Validating New Software for Semiautomated Liver Volumetry – Better than Manual Measurement?

Zusammenfassung


Ergebnisse: Die Ergebnisse des postoperativen CT-Scans korrelierten hochgradig mit den Ergebnissen der Verdrängungsvolumetrie (manuell: \( p=0.997 \); halbautomatische Software: \( p=0.995 \)). Mit der halbautomatischen Software fielen die Unterschiede zwischen dem vorhergesagten und dem tatsächlichen Volumen signifikant kleiner aus (33 % vs. 57 %, \( p=0.002 \)). Zudem lieferte die halbautomatische Software die Volumina der Gesamtleber fast 4 mal schneller (manuell: 6:59 ± 3:04 min; halbautomatisch: 1:47 ± 1:11 min).

Conclusion: Both methods for liver volumetry give an estimated liver volume close to the real one. The tested semiautomated software is faster, more accurate in predicting the volume of the resected liver part, gives more reproducible results and is less dependent on the user’s experience.

Abstract

Purpose: This prospective study compared a manual program for liver volumetry with semiautomated software. The hypothesis was that the semiautomated software would be faster, more accurate and less dependent on the evaluator’s experience.

Materials and Methods: Ten patients undergoing hemihepatectomy were included in this IRB-approved study after written informed consent. All patients underwent a preoperative abdominal 3-phase CT scan, which was used for whole liver volumetry and volume prediction for the liver part to be resected. Two different types of software were used: 1) manual method: borders of the liver had to be defined per slice by the user; 2) semiautomated software: automatic identification of liver volume with manual assistance for definition of Couinaud segments. Measurements were done by six observers with different experience levels. Water displacement volumetry immediately after partial liver resection served as the gold standard. The resected part was examined with a CT scan after displacement volumetry.

Results: Volumetry of the resected liver scan showed excellent correlation to water displacement volumetry (manual: \( p=0.997 \); semiautomated software: \( p=0.995 \)). The difference between the predicted volume and the real volume was significantly smaller with the semiautomated software than with the manual method (33 % vs. 57 %, \( p=0.002 \)). The semiautomated software was almost four times faster for volumetry of the whole liver (manual: 6:59 ± 3:04 min; semiautomated: 1:47 ± 1:11 min).

Conclusion: Both methods for liver volumetry give an estimated liver volume close to the real one. The tested semiautomated software is faster, more accurate in predicting the volume of the resected liver part, gives more reproducible results and is less dependent on the user’s experience.
**Introduction**

Liver volumetry is used to predict a patient’s liver volume by the use of imaging, usually with an abdominal CT scan. It is often used in the setting of living-donor liver transplantation to predict the size of the future graft and to ensure a certain volume of the remaining donor liver [1–5]. Liver volumetry is also important in patients undergoing extended liver resection. In both cases a minimal amount of functional liver is necessary to maintain sufficient metabolic and detoxifying function. Otherwise it can lead to a threatening scenario with acute liver failure, coagulopathy and multiorgan dysfunction [6].

Previous studies found a good correlation (p < 0.001) between liver volumes measured by liver volumetry with the help of a CT scan and the real liver volume, measured by water displacement [3, 7, 8]. Most of these studies evaluated their software in donors for living-donor liver transplantations. Patients undergoing liver resection have been studied less frequently [9, 10] but are equally important in the clinical routine.

Manual liver volumetry was shown to be a time-consuming procedure. Nakayama et al. measured 32.8 ± 6.9 minutes for one manual volumetry [8]. Automated liver volumetry programs promised to be faster. For example, Suzuki et al. found a mean time of 0.57 ± 0.06 minutes with their semiautomated software [11].

In the daily routine at our clinic, liver volumetry is performed with the help of a manual program, which gives the observer a lot of freedom in the definition of liver tissue and segments to be resected. Volumetry is performed by different observers with different experience levels. Although new observers are always introduced to the program and the volumetry, considerable variation is still possible in the definition of liver segments. This leads to intra- and interindividual differences. Semiautomated software for the detection and segmentation of liver tissue could be of great help in terms of a time reduction and volumetric measurement reproducibility. Several companies are working on such software programs and our department had the opportunity to test a prototype software, which is now also commercially available (CT Liver Analysis, Philips Healthcare, Best, NL).

A study was performed to compare the manual program for liver volumetry with a prototype version of the semiautomated software tool. The hypothesis was that the semiautomated software would be faster, more accurate and less dependent on the evaluator’s experience.

**Key points:**
- Both tested types of software allow exact volumetry of resected liver parts.
- Preoperative prediction can be performed more accurately with the semiautomated software.
- The semiautomated software is nearly four times faster than the tested manual program and less dependent on the user’s experience.

**Materials and Methods**

Written informed consent was obtained from all patients for this prospective IRB-approved study. 10 patients were included in this prospective study (4 women, 6 men), who underwent hemihepatectomy in our Department for Visceral Surgery. The mean age was 70 years (range: 56–83 years). The sample size was estimated to be high enough by our department for biostatistics in view of the expected differences between the methods. Surgery took place between 01/2012 and 01/2013. Underlying diagnoses were adenocarcinoma of the gall bladder (n = 1), cholangiocellular carcinoma (n = 1), liver abscess (n = 1), hepatocellular carcinoma (n = 2) and liver metastases (n = 5).

The resected parts of the liver had different sizes in each case. The resected Couinaud segments were V-VIII (n = 3), IV-VIII (n = 1), I-IV (n = 2), II+III (n = 2), IV-VIII+I (n = 1), V-VIII+IVa (n = 1).

All patients underwent a preoperative abdominal CT scan which is part of the normal preoperative workup. The scans were performed on a 64-slice CT scanner (Philips Brilliance 64, Philips Healthcare, Best, NL) with 120 kV and 200 effective mAs, a collimation of 64 × 0.625 mm and a reconstructed slice thickness of 3 mm. All patients were scanned with 3-phase CT (unenhanced, arterial phase, portal venous phase; timing with bolus tracking) after intravenous application of contrast material (0.5 g iodine per kilogram body weight; Imeron 400 mCT, Bracco Imaging, Konstanz, Germany). The delay for the start of the arterial phase scan and the portal-venous phase scan was set at 15 and 45 seconds, respectively, after a threshold of 100 Hounsfield Units was reached in the abdominal aorta. Image data of the portal-venous phase were used for volumetry.

As a gold standard, the resected parts of the liver were measured with water displacement volumetry immediately after resection in the operating room. Therefore, the resected piece of liver was placed into a basin completely filled with NaCl solution and the displaced fluid was collected and measured with a 1000 ml measuring cylinder.

Thereafter a CT scan of the resected liver, inserted in a box filled with formalin, was performed on the same CT scanner with 120 kV, 100 effective mAs and 3 mm reconstructed slice thickness. Volumetry was performed with two different types of software. The first one is part of the CT viewer integrated into the dedicated CT workstation (Extended Brilliance Workspace, Philips Healthcare, Best, NL) and routinely used in our department. Here, the borders of the liver must be defined per slice by the user. Slice interpolation is possible, but the user has to control the correct borders. The resulting volume is displayed in millili-
To measure parts of the liver, the user must exclude the unwanted anatomy by hand. This can be done on the volumetric image of the liver (Fig. 1).

The second software was a prototype software for liver volumetry and segmentation developed by Philips which is now commercially available (“CT Liver Analysis”, Philips Healthcare, Best, NL). Here, the liver volume is identified automatically, but the borders can be corrected by the user. In a second step, vessels are automatically identified and classified as portal, hepatic, or unclassified veins. Their volume is included in the total volume. Manual correction is possible. In a third step, for segment definition, the user must set nine points (bifurcation of right portal vein, vena cava inferior, right hepatic vein, mid hepatic vein, umbilical fissure, superficial and deep ligamentum venosum, end of left portal vein, left tip of the liver) from which Couinaud segments are calculated automatically. The volumes for every single segment are listed and can be accumulated to the respective volumes of the resected liver part (Fig. 2).

Volumetry of the preoperative CT dataset was performed by six users. Three of them were radiologists experienced in the use of the manual software and three of them were medical students and novices in CT volumetry. The radiologists had three, four and fourteen years of clinical experience and the medical students were in their fourth and fifth year of study. They all received the same introduction to the prototype software. Medical students received an additional introduction to the manual program. Each user performed test volumetry on three different datasets to become accustomed to the programs and to minimize a learning effect during the study. Thereafter, each user performed volumetry of the whole liver and of the resected segments with the manual program as well as with the semiautomated software for each of the ten livers. The gallbladder was excluded and tumors were included in the total liver volume. Resected segments were known from the operating room report and were made available to the users. In contrast to the approach in the clinical routine, the preoperative volumetry was also done after the time of surgery. For each method the measurement was repeated three times in a random order to avoid a learning effect. Time needed for volumetry and measured volumes were noted and analyzed separately for the two groups of observers.

Volumetry of the postoperative CT dataset of resected liver parts was performed by three users, two radiologists and one medical student. All of them had also done the preoperative measurements. This measurement was done as a quality check for accuracy of both volumetry modalities and not to assess differences between observers. The manual and semiautomated delineation of the resected liver part proved to be simple, because the liver and the circumfluent formalin had very different Hounsfield Units. This is why only three participants also did the postoperative measurements.

**Statistical Analyses**

Statistical analyses were done with SPSS for Windows Version 15.0 and performed in cooperation with the local Institute for Medical Informatics, Statistics and Epidemiology. Descriptive statistics including mean value, standard deviation and range were performed for measured times and volumes, in each case separately for resected and total liver.

The results of measured volumes were visualized with Bland-Altman plots [12]. For correlations the spearman correlation coefficient (-1 ≤ ρ ≤ 1) was used. Statistical tests to compare measured volumes were the Wilcoxon test and the Mann-Whitney U-test. For the analysis of the experience level, the use of Cohen’s Kappa was not recommended by our institute for statistics. Instead visualization with Bland-Altman plot was recommended. P-values ≤ 0.05 were considered significant.

**Fig. 1** The manual software (Extended Brilliance Workspace, Philips Healthcare, Best, NL). Here the previously determined total liver volume is already divided into the resected liver and the remaining part. The upper right picture shows the 3D reconstruction.

**Abb. 1** Die manuelle Software (Extended Brilliance Workspace, Philips Healthcare, Best, NL). Die vorher volumetrierte Gesamtleber wurde hier bereits in das zukünftige Resektat und den verbleibenden Leberteil untergliedert. Das obere rechte Bild zeigt die 3D-Rekonstruktion.
Results

An overview of all results can be seen in Table 1.

Liver Volume
In each case the mean volume of the total and the resected liver, measured on the preoperative dataset with the manual method, was greater than the volume measured preoperatively with the semiautomated software. The differences, both for the total and the resected volume, were statistically significant (p < 0.001).

Postoperative measurement of resected segments with CT scan shows results very close to water displacement volumetry with both methods. Differences are not statistically significant (manual: \( p = 0.557 \); semiautomated: \( p = 1.000 \)). Correlations to the gold standard were very strong with both methods (manual: \( p = 0.988 \); semiautomated: \( p = 0.988 \)).

Comparison of volumes measured preoperatively with volumes measured by water displacement shows that the manually predicted volume is always greater than the volume measured by water displacement (mean difference 305 ml (57%); correlation

<table>
<thead>
<tr>
<th></th>
<th>mean value measured by radiologists</th>
<th>mean value measured by medical students</th>
<th>mean value over all observers</th>
</tr>
</thead>
<tbody>
<tr>
<td>time needed to measure the total liver with the manual method [minutes:seconds]</td>
<td>5:00 ± 1:51</td>
<td>8:59 ± 2:45</td>
<td>6:59 ± 3:04</td>
</tr>
<tr>
<td>time needed to measure the total liver with the semiautomated software [minutes:seconds]</td>
<td>1:53 ± 1:13</td>
<td>1:42 ± 1:08</td>
<td>1:47 ± 1:11</td>
</tr>
<tr>
<td>time needed to measure the resected liver with the manual method [minutes:seconds]</td>
<td>2:02 ± 1:09</td>
<td>2:35 ± 1:53</td>
<td>2:19 ± 1:35</td>
</tr>
<tr>
<td>time needed to measure the resected liver with the semiautomated software [minutes:seconds]</td>
<td>4:16 ± 2:09</td>
<td>4:50 ± 2:07</td>
<td>4:32 ± 2:09</td>
</tr>
<tr>
<td>total volume measured preoperative with the manual method [ml]</td>
<td>1954 ± 667</td>
<td>2126 ± 707</td>
<td>2040 ± 691</td>
</tr>
<tr>
<td>total volume measured preoperative with the semiautomated software [ml]</td>
<td>1818 ± 572</td>
<td>1860 ± 579</td>
<td>1839 ± 574</td>
</tr>
<tr>
<td>resected volume measured preoperative with the manual method [ml]</td>
<td>1084 ± 764</td>
<td>1199 ± 785</td>
<td>1141 ± 775</td>
</tr>
<tr>
<td>resected volume measured preoperative with the semiautomated software [ml]</td>
<td>970 ± 625</td>
<td>1006 ± 695</td>
<td>988 ± 659</td>
</tr>
<tr>
<td>water displacement volumetry [ml]</td>
<td>837 ± 740</td>
<td>837 ± 740</td>
<td>837 ± 740</td>
</tr>
<tr>
<td>resected volume measured postoperative with the manual method [ml]</td>
<td>795 ± 603</td>
<td>795 ± 603</td>
<td>795 ± 603</td>
</tr>
<tr>
<td>resected volume measured postoperative with the semiautomated software [ml]</td>
<td>809 ± 620</td>
<td>809 ± 620</td>
<td>809 ± 620</td>
</tr>
</tbody>
</table>
The volume predicted with the semiautomated software as compared to the water displacement is bigger in some cases and smaller in others with an excellent correlation (mean difference 152 ml (33 %); correlation \(\rho = 0.939\)) (Fig. 3). Both differences are statistically significant (manual: \(p = 0.002\); semiautomated: \(p = 0.027\)).

**Measurement time**

The required mean time to determine total liver volume with the manual method was 6:59 ± 3:04 minutes (range: 2 – 18 minutes). With the semiautomated software the mean time was 1:47 ± 1:11 minutes (range: 1 – 8 minutes). So the semiautomated software is 3.9 times faster than the manual measurement. The difference is statistically significant (p < 0.001).

Measurement of the preoperative volume of resected liver parts took a mean time of 2:19 ± 1:35 minutes with the manual method and 4:32 ± 2:09 minutes with the semiautomated software. For the combination of both measurements, the semiautomated software is 1.5 times faster than manual volumetry (manual: 9:22 ± 3:09 minutes, semiautomated 6:20 ± 1:40 minutes). This difference is also statistically significant (p < 0.001).

**Experience level**

In the measurement of the total liver volume, the absolute difference between medical students and radiologists was on average smaller with the semiautomated software (41 ml with semiautomated software versus 171 ml manually measured), but the difference was not statistically significant (manual: \(p = 0.208\); semiautomated: \(p = 0.722\)).

In the measurement of the resected liver on preoperative scans, the differences between the two groups of users were also not statistically significant in both methods (manual: \(p = 0.300\); semiautomated: \(p = 0.912\)) (Fig. 4).

Comparing the results of the resected liver volume on preoperative scans with the real volume of the resected liver, radiologists had smaller differences with both methods (mean difference 305 ml manually and 134 ml with semiautomated software) than medical students (mean difference 362 ml manually and 170 ml with semiautomated software). The differences are statistically significant (radiologists manual: \(p = 0.002\); medical students manual: \(p = 0.002\); medical students semiautomated: \(p = 0.014\)) except for the difference between the volume measured by the radiologists with the semiautomated software and the real volume (p = 0.084).

Radiologists were faster in measuring the total liver and the resected volume with both methods, but the differences were not statistically significant (manual: \(p = 0.259\); semiautomated: \(p = 0.125\)).

**Discussion**

**Total Liver Volume**

Heinemann et al. measured volumes of 33 healthy livers post mortem by water displacement and found a mean liver volume of 1862 ml for the Caucasian population [13]. The present study provides results comparable to those of Heinemann. Suzuki et al. found a manually measured mean liver volume of 1486 ± 343 ml (DICOM viewer, Abras version 0.9.9) and an interactively measured volume of 1520 ± 378 ml (Volume Tracing in Advanced Vessel Analysis, Philips Healthcare) [11]. They used a similar software type for volume tracing as we did for manual volumetry, but with another tool for liver delineation. Their mean liver volume was 434 ml smaller than the volume found in the present study which might be due to different measurement tools.
D’Onofrio et al. used the same semiautomated software as we did but compared it to software running on a personal computer. They found a total liver volume of 1787.31 ml, which is comparable to the results found in the present study [14]. Certainly every method has its own limitations and it is difficult to compare absolute volumes across different studies. A general problem that can also affect the volume measurement is the slice thickness. We used slices with a thickness of 3 mm, because this is routine in our clinic and both programs can deal with this thickness. Hori et al. reported that if a maximum error of 5% is allowed, a slice thickness of 5 mm is exact enough and smaller slices make volumetry even more accurate. Thinner slices can additionally lead to the problem that the volumetry is more time-consuming [15].

Resected Liver Volume
So far water displacement is the best method to measure the real volume of resected liver parts [16] and better than measuring liver weight because density of liver tissue varies. Lemke et al. found densities between 0.67 g/cm³ and 1.66 g/cm³ [17]. Volumes measured by water displacement in the present study cannot be compared to volumes found in the literature, because we only measured resected liver parts which differ a lot in size, because different segments were resected in every case. However, D’Onofrio et al. also measured resected liver parts with different sizes with the same semiautomated software as used in the present study. They found a mean volume of resected liver parts of 1021.23 ml, which is comparable to our results, although they only used the weight of the surgical specimen as the gold standard [14]. Additionally, they did not give any information about the time needed for volumetry and reproducibility.

In our study both methods resulted in an overestimation of the real volume of resected liver parts in almost all cases. This overestimation was also found by Lemke et al. [2], who compared the weight of right liver lobes preoperatively in vivo and after resection and found a correction factor of 0.75. Niehues et al. also found a 13% overestimation of in vivo volumetry in a pig model [18]. They found that intraoperative blood loss is the main reason for overestimation. Hwang et al. found a difference between CT measurement and blood-free water displacement volumetry of 20% but only a difference of 4% between blood-filled graft volume and CT volumetry [19]. In view of these results, overestimation of liver volume in the present study can be fully explained. Additionally, comparison of CT volumetry of explanted liver parts and displacement volumetry did not suffer from this fluid problem and showed an excellent correlation with both methods.

Measurement time
Nakayama et al. measured 32.8 ± 6.9 minutes with their manual program and 4.2 ± 1.9 minutes with their automatic program [8]. Suzuki et al. found a mean time of 39.4 ± 5.5 minutes for manual volumetry and 0.57 ± 0.06 minutes for semiautomated software. With their “interactive software”, which was similar to our manual software, they needed 27.4 ± 4.6 minutes. This is much longer than the mean time per case found in the present study and might be explained by the use of another tool within the software [11]. In comparison with these studies the manual software tested in the present study seems to be considerably faster, even in inexperienced users. This can be explained by use of the interpolation mode, we used in this study, in which it is not necessary to define liver borders in every single CT slice. The time needed for semiautomated volumetry in the present study is comparable to the time found in literature. The time needed for measurement of resected parts was found to be a bit longer with the semiautomated software in the present study as compared to manual volumetry. The reason is the time that was needed to set the nine points to define the segments of the liver correctly. However, with the semiautomated software volumes of all liver segments and vessels are calculated within this time. With the manual volumetry it is only possible to get the volume of the liver part the user detaches from the formerly measured total volume. After all, the manual volumetry method used in the present study is already relatively fast, but the tested software is up to four times faster. In comparison to other programs discussed in the literature, the time gain can be even more substantial.

Experience level
In the abovementioned studies [8, 11, 14], just one user measured all volumes. Even if the radiologist is experienced, this can lead to a bias. Correct and repeatable results are also very important in the clinical routine. Friericks et al. performed a study with three equally trained observers, who re-measured livers in complicated cases only. The three observers worked together to measure one volume for one liver and no comparison of different results was made [7]. Radtke et al. had three observers (one trained radiologist and two untrained surgeons), but they also did not compare different results [1]. Sandrasegaran et al. performed a study to expose reproducibility and interobserver variations in liver volumetry, but they had just 2 observers and did not provide any information about their experience level. Additionally, just one observer repeated the measurement. They found extremely high inter- and intraobserver correlations (r = 0.999 and 0.997) [20]. The present study systematically assessed different levels of experience, which makes this study unique. It was found that inexperienced observers measured bigger liver volumes with both methods and also showed bigger differences between the resected volume and the real volume. Additionally, they needed longer for the measurement. However, the differences between the two observer groups were smaller if the measurement was made with the semiautomated software.

Limitations
Due to the study design, water displacement volumetry for the whole liver could not be performed. Some studies concerning liver volumetry used explanted livers to measure the real total liver volume [8, 17] but in these studies no measurement of resected liver parts was possible. In the clinical routine it is very important to get a realistic estimate of resected and remaining liver parts for both hemihepatectomy and living-donor liver transplantation. In the present study it was also not possible to get a gold standard of the remaining liver volume after surgery. But this is the part of the liver which is decisive for patient outcome [21, 22]. However, it could be shown that the volume of resected liver can be predicted very well, especially with the semiautomated software, and so the conclusion is acceptable that the remaining liver volume is predicted equally well.

Another limitation is that resected liver parts were very heterogeneous. Lemke et al. [2] only used right liver lobes and so the results are more homogenous and unconfounded by different numbers of segments. The patients in this study were 10 consecutive patients for partial liver resection and so the study population represents a normal mix of patients in the clinical routine. Additionally there is the problem that intraoperative cutting lines are not identical to the Couinaud segments. Couinaud di-
vides the liver into eight segments along hepatic veins and the vena porta with straight lines, but the vessels and the corresponding cutting lines are never straight. Fasel et al. [23] found that up to 51.6% of the liver area has been attributed to the wrong subsegment and Fischer et al. [24] stated that the volume of one segment could be overestimated by 24% or underestimated by 13%. In the present study it was a benefit that resected liver segments were already known when volumetry was performed. In the clinical routine it is an additional problem that it is only known which segments are planned to be resected and that the real cutting line during surgery can differ from this. The semiautomated software used in this study was more accurate in the prediction of resected liver volume, probably also due to the fact that it was possible to determine the size of every liver segment as opposed to drawing one straight cutting line through the liver. Especially in cases with irregular contours of resected segments (e.g. VI–VIII + I), the semiautomated software should deliver a more accurate volumetry. However, the existing incorrectness of the Couinaud segments remains a limitation for all preoperative volumetric methods.

Our study population comprised only ten patients, so the semiautomated software should be tested in a larger population in further studies. Furthermore, the software has some extra tools which are not tested in the present study, but could be of interest for future studies, for example the preoperative planning of radiofrequency ablation.

**Practical Applications**
Both methods for liver volumetry provide an estimated liver volume close to the real one. The tested semiautomated software is faster, more accurate in predicting resected liver volume, less dependent on user experience and more reproducible than the manual method and thus allows a more standardized liver volumetry.

**Clinical relevance**
- This study validates the use of both types of tested software for preoperative evaluation of patient liver volume (total liver volume and volume of liver parts that are planned to be resected).
- The new semiautomated software is considerably faster than the manual method and most other types of reported software and allows an easy integration of liver volumetry into routine image evaluation.
- Additionally, it is less dependent on the user’s experience, which also alleviates integration into routine imaging.

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