Retrospective Study

Three-dimensional morphometric analysis for hepatectomy of centrally located hepatocellular carcinoma: A pilot study

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Abstract

AIM: To describe a three-dimensional model (3DM) to accurately reconstruct anatomic relationships of centrally located hepatocellular carcinomas (HCCs).

METHODS: From March 2013 to July 2014, reconstructions and visual simulations of centrally located HCCs were performed in 39 patients using a 3D subject-based computed tomography (CT) model with custom-developed software. CT images were used for the 3D reconstruction of Couinaud’s pedicles and hepatic veins, and the calculation of corresponding tumor territories and hepatic segments was performed using Yorktal DMIT software. The respective volume, surgical margin, and simulated virtual resection of tumors were also estimated by this model preoperatively. In addition, all patients were treated surgically and the results were retrospectively assessed. Clinical characteristics, imaging data, procedure variables, pathologic features, and postoperative data were recorded and compared to determine the reliability of the model.

RESULTS: 3D reconstruction allowed stereoscopic identification of the spatial relationships between physiologic and pathologic structures, and offered quantifiable liver resection proposals based on individualized liver anatomy. The predicted values were consistent with the actual values for tumor mass volume ($82.4 \pm 109.1$ mL vs $84.1 \pm 108.9$ mL, $P = 0.910$), surgical margin ($10.1 \pm 6.2$ mm vs $9.1 \pm 5.9$ mm, $P = 0.488$), and maximum tumor diameter ($4.61 \pm 2.16$ cm vs $4.53 \pm 2.14$ cm, $P = 0.871$). In addition,
the number and extent of portal venous ramifications, as well as their relation to hepatic veins, were visualized. Preoperative planning based on simulated resection facilitated complete resection of large tumors located in the confluence of major vessels. And most of the predicted data were correlated with intraoperative findings.

CONCLUSION: This 3DM provides quantitative morphometry of tumor masses and a stereo-relationship with adjacent structures, thus providing a promising technique for the management of centrally located HCCs.

Key words: Centrally located; Hepatectomy; Hepatocellular carcinoma; Liver; Three-dimensional model

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Core tip: Relatively accurate and convenient measurements of morphometric parameters of tumor masses using radiology is important for planning surgical strategy, especially for centrally located hepatic tumors, which should be individualized in each patient with the aim of preserving major vascular branches. In this study, we describe a three-dimensional model to accurately reconstruct the relationships between the tumor, hepatic veins, and Glissonian pedicles for centrally located hepatocellular carcinomas, which is essential for correctly defining the hepatic segments and the limits of tumors with wide variations in anatomy.

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INTRODUCTION

Centrally located hepatocellular carcinomas (HCCs) are traditionally characterized as tumors in Couinaud’s segments IV, V, or VIII of the liver. Extensive major hepatectomy or mesohepatectomy often offers the best chance of cure. However, extensive hepatectomy may sacrifice a large amount of functioning liver and result in suboptimal residual liver volume, causing hepatic failure or death. The en bloc resection of Goldsmith and Woodburne’s left medial and right anterior segments or Couinaud’s segments IV, V, and VIII (mesohepatectomy) have always been satisfactory, but are technically demanding, and often can not be performed safely or are associated with a high risk of tumor recurrence. Therefore, a mathematic finite element model which can demonstrate the structural relationship and provide relatively accurate staging of hepatic tumor masses is urgently required. In addition, such a model is also crucial for determining appropriate treatment, guiding operative strategy, and predicting the prognosis of patients with centrally located HCCs.

The diagnosis of intrahepatic masses has significantly changed over the past decade from the use of invasive procedures such as angiography or biopsy to noninvasive imaging including contrast-enhanced ultrasound (US), multidetector-row computed tomography (MDCT), and magnetic resonance imaging (MRI). CT is the most commonly used imaging modality in diagnosing intrahepatic masses due to its widespread availability and short examination time, and it was estimated that the overall accuracy of MDCT for detection and characterization of HCC was 89% and 43%, respectively, compared with pathologic examination. In addition, MDCT provides detailed mapping and assessment of hepatic arteries, portal veins, and hepatic veins, which can be reconstructed to provide angiographic pictures and is able to replace direct angiograms. However, the anatomic and vascular pathologic details provided by the MDCT scanners do not completely meet the requirements for preoperative planning.

Considering the known difficulties of virtual simulation of centrally located tumor masses by radiologic imaging, we constructed a three-dimensional morphometric analysis model (3DM) of tumor reconstruction with custom-made software, as only a few studies have explored the accuracy and reliability of data-processing using 3D models. A risk analysis was also included in the preoperative planning by calculating the volume of tumor and peritumor territories and visualizing the relationships between the masses, portal veins, hepatic veins, and bile ducts, which is essential for correctly defining the hepatic segments, as well as the limits of a tumor with wide variations in anatomy. Therefore, the aims of this study were to describe a customized application framework using Yorktal DMIT software for the 3DM reconstruction and assessment of the morphology of centrally located HCCs on the basis of micro-CT data, and to analyze its reliability in pre- and intraoperative assessment.

MATERIALS AND METHODS

Study participants

Fifty-three patients with complex centrally located HCC masses referred to our institution for surgical treatment from March 2013 to July 2014 were retrospectively investigated in this study. We used a revised definition for centrally located HCC, previously described as “carcinoma adjoined to the porta hepatitis, < 1 cm from major vascular structures [including the inferior vena cava (IVC), main portal branches, and main trunks of the hepatic veins] and usually located in Couinaud’s segment I, IV, V, VIII, or at the junction of the central
multiphase CT scans were obtained using a 64-section addision, different functional application frameworks format was transferred from Dicom to Bitmap. In module encapsulates a specific function. Parameters the operation interface are called modules, and each its graphic user interface (Figure 1). The boxes on provides a visual data processing environment on 3D models of the hepatic anatomy. The DMIT package dimensional CT images to generate highly accurate processing. It is used for the segmentation of two- arteriovenous phase, and 150 s to the end of the portal phases were obtained by adding 18 s to the time of peak aortic enhancement, 30 s to the end of arterial phase, and 150 s to the end of the portal venous phase, respectively. Scanning parameters were as follows: collimation, 64 rows × 0.5 mm; gantry rotation speed, 0.6 s; section thickness, 5 mm; image reconstruction increment, 1 mm; 12 kVp; and effective tube current-time charge, 450 mAs.

CT scanning All patients underwent three-phase dynamic contrast-enhanced CT at initial diagnosis. Contrast-enhanced multiphase CT scans were obtained using a 64-section scanner (Light Speed VCT; General Electric Corp., Fairfield, CT, United States). Arterial, portal venous, and delayed phases were obtained by adding 18 s to the time of peak aortic enhancement, 30 s to the end of arterial phase, and 150 s to the end of the portal venous phase, respectively. Scanning parameters were as follows: collimation, 64 rows × 0.5 mm; gantry rotation speed, 0.6 s; section thickness, 5 mm; image reconstruction increment, 1 mm; 12 kVp; and effective tube current-time charge, 450 mAs.

Description of the application framework DMIT is software specifically developed by the Yorktal Corporation (Shenzhen, China) for medical image processing. It is used for the segmentation of two-dimensional CT images to generate highly accurate 3D models of the hepatic anatomy. The DMIT package provides a visual data processing environment on its graphic user interface (Figure 1). The boxes on the operation interface are called modules, and each module encapsulates a specific function. Parameters measured by CT were imported and included in the customized application framework, and then the data format was transferred from Dicom to Bitmap. In addition, different functional application frameworks can be established with different image modules (Figure 1), which can be combined with complex image processing networks. Taken as a whole, the various modules comprise a data-flow framework.

3D finite element modeling The 3D simulation model was composed of Couinaud’s segments 1975, revised in 1983). All eligible patients were provided written informed consent. This study was approved by the Ethical Committee of the Cancer Institute and Hospital of the Chinese Academy of Medical Science and was performed in accordance with principles of Good Clinical Practice and Declaration of Helsinki guidelines (1975, revised in 1983).

Volume calculation Quantitative information on the volumes of the eight Couinaud’s segments, removed tumor masses, nontumorous parenchyma of the resected liver, and the untouched surface during canal preparation was obtained. The volume of the corresponding sub-territory at risk of an impaired hepatic venous outflow or portal vein inflow was also calculated and formed the basis of the ratio analysis. The volume of large vessels, including the inferior vena cava and the extrahepatic portal vein, the major fissures, and the gallbladder fossa were excluded. The functional liver mass was calculated by subtracting the volume of the potentially resected and blood supply affected zone from the mass of the remnant liver. Thresholds for the ratio of functional liver mass to nontumorous parenchymal volume of the whole liver were set at 50% and 40%, respectively, for patients with chronic liver diseases and without underlying liver disease to predict the resectability of hepatic tumor mass. When the ratio exceeded the threshold, the resection was
based on the direction and diameter of the hepatic vessels was also carried out. By using this method for data analysis, individualized territories that were supplied or drained by a certain vascular branch were fully identified automatically.

Resection margin
Preoperative resection margin was estimated by measuring the minimal distance between the remnant parenchymal border and tumor rim in the predicted resection plane. We calculated the distance in a preinstalled algorithm where the predicted margin equaled the distance between slice thresholds. Postoperative actual resection margin was measured by calculating minimal vertical parenchymal thickness in the resected tumor specimen surface. The preoperative estimated and postoperative actual resection margins were then compared to assess the accuracy of the 3DM.

Virtual resection and surgical guiding
The operative procedure for liver resection was then imitated in this complex image-processing network. Environments for anatomic curative resections defined as mesohepatectomy (removal of segments IV, V, and VIII), right anterior sectionectomy (removal of segments V and VIII), segment IV resection, caudate lobe resection, or other non-anatomic irregular hepatectomies were established according to tumor size, location, degree of hepatic cirrhosis, and individual resection ranges in individual patients. The

considered safe. If the calculated functional liver mass of the remnant was below the currently accepted limits, the planned procedure carries a high risk for the development of a small-for-size syndrome.

A specialist in mathematics was invited to assist this study in assessing the corresponding volumes in order to monitor software calculation deviation. The verification formula was as follows:

\[ V = \frac{M}{\Sigma} \frac{d}{\Sigma} \frac{N_i}{\Sigma} \frac{L_{ij}}{\Sigma} \]

where \( d \) is distance between the two layers, \( e \) is distance between the two lines, \( M \) is the number of layers, \( N_i \) is the number of lines in layer \( i \), and \( L_{ij} \) is the length of line \( j \) in layer \( i \). The data were then compared with those obtained from the software workstation to monitor reliability.

Vessel quantitative analysis
The enhanced CT data of the vessels were extracted automatically using a standard threshold technique due to the use of a contrast agent. An algorithm based on the fractal approach recognized the vessels starting from a seed point near the major branches and gradually searched for all ramification structures with a diameter > 1 mm. The transectional diameter and bending angle of vessel canals were also calculated with individualized wide variations, allowing intuitive interpretation and measurement (Figure 2). The resulting vessel tree was visualized using different colors for the hepatic artery, portal vein and hepatic vein systems. Calculation of the portal venous supply and the hepatic venous drainage area in each area based on the direction and diameter of the hepatic vessels was also carried out. By using this method for data analysis, individualized territories that were supplied or drained by a certain vascular branch were fully identified automatically.

Figure 1  Data processing environment (yellow arrow) was demonstrated by the DMIT software package, and each module encapsulated a specific function. A: Transverse; B: Sagittal; C: Coronal sections were dissected and reconstructed on its D: Graphic user interface.
established 3DM of the liver was then imported to the intraoperative computer workstation to guide the surgical resection of hepatic tumor masses, which was viewed from the visceral and diaphragmatic surfaces, and simulation of the whole process was also performed with a virtual irregular dissection plane in the system. Prior to division of the parenchyma, a selective and dynamic region-specific vascular occlusion (SDRVO) technique\(^{(1)}\) was also used and appropriate areas were selected for inflow hepatic blood occlusion depending on tumor location and the resection area. In cases where tumors were adherent to major vascular structures, we carefully dissected and resected lesions away from the vascular surface using a cavitation ultrasonic surgical aspirator (CUSA). When vascular wall injury or rupture occurred, stay sutures were applied for control of hemostasis and bile leaks. From the workstation, we also investigated the cross-sectional images before and after canal preparation and calculated the untouched surface in the canal preparation three-dimensionally. The viewing direction and dissection plane were presented in the graphic interface and could be chosen arbitrarily. The relationship between the dissection plane and the tumor edge was followed in real time. With the direction of the dissection plane modified when needed, the remnant functional liver volume, venous territories, and affected vascular tree were automatically calculated (Figure 3). The ratio of pre-and postoperative volumes of sound liver tissue was

Figure 2 Vascular tree reconstruction. Reconstruction was based on A: Computed tomography data; B: Patient’s individual vascular territories for different vessel stratifications were calculated, including C, D: Specified angle, diameter, and length.

Figure 3 Virtual dissection plane. A: The plane was adjusted in real time; B: The corresponding liver volume was automatically calculated.
Results

Patients and tumor characteristics

The demographic, clinical, and pathologic characteristics of the 39 patients with a mean age of 54.3 ± 12.1 years (range: 32-80 years) are shown in Table 1. All patients had complete simulation data and subsequently underwent liver resection. Cirrhosis was found in 24 (61.6%) patients in the background liver on histological examination, with hepatitis B as the most common cause of chronic liver disease. All patients in this study had a liver function of Child-Pugh class A and the median 15 min retention rate of ICG (ICG-R15) was 5.2%. Three patients had an ICG-R15 > 20% and were high-risk patients for surgical treatment, but underwent successful hepatectomy. There was no 30-day operative mortality or serious complications that required additional surgery. Eight complication events occurred in six (6/39; 15.4%) patients. All these postoperative complications resolved after conservative treatment. Child-Pugh C status occurred transiently on postoperative day 7 in 4/39 (10.3%) patients, which was managed successfully when patients were discharged. The mean duration of postoperative hospitalization was 9.1 ± 2.3 d (range: 5-16 d).

Digitized 3DM

3D images of the liver, vascular system, bile duct system, and adjacent organs were reconstructed and the manipulation environment presented the model with high-quality visualization (Figure 4). The framework provided 3D quantitative information with a color-coded map of the five lobes and eight segments using Couinaud’s method, which quantified the characteristics of the internal and external anatomy of the tumor masses. Tumor infiltration of vessels, liver capsule, or adjacent tissues were identified and demonstrated more precisely compared with the original CT data. The hepatic artery, portal vein, and hepatic vein system were stained red, light blue, and dark blue, respectively. Individual segments or organs could be added or concealed arbitrarily to clearly represent the target structure. In cases where tumors were adherent to major vascular structures, the tumor masses were concealed to demonstrate whether intravascular invasion had occurred. In addition, the nutritional arteries for tumor tissue were also viewed to guide surgical operation and postoperative transarterial chemoembolization.

Statistical analysis

All values are expressed as a median or mean ± standard deviation. Student’s t-tests were used to evaluate the differences between comparisons. Correlations were presented as scatter plots and used to assess the predictive accuracy of the 3DM in preoperative evaluation of volume, resection margin, and tumor diameter. A P < 0.05 was considered statistically significant. All analyses were performed using SPSS 17.0 statistical software (SPSS Inc., Chicago, IL, United States). The statistical methods of this study were reviewed by a biostatistician from the medical statistical department in our hospital.

Table 1  Patient and tumor characteristics a (%) 

| Variables                  | Value   |
|----------------------------|---------|
| Gender                     |         |
| Male                       | 34 (87.1)|
| Female                     | 5 (12.9) |
| Hepatitis B carrier        | 37 (94.8)|
| Hepatitis C carrier        | 2 (5.1)  |
| ICG-R15                    | 7.1% ± 5.9% |
| Pathologic characteristics |         |
| Fibrosis score F0          | 15 (38.4) |
| Fibrosis score F1          | 24 (61.5) |
| Tumor diameter (cm)        | 4.5 ± 2.1 |
| Resection margin (mm)      | 9.1 ± 5.9 |
| Vascular adhesion          | 11 (28.2) |
| Liver capsule invasion     | 24 (61.5) |
| Major vascular invasion    | 3 (7.7)  |
| BCLC staging               |         |
| Stage A                    | 25 (64.1) |
| Stage B                    | 11 (28.2) |
| Stage C                    | 3 (7.7)  |
| Surgical procedure         |         |
| Hemi-hepatectomy           | 7 (17.9)  |
| Meshepatectomy             | 5 (12.8)  |
| Segmentectomy              | 13 (33.3) |
| Irregular resection        | 14 (35.9) |
| Postoperative complications|         |
| Massive hemorrhage         | 2 (5.1)  |
| Bile leakage               | 2 (5.1)  |
| Massive ascites            | 3 (7.7)  |
| Pleural effusion           | 1 (2.6)  |
| Hospital mortality         | 0 (0.0)  |

Data are expressed as mean ± SD or n (%). BCLC: Barcelona Clinic Liver Cancer; ICG: Indocyanine green.
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addition, a relatively large right posterior branch in five cases originated from the portal vein. At the second level ramification, the mean number of branches originating from the left and the right portal vein was 18 (range: 11-38). For the classification of hepatic veins, three types of veins were found. The most common type (approximately 56%) belonged to the left-middle and right form, in which the left and middle hepatic veins flowed into a confluence and then joined the IVC, but the right vein joined it alone. Second, the left-middle-right type accounted for 37%, in which three hepatic veins joined the IVC separately. Third, the left-middle-right-right posterior type accounted for approximately 7%, in which the right posterior supramarginal vein and the main right vein joined the IVC separately.

Vascular variations were also demonstrated and evaluated; right posterior inferior hepatic veins were identified in 31/39 (79.4%) cases, caudate hepatic veins were confirmed by a mean of six branches in each patient with a median diameter of 3.7 mm, and the superior suprarenal vein was also found to converge into the right posterior hepatic veins in 23.1% (9/39) cases.

**Volumetry measurement by 3DM**
Quantitative information regarding the volume of tumor masses, peritumor parenchyma of the resected liver, and the functional liver mass was obtained. The mean and median whole liver volume calculated by DMIT software were 1348.9 ± 179.2 and 1310 mL, respectively (n = 39; range: 1076-1739 mL), which were less than those by physical measurement (1351.2 ± 185.1 and 1330 mL, respectively). However, the difference was not statistically significant (P = 0.954) (Figure 6A). The mean volume of tumor mass and functional liver mass measured using the software workstation calculation were 82.4 ± 109.1 mL and 1022.1 ± 153.5 mL, respectively, similar results regarding the volume of tumor mass were also measured by the mathematics specialist (84.1 ± 108.9 mL) (P = 0.910). The average κ between the 3D software calculation and manual counting was 0.93 ± 0.12. The functional liver mass could not be computed.
by conventional planimetric MDCT data. The ratio of functional liver mass to nontumorous parenchymal volume of the whole liver ranged from 55.7 to 88.1%, and no cases developed a small-for-size syndrome.

**Accuracy of computed resection margin and tumor diameter**

In 36/39 resections, the actual margin achieved from the resected specimen ranged from 1 to 21 mm, with a median of 9 mm. The predicted and actual margins did not differ significantly (10.1 ± 6.2 mm vs 9.1 ± 5.9 mm, \( P = 0.488 \)) (Figure 6B). The resection margin could not be determined by planimetric MDCT data. Three patients with centrally located tumors adherent to or compressing major vessels who demonstrated a 0 mm resection margin in the simulation system ultimately underwent successful hepatectomy with exposure of the tumor surface.

The predictive accuracy of the 3DM software for
preoperative calculation of maximum tumor diameter was assessed by comparing results with postoperative pathologic examinations. Simulated maximum tumor diameter was consistent with the pathologic maximum diameter (4.61 ± 2.16 cm vs 4.53 ± 2.14 cm, \( P = 0.871 \)) (Figure 6C).

**Virtual removal of tumor masses**

All cases withstood radical hepatectomy using DMIT for prediction. And the high predictive accuracy for risk analysis was remarkable. The environments for mesohepatectomy, right and left hepatectomies, segmentectomy, or irregular hepatectomies were simulated and conducted by different methods for the various circumstances. During parenchymal dissection using the SDRVO maneuver, the origin of the right-left portal vein and three dorsal hepatic veins were divided and identified as landmark structures, along which the tumor masses deeply located were detected precisely and the dissection lines were marked. The line of dissection was adjusted when the safety margin was guaranteed, and the vessels or bile ducts located in the security margin were also detected. By combining this information, major pedicles were well preserved during real-time surgical guiding on the computer-assisted workstation. Clipping the first- or second-order level branches of the portal vein and hepatic vein resulted in a prompt calculation of the affected area during curative resection. To secure maximal residual liver volume and minimal vascular tree injury, the tumor masses adherent to or compressing major vessels were meticulously dissected from the vascular walls.

Simulated 3D resection in one case showed that a huge HCC which was fixed at the confluence of the right and middle hepatic veins was feasible for complete resection. However, it could not be judged definitively by the conventional data (Figure 4). In another case, hepatectomy of the left lobe appeared possible after conventional ultrasound imaging and CT scan assessment. However, 3D reconstruction revealed an infiltration into the middle hepatic vein and ultimately mesohepatectomy with middle hepatic vein ligation at the root was performed.

DISCUSSION

Surgery remains the most effective treatment and provides a chance of cure for patients with centrally located HCCs. Conventional extensive hepatectomy carries a considerable risk of liver failure due to compromised liver functional reserve, particularly in patients with chronic liver disease. The nomenclature for mesohepatectomy, defined according to the Brisbane 2000 system\[^{15}\], is also referred to as middle hepatic lobectomy, central hepatectomy, and central bisectionectomy in the literature. This procedure often preserves more liver parenchyma and is theoretically associated with a better recovery in the short term\[^{4}\].

However, mesohepatectomy is also difficult, time-consuming, and a technically demanding procedure\[^{14}\]. Lee et al\(^{2}\) retrospectively reviewed 436 patients with HCCs operated on with curative intent and reported mesohepatectomy in only 6.2% of patients. The presence of two hepatic parenchymal transections with proximity to important vascular structures makes it technically more complex than hemi-hepatectomy. Moreover, in clinical practice, we found that a large number (> 60%) of patients with centrally located HCCs had tumors adherent to or compressing major vascular structures. Therefore, the operation fields are often bordered by two cut surfaces and with exposure of important structures, such as the great vessels and main branches of the bile duct. Improper ligation of these important branches may result in ischemia or necrosis of the residual liver, and may lead to liver failure and death\[^{15}\].

Due to the great variability of Glissonian pedicles and hepatic veins, preoperative understanding of the relationship between the tumor and these structures is of great importance. Recently, with the wide usage of intraoperative ultrasonography and a CUSA, major vessels and intrahepatic bile ducts can be localized, visualized, skeletonized, and meticulously controlled. Lee et al\(^{2}\) recommended the use of cholangiography during preoperative MRI or intraoperative exploration to characterize the HCC, which can provide information on bile duct anatomy, including variations and the relationship with the tumor, which might help prevent bile duct injury. They demonstrated that after completion of the resection, any bile leak from the resection planes could be detected by infusion of water and air simultaneously via the cystic duct. In their study, preoperative angiography and reconstruction of computed tomograms were used to assess tumor resectability and to determine the resection line. Fang et al\(^{16}\) described an abdominal image processing system to reconstruct a 3DM of the liver based on CT scan data for volume calculation and identification of vascular variations. The reconstructed model of the abdominal blood vessels and the liver was digitally consistent with the anatomy, different methods were available for selection, and liver transplantation was subsequently simulated. However, to the best of our knowledge, reports of 3D geometric visualization specialized for centrally located HCCs are rare.

It is well known that hepatic functional reserve is highly related to the quantity and quality of liver cells. Previous work has shown that the larger the resected normal liver volume, the greater the risk of liver failure\[^{17}\]. Hence, estimating the percentage of the resected nontumorous parenchymal volume and the ratio of functional liver mass is necessary. In the present study, we designed a morphometric analysis model of tumor reconstruction with DMIT software based on MDCT scans, which included all anatomic structures that were relevant for surgical
resections. Computerized 3D CT-based visualization of the liver is a fast, standardized, and noninvasive procedure that may replace multiple and invasive diagnostic approaches. This system demonstrated accuracy in predicting the liver resection volume as well as the surgical resection margin. Yamanaka et al.\(^\text{[18]}\) used a simulation system to validate volumetric accuracy, and compared the predicted liver resection volume with actual weight of the resected specimen, assuming that 1 g of liver tissue had a volume of 1 mL. They concluded that in patients undergoing major hepatectomy, a strong positive correlation was evident between simulation-predicted liver resection volume and actual weight of the resected specimen. Nevertheless, the density of liver tissue is not completely equal to that of water (1 g/mL) and always depends on the degree of cirrhosis. When the degree of cirrhosis is higher, the density of liver tissue is often greater (> 1 g/mL). In our study, we invited a mathematics specialist to assist in assessing the volume of functional liver mass and tumor mass in order to monitor software calculation deviation. Using an algebraic and geometric algorithm, the volume can be verified in a more objective way. The mean whole liver volume and tumor mass volume calculated by DMIT software demonstrated high similarity to physical measurement (κ = 0.93 ± 0.12).

Some centrally located HCCs are often adherent to or compress major vessels. The presence of two cut surfaces with proximity to important vascular structures makes it technically more complex than hemi-hepatectomy. Moreover, large tumors located in the central portion of the liver are usually associated with an increased risk of intraoperative bleeding\(^\text{[9]}\). In the present series, preoperative 3D simulation facilitated visualization of the crucial extra- and intrahepatic portal vein anatomy, recognition of hepatic vein variants, and determination of the optimal point of surgical division. Computer supported visualizations also enable virtual display of the divided Couinaud’s pedicle branches at the site of the resection surface. In addition, we applied the SDRVO technique, which was reported to control intraoperative bleeding, to avoid ischemia and ischemia-reperfusion injury of the entire liver. Maintaining portal vein blood flow reduces intraoperative visceral congestion and facilitates a more rapid postoperative recovery. The longer inflow occlusion time also allows surgeons to dissect, skeletonize, and manage major vessels and bile ducts in a more relaxed manner, allowing removal of more complex centrally located HCCs. In this study, the digitized reconstruction of the hepatic portal vein and proper hepatic artery converged in the porta hepatis, which made it possible to distinguish all the variations clearly so that the surgeons were able to avoid injury to the variant hepatic vessels during the SDRVO technique.

Although three patients with centrally located tumors adherent to or compressing major vessels demonstrated a 0 mm resection margin in the simulation system, resection with exposure of the tumor surface was ultimately carried out safely. In the software interface, the safety margin was marked by setting a threshold calculated from the minimum safety distance. By combining this information with the image of the segmented vessels, the vessels located in the safety margin were detected. During the operation, tumors were meticulously dissected from the exposed surface of the main vascular structures, and CUSA and sutures were applied for vascular surface dissection and vascular wall injury repair. The result of a preoperatively evaluated 0 mm resection margin obtained by the simulation system was not considered a contraindication for resection of centrally located HCCs that were adherent to or compressed major vessels. This technique provides an opportunity for hepatectomy with exposure of the tumor surface, and although technically demanding, it can be performed safely.

Yu et al.\(^\text{[19]}\) reported that adjuvant radiotherapy for centrally located HCCs after narrow-margin hepatectomy was technically feasible and relatively safe, and a post-hoc subgroup comparison showed that adjuvant radiotherapy considerably improved recurrence-free survival. As the growth pattern of HCCs is usually pushing rather than invading, and most intrahepatic recurrences arise from multicentric carcinogenesis or are distant from the resection margin, obtaining a wide negative surgical margin is usually not necessary\(^\text{[14,18-21]}\). The predictive accuracy of the 3DM software for preoperative BCLC staging in this study was also significantly higher than that by MDCT assessment. As the maximum tumor diameter can only be measured in the transectional plane by conventional CT imaging, our simulation allowed not only a more accurate, but also a more detailed stereoscopic measurement of the maximum tumor diameter, including whether there was vascular invasion or portal hypertension. Therefore, the application of virtual 3D software was useful in preoperative staging and in making appropriate treatment decisions.

All the patients in this study had a liver function of Child-Pugh class A, and the median ICG-R15 was 5.2%. Three patients had an ICG-R15 > 20%, which was too high for major hepatic resection to be performed in cirrhotic patients. However, when using DMIT for prediction, the decision to perform hepatectomy was made. Through virtual tumor resection, the surgeon can judge the parenchyma of organs, identify areas at risk of insufficient blood supply or blood drainage, and estimate the postoperative liver function. Depending on the exploration of various strategies and the results of different risk-analysis calculations, the optimal surgical strategy can be chosen and documented, and the potential benefit from preserving as much functional liver mass as possible can also be predicted. Therefore, morbidity and mortality rates in the present
Innovations and breakthroughs

The diagnosis of intrahepatic masses has significantly changed over the past decade from the use of invasive procedures such as angiography or biopsy, to noninvasive imaging including contrast-enhanced ultrasound, multidetector-row computed tomography (MDCT), and magnetic resonance imaging. CT is the most commonly used imaging modality for diagnosing intrahepatic masses due to its widespread availability and short examination time, and it was estimated that the overall accuracy of MDCT for the detection and characterization of hepatocellular carcinoma is 89% and 43%, respectively, compared with pathologic examination. However, the anatomic and vascular pathologic details provided by MDCT scanners do not completely meet the requirements for preoperative planning. Therefore, a mathematical finite element model that can demonstrate the structural relationship and provide relatively accurate staging of hepatic tumor masses is necessary. In addition, this model is also crucial for determining appropriate treatment, guiding operative strategy, and predicting the prognosis of patients with centrally located HCCs. To overcome these disadvantages, the authors constructed a morphometric analysis model of tumor reconstruction using DMIT software based on MDCT scans, which included all anatomic structures that were relevant for surgical resections. This computerized three-dimensional model is a fast, standardized, and noninvasive procedure that may replace multiple and invasive diagnostic approaches. It can accurately reconstruct the relationships between the tumor, hepatic veins, and Glissonian pedicles in centrally located HCCs, which is essential for correctly defining the hepatic segments and the limits of a tumor with wide variations in anatomy.

Applications

The study results suggest that the three-dimensional model is potentially advantageous and could be implemented routinely for centrally located HCCs, which are more complicated and technically demanding. In these single liver-tumor treatment center, hepatectomy guided by the three-dimensional model was associated with lower rates of complications, shorter postoperative hospitalization, and faster recovery. Therefore, our virtual hepatectomy should be implemented routinely for centrally located HCCs, which are more complicated and technically demanding. More prospective cohort studies are necessary to investigate the advantages and convenience of 3D interactive visualization and quantitative evaluation that is ready for routine use during perioperative treatment of centrally located HCCs.

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