vs. 52.7%, P = 0.001). The 3D printing models may therefore be of great value to obtain a more accurate and safer transection of the biliary tract in the donor.

3D printing models and LDLT in pediatric patients

In pediatric LDLTs, the left lateral lobe (segments 2 and 3) grafting is a very well standardized and safe procedure [84]. However, large-for-size grafts [a graft to recipient weight ratio (GRWR) > 4%] and inappropriate hepatic venous outflow still remain common reasons of surgical failure. Large grafts placed in a small abdominal cavity can lead to an impaired allograft oxygenation and a compression or torsion of the portal and/or hepatic veins causing PV thrombosis and/or hepatic outflow obstruction [85–87]. Therefore, a very precise surgical planning and implantation procedure are needed in such constellation.

Soejima et al. [36] evaluated an 11-month-old girl post-Kasai surgery using 3D printing models. The estimated left lateral segment graft volume was 295 mL, corresponding to a GRWR of 4.9%. After reassessment, including a partial S2 liver resection, the weight of the allograft could be reduced to 245 g corresponding to a GRWR of 3.8%, avoiding a large-for-size grafting. Ishii et al. [37] used 3D printing technology to evaluate vascular variations in a case of biliary atresia in situs in versus totalis. The sterilized 3D printing models were brought into the operative field and used as an intraoperative navigation tool. This recipient presented an unconventional arterial anomaly, the right hepatic artery originating from the celiac axis and reaching dorsally in the hepatoduodenal ligament at the right edge of the caudate lobe. Hepatectomy was challenging based on the documented anatomical variations, and the liver could be removed without damaging the right hepatic artery. Moreover, the industrial CT scan of the patient-specific 3D liver model revealed that the gaps between the liver model and the original data were < 0.4 mm in the 90% area, < 0.8 mm in the 98% area, and 1.53 mm at the maximum.

Wang et al. [38] looked at the impact of 3D printing models comparing ten 3D printing guided LDLTs to 20 non-3D printing guided LDLTs. The 3D printing group had a significantly shorter operative time (2.3 ± 0.4 vs. 3.0 ± 0.4 h, $P < 0.001$) and less cost (17.1% lower) (34600 ± 6600 vs. 41700 ± 10400 RMB, $P = 0.03$) compared to the non-3D printing group. They also concluded that 3D printing models can help minimize the risk of large-for-size syndrome and graft reduction.

Conclusions

3D printing technology is used more and more frequently in complex liver surgery and transplantation. 3D printing models can visualize and calculate very precisely the anatomy and diameter of blood vessels, bile ducts, their relationship with liver tumors and finally to give a precise idea about total and RLVs. Although 3D modeling and printing may be superior to "traditional" state-of-the-art 2D imaging in relation to the planning of advanced liver resection and LDLT procedures and to improve the tactile evaluation of the operative field, more research will be needed to confirm its real superiority. Future technical development is expected to overcome the inconvenience of increased cost and time-consumption.

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CRediT authorship contribution statement

Jian-Peng Liu: Conceptualization, Writing – original draft. **Jan Lerut:** Writing – review & editing. **Zhe Yang:** Conceptualization, Funding acquisition. **Ze-Kuan Li:** Writing – original draft. **Shu-Sen Zheng:** Conceptualization, Validation, Funding acquisition, Writing – review & editing.

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Ethical approval

Not needed.

Competing interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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