Clinical Science

Planning of anatomical liver segmentectomy and subsegmentectomy with 3-dimensional simulation software

Takeshi Takamoto, M.D., Ph.D.*, Takuya Hashimoto, M.D., Ph.D., Satoshi Ogata, M.D., Ph.D., Kazuto Inoue, M.D., Ph.D., Yoshikazu Maruyama, M.D., Akiyuki Miyazaki, M.D., Masatoshi Makuuchi, M.D., Ph.D.

Division of Hepato-Billiary-Pancreatic Surgery, Japanese Red Cross Medical Center, Tokyo, Japan

KEYWORDS:
Liver hepatectomy; Subsegmentectomy; Anatomic segmentectomy; 3D simulation analysis; Hepatocellular carcinoma

Abstract

BACKGROUND: The aim of this study was to evaluate whether 3-dimensional (3D) simulation software is applicable to and useful for anatomic liver segmentectomy and subsegmentectomy.

METHODS: A prospective study of 83 consecutive patients who underwent anatomic segmentectomy or subsegmentectomy using the puncture method was performed. All patients underwent 3D simulation analysis (SA) preoperatively for planning operative procedures. The clinical information acquired by 3D SA and the consistency of virtual and real hepatectomy were evaluated.

RESULTS: The time needed for completing 3D SA was 18.3 ± 6.7 minutes. Three-dimensional SA proposed resection of multiple segments or subsegments in 29 patients (35%). It also helped complement the resection line in 26 patients (31%) who lacked a bold staining area on the liver surface. The volume of segment or subsegment calculated by 3D SA was correlated with the actual resected specimen (R² = .9942, P < .01). The bordering hepatic veins were clearly exposed in 71 patients (86%), in accordance with completed drawings by 3D SA.

CONCLUSIONS: Three-dimensional SA showed accurate completed drawings and assisted liver surgeons in planning and executing anatomic segmentectomy and subsegmentectomy.

© 2013 Elsevier Inc. All rights reserved.

Anatomic segmentectomy and subsegmentectomy have been proposed as means of improving the curability of surgical treatment for hepatocellular carcinoma (HCC).1,2 Because HCC has a tendency to metastasize via the portal vein, the resection of liver parenchyma fed by portal venous branches bearing the tumor is a logical method for eliminating potential intrahepatic metastases.3 This procedure not only has the advantage of preserving the liver parenchyma, especially in patients with impaired liver function,1 but it also provides a survival benefit compared with nonanatomic partial resection.2,4–7 However, it is necessary and requires careful preoperative evaluation to select the adequate target segment or subsegment considering the tumor location and the individual variation of portal branches. And despite several ingenious methods proposed by liver surgeons,8–10 these surgical techniques require technically demanding processes, including the revelation of segment borders on the liver surface and liver parenchymal resection exposing the hepatic venous tributaries, which exist on the boundary between the segments, with the assistance of intraoperative ultrasonography.1

The authors declare no conflicts of interest.

* Corresponding author. Tel.: +81-3-3400-1311; fax: +81-3-3409-1604.
E-mail address: takamoto@nifty.com

Manuscript received December 4, 2012; revised manuscript January 21, 2013

0002-9610/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjsurg.2013.01.041
Around 2000, several 3-dimensional (3D) simulation software packages were developed to deal with the enormous quantity of imaging data acquired by advanced imaging modalities, such as multidetector computed tomography. These software packages aid in understanding the complex architecture of intrahepatic vessels and allow the evaluation of the volume and the territory supplied by any selected vessel. However, these first-generation software programs take 1 to 3 hours to complete a 3D analysis. Considering the limited clinical impact of these methods, virtual hepatectomy was initially performed using desktop computers with limited efficiency and accuracy. In this study, we used a new 3D simulation software program that has been improved with new algorithms and various aids for segmentation. We adapted this software for use as a preoperative analysis during anatomic segmentectomy or subsegmentectomy planning to evaluate the software’s accuracy and contribution to the procedure.

Methods

Process of virtual hepatectomy using 3D simulation software

The image analysis was performed using Synapsee VINCENT (Fujifilm Medical, Tokyo, Japan). This simulation software was implemented as a plug-in in the processing workstation (a Dell Precision T5400 [Dell Computer, Round Rock, TX] running Windows Vista 64-bit [Microsoft Corporation, Redmond, WA], with 8 GB random-access memory). One-millimeter-thick images acquired during a dynamic study using multidetector computed tomography were reconstructed using the following 3 steps (Fig. 1):

1. Liver segmentation: The liver parenchyma was semi-automatically extracted from consecutive computed tomographic (CT) images. A rough 3D image of the liver was made in a few seconds using a shape recognition algorithm, which is also used in digital cameras as face recognition technology. Then, after shaving the run-over area, the exclusion of the intrahepatic vessels was performed manually.

2. Three-dimensional reconstruction of the portal vein, hepatic vein, and tumor: By setting the start point and the direction, the automatic algorithm, which was developed by modifying the threshold-based region-growing technique, selects consecutive voxel data with appropriate CT values and branching angles. As for the portal vein, the stem of the main portal vein is set as a seeding point and the direction is set for the peripheral side; the portal tree is then extracted automatically. The additional setting of seeding points is usually necessary to extract the peripheral thin branches for complete segmentation. Each hepatic vein is also extracted using the same procedure from the direction of the confluence to the inferior vena cava. The tumor was designated in the axial images. Finally, the extracted portal vein, hepatic veins, and tumors were overlapped, and 3D images were created.

3. Virtual hepatectomy: The vascular perfusion territory was calculated using an algorithm based on the Voronoi tessellation. The territory belonging to any selected vessel is bordered by a line that runs at an equal distance from the surrounding vessels. A virtual hepatectomy for the anatomic segmentectomy or subsegmentectomy is performed by extracting the perfusion territory of a target portal vein followed by its subtraction from the whole liver. On the completed drawing of the segmentectomy or subsegmentectomy, not only the shape of the cut surface but also the position of landmark vessels, such as the stem of the portal branch and the tributaries of the hepatic veins bordering the selected segment or subsegment, after the anatomic liver resection, are visible (Fig. 2).

Clinical study

Patient selection. From September 2009 to April 2012, consecutive patients undergoing anatomic segmentectomy or subsegmentectomy using the puncture technique were eligible for enrollment in this study. Patients whose imaging data were not available or not suitable for 3D simulation analysis were excluded.

Preoperative examination and operative procedure planning. In addition to the routine screening test, liver function was evaluated by the indocyanine green retention rate at 15 minutes in all the patients. All hepatectomies were planned according to the criteria based on the indocyanine green retention rate at 15 minutes (Makuuchi’s criteria). Computed tomography was performed using a 64-row multidetector CT scanner (Aquilion 64; Toshiba Corporation, Tokyo, Japan) using the following parameters: tube voltage, 120 kVp; slice collimation, 1 mm; and rotation time, .5 seconds. Patients received 100 to 135 mL of an iodinated contrast agent (Iomelon [iomeprol]; Eisai, Tokyo, Japan) administered intravenously using an automated injector system over 32 seconds. To display the portal and hepatic venous anatomy, additional CT image sets were acquired at 70 and 140 seconds after arterial imaging.

After 3D reconstruction of the liver, anatomic segmentectomy or subsegmentectomy planning was simulated as follows. First, the portal pedicle supplying the tumor is detected by reconstructed 3D images. Then, by selecting the root of the portal venous branch, the territory of the portal pedicle is extracted. When part of the tumor is out of the extracted territories, additional resection of segment or subsegment is proposed. Another portal pedicle nearby is selected as a second target, and extraction is added. This procedure is repeated until the tumor is surrounded by selected territories.
Operation procedure. An anatomic segmentectomy or subsegmentectomy was performed as reported previously. In brief, after a laparotomy with a J-shaped incision, the entire liver was scanned using intraoperative ultrasonography (ProSound alpha-7: Hitachi-Aloka, Tokyo, Japan) equipped with a microconvex probe (5-MHz to 7.5-MHz frequency), and the tumor locations were mapped. A thoracotomy along the 9th intercostal space was added if the tumor was located in the S7 or S8 region. The portal branches were identified, and 3 to 5 mL indigo carmine dye (Indigocarmine Injection 20 mg/5 mL; Daiichi Sankyo, Tokyo, Japan) was injected into the sites distal to the point at which they needed to be ligated. The speed of the injection was controlled with reference to the ultrasonographic findings to prevent the dye from flowing back into nontargeted portal branches. Additional branches were punctured, as necessary, depending on the location of the tumor. The stained surface of the liver was marked with electrocautery. Under intermittent inflow occlusion by clamping of the hepatoduodenal ligament or hemihepatic inflow occlusion, the parenchyma was dissected using the clamp-and-crush method. Intraoperative ultrasonography was used during the liver transaction to provide an understanding of the relationship between the transection line and the landmark hepatic veins and portal branches. A patient who underwent an S8dor

Figure 1  Concepts of the 3D simulation software Synapse VINCENT. Step 1: segmentation of the whole liver. A prescribed form of the liver, such as the location, rough shape, and particular range of CT value, is transformed and adjusted to the individual liver (A), and the whole liver is extracted from 2-dimensional CT images in a few seconds (B). Step 2: segmentation of the vascular (portal vein, hepatic vein, and hepatic artery). By starting at the stem and its direction (yellow arrow) of the portal vein (pink colored), the automatic algorithm passes through the data set to find connected structures in prescribed condition, such as CT value and branching angle (C,D). This procedure is repeated to extract all the peripheral vessels. The segmentation of hepatic veins is continued in the same way from the confluence of inferior vena cava. Step 3: concept of virtual hepatectomy using the Voronoi tessellation (E,F). The territories of points I, II, III, and IV are drawn as blue, light blue, pink, and yellow, respectively. Each point such that the borders of the regions are equidistance from the 2 nearest points. Point p belongs to point II (E). This concept is applied to 3D analysis. The territories of P2 and P3 are described as green and yellow territory, respectively. The tumor (red) is included in the yellow territory, S3 (F).
subsegmentectomy is shown in Fig. 2. The resected specimen was promptly weighed after the resection.

**Estimation of outcome.** The following points were evaluated to compare the virtual hepatectomy and the actual hepatectomy:

- Preoperatively, the time needed to reconstruct and calculate the target segment or subsegment using a 3D analysis was recorded.
- Intraoperatively, the stained area on the surface of the liver was classified as bold, traceable, or not visible, according to its appearance.
- The appearances of the landmark vessels, such as the hepatic veins bordering the segments or subsegments and stump of the portal branches, on the raw surface of the liver after transection were classified as clear, hazy, or invisible, with judgment and agreement by all surgeons participating in the operation.

If the target portal branches were changed from the preoperative plan after the intraoperative evaluation, the area of the newly selected segment or subsegment was recalculated and presented immediately during the operation. When the stained area appearing on the liver surface was not bold and clear enough to draw the complete line for resection, the line was complemented with reference to the picture of 3D analysis. Intraoperative ultrasonography was used to confirm that the portal pedicle running to the complemented area derived from the target portal pedicle.

To validate the preoperative planning using the 3D simulation software, the actual weight of the resected specimen was compared with the calculated volume of the matching segment or subsegment. The relationship between the computed volume and the weight of the resected specimen was applied using a linear regression model, and an approximation formula was derived. The discrepancy ratio between the computed volume and the weight of the resected specimen was also evaluated between the stratified groups. The discrepancy ratio was defined as the absolute value according to the following formula: \( \left[ 1 - \frac{\text{computed weight of the specimen calculated using the approximation formula}}{\text{actual weight of the specimen}} \right] \times 100\% \).

Postoperative complications were investigated and graded according to Clavien’s classification.  

**Statistical analysis**

Continuous data are expressed as mean ± SEM and were compared using Student’s \( t \) tests or Welch tests, as
appropriate. Categorical data were compared using Pearson’s chi-square tests or Fisher’s exact test, as appropriate. Correlations were presented as scatterplots and were analyzed using Pearson’s test (JMP version 9; SAS Institute Inc, Cary, NC). P values <.05 were considered statistically significant.

Results

Patients

From September 2009 to April 2012, 433 hepatectomies were performed at a Japanese Red Cross medical center. Among them, liver segmentectomy or subsegmentectomy using a puncture technique was performed in 88 patients. However, 5 patients were excluded. Three of these patients had portal venous tumor thrombosis, and their CT data were not suitable for complete portal venous reconstruction. The other 2 patients were allergic to the contrast material used for the CT scan. Consequently, 83 patients were eligible for inclusion in this study (Fig. 3). Table 1 shows the demographic and clinical features of the selected patients.

Contribution of 3D simulation analysis in preoperative planning

In 29 of 83 patients (35%), the 3D simulation analysis predicted that the tumor was located on the border of the first extracted segment or subsegment. Staining of multiple portal veins was proposed. A patient with HCC located on the border between S8 dor and S8 vent is shown in Fig. 4. The staining of both portal branches was scheduled with reference to the 3D simulation analysis.

All the reconstructions using the 3D simulation software were performed by a surgeon (T.T.) who participated in all the operations. The time needed for the virtual hepatectomy, from the reading of the CT data to the computation of the territory of a target portal branch, was 18.3 ± 7 minutes.

Estimation of operation procedure

The resected segments ranged all over the liver, from S2 to S8 (Table 2). Anatomic segmentectomy or

Table 1  Demographic and clinical features of patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (y) (range)</td>
<td>65 (26–81)</td>
</tr>
<tr>
<td>Men/women</td>
<td>61/22</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>61</td>
</tr>
<tr>
<td>Metastatic liver tumor</td>
<td></td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>18</td>
</tr>
<tr>
<td>Neuroendocrine tumor</td>
<td>3</td>
</tr>
<tr>
<td>Duodenal cancer</td>
<td>1</td>
</tr>
<tr>
<td>Repeated hepatectomy</td>
<td>21</td>
</tr>
</tbody>
</table>
subsegmentectomy with the puncture technique can be performed anywhere in the liver except for the S1 region.

In all patients, the staining area was visible on the liver surface. Fifty-seven patients (68%) exhibited bold staining, and a clear border of the segment or subsegment was visualized. However, the stained area appeared light colored and was barely traceable in 26 patients (31%). In such instances, the liver resection line was complemented by referring to the drawing of 3D simulation analysis and intraoperative ultrasonography (Fig. 4). The hepatic veins were obvious on the completed drawings and were longitudinally visible on the actual cut surface of the liver in 70 patients (84%).

**Computed volume and weight of the resected specimen**

The relationship between the computed volume and the weight of the resected specimen is shown in Fig. 5. The linear approximation formula was as follows: actual specimen weight (g) = .9586 × computed volume (mL) + 3.2065 ($R^2 = .9942, P < .01$).

**Examination of discrepancy ratio**

Further estimation of the discrepancy ratio was performed between stratified groups (Fig. 6). The discrepancy ratios between the group with bold stained area appearance and those with traceable appearance were 4.5 ± 5.0% and 9.6 ± 6.7%, respectively. The discrepancy ratio was lower in the bold group ($P = .0003$). The resected segment or subsegment was classified as the left liver (S2, S3, and S4), the right paramedian sector (S5 and S8), and the right lateral sector (S6 and S7). When the resected segments or subsegments extended over 2 sectors, the specimen was classified according to the sector to which the thicker portal vein or larger segment or subsegment belonged. The discrepancy ratios for the left liver, right paramedian sector, and right lateral sector were 5.0 ± 1.5%, 7.1 ± 1.0, and 5.6 ± 1.2%, respectively, and no significant differences were observed.

The discrepancy ratios for groups classified according to the number of punctured portal branches (1, 2, and 3 or 4 branches) were 6.4 ± .8%, 6.4 ± 1.3%, and 2.6 ± 2.5%, respectively ($P > .14$). No significant difference was found between groups undergoing initial hepatectomy and those...
undergoing repeat hepatectomy (6.4 ± .8% vs 5.2 ± 1.3%, respectively, P = .42).

Postoperative outcomes

Postoperative complications were observed in 23 patients (28%). Twenty patients (24%) experienced grade I or II complications according to the Clavien-Dindo classification, including surgical-site infection (n = 7), transient bile leakage (n = 6), pleural effusion (n = 3), ascites (n = 1), temporary bowel obstruction (n = 1), inflammation of the prostate (n = 1), and mental disorder (n = 1). There was no reoperation (class IIIb), class IV/V, or 90-day mortality.

Comments

In this study, we used the 3D simulation software Synapse VINCENT to examine patients scheduled to undergo anatomic segmentectomy or subsegmentectomy using the puncture method and showed the consistency of this methodology. Three-dimensional simulation analysis supports surgeons in selecting the target portal veins preoperatively. And intraoperatively, it assisted confirming and complementing the liver resection line.

Several investigators have reported good correlations between the actual weight of the resected liver specimen and the volume calculated using other 3D simulation software.14,22 However, we attempted to show 2 clear differences from previous reports. First, we applied new 3D simulation software that was developed using an invented algorithm, various imaging technologies, and topologic knowledge aimed at easy handling and time-saving for 3D reconstruction. As a result, less than half the working time was required to complete the virtual hepatectomy compared with the reports using other software packages.14,16 Second, unlike previous reports containing heterogeneous types of hepatectomy, we focused on segmentectomy or subsegmentectomy using the puncture method. With this operative procedure, arbitrary drawing of the liver resection line can be avoided in both the virtual hepatectomy performed with 3D simulation software and the real hepatectomy.

Remnant liver volume is known to affect postoperative liver failure and morbidity.23–25 A precise preoperative estimation of the future remnant liver volume is indispensable for liver surgeons. We selected the extent of the hepatectomy, which can preserve future remnant liver volume according to criteria based on the indocyanine green retention rate at 15 minutes.18,26 This selection is an important part of preoperative planning, with the potential to lower the rates of postoperative liver failure and mortality to zero.27

As a preoperative volumetry technique, a method involving the piling up of the areas traced from the axial CT images, the so-called planimetric or hand-trace method, has been widely used.28,29 The planning of a left or right hepatectomy and sectoriectomy using this traditional method is relatively easy to perform, and a certain degree of accuracy in the volumetry can be achieved because the apparent major hepatic veins run the boundary of the segments or subsegments. However, for the planning of a segmentectomy or subsegmentectomy, the planimetric method

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Operative procedure and postoperative outcome after anatomic segmentectomy or subsegmentectomy with puncture technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>Value</td>
</tr>
</tbody>
</table>
| Resected segment or subsegment | S2 7  
|  | S3 5  
|  | S4sup 2  
|  | S4sup + S8 1  
|  | S4inf + S5 1  
|  | S5 2  
|  | S5 + S6 1  
|  | S5 + S6 + S7 1  
|  | S5 + S8 1  
|  | S6 7  
|  | S6 + S7 1  
|  | S7 18  
|  | S7 + S8dor 2  
|  | S7 + S8 1  
|  | S8 12  
|  | S8dor 11  
|  | S8vent 10  |
| Number of stained portal branches | 1 54  
|  | 2 23  
|  | 3 5  
|  | 4 1  
| Stained area appearance on the liver surface | Bold 57  
|  | Traceable 26  
| Depiction of anatomic landmarks | Clearly 71  
|  | Hazy 12  
| Concomitant liver resection | No 59  
|  | Yes (limited resection) 24  
| Number of concomitant resections | 2.5 (1–34)  
| Preoperative indocyanine green retention rate at 15 min (%) | 11.1 (3.1–43.7)  
| Operation time (min) | 441 (147–1,550)  
| Total Pringle time (min) | 74.5 (14–249)  
| Blood loss (mg) | 595 (40–3,110)  
| Red blood cell transfusion | 6  
| Postoperative complication | None 60  
|  | I/II 10/10  
|  | IIIa/IIIb 3/0  
|  | IVa/IVb/V 0/0/0  
| 90-d mortality | 0 |

Data are expressed as numbers or as median (range).
becomes difficult and time-consuming and involves measurement error, especially when the hepatic venous tributaries bordering the segments are not clear. In such instances, 3D simulation software is superior. A precise estimation of future remnant liver volume can be critical when deciding the extent of an anatomic resection in patients with impaired liver function. Several practical 3D simulation software, such as Hepavision (MeVis Medical Solutions AG, Bremen, Germany) and OVA (Hitachi, Tokyo, Japan), have been developed, and their usefulness and accuracy have been discussed. With all these techniques, however, a few hours are required to complete the 3D images, and this time-consuming aspect has hindered their application. For example, some software requires not only the branching of the vessels but also their thickness to be entered; other software requires the portal trees to be separated from the hepatic venous trees. Thanks to several innovative devices that overcome these troublesome procedures, Synapse VINCENT requires <20 minutes to extract the target territory, enabling surgeons to participate in the use of the software for operative planning. At our institution, all liver resections are now preceded by 3D analyses performed by liver surgeons.

Anatomic liver resection is a reasonable procedure for preventing metastases of HCC via the portal vein and is an almost established option for improving the prognostic outcome. However, some investigators have attempted to provide evidence against its prognostic efficacy. One reason for this discordance is the absence of approved quality indicators for anatomic liver resections. Actually, the accomplishment of an anatomic liver resection (ie, the complete removal of the target segment or subsegment) is difficult to prove and has rarely been conducted. By comparing the cut surface of the liver to the predicted completed drawing and confirming the concordance between the computed volume of the segment or subsegment and actual weight of the specimen, 3D simulation software can be used as a quality indicator for anatomic liver resection. Thus, the above argument should be resumed with the addition of this quality evaluation.

Anatomic segmentectomy or subsegmentectomy was advocated in 1985 by 1 of the authors (M.M.). In this study, high-quality hepatectomies were performed by a team led by this experienced surgeon, who has continued to improve anatomic liver resection techniques for 30 years. This experience may have contributed to the good accordance between the predictions of the 3D simulations and the actual operations.

Although 3D simulation software can produce accurate completed drawings, it provided critical preoperative proposal and intraoperative assistance only for one-third of patients. However, recognition of the segment where the tumor is located is not easy with 2-dimensional CT imaging, and successful staining is unpredictable preoperatively. It is reasonable to apply 3D simulation analysis for all patients undergoing anatomic segmentectomy or subsegmentectomy.
subsegmentectomy. Another limitation of 3D simulation analysis is that it cannot yet be used to navigate during a hepatectomy in real time. Actually, an anatomic segmentectomy or subsegmentectomy still relies on the space perception ability of liver surgeons using intraoperative ultrasonography and requires advanced techniques, including puncture and dye injection into the target portal branch, liver resection exposing the bordering hepatic venous tributaries, and ligation of the target portal branch at the planned location. Technological improvements should be continued until software can be used to guide liver resections in real time.

Conclusions

Our study demonstrated the accuracy and timesaving benefits of 3D simulation software. We have also suggested a new role for 3D simulation software: providing assistance for anatomic segmentectomy or subsegmentectomy. This modality could also be used as a quality indicator for this technically demanding procedure.

Acknowledgment

We express our appreciation to Jun Masumoto for his engineering guidance with Synapse VINCENT.

References