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AUTOMATED CT- VOLUMETRY OF RESECTED LIVER SPECIMEN: COMPARISON TO INTRAOPERATIVE VOLUME AND WEIGHT MEASUREMENTS AND CALCULATION

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Abstract:

Background: With rapid growth of machine learning and image analysis techniques, highly accurate CT automatic volumetry methods may substitute for the manual method in clinical liver volume calculation and giving a close correlation between intra-operative liver volume or weight measurements and virtually measured liver volume. The purpose of our study is to evaluate the effectiveness and advantages of automated CT volumetry in the assessment of liver volume in living donor liver transplantation and to compare this technique and its results with those calculated intra-operatively.

Material and Methods: Between February 2017 till February 2019 comparative study was conducted on dynamic contrast enhanced hepatic CT scans of 16 potential living liver donors in Theodor Bilharz Research Institute. The potential donors were investigated using 32 channel multi-detector rows CT scanner (Alexion; Toshiba medical systems) and Automated CT liver volumetry was performed on Myrian workstation using Myrian® XP-Liver software. Potential donors underwent liver transplantation; consequently post-operative weights of the graft were available for comparison with automated CT volumetry results.

Results: After collection of data from preoperative automated volumetry and actual graft weights, we analyzed the degree of difference between the real graft weight and preoperative automated volumetry of the right lobe excluding middle hepatic vein. The average processing time for the automated volumetry was 3.09 ± 0.44 min/case (range, 2.37 – 4.02 min/case), The average volume using automated method was 1035.38 ± 115.79 cm3 (range, 883 – 1217 cm3), while the actual graft weight was 930.63 ± 123.24 gm (range, 700 – 1090 gm) which achieved excellent agreement with the actual graft volume without statistical significance (P value = 0.068). We also found that majority of cases show overestimated the graft weight. Our study showed that automated software with 75 % of cases having less than 15% difference from real graft weight using automated CT volumetry.

Conclusion: Automated CT liver volumetry significantly reduced the time required for volumetry of the liver, accurately predicted the preoperative liver volume and provided

acceptable measurements intra-operative weight/volume of the grafts that can be considered sufficiently accurate for determination of weight/volume of liver graft for surgery.

Key Words: CT automated volumtery – Liver donor – Myrian® XP-Liver software

INTRODUCTION:

Liver transplantation is the most effective treatment for patients with end-stage hepatic disease (1). The size of the liver is considered to be an important prognostic factor in patients candidate for liver transplantation. Imaging techniques have been used for obtaining quantitative measurements of liver volume (2).

Evaluation of total and segmental liver volumes is crucial because assuring appropriate graft size is one of the major predictors of a safe, successful outcome for both donor and recipient (3). At many institutions, contrast-enhanced Multidetector CT (MDCT) is the most widely used radiographic imaging technique for preoperative imaging to assess liver volumes (4).

A liver remnant measuring 30–40% of the original liver volume is required for the donor to survive. A minimum of 40% of the standard liver mass, which is calculated from body surface area, is needed by the recipient. Overestimation of the donor's standard liver volume (SLV) may result in excessive hepatic resection leading to liver failure, while underestimation of the recipient's SLV may result in small-for-size graft syndrome (5).

Manual volumetry on CT images is the current "gold-standard" for liver volume calculation. Although manual volumetry can deliver a relatively accurate result, the lengthy and tedious operation, subjective determination, and intraobserver and interobserver disagreement discourage its usage in routine clinical work (6).

Determination of hepatic volumes using manual tracing is both uncomfortable and time-consuming, requiring an average of greater than 60 minutes in post-processing duration.

With the rapid growth of machine learning and image analysis techniques, highly accurate automatic volumetry methods may substitute for the manual in clinical liver volume calculation (7). Various studies have demonstrated a close correlation between intra-operative liver volume or weight measurements and virtually measured liver volume. The purpose of our study is to evaluate the effectiveness and advantages of automated CT volumetry in the assessment of liver volume in living donor liver transplantation and to compare this technique and its results with those calculated intra-operatively.

PATIENTS AND METHODS

This comparative study was conducted on dynamic contrast enhanced hepatic CT scans of 16 potential living liver donors in Theodor Bilharz Research Institute during the period from February 2017 till February 2019. The potential donors were investigated using 32 channel multi-detector rows CT scanner (*Alexion; Toshiba medical systems*).

All potential donors underwent 1st step laboratory investigations to enter the 2nd step investigations for living donor liver transplantation operations. All potential donors were of average weight and physically fit for operation with no history of any medical diseases. Potential donors underwent liver transplantation; consequently post-operative weights of the graft were available for comparison with automated CT volumetry results.

Inclusion criteria include the candidates for living donor liver transplantation, normal renal functions with no specific sex or age group predilection. Imaging of the candidates for liver transplantation:

Patient preparation:
All potential donors were instructed to fast for food for six to eight hours prior to examination. The potential donors were taught how to hold breath during examination when requested, to ensure their cooperation. We explained the procedure and its duration to the donor and answered any questions. (*An informed written consent was obtained from all potential donors before entering the scanner room*). A suitable wide pore (18-20 gauge) cannula was introduced though antecubital vein. The potential donors lied in supine position on CT gantry.

Technical Specifications:
One scout was acquired in antero-posterior view. The examination was planned on the scout from the level of the top of the right diaphragmatic cupola (Hepatic Dome) till 20 cm caudally in pre-contrast and post-contrast sequences. The pre-contrast series were performed using the following scan parameters: *2-mm slice thickness, X-ray tube voltage 120 kVp, current 150 mA, and 0.75-sec rotation time.* Each potential donor received between 120 to 150 mL of low osmolar non-ionic intravenous contrast agent (*Ultravist or Omnipaque*) using an automatic pump according to the donor's weight (1.5–2 ml/kg) at a flow rate 4–5 ml/s. Arterial phase scanning was achieved by contrast agent tracing. Specifically, the scanning was automatically triggered 8 second after the vascular CT value in the diaphragmatic section of the abdominal aorta reaches 100 HU. The portal dominant phase was started similarly as the 1st one (about 40 seconds post-injection). Then the 3rd and 4th phases (venous phases) were started after a delay of 10 seconds from the end of the 2nd phase to the end of the whole examination. All images were transferred to the workstation *(Myrian® XP-Liver workstation)* for post processing.

Post-processing

Automated CT liver volumetry was performed by experienced radiologist specializing in liver imaging on *Myrian workstation* using *Myrian® XP-Liver software*. The hepatic venous phase images were used to maximize the intensity difference between the liver parenchyma and non-liver tissue. First, Myrian program for automated liver extraction was applied to 1 mm CT images and the liver boundaries were obtained automatically. We edited the boundary to enhance the accuracy of volumetry. A virtual hepatectomy plane was defined on the 3D hepatic vein models and axial images, for segmental volume analysis. The total and lobar volumes of liver ware calculated. The time required to complete the automatic tracing for each case was recorded.

After opening the workstation, you will be able to load a local exam, or to import CD/USB data from the main patient list. There are two ways to open a study, either with Generic MPR mode for a basic review with MPR / MIP / 3D, either with XP-Liver Multiphase protocol to access the advanced liver segmentation module. It is possible to select multiple Series inside a study folder. Once you opened your selection of series with the XP-Liver Multiphase protocol, the workspace will open, all the images will load, and an automatic synchronization will be processed.

In the first Viewport Layout, you have all the phases displayed, in a synchronized interface: Zoom, navigation, panning and windowing are synchronized between the views. In the 3D Viewport Layout, you will have your 2D images on the left, and the 3D results on the right, letting you change between the different phases manually to do the different segmentation. The segmentation tools are very powerful and they have to be used carefully, and always in the same steps.

There are 3 steps to go through: a) select the ROI (*Region of interest*) you want to work on, b) select the tool you want to use, c) let the process finish before moving to any next step.

Tool number 1 is used for the segmentation. It will be used on all the ROI the same way: Select the good ROI, select the tool and click in the good anatomic region. ***Tool number 2*** is used to do correction. It can be used on both 3D and 2D, but they have a different behavior: **In 3D**: Easy for Fast and big correction. Doing a contour on the 3D will erase the selected ROI. **In 2D**: It can be used to Delete or Create ROI volume with multiple contours. ***Tool number 3*** is used for the surgery planning. You will be able to use this tool on 2D or on 3D by drawing a cutting surface and creating different lobes/Segments (Figure 1).

Figure 1- segmentation Tools.

The cutting surface tool bar can also be used on 3D or on 2D. Please make sure you selected the good ROI in the list before starting to cut. The 3 steps of the cutting process are: a) draw the cutting surface and edit it, b) validate the cutting, c) click on the part you want to remove. *It's possible to do a new cutting surface, after selecting the correct ROI and starting the process again* (Figure 2).

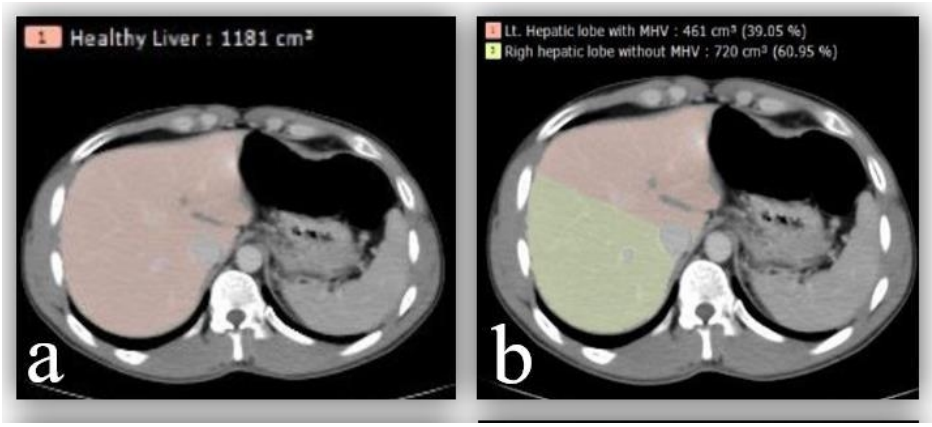

Figure 2. (a & b): axial cuts of the liver venous phase showing: (a) automated volumetry of the whole liver volume, (b) automated volumetry of the right hepatic lobe excluding the MHV "green color".

Intraoperative data measurement:
During bench surgery, the right liver lobe was flushed with an organ perfusion solution. After all the intra-hepatic liquid media has drained to a large extent, the weight of the resected right liver lobe was determined with a calibrated electronic laboratory scale. It is widely accepted that studies using pre-operative and intra-operative liver volumetric measurements are based on the assume that the density value is on the order of 1.00 g/mL, to facilitate the conversion of volumetric values to weight values.

Statistical Analysis:
Whole liver volume, volume of right hepatic lobe without MHV and estimated graft weight were presented as mean (±standard deviation [SD]), and (minimum, maximum) values. We compared the results obtained with automated liver volumetry. The difference between preoperative automated volumetry and real graft weight was graded into minimal difference (≤15%) and big difference (>15%).

RESULTS

This comparative study was conducted on dynamic contrast enhanced hepatic CT scans of 16 potential living liver donors in Theodor Bilharz Research Institute during the period from February 2017 till February 2019. The 16 potential donors consisted of 12 males and 4 females with age ranging from 18 – 47 years with a mean of 29.19 ± 8.27 years, as shown in Table 1 and Figure 3.

Table 1. Age and sex distribution of the included potential donors.

		Total no. = 16
Age	Mean ± SD	29.19 ± 8.27
	Range	18–47
Sex	Female	4 (25%)
	Male	12 (75%)

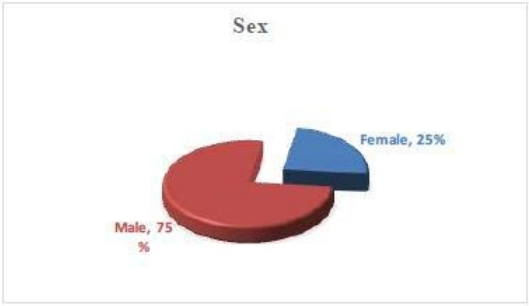

Figure3. Sex distribution of the included potential donors.

The average automated whole liver was 1620.24 ± 329.83 cm3 (range, 1181 – 2434 cm3) as shown in Table 2 and Figure 4.

Table 2. Automated whole liver volume.

Method	Volume		Error %
Automated whole liver volume	Mean ± SD	1620.24 ± 329.83	-0.8 % ± 3.92
	Range	1181 – 2434	

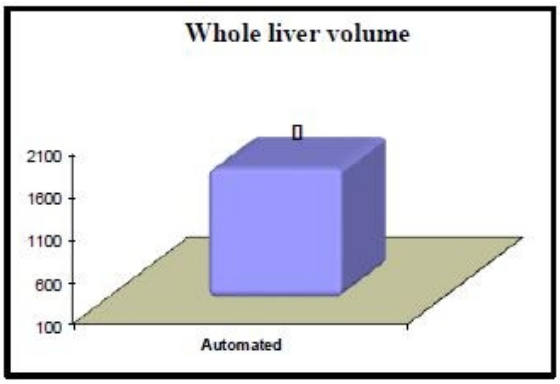

Figure 4. Mean whole liver volumes of automated volumetry.

Duration of Automated CT Volumetry

The average processing time for the automated volumetry was 3.09 ± 0.44 min/case (range, 2.37 – 4.02 min/case) as shown in Figure 5.

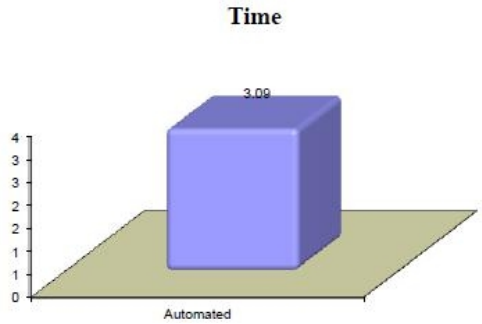

Figure 5. Mean processing time of automated volumetry.

Intraoperative Actual Graft Weight Measurements

The potential donors underwent liver transplantation surgery and the planned grafts were excised and transplanted to their recipients after excision of their original liver. The Grafts were weighed intra-operatively, and then compared with the preoperative estimated automated volume. In all donors, the graft involved the right hepatic lobe to the right of the middle hepatic vein. After collection of data from preoperative automated volumetry and actual graft weights, we analyzed the degree of difference between the real graft weight and preoperative automated volumetry of the right lobe excluding middle hepatic vein. The absolute graft weight was considered to be the actual graft volume because the liver has nearly the same density as water.

Majority of cases overestimated the real graft weight. Underestimation was seen in 2 cases from the automated CT volumetry. Absolute values of differences between preoperative automated volumetry and real graft weight were summarized and graded into minimal difference (≤15%) and big difference (>15%) as shown in Table 3, according to Mussin et al. (8)

Table 3. Grading of difference between estimated automated graft volume and real graft weight.

Difference	Automated volumetry (n = 16)
Minimal difference (≤15%)	10 (62.5%)
Big difference (>15%)	6 (37.5%)

The average volume using automated method was 1035.38 ± 115.79 cm3 (range, 883 – 1217 cm3), while the actual graft weight was 930.63 ± 123.24 gm (range, 700 – 1090 gm), as shown in Table 4.

Table 4. Summarizes the comparison of right hepatic lobe liver volumes excluding MHV using automated method & actual graft weight.

Method		Volume	Deviation from actual graft volume
Automated Rt. Lobe excluding MHV	Mean ± SD	1035.38 ± 115.79	12.35 ± 16.22
	Range	883 – 1217	-8–43%
Actual graft weight	Mean ± SD	930.63 ± 123.24	Not applicable
	Range	700 – 1090	

Automated volumetry also achieved excellent agreement with the actual graft volume without statistical significance (P value = 0.068) as shown in Table 5.

Table 5. Shows agreement between automated volumetry and actual graft weight.

	Actual graft weight	Automated Rt. Lobe excluding MHV	Paired t-test		
			t	P-value	Sig.
Mean ± SD	930.63 ± 123.24	1035.38 ± 115.79	-2.158	0.068	NS
Range	700 – 1090	883 – 1217			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

Bland-Altman plots for assessing agreement between preoperative automated volumetry and actual graft weight are shown in Figure 6. It shows that almost all points fall in the 95% limit-of-agreement confidence region, which indicates that automated liver volumetry achieved excellent agreement with actual graft weight.

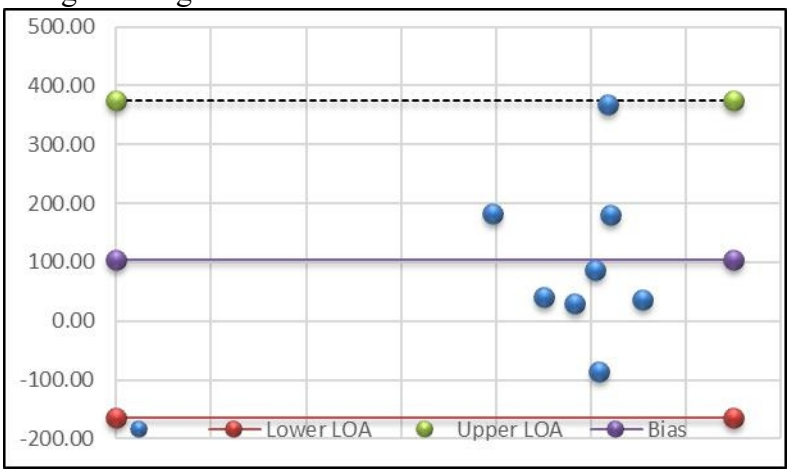

Figure 6. Bland-Altman plots for agreement between preoperative automated volumetry and actual graft weight.

DISCUSSION

Living donor liver transplantation is an effective, life sustaining surgical treatment in patients with end-stage liver disease and a successful liver transplant requires a close working relationship between the radiologist and the transplant surgeon (2).

Optimal graft size is an important element of both the donor evaluation and the excellent outcome of LDLT. Therefore, it is necessary to have a reliable preoperative estimation of appropriate graft size that will meet the metabolic demands of the recipient and at the same time provide an adequate liver remnant volume for donor safety (8).

It is important to use no more than 70% of the donor liver volume and that the graft be of the appropriate weight for the recipient. We take extreme care to leave 30% of the total liver volume in the donor and to obtain a volume/weight ratio for the recipient of between 0.8% and 2.9% (9). Due to advances in technology, several computer-aided protocols and commercially available standalone specialized virtual software systems have recently been advocated to simplify the volumetry calculation and hasten its process. However, each software has its own strengths and weaknesses (8).

In our study, we utilized Myrian workstation using Myrian® XP-Liver software as an automatic liver volume calculation program that uses data obtained from CT examinations. We utilized 32 channel multi-detector rows CT scanner (Alexion; Toshiba medical systems). Although our automated volumetry software carefully extracted liver borders on each CT section, some measurement errors did occur. Because the areas were extracted on the basis of their CT number, the errors may be attributable to a partial volume effect at the liver edge, to proximity of the adjacent tissue with attenuation similar to that of the liver parenchyma and/or to exclusion of intrahepatic regions that have CT numbers different from those of the surrounding parenchyma. To overcome this point in automated liver volumetry, we applied manual correction, which was accomplished rapidly with routine manipulations.

We aimed reducing the difference between the preoperative measured volume and actual liver volume (or weight) measured at surgery.

Our study included 16 cases to evaluate the automated volumetry. Other studies included: 35 cases as in a study done by Nakayama et al. (7) and 18 cases in a study done by Suzuki et al. (5). We estimated the average total processing time for the automated volumetry, and it was 3.09 ± 0.44 min/case (range, 2.37 – 4.02 min/case). In a study conducted by Suzuki et al., the average automated volumetry time was 4.1 ± 1.5 min/case (range, 2.3 –7.7 min/case), while in a study conducted by Nakayama et al., the average automated volumetry time was 4.4 ± 1.9 min/case (range, 3.0 – 7.0 min/case). For a right hepatectomy, the liver is divided into lobes with an imaginary line drawn along the middle hepatic vein, leaving the vein on the donor side, and then the volume of the right liver and the remaining liver tissue are calculated. The same radiological

protocol and volumetric analysis program were used in all of our cases. Millimetric deviations seen on the tracing of the middle hepatic vein may cause great discrepancies in the volumetric assessment. The demarcation line can be seen during the operation after temporary closure of the right portal vein and the right hepatic artery is achieved (9).

Our study showed that preoperative automated volumetry achieved excellent agreement with the estimated graft volume without statistical significance, *P value* = 0.068 for automated volumetry. We also found that majority of cases show overestimated the graft weight. Our study showed that automated software with 75 % of cases having less than 15% difference from real graft weight using automated volumetry. Also in a study presented by Mussin et al. (8), automated software significantly calculated right liver volumes having less than 15% difference from real graft weight. This may be attributed to small number of cases in our study. When we compared the values of corresponding preoperative automated volumetric measurements and intra-operative weight measurements, the mean preoperatively measured values showed a deviation of – 8 to 43 %% from the intra-operatively measured values with mean deviation amounted to 12.53 %, and a standard deviation of 16.22 %. In contrast to a study conducted by Lemke et al. (10) measurement results revealed a substantial discrepancy between the intra-operative and the preoperative measurements with mean value of 34.3%. In a study presented by Nakayama et al., it showed that liver volume measured with CT volumetry is also overestimated compared with the actual liver volume measured after resection. According to the literature, a deviation of some 10% is to be expected in an automatically calculated preoperative volume assessment. Liver volume calculations in donors aged less than 36 years have been reported to be closer to intraoperative measurements as reported by previous studies conducted by Yonemura et al. (11) and Kayashima et al.(12). We did not study the effect of age on liver volume calculations.

The main possible explanation for this phenomenon is that actual liver volumes are measured with less blood in the hepatic vessels. Therefore, exclusion of major hepatic vessels may be desirable. ***Kim et al. (1),*** developed automated volumetry without blood for the right lobe. In our study, we did not exclude major blood vessels or biliary structures from the automated volumetry, yet it can be done using Myrian software.

Other explanation is that the actual cutting line of the graft is determined by temporary clumping of the hepatic vessels, so it may differ from the preoperative estimation**.** CT volumetric error can, to some extent, be attributed to the variable physiologic density of the hepatic graft. In our study, CT volumetric values were converted to weight values on the basis of the general assumption that the density of the hepatic tissue was 1.00 g/mL. However, results from a study done by Lemke et al. on 16 live liver donors indicated that mean hepatic density was approximately 12% higher than 1.00 g/mL, and substantial individual variations of density occurred**.** Similarly, Karlo et al. (13) suggested a factor of 0.85 for CT to convert volume to weight, but their result is limited and may not apply to living liver donors because the resected hepatic specimens in that series had underlying diseases that might have resulted in a density different from that of normal liver. Hepatic steatosis also may affect the density of the hepatic graft and the conversion factor. In conclusion, we found automated CT liver volumetry performed with the Myrian® XP-Liver software significantly reduced the time required for volumetry of the liver, accurately predicted the preoperative liver volume and provided acceptable measurements intra-operative

weight/volume of the grafts, we concluded that automated CT liver volumetry provides acceptable volumetric measurements that can be considered sufficiently accurate for determination of weight/volume of liver graft for surgery.

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