Hepatoma Research

Review

Preoperative planning in paediatric liver tumour surgery - a literature review

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Abstract

Radiological assessment is evolving rapidly, including in paediatric liver tumour surgery. There are advancements in the fields of conventional radiology, 3D imaging and preoperative planning. This article presents the current research in paediatric liver imaging for liver tumour surgery and shows the results of a systematic search in computer-aided liver surgery in children. Sixteen original papers were found. We summarise the progress made and offer the directions in which further research could go. Computer-assisted surgery is a promising field for research and clinical application.

Keywords: Paediatric liver tumours, computer-assisted surgery, preoperative planning, paediatric hepatectomy, segmentation

INTRODUCTION

In 1998, Marescaux *et al.*[1] described an astounding attempt to apply virtual reality to liver surgery. The authors concluded that surgical planning, training and teaching of liver surgery will be possible using virtual reality concepts. This work has had a significant impact on the development of many new medical technologies. Above all, it has influenced the imagination of surgeons, engineers and computer scientists

who are in pursuit of change in medical practice. According to the Web of Science (accessed February 2021), the paper has been cited 184 times. However, Marescaux and his team were not the only representatives of this avant-garde. Many others wanted to become a part of the surgical innovation movement, too.

Since that time, information technology, augmented reality, virtual reality, 3D printing and other similar technologies have changed medicine[2]. Many ideas have already been implemented, while others are being rapidly developed. Surgical innovation has always been fundamental to surgical progress[3], and it seems even more apparent at present.

The practice of surgery is changing, and the technological impact can be clearly seen during surgical teaching and learning, as noted by Langridge *et al.*[4]. Additive manufacturing has become a fascinating research topic in anatomy education, surgical training and preoperative planning. Even though this research field is still in its infancy from the point of view of clinical outcomes, technology's impact will probably change the surgical landscape very soon. Technology is becoming cheaper and hence readily available. For instance, Witowski *et al.*[5] proposed in 2017 a cost-effective liver model printed using fused deposition modelling technology. The costs of printing are less than $150. Witowski was still a medical student at the time he published these findings.

In 2011, a new concept of so-called precision medicine emerged and was published by the National Research Council of the United States[6]. In this model, clinical treatment decisions and other practices are matched to a specific patient or a particular subgroup of patients. The treatment is customised to the patient, and the surgery is tailored to the patient as well. However, the idea of precision liver surgery has been around for a bit longer. Dong *et al.*[7] made the scientific community aware of the need for a paradigm shift in liver surgery for the first time in 2006. He called this idea "precision liver resection"[8], but it later evolved to the term "precision liver surgery"[9].

The COVID-19 pandemic has further increased the speed of changes and implementation of telemedicine and other digital technologies. Thus, we can observe more adoption and translation of technology into healthcare.

Inevitably, the old "see one, do one, teach one" paradigm has been shifting[10,11]. Now, it seems to be the 4Ps: plan, prepare, perform and perfect.

This systematic review aims to present studies on computer-aided surgical methods used in paediatric liver surgery, discuss the scientific methods used and provide new perspectives on preoperative planning. This review also aims to discuss progress of the radiological assessment. This paper is organised according to the following sections: plan (radiological assessment), prepare and perform (systematic review) and perfect (discussion).

METHODS

A comprehensive, focused literature search was conducted and performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines[12].

Data sources

We performed a systematic search using our search strategy in MEDLINE®, PubMed®, EMBASE and Ovid scientific electronic databases. The keywords were selected based on a recently published mapping of

research on surgery with mixed reality[13] and crucial articles to create a broader search. The search strategy is described in Table 1. It was conducted on 25 January 2021, and the initial results were screened by three reviewers to identify relevant studies.

Inclusion and exclusion criteria
Original studies concerning liver surgery in children, preferentially hepatic tumour surgery, were included. In addition, studies concerning virtual reality, augmented reality, mixed reality and 3D printing were included. We excluded articles expressing individual opinions (letters or commentaries), reviews and studies concerning adults, bioengineering and non-medical publications. Studies that did not mention patient age were also excluded.

Data extraction and analysis
Extracted information included: type of imaging studies performed, software or service used, number of patients, 3D imaging modality, measured outcome variables, the main results and the advantages and disadvantages of different methods.

PLAN (RADIOLOGICAL ASSESSMENT)

Imaging is the critical components of precision medicine[14] and precision liver surgery. The surgeon expects exact, relevant information from the radiologist. Advances in cross-sectional imaging allow better treatment efficacy and patient safety[15].

The aim of liver tumour imaging is to answer the following questions: is the tumour present, is it malignant or benign and, most importantly, whether complete surgical resection is plausible. To answer them, one should choose the best imaging modality.

The clinician has three main methods of cross-sectional liver evaluation available: ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI).

Due to the wide accessibility and patients' small size, US is the primary diagnostic tool for assessing liver tumours in the paediatric population. One can describe the lesion's size, character (solid *vs.* cystic) and vascularity during ultrasound examination. This assessment is quick and relatively inexpensive. It may be difficult to establish the lesion's extent due to the small field of view, especially when the tumour is large. The inspection for local and distant metastases may be uncertain as well.

Radiation-free imaging, similar to US, is favourable for children as they are much more susceptible to ionising radiation than adults and they are prone to developing radiation-associated side effects, including cancer[16].

Doppler (colour, power, pulsed, *etc.*) mode can be used to identify the presence or absence of blood flow in a mass, lesion or tumour thrombus in the portal vessels. The characteristics of doppler signal may suggest the organ of origin[17].

Somewhat new, but supported with multiple publications (unfortunately, mainly concerning adults and only scarcely paediatric population), contrast-enhanced ultrasound (CEUS) is emerging as a new liver tumour evaluation method (even though it has been known for over 20 years).

Table 1. Details of the query search strings used in this systematic review

Search query	Results
"Computer-assisted" (All Fields) AND {["paediatrics" (All Fields) OR "pediatrics" (MeSH Terms) OR "pediatrics" (All Fields) OR "paediatric" (All Fields) OR "pediatric" (All Fields)] AND ["liver" (MeSH Terms) OR "liver" (All Fields) OR "livers" (All Fields) OR "liver s" (All Fields)]}	217
{["Virtual" (All Fields)] AND ["pediatric" (All Fields)]} AND ["liver" (All Fields)]	35

Duplicate articles were removed from the results. The search was performed on 25 January 2021.

Inspired by the contrast agents used in other imaging modalities, ultrasound contrast agents (UCAs) are used to enhance the US's resolution in order to more easily assess the lesion's character. Because of their physical size (1-10 μm, i.e., equal to or smaller than red blood cells), UCAs act as blood pool agents and depict both the microvasculature and the macrovasculature[18].

CEUS has been approved globally for liver imaging, most recently in the USA[19]. The detection rate of CEUS is comparable to the results of contrast-enhanced magnetic resonance imaging and contrast-enhanced computed tomography (CECT)[20]. Moreover, UCAs have been proven to be safer than MRI contrast agents (the risk of an anaphylactic reaction is 1:10,000, with few adverse events, and no serious adverse events have been reported)[21,22]. The European Federation of Societies for Ultrasound in Medicine and Biology in 2017 stated that UCAs have a good safety profile in adults, and the data in children suggest they are as safe for use in the paediatric population[23]. UCAs are also cheaper than MRI or CT.

Examples of hepatic lesions that can be evaluated using CEUS are haemangiomas, telangiectasias and regenerative nodules. They have a characteristic enhancement pattern similar to the one seen on MRI[24].

More recent publications show that CEUS might be a valuable tool for preoperative assessment of the tumour, as 3D-CEUS volume calculations provided consistent measurements across different readers with almost perfect inter-rater agreement[25] and proved to be accurate. Ablation planning based on 3D US/CEUS-CT/CEUS fusion imaging has proved to be feasible for liver tumours[26].

Unfortunately, even with Doppler US and the addition of CEUS, the lesion's real character is hard to establish based solely on US.

Therefore, high-resolution CECT and MRI have become the imaging modalities of choice for detailed anatomical assessment of primary paediatric liver tumours[27]. The main drawback of both CT and MRI examinations is that they both require sedation in children under 5 years old (and sometimes in older children).

A single portal venous phase CT is generally sufficient when a CT is performed in a paediatric patient to assess a hepatic mass lesion-the lesion's size, vascularity and anatomical position can all be evaluated using solely this phase. The other phases (non-contrast, arterial and delayed) add little diagnostic information[28].

Other risks related to CT (apart from radiation) include the need to use oral and intravenous contrast agents because paediatric patients have little perivisceral fat, making anatomic organs delineation difficult in many cases[29].

Simultaneously, modern scanners produce high-quality isovolumetric images that can be reconstructed in multiple imaging planes[25].

Up to date, MRI seems to be the best imaging modality in liver lesions assessment. Several publications have shown that MRI is superior for lesion characterisation of liver pathology when compared to CT. It is only moderately better for lesion detection but contributes clinically crucial additional information in a sizeable number of patients[30-32].

MRI has the advantages of providing excellent soft tissue contrast without exposing the patient to ionising radiation. Advances in both MRI hardware and software technology have significantly contributed to the detection, characterisation and staging of hepatic neoplasms[33].

MRI in paediatric patients can be performed with either 3 or 1.5 T systems[34]. Imaging at 3 T has a better signal-to-noise ratio and spatial resolution than 1.5 T imaging when combined with acceleration techniques such as parallel imaging and compressed sensing[35], which makes it preferable in younger children[36,37].

Although new, but with proven advantages, hepatobiliary agents have been used to evaluate the biliary system's anatomy, function and pathology[38].

There are three FDA-approved MR contrast agents with differing degrees of hepatocyte uptake and biliary excretion. Gadoxetic acid is discussed in more detail in this paper. It has been marketed in the US since 2008 (approved as Primovist® in Europe since 2004). Almost 50% of gadoxetic acid is taken up by hepatocytes and excreted into biliary canaliculi[39]. Hepatobiliary phase liver imaging shows peak contrast enhancement at 20 min with a persistent enhancement for more than 2 h[40]. The early enhancement is the main reason this agent is preferred in the paediatric population[41]. Gadoxetate is safe in children older than two months[42]. The advantages of gadoxetate are improved characterisation of liver lesions, enhanced detection of metastases, better evaluation of the relationship of tumours to the biliary tree (to evaluate the biliary tree for benign disease and for tumours communicating with the biliary tree[43]) and increased diagnostic confidence of focal nodular hyperplasia (FNH) differentiation from liver metastases[39]. If needed, they can guide the biopsy of more suspicious lesions[44]. This last benefit is significant in children who have been treated for a primary tumour, as there is an increased incidence of FNH in those patients[45].

PREPARE AND PERFORM (SYSTEMATIC REVIEW)

We found 16 relevant articles that contribute to the application of 3D visualisation in paediatric liver surgery. The papers are summarised in Tables 2 and 3. Table 4 summarises the outcome measures used in the reviewed research studies.

Plumley *et al.*[46] were the first to describe the role of helical (spiral) CT scan, with 3D reconstruction, in the preoperative assessment of solid paediatric tumours. From the nine described cases, one patient was a child with hepatoblastoma. The surgical treatment was feasible after performing the spiral-CT scan and 3D reconstruction, even though initially the tumour seemed unresectable. The authors believed that the excellent resolution of vascular structures and the ability to evaluate the tumour's 3D relationship to these structures in multiple projections allow preoperative surgical strategies that result in safe and complete surgical resection of tumours.

Table 2. A concise description of relevant articles, sorted by year of publication (ascending) and the last name of the first author

Ref.	Year of publication	Study type	Study description	Sample size
Plumley *et al*.[46]	1995	Case report	Assessment of tumour size and location in relation to vital structures	1 (9)*
Fuchs *et al*.[47]	2005	Evaluation study	Preoperative 3D visualisation and virtual resection	4 (11)*
Dong *et al*.[48]	2007	Validation study	Comparison between 3D preoperative reconstruction *vs.* conventional CT	18
Fuchs *et al*.[49]	2010	Evaluation study	Description of experience with the use of software assistants	12
Souzaki *et al*.[50]	2013	Case report	Description of a novel augmented reality navigation system	1 (6)*
Souzaki *et al*.[51]	2015	Case report	3D-printed liver model based on preoperative CT scan	1
Su *et al*.[52]	2015	Evaluation study	Experience with a computer-assisted surgery system in liver resections	21
Soejima *et al*.[53]	2016	Case report	Description of a 3D-printed model of a liver graft and the recipient's body	1
Su *et al*.[54]	2016	ComparativeRetrospective	Comparison between 3D preoperative reconstruction *vs.* conventional CT	26
Warmann *et al*.[55]	2016	Evaluation study	Description of experience with the use of software assistants	24
Zhang *et al*.[57]	2016	Validation study	Comparison between 3D preoperative reconstruction *vs.* conventional CT	21
Janek *et al*.[58]	2017	Evaluation study	Experience with a computer-assisted surgery system in liver resections	5
Zhao *et al*.[59]	2017	Evaluation study	Evaluation of a computer-assisted surgery system in preoperative surgical planning and intraoperative navigation	5
Wang *et al*.[60]	2019	Validation study	Application of 3D-printed liver models in paediatric living-donor liver transplant	30
Esaki *et al*.[61]	2020	Validation study	Segmentation and volumetry of a liver graft using U-Net convolutional neural network	100/20#
Ishii *et al*.[63]	2020	Case report	Experience with patient-specific 3D-printed liver model based on preoperative CT	1

*The number refers to patients with liver tumours; the number in parentheses refers to the number of all patients. #100 patients were used for learning and 20 patients for validation. Note that not all patients were children in this study.

Fuchs *et al*.[47] published in 2005 one of the first reports of using 3D CT reconstructions in paediatric liver surgery. The authors found an excellent correlation between 3D reconstructions and the findings during surgery. Tumour resections could be planned more precisely. Especially the colour-coded determination of risk margins seemed to be useful. The authors used MeViS services (Fraunhofer Institute for Digital Medicine). Within this service, surgeons receive images of the individual cases comparable to a personal anatomical textbook together with an automatic risk analysis. Through the analysis of separate liver territories (according to the portal venous drainage), the authors also noted variations of the Couinaud's classification. Individual differences in the segmental borders within the liver were found. The authors also stated that anatomic variants could be demonstrated and evaluated reliably.

Dong *et al*.[48] in 2007 analysed large tumours (> 30% of hepatic mass) or tumours at the hepatic hilum. Three-dimensional CT imaging provided high-quality images of the tumours and their borders and the tumour location relative to vital hepatic blood vessels (before this technique, angiography was used, which had many disadvantages). As the surgeons identify hepatic blood vessels before surgery, they can reduce the risk of massive haemorrhage. The authors concluded that 3D reconstruction offers a more accurate method than traditional imaging techniques. It could help the surgeon identify the tumour borders precisely and devise a comparatively safe surgical strategy.

Table 3. A summary of the types of preoperative imaging studies used, as well as the software and types of technology implemented in the study

Ref.	Preoperativestudy used	Software used	What was performed
Plumley *et al.*[46]	CT	No data	3D reconstruction
Fuchs *et al.*[47]	CT	MeVis service	3D reconstruction
Dong *et al.*[48]	CT	4D Recon Card Wizard (Siemens)	3D reconstruction
Fuchs *et al.*[49]	CT	MeVis service	3D reconstruction
Souzaki *et al.*[50]	CT/MRI	Virtual Place 300, AZE Co (Now AZE Virtual Place, Cannon)	Augmented reality
Souzaki *et al.*[51]	CT	ZedView, 3D Doctor, FreeForm, CATIA	3D printing
Su *et al.*[52]	CT	Higemi	3D reconstruction
Soejima *et al.*[53]	CT	Free Form, K's Design Lab	3D printing
Su *et al.*[54]	CT	Hisense CAS system	3D reconstruction
Warmann *et al.*[55]	CT/MRI	MeVis service	3D reconstruction
Zhang *et al.*[57]	CT	Hisense CAS system	3D reconstruction
Janek *et al.*[58]	CT	MeVis service	3D reconstruction
Zhao *et al.*[59]	CT	Hisense CAS system	3D reconstruction
Wang *et al.*[60]	CT/MRI	IQQALiver; EDDA Technology	3D printing
Esaki *et al.*[61]	CT	U-Net and three-dimensional (3D) workstations (3DWS)	Deep learning
Ishii *et al.*[63]	CT	Synapse Vincent (Fujifilm)	3D printing

Table 4. Outcome measures

Ref.	Measured outcomes
Plumley *et al.*[46]	Recurrences, kidney function, changing the operation plan
Fuchs *et al.*[47]	The margin of resection, intraoperative complications, portal venous thrombosis
Dong *et al.*[48]	Operation time, blood loss, mortality, surgeons subjective opinion
Fuchs *et al.*[49]	The margin of resection, intraoperative complications, portal venous thrombosis
Souzaki *et al.*[50]	Operation time, reoperations, mortality, intra- and postoperative complications
Souzaki *et al.*[51]	Recurrence, the margin of resection
Su *et al.*[52]	Operation time, blood loss, blood transfusion, mortality
Soejima *et al.*[53]	Operation time, blood loss, blood transfusion, mortality, postoperative complications
Su *et al.*[54]	Operation time, blood loss, blood transfusion, mortality, postoperative complications, recurrence, RSLVR
Warmann *et al.*[55]	Mortality, the margin of resection, changing operation plan
Zhang *et al.*[57]	Operation time, blood loss, intra- and postoperative complications, postoperative stay, the margin of resection, recurrence
Janek *et al.*[58]	Blood loss, blood transfusion, recurrence, bilirubin levels, the volume of post-resection liver residue
Zhao *et al.*[59]	Operation time, blood loss, blood transfusion
Wang *et al.*[60]	Operation time, blood loss, mortality, intra- and postoperative complications, inpatient stay, cost
Esaki *et al.*[61]	Liver and spleen volume measurement
Ishii *et al.*[63]	Operation time, blood loss, intraoperative complications

In 2010, Fuchs *et al.*[49] proposed an approach to the planning of surgical treatment of liver vascular malformations in children. This approach incorporated MeVis LiverAnalyzer and MeVis LiverExplorer (Mevis, Bremen, Germany). Twelve children were diagnosed with hepatic vascular malformations. The patients were assessed for Rex shunt procedure and other interventions. Liver segmentations were performed using the livewire segmentation technique. This semiautomatic technique needs user input to set anchors around the region of interest. The smallest "cost path" is then drawn from the anchor to the pixel where the pointer is. The path is changed whenever the user moves the pointer.

The authors found that virtual reconstructions provided information that was not obtained through conventional imaging techniques. They qualitatively explored the possibilities for the use of 3D imaging. The only measurable result provided is the number of procedures performed: seven patients received interventions (out of twelve). The authors also found that combining reconstructions from different CT phases on one 3D image provided further useful information. The authors had difficulty distinguishing between portal branches and collaterals, and reduced contrast in the post-thrombotic vessels did not allow proper identification.

In 2013, Souzaki *et al.*[50] presented an augmented reality navigation system for endoscopic and open surgery. In their case series, one patient had been diagnosed with hepatoblastoma. Initial CT and MRI studies were performed with multimodality markers (Chiyoda Technol, Tokyo, Japan) fixed to the patient's body surface. 3D images were reconstructed using 3D viewer software (Virtual Place 300, AZE Co Ltd., Tokyo, Japan). Each multimodality marker's coordinates were obtained with an optical tracking device (Polaris, Nrthern Digital Inc., Ontario, Canada). A video camera registering the surgical image had a rotary encoder to measure the rotation parameters. Liver borders were detected by the system, and preoperative 3D images were superimposed onto video camera live images on the screen. The authors' most significant difficulty was concerning motion and deformation of the intraoperative images of the liver. Respiratory movement and deformation caused by pressure are essential factors that create differences between the images and reality. Due to intraoperative organ movement, it was impossible to follow the intraoperative organ deformations. The authors also found that the 3D image projected onto 2D monitors produced dissatisfying results.

Souzaki *et al.*[51] published in 2015 a case report of using a 3D-printed liver model based on preoperative CT for a PRETEXT IV hepatoblastoma case, located at the porta hepatis after the neoadjuvant chemotherapy. The model was created in a 3D workstation with ZedView, 3D Doctor, FreeForm (analytical software) and CATIA, a three-dimensional interactive application. The model was printed on an Objet 500 connex 3 printer (Stratasys, USA) with the tumour, hepatic veins and portal veins seen through a translucent body. The tumour was resected completely. The surgical margins were negative, and the patient was discharged home. No recurrence was detected for a year. The authors found that the object can be sterilised and held in the surgeon's hand during surgery. Compared with 3D images, the authors found that the 3D model after fabrication cannot be changed and manipulated during surgery.

Su *et al.*[52] published, also in 2015, a case series of 21 paediatric patients with complex liver tumours. The authors used Hisense Gemini 3-dimensional Medical Imaging Reconstruction (HIGEMI) and a computer-assisted surgery (CAS) system. The images were segmented using the seeding technique. They segmented the liver, tumour, hepatic arteries, portal vein, hepatic veins and inferior vena cava. The authors recorded histopathological reports, duration of surgery, intraoperative blood loss, transfusions and complications. One patient died. This is the only paper that mentions the HIGEMI system.

Soejima *et al.*[53] described the case of an 11-month-old girl with biliary atresia after Kasai surgery who had to undergo a liver transplant. The transplant turned out to be large-of-size and impossible to perform from the CT image's initial calculations. For a more detailed analysis of this area's anatomy, the researchers decided to make 3D models of the donor and recipient liver. ZedView (Data Design, Nagoya, Japan) software was used to prepare the models. Thanks to those models, the resection line was changed to a more optimal one, and the operation was planned. The surgery proceeded without intraoperative complications; only slight blood loss was noted, and transfusion was not needed. Unfortunately, the postoperative course was complicated by infection. The patient died due to an intracranial haemorrhage 135 days after the

transplant (while the graft was still functioning).

Su et al.[54] described a study conducted on 26 children aged 22 days to 36 months with giant liver tumours. The Hisense CAS system was used in the reconstruction group and CT workstation examination in the control group. Based on the reconstruction, the procedure was simulated. The 3D images were also displayed in the operating room during the operation. It was concluded that the 3D images can precisely locate the tumour and its vascularisation. Eight patients received blood transfusions, and the mean operative time was shorter in the study group. The mean intraoperative blood loss was lower in the study group. Both differences were statistically significant.

Warmann et al.[55] designed a study that aimed at defining the role of computer-aided surgical planning in children with advanced hepatic tumours, i.e., those affecting three or four sectors of the liver. The primary outcome was the possibility to avoid liver transplantation. The authors used the MEVIS service. Surgical planning is offered by MEVIS as a commercial product, and results are embedded in a 3D interactive PDF file[56]. Sixty-three patients were evaluated, but only 24 had computer-aided surgical planning performed. Most of the patients had a CT-scan, but, interestingly, the authors did not see any difference in quality between CT scans and MRI scans. The authors stated that the 14 patients with hepatoblastoma affecting three or four liver sectors post-chemotherapy (POST-TEXT III or IV) were potential candidates for liver transplantation, but, finally, only two patients were qualified for a liver transplant. The authors observed close relationships between computer-aided surgical planning and intraoperative findings. Resection margins were free of tumour cells. The authors found variations and significant differences in segmental distribution between the patients. Variations in segment volume were presented as mean percentage and ranges. They analysed the disease-free survival rates of the hepatoblastoma patients, and the overall survival rate was 90% after five years.

In 2016, Zhang et al.[57] published a cohort study comparing two groups of children who underwent hepatectomy. Before surgery, all children had CT scans performed. CT images of eleven children were reconstructed using Hisense CAS, and 10 children were operated on without performing 3D reconstructions of the images. The two study groups were compared. No positive margins, no complications and no recurrences of the disease were noted in both groups. The authors stated statistically shorter surgery duration, less intraoperative bleeding and shorter hospital stay in the reconstruction group.

Another study was published in 2017 by Janek et al.[58]. They also used MeVis distant services for surgical planning. Their cohort consisted of five children diagnosed with hepatoblastoma. Post-surgical liver volume was 28%-70%, and none of the children suffered from post-resection liver failure. Liver volumetry was performed in OsiriX (at the time of diagnosis) and by MeVis (after neoadjuvant chemotherapy). The lowest recorded FRL equalled 28% and was well tolerated. The authors also used OsiriX for liver volumetry but found the analysis time-consuming. The authors also stressed that risk analysis performed by MeVis is fundamental, and the 3D topographic-anatomical visualisation is complete. The analysis by MeVis also contains suggested resections with calculations of liver volumes. In one of the patients, the authors used Biliskopin™ for the analysis of the biliary tract. The price of the MeVis analysis is about 700-800 euros, as stated by the authors.

Five children with hepatic mesenchymal hamartomas participated in a study by Zhao et al.[59]. The children were 8-24 months old. 3D liver reconstructions were prepared for all children based on CT examinations, including three children using the Hisense CAS software. With this software, a virtual hepatectomy was performed with the calculation of the residual volume. Based on the simulation, the optimal surgical

technique was selected. The paper presents values such as the time of surgery, bleeding and the need for blood transfusion concerning the tumour's size. There were no postoperative complications in any of the patients. Patients were followed-up for one year - no recurrence occurred. The intraoperative appearance of the liver was consistent with the reconstruction image. Reduced blood loss and shorter surgery time were also found in reconstructive patients. It was also noted that such reconstructions can be useful for learning by students and young surgeons.

Another experience was published by Wang *et al.*[60] Thirty patients requiring living donor liver transplantation were enrolled in the study. In this study, a preoperative simulation was carried out, and models were created on its basis. The segmentation method was not given-the organ volume was calculated automatically. The median age of recipients was 23 months in the study group and 11 months in the control group. The median age of the donors was 34 and 35 years, respectively. The authors pointed out the disadvantage of 3D reconstruction displayed on a flat screen. Printed models allow better 3D visualisation. Additionally, thanks to transparent silicone for parenchyma, it is easy to visualise the internal course of the vessels and the tumour's location. Ultimately, no statistically significant difference was found for surgery, blood loss, length of stay, cost or survival. Fewer patients had complications, but the result was also statistically insignificant. The duration of donor surgery was significantly shortened. Follow-up lasted an average of 35 months.

Esaki *et al.*[61] published a paper that is unlike the other works presented in this review. They proposed a method that uses a convolutional neural network (U-net), developed for biomedical image segmentation at the Computer Science Department of the University of Freiburg[62]. U-net is provided as open-source software. The method was used for automatic segmentation of liver graft volume of paediatric liver transplant patients. The accuracy of automatic segmentation was assessed after the network learned using 100 patient datasets. The accuracy was measured using Dice similarity coefficients on 20 patient datasets. The accuracy rate for liver graft was 87.10% ± 4.70%. The authors used a neural network to accelerate the segmentation process. Computed tomography datasets were used for training of the neural network and for verification of its efficacy. The segmentations created by the U-net were compared to those made by an experienced radiology technician and verified by radiologists.

Ishii *et al.*[63] described a single case of using a 3D-printed model for a 22-month-old girl with biliary atresia, leading to a liver transplant. An additional anatomical difficulty was situs inversus - a rare congenital defect causing all internal organs' vertical inversion. During the model's standard creation, the accuracy was assessed by scanning with an industrial CT system. After sterilisation, the printed model was taken to the operating room to compare its anatomy with the actual patient. The authors pointed out that the perception of the dorsal side of liver anatomy is more straightforward, thanks to the 3D model that could be easily rotated in the hands. The operation time was 646 min, blood loss was 425 mL, and the operation was completed without any intraoperative complications. The developers noted and quoted the time it takes to create the model: it took about 30-60 min to generate STL files from the original CT data. Then, it usually took about three days to produce 3D liver models from STL files. An additional day was needed for ethylene oxide sterilisation. Accordingly, the entire process takes 4-5 days.

DISCUSSION (PERFECT)

Complete surgical resection of hepatoblastoma is considered the most crucial step to achieve long-term survival[64]. Open surgery is most commonly performed[65], but laparoscopic liver surgery is also a feasible, yet very rarely used, approach[66]. The International Laparoscopic Liver Society members encourage routine use of laparoscopy in local liver resections and left lateral segmentectomies[67]. One of the reviewed studies,

by Souzaki *et al.*[50], utilised an augmented reality navigation system in laparoscopic surgery for two cases (Wilms' tumour and bronchogenic cyst). In the hepatoblastoma case, the augmented reality navigation system was used for open surgery. The authors' main hindrance was the increasing difference between the AR image and reality with the operated organs' displacement and compression. The system could not follow organ deformations. Marescaux *et al.*[68] reported the first real-time AR laparoscopic adrenalectomy. That system used manually assisted deformable registration. Haouchine *et al.*[69] proposed another solution for rigid registration and published a paper the same year as Souzaki *et al.*[51]. Haouchine *et al.*[69] suggested a real-time, physics-based system able to automatically register deformable organs using stereo endoscopy. It was shown in 2009 that stereoscopic endoscopes can take accurate anatomical measurements[69].

Because excellent knowledge of the liver's anatomy is crucial for successful resection (or transplantation) and protection of the vascular inflow and outflow to the remaining liver[65], it is believed that 3D visualisation may help in the surgical treatment of liver tumours.

All of the reviewed papers speak favourably of computer-aided surgery. However, Warmann *et al.*[55] claimed that, owing to 3D reconstructions, 12 out of 14 hepatoblastoma patients could avoid transplantation. Dong *et al.*[48] also stated that 3D surgical planning allowed more comfortable and safer dissection. The authors declared that this technique should be applied especially in large or complex liver tumours.

The critical, post-resection volume of the liver is called the future liver remnant (FLR). This is an essential concept because it was proven that, in the case of FLR < 20%, more than half of patients develop severe postoperative complications, while, for FLRs > 20%, the risk of liver failure is 13%[70]. Vauthey *et al.*[71] stated that the minimal safe FLR volume is 25% for cases of extended right-sided hemihepatectomy. Shoup *et al.*[72] also found that an FLR volume that is less than 25% is a significant risk for hepatic dysfunction. There is no consensus regarding the minimal FLR that is safe for liver surgery in children.

Most of the studies used medical imaging datasets obtained from CT studies. Only Souzaki *et al.*[50], Warmann *et al.*[55] and Wang *et al.*[60] reported the use of data from MRI studies. This is because MRI images are less accurate, have a higher signal-to-noise ratio than CT and have lower image contrast differences between tissues. Fuchs *et al.*[49] noted that the spatial resolution of CT allows for more detailed reconstructions when compared to MRI. In addition, the thickness of the slices is essential for 3D reconstructions. The problem also lies in inhomogeneous signal intensities. Those obstacles can be avoided through the proper design of an MRI protocol[73]. However, good communication between the radiologist, MRI team and the person who wants to use the MRI dataset for 3D reconstruction is necessary.

Liver volumetry is one of the essential computer-aided surgical tools. IT can be performed by surgeons alone. Van der Vorst[74] presented accurate volumetric measurements using Osirix® (Pixmeo, Geneva, Switzerland). Dello *et al.*[75] compared volumetry done in Osirix® and ImageJ by non-radiologists on personal computers and compared the results with radiological software iNtuition® (National Institute of Health, USA). The results were accurate. In another paper, Dello *et al.*[76] presented how to perform liver volumetry in ImageJ. Lodewick *et al.*[77] compared volumetry in OsiriX® and iNtuition® and also found no differences in measured volumes, but they also stressed that auto-segmentation with iNtuition® is three times faster than manual volumetry in OsiriX®. In the reviewed articles, volumetry was performed by radiologists or software engineers.

The currently used systems rely on software assistants[57] that use specific software packages such as iNtuition®, Fraunhofer MeVis or Visible Patient Planning™ (Ircad, France; not mentioned in the reviewed articles). Those software packages or services include medical image analysis with deep learning and machine learning techniques: automated organ segmentation in CT and MR, automatic liver lesion detection and segmentation, automatic vessel segmentation in contrast - enhanced CT, *etc*. Several open-source neural networks exist that can perform automatic segmentation tasks, such as U-net[78]. A complete automated liver segmentation problem is not fully solved yet, although the situation has changed since 2009[79] thanks to deep neural networks[80,81]. The paper by Ibtehaz *et al*.[78] is different from the other reviewed articles, as it describes U-net's use in automatic volumetry of liver graft.

Several well-designed review have been published recently on augmented and virtual reality in oncologic liver surgery[14], 3D printing in liver surgery[82], 3D printing in general medical setting[83], precision hepatectomy[84] and liver segmentation techniques[85]. However, we feel that this landscape is incomplete due to the lack of a comprehensive review of recent advances in radiological assessment of the liver focused on preoperative liver surgery planning in the paediatric population. We believe that this focused approach on the topic is essential because it enables a thorough analysis of the achievements in the field. In other words, it allows us to define "where we are".

The reviewed studies have mostly evaluative characteristics or are simply case reports. Only Zhang *et al*.[57], Su *et al*.[54] and Wang *et al*.[60] compared the results of patients who had computer-aided surgical planning performed with patients without additional planning. However, there is a high risk of bias in those studies, mainly confirmation bias. Due to the low numbers of patients in the groups, the studies may be underpowered and not show significant results. More prospective, comparative studies with well-defined outcome measures should be performed. It is also not known whether the computer-aided preoperative planning should be used in all cases or only in complex cases.

It is also not known how surgeons perceive different types of 3D preoperative planning. What is the difference between 3D-printed object, 3D visualisation seen on a computer screen and using 3D glasses or mixed reality glasses? Even subjective opinions of surgeons would be helpful to choose the best tool for further evaluation. The use of these advanced methods during surgery may be problematic because, for now, they need active input from the surgeon (to hold the 3D-printed model or ask someone to hold and move the model for her/him).

Most authors used 3D reconstructions presented on monitors and 3D-printed objects. The application of augmented reality utilising stereo head-mounted displays enabling holographic imaging has not been described yet in paediatric liver tumour surgery. An example of such a device is Microsoft's HoloLens™. The 3D models can be manipulated during surgery by the operating surgeon and tracked by hand gestures and voice commands. The use of HoloLens™ in adult liver surgery has been described[86], and the results are favourable.

On the other hand, a holographic image still needs to be set appropriately (zoomed-in or out, rotated, *etc*.). When overlying the operated organ, the holographic image may partly cover the organ and distract the surgeon. In addition, the 3D-printed models and 3D visualisations presented on the screens may be a source of distraction. It has not been yet resolved whether computer-aided surgery is beneficial only before the operation (preoperative planning) or during the surgery, despite all enthusiasm. This may also be a question of a long learning curve. In addition, there is a possibility that experienced surgeons will be less likely to use novel technologies. However, this technology may also work as a booster of a learning curve in

hepatobiliary surgery because it seems much more comfortable to grasp the anatomy while using 3D models and visualisations.

Another promising advancement is cinematic rendering (Siemens Healthineers), a new type of 3D imaging with a realistic photo quality visualisation. This novel rendering algorithm simulates the propagation and interaction of light passing through the volumetric images. Elshafei *et al.*[87] compared cinematic rendering with conventional computed tomography imaging in a randomised, two-sequence crossover study. Cinematic rendering allowed for faster and more correct comprehension of the surgical anatomy. A similar conclusion was drawn by Binder *et al.*[88] who studied cinematic rendering in preclinical anatomy education. The use of cinematic rendering of focal liver masses was described in 2019[89].

CONCLUSIONS

Paediatric liver tumours are rare, and, in some complex cases, the treatment approach has to be made individually. This is one of the instances where 3D imaging starts to play a role. It is possible that computer-aided surgical planning will become routine in all major surgeries. Due to technical advances, the process will become more automatic and will take less time. It will also become more available and affordable.

One of the main aims of virtual imaging is organ preservation in cases of locally advanced liver tumours. As for now, the impact of virtual imaging has rarely been analysed in the paediatric population. 3D reconstructions can allow for more aggressive surgical treatment when spatial relationships and crucial anatomical structures are depicted.

The conclusions of the reviewed articles are very enthusiastic, and the progress that has already been made in the field of computer-aided paediatric liver surgery is impressive. It is time to design studies appropriate for measuring the new technologies' effects on liver surgery outcomes.

The learning curves of those new technologies certainly have to be included in the study designs.

DECLARATIONS

Authors' contributions
Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Kościuszko D, Anzelewicz S, Czauderna P
Participated in the discussion, prepared tables and shaped the overall structure: Niemirycz-Makurat A, Gołębiewski A, Kościuszko D
Prepared the final manuscript: Kościuszko D, Niemirycz-Makurat A, Anzelewicz S

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All authors declared that there are no conflicts of interest.

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