Original Article

Clinical practice guidelines for precision diagnosis and treatment of complex liver tumor guided by three-dimensional visualization technology (version 2019)

Chinese Society of Digital Medicine; Liver Cancer Committee of Chinese Medical Doctor Association; Clinical Precision Medicine Committee of Chinese Medical Doctor Association; Digital Intelligent Surgery Committee of Chinese Research Hospital Association

Abstract: Virtual resection of liver structures guided by three-dimensional visualization technology (3DVT) has been extensively used in China. This technique provides a safe and effective method for accurate diagnosis of liver tumors and has important applications in preoperative evaluation, surgical planning and intraoperative guidance of liver cancer surgeries. The technical advantages and clinical significance of 3DVT in the diagnosis and treatment of complex liver tumors have been recognized. In order to standardize the application of 3DVT in the precision diagnosis and treatment of complex liver tumors, this guideline provides explanations and recommendations in the following aspects: (1) the establishment of homogenization processing and quality control system of 3D reconstruction; (2) the establishment of 3D reconstructed models of abdominal organs and lesions; (3) the individualized classification and quantitative analysis of blood vessels based on 3DVT; (4) 3DVT-based classification and grading of hepatic vessels in complex hepatic tumors; (5) evaluation system for surgery evaluation after reconstruction of the 3D visualization model; (6) application of 3D printing in complex hepatectomy; (7) virtual reality technology; (8) ICG fluorescence imaging; (9) multi-modal images for real-time navigation; (10) three-dimensional visualization to guide the preoperative surgical planning of precision hepatectomy; (11) application of 3DVT guidance in other therapeutic methods of hepatocellular carcinoma; (12) application of 3DVT in follow-up evaluation of the patients after liver cancer surgeries. 3DVT for visualization of the liver structures has important clinical values for accurate preoperative evaluation, preoperative planning and surgical navigation of complex liver tumors, and it facilitates precision surgeries to improve the outcomes and promote postoperative recovery of the patients.

Keywords: three-dimensional visualization; three-dimensional printing; virtual reality; fluorescence imaging; complex liver tumors; hepatectomy

INTRODUCTION

Currently, there are different definitions for complex liver tumors: (1) centrally located hepatocellular carcinoma spreading to the porta hepatis; (2) tumors with vascular variations inside the liver; (3) intrahepatic vascular malformations caused by liver compression due to its large size; (4) hepatic malignancy with tumor thrombus in the inferior vena cava and/or the right atrium; (5) giant tumor regardless of its characters for which extended hepatectomy is planned; or (6) liver tumors encroaching on segments I and VIII to require complex hepatectomy[1-3].

Three-dimensional (3D) visualization technology (3DVT) for liver tumors encompasses the techniques involved in displaying, describing, and interpreting the 3D anatomy and morphological features of liver tumors. With the aid of computed tomography/magnetic resonance imaging (CT/MRI), 3DVT allows accurate description and interpretation of the morphology and spatial distribution of the targets including the liver, biliary tract system, blood vessels, and pathological tissues through such computer image processing techniques as data analysis and calculation, imaging fusion, segmentation, and visualization. This technique makes possible intuitive, accurate, and fast visual identification of the targets and thus offers decision-making support to preoperative diagnosis, individualized surgical planning, and selection of the surgical approach.

When using more conventional diagnostic imaging methods for liver tumors such as ultrasonography, CT, and MRI, clinicians have to rely on 2D information to deduce 3D structures. The results rely heavily on their personal experience. Nonetheless, the limitation and uncertainty of their experience may lead to uncertainty and inconsistency in reconstructed structures, which may

hinder accurate preoperative assessment, resulting in a relatively high incidence of postoperative complications.

With the development of CT scanning techniques, more distinct and substantial image datasets of liver tumors are available to provide large amounts of diagnostic information that facilitates the research of 3DVT for liver tumors. Current advances in modern imaging technologies, including 3DVT, 3D printing, multimodal image fusion, virtual reality, and ICG fluorescence imaging[4] have promised a further increase in the diagnostic efficacy of the liver diseases. In 2017, "the Expert Consensus on the Application of 3DVT for the Accurate Diagnosis and Treatment of Complex Liver Tumors" was published in the *Chinese Journal of Practical Surgery*. It has received widespread acceptance nationwide after 3 years of clinical practice. A meta-analysis reported that the application of 3DVT in the diagnosis and management of primary hepatocellular carcinoma showed significant advantages over the control group in terms of intraoperative blood loss, postoperative complications, recovery of postoperative liver function, operation time, hospitalization time, and short-term postoperative tumor recurrence. According to the 2017 version of the Expert Consensus, this guideline, based on the efforts of the Chinese Society of Digital Medicine, Chinese Research Hospital Association of Digital Surgery Committee and Chinese experts in relevant fields, aims to standardize the application of 3DVT, 3D printing technology, virtual reality and fluorescence imaging technology in precision diagnosis and treatment for complex liver tumors.

This Guideline follows the Grading of Recommendations Assessment, Development and Evaluation (GRADE), which divides the quality of evidence into high, moderate, and low or very low levels, reported herein by tagging with the letters A, B and C, respectively (Tab.1). The strength of the recommendations given herein, based on the GRADE grid method[5-7] (Tab.1), is described as strong (1) and weak (2). The experts and patient representatives who participated in the formation of recommendations signed a declaration of no conflict of interest in advance, which was checked by the secretariats of guideline committees.

Tab.1 Quality of evidence and strength of recommendations

Grade	Classification	Content
Quality of evidence		
High	A	We are very confidence that the true effect lies close to that of the estimated effect.
Moderate	B	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimated effect, but there is a possibility that it is substantially different.
Low or very low	C	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimated effect; we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimated effect.
Strength of recommendation		
Strong recommendation	1	The desirable effects outweigh the undesirable effects.
Weak recommendation	2	The desirable effects possibly outweigh the undesirable effects.

1 Homogenization processing and quality control system of 3D reconstruction

In the process of generating 3D models, manual segmentation is usually required besides automatic segmentation. Therefore, only by following the homogenization processing and quality control system can a high-standard 3D reconstruction and comprehensive evaluation of diseases be achieved.

1.1 Quality control of CT image data of complex liver tumors

The setting of scanning parameters and storage of the CT images (typically with a 64-slice helical CT scanner): the conventional supine position is chosen for a plain scan from head to foot. The range is from the top of the diaphragm to the inferior margin of the liver. The scanning parameter setting is 120 kV and 250 mAs, with the detector combinations of 0.625×64, slice thickness of 1.0 mm, an interval of 1.0 mm, and a screw pitch of 0.984. The time for one revolution of the bulb tube is 0.5 s. The delayed scan of the arterial phase is 20-25 s, and that of the portal phase is 50-55 s. The image data acquired are put into CT postprocessing workstation after the scan, and a disk is burned to store the three-phase data (the plain, arterial, and portal venous phases)[8].

Recommendation: Surgeons should work together with radiologists and radiographers to optimize the scanning parameter based on the tumor location, vessels adjacent to or invaded by the liver tumors, and the specific circumstances where CT scan is performed. The high-quality triple-phase helical CT data are the basis for constructing a 3D visualization evaluation model (strong recommendation).

1.2 Study of homogenization processing and quality control system of 3D reconstruction for complex liver tumors[8]

The establishment of the quality control system for 3D visualization evaluation is vital for scientific understanding of the diseases. Three-dimensional

reconstruction should follow the quality control and homogenization research criteria: (1) the patient should be instructed to hold his/her breath during scanning to avoid the difficulties in image segmentation and registration; (2) the quality of the original CT images should meet the minimum requirement of the 3D reconstruction software; (3) 3D reconstruction should be carried out by qualified professionals; (4) 3D models should be manually checked and modified by a senior surgeon and a radiologist. Only after standardization and strict quality control can the 3D visualization models be used to guide clinical practice.

　　A standardized process of 3D reconstruction for complex liver tumors is currently unavailable in China. Failure to maintain standard procedures during the scan will lead to erroneous results, which has a direct impact on the understanding of the patient's performance status, the selection of surgical options and surgical navigation. Meanwhile, inconsistent operating standards also affect the accuracy of evaluating the clinical efficacy in different centers, thus causing great inconvenience to clinical practice and scientific research. To better apply 3DVT in the field of liver diseases, standardized evaluation and homogeneous operation flow are urgently needed. We previously proposed the quality control system and 3DVQS based on the 3 criteria concerning preoperative 3D surgical simulation, intraoperative 3D surgical navigation, and postoperative 3D reconstruction; they are further modified into 16 criteria, as elaborated in Tab.2[15,16].

Recommendation: An adequate quality control system must be established for 3D reconstruction of complex liver tumors. The reconstruction process should be carried out by qualified surgeons and radiologists and validated by senior physicians (strong recommendation).

2　Construction of individualized 3D models for abdominal organs and lesions

The acquired DICOM data should be imported into the independently developed MI-3DVS for data segmentation. The original 2D images of the abdominal organs, lesions and vascular system can be reconstructed automatically utilizing volume rendering for interactive 3D segmentation, regional self-growth method, and surface rendering with the intrahepatic vascular branches reaching the level of 3-4 [9]. Based on the automatically generated liver contour and vascular model, clinicians and radiologists should work together to determine, manually check and modify the lesion scope to ensure the accuracy of reconstruction.

Recommendation: For patients with complex liver tumors scheduled for hepatectomy, clinicians and radiologists should cooperate to establish a standardized and individualized 3D visualization model (strong recommendation).

3　Individualized classification and quantitative analysis of blood vessels based on 3D visualization

Anatomical variations of the hepatic artery [10], hepatic vein[11] and portal vein[12] are common. A 3D visualization analyses of these blood vessels identify (1) the 3D distribution of blood vessels; (2) the course and variation of blood vessels, and (3) their spatial relationship with the tumors. Priority should be given to the assessment of vascular variations, which is helpful to the selection of a hepatectomy plane. The distance between the tumor and adjacent important vessels can be accurately estimated by classification according to the degree of compression or invasion of various blood vessels and vessels involved in the liver [13]. Accurate individualized vascular classification and quantitative analysis have important significance for guiding clinical diagnosis, surgical planning, and implementation of precision surgery.

3.1　Individualized arterial classification with 3D visualization

The incidence of hepatic artery variation is approximately 45%. Michels et al[10] divided them into 10 types. In type I, the common hepatic artery is from coeliac trunk artery; in type II, the left hepatic artery is from left gastric artery; in type III, right hepatic artery is from the superior mesenteric artery; in type IV, the left hepatic artery is from the left gastric artery, and the right hepatic artery is from the superior mesenteric artery; in type V, the accessory left hepatic artery is from the left gastric artery; in type VI, the accessory right hepatic artery is from the superior mesenteric artery; in type VII, the accessory left hepatic artery is from the left gastric artery, and the accessory right hepatic artery is from the superior mesenteric artery; in type VIII, the accessory left hepatic artery is from the left gastric artery, the right hepatic artery is from the superior mesenteric artery (or the left hepatic artery is from the left gastric artery), and the accessory right hepatic artery is from the superior mesenteric artery; in type IX, the common hepatic artery is from the superior mesenteric artery; in type X, the common hepatic artery is from the left gastric artery;

Recommendation: For patients with complex liver tumors scheduled for hepatectomy, these variations identified through 3D visualization analysis of the hepatic artery is crucial to clinical diagnosis, interventional therapy, and guiding precision surgery (weak recommendation).

3.2　Individualized portal vein classification with 3DVT[12]

The variation of the portal vein is also common, which can be classified into 5 types according to the analysis by 3DVT. These variations include: (1) the normal type, where the main portal vein is divided into left and right branches in the porta hepatis; (2) Type I variation, where the main portal vein is divided into left, right anterior and right posterior branches, resembling a trident; (3) Type II variation, where the main portal vein sends out the right posterior branch and then goes upward to divide into left and right anterior branches; (4) Type III variation, where the right portal vein is divided horizontally into anterior and posterior branches; and (5) Type IV variation, where the horizontal part of the left portal vein is missing, in rare cases, the left portal vein is from the right anterior branch.

Recommendation: For patients undergoing hepatectomy for complex liver tumors, portal vein classification based on 3DVT is recommended to understand the vascular course, variations and its spatial relationship with tumors

Tab.2 Process Measures

	Criteria	Points
1	Diagnosis of liver diseases by preoperative imaging (ultrasound, CT or MRI)	+1
2	Patients fast for at least 4 hours prior to the CT scan, orally take 0.5 L-1.0 L of clear liquid 20 to 30 mins before the exam and take another 500 ml before the exam.	+1
3	Train the patient to hold their breath in full inspiration before scanning and instruct them to do so during each scan phase to achieve maximum management of artifacts due to respiratory motion.	+1
4	Select 64-slice or above spiral CT scanning with a slice thickness of 0.625 to 1.0 mm.	+1
5	CT scanning ranges from the top of the diaphragm to the lower level of both kidneys, and perform dynamic abdominal scan after intravenous contrast medium administration; perform CT celiac arteriography. The arterial phase, portal venous phase and delayed phase scans start at a delay of 20-25 s, 50-55 s, and 2 minutes, respectively.	+1
6	3D reconstruction should be performed by attending physicians or a level above who are engaged in the diagnosis and treatment of liver diseases.	+1
7	Evaluate the integrity of the course, shape and continuity of hepatic artery reconstructed by 3D visualization to determine whether a manual revision is required (manual revision is unnecessary when the tertiary branches of artery can be reconstructed).	+1 (no manual revision); -1 (manual revision required)
8	Evaluate the integrity of the course, morphology and continuity of hepatic vein reconstructed by 3D visualization to determine whether a manual revision is required (Manual revision is unnecessary if the tertiary branches of hepatic vein can be reconstructed).	+1 (no manual revision); -1(manual revision required)
9	Evaluate the integrity of the course, morphology and continuity of portal vein reconstructed by 3D visualization to determine whether a manual revision is required. The branches of the portal vein system with the diameter ⩾5 mm should be reconstructed (it is unnecessary if the tertiary branches of portal vein can be reconstructed)	+1 (no manual revision); -1(manual revision required)
10	Evaluate its course, morphology, continuity and integrity of the 3D reconstructed biliary tract (manual revision is unnecessary if the tertiary branches of the biliary tree can be reconstructed).	+1 (biliary system reconstructed); -1 (no biliary system reconstructed)
11	Evaluate the morphology, size and distribution of lesions in the 3D reconstructed model and whether they are consistent with CT images.	+3 (basically consistent, no manual revision required); +2 (mostly consistent, manual revision required); -1 (inconsistent, manual revision required)
12	The overall 3D model should be validated by at least 2 abdominal imaging attendings and at least 2 attending hepatologists in comparison with the original CT images, and finally confirmed by a senior physician.	+1
13	Perform simulation surgery based on the 3D model. The simulation of various schemes should be carried out, and the optimal surgical approach and surgical resection plane should be selected by two attending physicians, and finally confirmed by a senior physician.	+2
14	A multi-disciplinary team (MDT) should be formed based on the individualized 3D model and the results of clinical examinations; liver surgeons undertake the main tasks, assisted by the departments of hepatology, oncology, endoscopy, interventional therapy and radiotherapy.	+2
15	The consistency between preoperative 3D models and intraoperative conditions (lesions, vascular variance and range of hepatectomy) should be assessed.	+3 (completely consistent); +2 (basically consistent); -1(inconsistent)
16	The volume of the virtual resected liver should be compared with that of the actual resected liver (reference standard is intraoperative dewatering method). The volume error (<5%) is completely consistent, the volume error (<10%) is basically consistent, and the volume error (>10%) is inconsistent.	+3 (completely consistent); +2 (basically consistent); -1 (inconsistent)
Total score (24, 100%)		

(strong recommendation).

3.3 Individualized three-dimensional visualization hepatic vein classification[11]

In hepatic surgery, the vascular control of hepatic vein is crucial to the entire procedure. It is important to summarize the character of hepatic vein and identify the variations to reserve normal hepatic tissues to the greatest extent. Based on the research on the classification of hepatic vein using 3D visualization technology, the variation of inferior right hepatic vein and hepatic veins for segments IV and VIII are more valuable for hepatic surgery.

Recommendation: In the formulation of surgical plans, it is necessary to classify hepatic veins based on 3D visualization technology, especially the variation of right inferior hepatic vein, and the veins for segments IV and VIII.

4 3DVT-based classification and grading of hepatic vessels for complex hepatic tumors[14-15]

Hepatectomy mainly involves the portal vein, hepatic vein, inferior vena cava and hepatic artery system. Therefore, this guideline proposes a 3DVT-based classification system for hepatic vessels for complex liver tumors to guide the operation (Tab.3).

Tab.3 Three-dimensional visualization classification of complicated hepatocellular carcinoma

Type	Grading
Type I: Tumor involving portal vein	
Type I a: Tumor involving the right branch of portal vein	
Type I b: Tumor involving the left branch of portal vein	
Type II: Tumor involving hepatic vein	Grade 0: Vessels are not compressed by tumors.
Type II a: Tumor involving right hepatic vein	
Type IIb: Tumor involving middle hepatic vein	Grade 1: Vessels are compressed but not invaded by tumors.
Type II c: Tumor involving left hepatic vein	Grade 2: Vessels are invaded but not interrupted by tumors.
Type III: Tumor involving hepatic artery	
Type III a: Tumor involving right hepatic artery	
Type III b: Tumor involving left hepatic artery	Grade 3: Tumor invasion with continuity interruption of blood vessels
Type IV: Tumor involving inferior vena cava	
Type V: Tumor involving abdominal aorta	

Recommendation: Hepatic vessels of complex liver tumors should be classified by 3DVT to provide anatomical guidance for hepatectomy (weak recommendation).

5 Evaluation system for surgery simulation after 3D visualization model reconstruction

5.1 3DVT-based individualized liver segmentation

The Couinaud classification in clinical use benefits from the results of in vitro liver cast study, and its coincidence rate is only 20%-30% among the general population. If digital medical technology can be used in liver segmentation, the individualized segmental partition can be performed based on blood topological relation for each patient and displayed in 3D visualization images. Each functional segment is supplied by the portal vein and drained by the hepatic vein[16]. There could be segments 7, 9, or 10 when intrahepatic vascular variation occurs. Regular and irregular liver segments can be precisely divided using 3DVT. Therefore, individualization can be achieved to increase the accuracy practically.

Recommendation: For patients undergoing hepatectomy for complex liver tumors, individualized liver segmentation should be performed before surgery (strong recommendation)

5.2 Individualized liver volume calculation based on 3DVT

Currently, there are 3 approaches to calculate the liver volume: (1) the computational formula of the liver volume[17]; (2) manual volumetry based on sectional data such as CT images[18]; (3) 3D reconstruction of CT images, through which the liver volume was calculated by 3D reconstruction based on the principle of voxel[19].

When the software is developed, the sum of dots (voxel) of the liver volume is calculated. Drainage and standard block methods are used to measure and proofread the volume. Total volume divided by the total dots makes the volume, and then the standard for the volume represented by each dot is obtained. Reports have shown that 3DVT-based calculation achieves accurate estimation of the liver volume[20-21].

Recommendation: For patients undergoing hepatectomy for complex liver tumors, individualized liver volumetry should be performed before surgery (strong recommendation).

5.3 Preoperative simulation surgery

The 3D model is imported into the simulation surgical system when individualized liver segmentation and volumetry are completed. By using the virtual environment, simulation surgical instruments and force feedback devices created by this system, simulation surgery is performed on the reconstructed 3D model to better understand the tumor location and the spatial relationship between the tumor and the intrahepatic vascular systems.

Recommendation: Preoperative simulation surgery could be performed when the hospital has adequate equipment. In recent years, for patients who may

potentially have insufficient remnant liver volume or who can not receive a major hepatectomy, partial associating liver partition and portal vein ligation for staged hepatectomy or portal vein embolization can be an option (weak recommendation).

6 Application of 3D printing in complex hepatectomy[22]

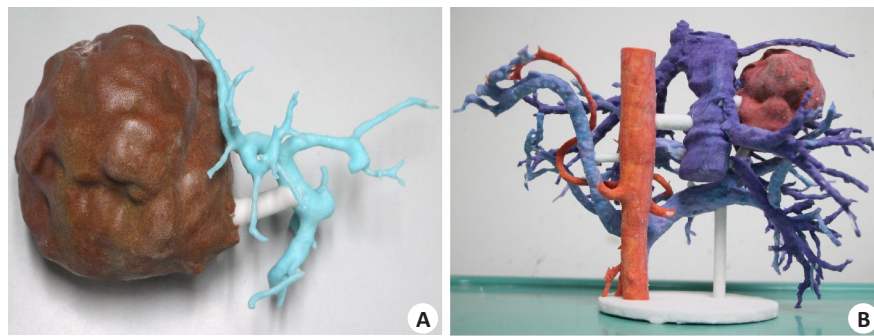The 3D printed model based on 3DVT can faithfully represent the characteristics of the intracorporeal organs (Fig.1). With this technique, the location, size and shape of the tumor are faithfully represented, and the spatial relationship between the tumor and the vascular systems can be observed from different angles; this technique also provides real-time indirect navigation during the surgery and allows rapid recognition and localization of the vital positions.

Recommendation: For patients undergoing hepatectomy

Fig.1 Complex hepatectomy guided by 3D printing technology. **A**: A 3D printing model of rare vascular aberration (segment IV portal vein stems from the right anterior branch); **B**: Type III variation of the portal vein and the inferior right hepatic vein draining into the inferior vena cava (posterior view).

for complex liver tumors, preoperative 3D printing can be used to guide surgery if the essential equipment is available (weak recommendation).

7 Virtual reality (VR) technology[4, 14-15]

VR technology provides surgeons with a variety of sensory simulations for preoperative planning and enriches the understanding of pathological changes. The STL format file of the 3D visualization model of complex liver tumors is imported into Unreal Engine 4 (UE4), and modeled in the VR environment. The individualized 3D model can be displayed in the VR environment. The operators can be integrated into the VR environment by wearing VR glasses and manipulating handles. Through the immersive human-computer interaction mode, the patients' individualized 3D model can be observed and manipulated stereoscopically in a manner closer to the real surgical experience.

Recommendation: It is suggested that a preoperative VR study be performed for patients scheduled for hepatectomy for complex liver tumors when adequate equipment is available (weak recommendation).

8 Indocyanine green (ICG)-fluorescence imaging

ICG fluorescence imaging can help to define the demarcation of tumors at the molecular and cellular levels, determine the resection line of lobe or segmental hepatectomy and detect small lesions or metastases. During the operation, the liver should be scanned using fluorescence detection equipment. The characteristics of the fluorescence signal of liver tumors and intraoperative rapid frozen pathology reports can be combined to preliminarily determine the differentiation degree of the space-occupying lesions in the liver (such as primary liver cancer). The residual tumor lesions and bile leakage can also be detected on the liver section after hepatectomy [23] to guide anatomical, functional, and radical hepatectomy for liver cancer[24].

Recommendation: ICG fluorescence detection should be performed preoperatively and intraoperatively in patients undergoing liver resection for complex hepatic tumors. Positive staining, negative staining or ultrasound-guided portal vein puncture and segmental staining can be selected during surgery according to the requirements of the surgical planning (strong recommendation).

9 Multi-modal images for real-time navigation[25]

Preoperatively, the portal venous-phase CT images and Gd-EOB-DTPA-enhanced MRI images are automatically registered and fused by the Mitworkbetch software. The fusion of CT-MRI images can provide more pathological information and improve the accuracy of diagnosis. At the same time, the CT-MRI-based 3D model and the virtual surgical images reconstructed are brought into the operating room to guide the critical procedures of the operation. The use of ICG fluorescence imaging makes possible the fusion of multi-modal images, which helps to define tumor demarcation, detect small lesions, and improve surgical precision[9]. Besides, during 3D surgical planning before the actual operation, the issues such as spatial and temporal separation and the lack of accuracy can be addressed by enhanced reality technology combined with multi-modal images to achieve a satisfactory real-time navigation effect.

Recommendation: Real-time navigation with multi-modal image fusion can be used in hepatectomy for hepatic tumors when adequate equipment is available (weak recommendation).

10 Surgical planning for 3DVT-guided precision hepatectomy

10.1 Surgical planning for complex hepatectomy in cases of hepatic vein variations

While it is challenging to detect hepatic vein variation with CT or MRI, 3DVT can display these variations in individual patients. The anatomy and variations of the segment IV and the inferior right hepatic vein are crucial in right hemihepatectomy. The segment IV vein drains mainly into the left and middle hepatic veins. Fig.2 shows that in a specific case where the segment IV hepatic vein drains into the left hepatic vein, removal of the middle hepatic vein is safe in right hemihepatectomy[26].

Recommendation: For patients undergoing right hemihepatectomy for liver tumors, 3DVT helps to identify the segment IV and the inferior right hepatic veins (strong recommendation).

10.2 Surgical planning for complex hepatectomy in cases of portal vein variations

With 3DVT, the course and variation of the portal vein can be clearly displayed preoperatively. Adequate surgical planning based on the variation types of the portal vein can significantly reduce the risk of vascular injuries and preserve more hepatic tissues, as exemplified by narrow-margin right hemihepatectomy in cases of type III variation of the portal vein (Fig.3) or in cases of specific variations of the portal vein. The segment IV of the portal vein stems from the right anterior branch. In a right hemihepatectomy, the trunk of the right portal vein needs to be severed, which causes insufficiency in blood supply of the segment IV. In such cases, narrow-margin right hemihepatectomy is a better option. Segment 4 of the portal vein from the right anterior branch is separated and protected, and the narrow-margin right hemihepatectomy is then performed (Fig.4).

Recommendation: For patients undergoing hepatectomy for complex liver tumors, preoperative analysis using 3DVT is essential, which helps to identify and classify potential variations of the portal vein, determine liver segmentation and calculate the volume, thus facilitating the decision-making on the surgical plan (strong recommendation).

10.3 Narrow-margin hepatectomy is a choice in patients with insufficient liver volume following hepatectomy[27]

Narrow-margin right hemihepatectomy is an innovative procedure for the treatment of right hepatic tumor(s) in cases where (1) post hepatectomy liver failure may occur if standard right hemihepatectomy is performed; (2) parts of the sections V and VIII are preserved after partial right hepatectomy; (3) a normal type of the right portal veins is found, and the residual hepatic cross-section meets the requirements of the guidelines; and (4) the stub of the portal vein in sections VI and VII or the right posterior portal vein can be seen after hepatectomy. In such a complex hepatectomy, 3DVT can display the vessels that need to be severed or preserved, thus helping to preserve sufficient residual liver and maximally ensure the safety of the patient during tumor removal (Fig.5).
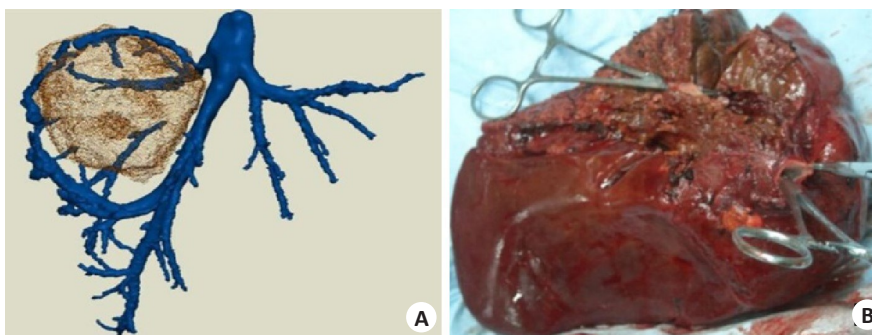

Fig.2 Three-dimensional visualization technology displays the middle hepatic vein to be removed in right hemihepatectomy. (**A**) the removed tissues in the actual operation (**B**). The tumor is located in the right liver, and the segment IV hepatic vein drains into the left hepatic vein, so segment IV is not affected after removal of the middle hepatic vein.
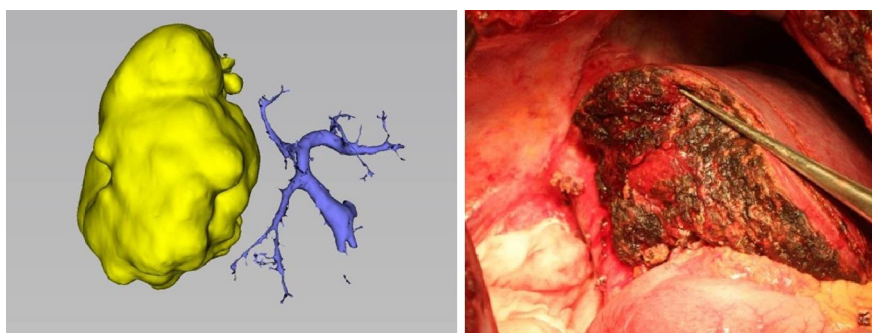

Fig.3 Narrow margin right hemihepatectomy is chosen for patients with type III variation of portal vein.
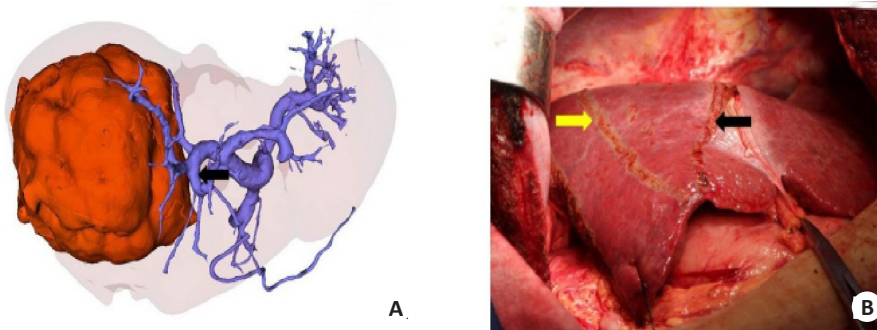
Fig.4 Preoperative surgical planning and actual operation of complex hepatectomy in a patient with anatomical variation of the portal vein. **A**: Blood supply of segment IV from the right portal vein is shown in three-dimensional visualization image (black arrow); **B**: Temporary blocking the trunk of the right portal vein shows that the ischemia area is around the falciform ligament (black arrow indicates the boundary of the right three sections, and the yellow arrow indicates the actual boundary of the left and right liver). The narrow margin right hemihepatectomy is performed and some part of segment V and VIII is preserved.
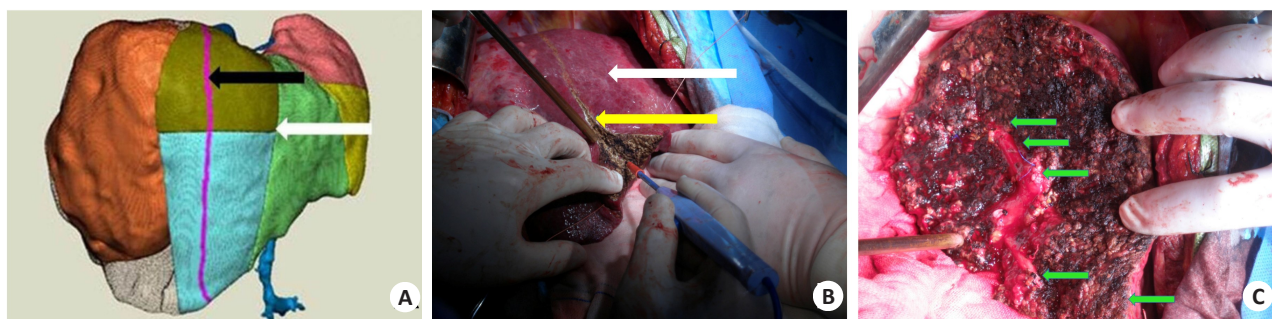

Fig.5 Narrow-margin right hemihepatectomy guided by 3DVT. **A**: Preoperative surgical planning based on 3DVT (the white arrow indicates the boundary of left and right liver, and the black arrow points the boundary of narrow-margin right hemihepatectomy); **B**: In the actual procedure, the yellow arrow shows the boundary of narrow-margin right hemihepatectomy and the white arrow shows the boundary of the left and right liver; **C**: The course of segments V and VIII portal vein and the nub of segments VI and VII are observed in the dissected plane after removal of the tumor.

Recommendation: 3DVT-guided narrow-margin right hemihepatectomy is a choice for patients with insufficient liver volume after right hemihepatectomy. Precision removal of the lesion can be performed to ensure the patient's residual liver function and surgical safety (strong recommendation).

10.4 3DVT-based classification and surgical planning for centrally located liver tumors

A centrally located liver tumor refers to one located mainly in segments I, IV, V, and VIII. Due to its particular location and involvement of the important intrahepatic vascular system, the resection of such tumors can be extremely difficult and risky. The application of 3DVT better ensures the surgical safety by allowing individualized preoperative surgical planning [13-14] (Tab.4).

Recommendation: For centrally located liver tumors, 3DVT-based classification and surgical planning can be essential to preserve more liver parenchyma and achieve the goal of precision hepatectomy (strong recommendation).

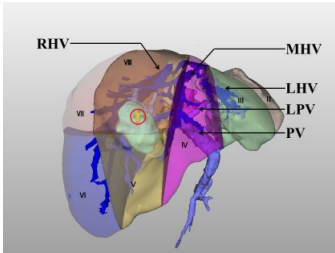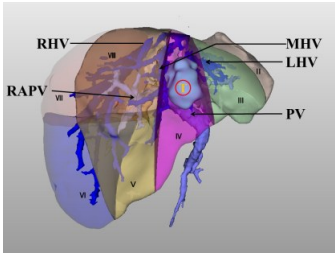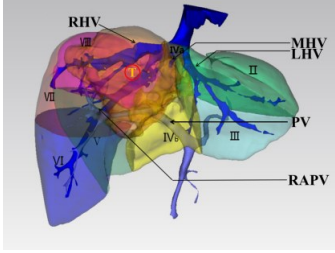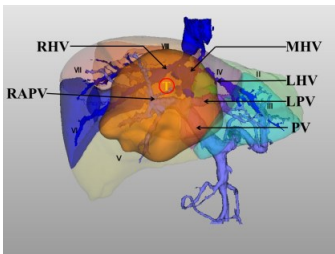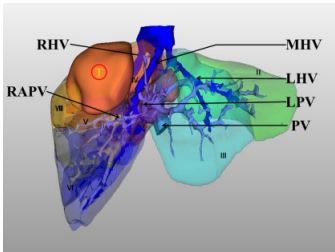### 11 3DVT guidance for other therapeutic methods of hepatocellular carcinoma

Transarterial chemoembolization (TACE) is a useful treatment modality for hepatocellular carcinoma [28]. With 3DVT, the main blood artery supply and its small branches supplying the tumor can be displayed, and the hepatic artery variations can be assessed in an accurate 3D "vessel-tumor" model. 3DVT also provides a preoperative 3D approach to radiofrequency ablation and argon-helium knife technology for percutaneous liver tumors and allows accurate measurement of the volume of intraoperative electrode probe failure range.

Recommendation: For patients undergoing TACE, tumor ablation, and argon-helium knife, 3DVT can be used to evaluate the condition of the hepatic artery (weak recommendation).

12 Application of 3DVT in postoperative follow-up of patients with liver cancer

No matter what treatment procedures are chosen for patients with hepatocellular carcinoma, regular follow-up of the patients is essential. Ultrasonography [29], hepatic tri-phase contrast-enhanced helical CT, and Gd-EOB-DTPA-enhanced MR imaging [30] are used to track the outcomes of the patients dynamically. In cases experiencing neoplasm recurrence, reevaluation with

Tab.4 3D visualization classification and surgical planning for centrally located liver tumor

Classification	Description	Surgical methods
	Type I: The tumor is in the liver parenchyma of segments V, VIII, or both, characterized by their close proximity to or even direct invasion of the adjacent portal vein. They do not adhere to or compress the right hepatic vein trunk.	Resection of segments V, VIII ± partial resection of segment IV
	Type II: The tumor is in the liver parenchyma of segments IV a, IV b, or both, characterized by its proximity to or even direct invasion of the left hepatic vein trunk. In addition, it does not adhere to or compress the left hepatic vein trunk.	Resection of segments IV a and IV b or left hepatectomy
	Type III: The tumor occupies most liver parenchyma of segments IV, V, and VIII, characterized by a wide and deep invasion of the parenchyma, or their proximity to the middle hepatic vein.	Central bisectionectomy (resection of segments IV, V, and VIII ± I)
	Type IV: This type of liver tumor occupies most liver parenchyma of segments IV, V, and VIII, characterized by their close proximity to, or direct invasion of, the left/right portal vein trunk or the left/right hepatic vein.	Resection of segment IV, V, VI, VII, VIII. Resection of segment II, III, IV, V, VIII. Reduced right trisectionectomy or reduced left trisectionectomy. Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS).
	Type V: This type of liver tumor occupies the superficial liver parenchyma of segments IV, V and VIII. The lesions are not close to either the portal branch or the hepatic vein.	Hepatectomy with a negative margin

3DVT can provide 3D anatomical evidence for guiding the treatment.

Recommendation: Ultrasonography, hepatic tri-phase contrast-enhanced helical CT and Gd-EOB-DTPA-enhanced MR imaging should be performed regularly in postoperative patients. Comparing the 3D reconstruction results with the preoperative 3D images may help in the dynamic monitoring of tumor recurrence.

Conclusion

In the clinical setting, hepatectomy for complex liver tumors poses a challenge. 3DVT shows obvious advantages over conventional 2D imaging modalities in the treatment of complex liver tumors. Real-time guidance by ultrasonography is also vital to enhance the accuracy of surgical operation. For patients undergoing hepatectomy, adequate protection of the liver function during the perioperative period is of equal importance to the surgical techniques[31-32].

In conclusion, for patients undergoing hepatectomy for complex liver tumors and those who are tentatively diagnosed by ultrasonography and CT, 3DVT-based analysis of the target lesion is recommended due to high risk and difficulty in the surgical operation. Hepatic 3D

printing evaluation, VR evaluation, and intraoperative ICG fluorescence detection can be used when equipment is available. These technologies are expected to play significant roles in enhancing the precisions of preoperative diagnosis and surgical operations and in improving the outcomes of the patients with complex liver tumors.

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中华医学会数字医学分会；中国医师协会肝癌专业委员会；中国医师协会临床精准医学专业委员会；中国研究型医院学会数字智能化外科专业委员会

摘要：基于肝脏三维可视化的虚拟肝切除在中国得到越来越广泛的应用，为肝脏肿瘤精确诊断、术前评估、手术规划和术中精准指导提供了安全而有效的方法，该技术在复杂性肝脏肿瘤诊治中的技术优势及重要意义也已逐渐得到认可。为规范三维可视化技术在复杂性肝脏肿瘤的精准诊疗中的应用，本指南对以下几个方面进行了研究：（1）三维重建同质化处理与质控体系的建立；（2）个体化腹腔器官和病灶的三维可视化模型的建立；（3）三维可视化个体化血管分型和量化分析；（4）复杂性肝脏肿瘤肝脏血管三维可视化分型、分级；（5）三维可视化模型建立后的手术模拟评估体系；（6）三维可视化肝脏3D打印在复杂性肝切除术的应用；（7）虚拟现实技术；（8）ICG分子荧光成像；（9）多模图像融合实时导航技术；（10）三维可视化指导精准复杂性肝切除术的术前规划；（11）三维可视化技术对肝癌其他治疗手段的指导作用；（12）三维可视化技术对肝癌手术后复查的指导作用。肝脏三维可视化技术为复杂性肝脏肿瘤的术前精准评估病情、术前规划、手术导航等实施提供了新的方法，为病人获得最佳的康复效果发挥强而有力的支持作用，具有重要的临床应用价值。

关键词：三维可视化/3D打印；虚拟现实；荧光影像；复杂性肝脏肿瘤；解剖性/功能性/根治术/肝切除术