Liver volumetry performance of a fully-automated, post-processing solution for whole-organ and lobar segmentation based on MDCT imaging

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Accurate liver volumetry is of utmost importance in preoperative assessment preceding liver donation and treatment planning of surgical and intraarterial interventions.[1,2,3,4] At many institutions, contrast-enhanced Multidetector CT (MDCT) is the most widely used radiographic imaging technique for assessment of longitudinal disease evolution and to perform preoperative imaging, in particularly evaluating vascular hepatic supply and drainage, hepatic parenchyma enhancement characteristics, disease location and relationships to hepatic arterial and venous as well as portal vasculature, and, eventually, liver volumes.

Determination of hepatic volumes using manual tracing is both cumbersome and time-consuming, requiring, historically, on average of greater than 30 minutes in post-processing duration.[5,6] Additionally, this technique suffers from substantial inter- and intraobserver variability. These limitations of manual segmentation techniques have created the impetus to develop semi-automated interactive segmentation techniques. Even though resulting improvements in accuracy of liver volumetry has been observed, still substantial measurement variability and considerable post-processing durations characterized these semi-automated interactive segmentation techniques.[6,7,8,9,10]

A prerequisite for any quantitative measurement technique is to optimize and balance accuracy and precision thereby establishing outputs as reproducible and standardizable biomarkers, such as liver volumes, which then can be reliably incorporated into both clinical trials and longitudinal comparisons assessing disease evolution. Recent initiatives such as the Quantitative Imaging Biomarkers Alliance (QIBA) and the American College of Radiology Imaging Network (ACRIN) sought to identify sources of variation that may contribute to overall measurement error. These standardization initiatives are crucial to permit comparisons independent of imaging and post-processing platforms, clinical sites and time of imaging. The goal is to standardize all factors contributing to overall measurement error and to limit the within-subject coefficient of variation to a value of smaller than 20%. Thereby, any change in within-patient measurement greater than 40% can confidently be attributed to disease evolution and / or therapy effect.[11]

The purpose of this White Paper was to evaluate the performance of a fully automated, post-processing solution for whole-liver and dual-seed lobar segmentation based on MDCT image datasets assessing whether fully-automated whole-liver and dual-seed lobar segmentation can be achieved with high precision in the in-vivo patient populations.

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Materials and Methods

In-vivo Patient Population

The institutional database was accessed to identify patients who had received both, a multiphasic contrast-enhanced CT and also had an MRI of the liver within three months, for the indication of evaluation of chronic liver disease during the time period from 01/2011 – 12/2011.

Exclusion criteria included (i) morphologic features of cirrhosis, (ii) history of prior liver / biliary surgery or liver tumor ablation procedures, and (iii) one or more liver lesions greater than 3 cm in size identified by CT or MRI, and (iv) portal or hepatic vein thrombosis. A total of 25 patients were enrolled. Of the 25 patients, 12 were male, with an average age of 68.2 years ± 11.5 (range 44 - 83 years); and 13 were female, with an average age of 55.4 ± 16.4 years (range 27 - 86 years).

MDCT Acquisition

All MDCT in-vitro and in-vivo examinations were performed on a commercially available 128-MDCT scanner. An x-ray tube voltage of 120 kVp and dose-modulated effective reference x-ray tube current of 200 mAs with a gantry rotation time of 0.5 secs and a target pitch of 0.8 were applied, acquiring image series with a collimation of 128 x 0.6 mm, using a matrix size of 512 x 512 pixels, resulting in an in-plane pixel size of 0.76 mm, reconstructing 0.6 mm thin images. Individual contrast bolus-tracking was performed during repetitive low-dose acquisitions at 120 kVp / 40 mAs and placement of a threshold region-of-interest (ROI) within the abdominal aorta at the level of the diaphragm, plotting HU contrast wash-in to a level of 150 HU following contrast administration of 100 ml 320 mg I / ml contrast agent administered at 4 ml / sec injected into a right antecubital vein using a CTA injector. The diagnostic arterial and portal-venous cranio-caudal helical hepatic MDCT acquisition commenced 12 secs and 60 secs post 150 HU wash-in, respectively.

Manual vs. Automated Liver Volumetry performing Whole-Organ and Lobar Segmentation

Liver volumetry of in-vivo patient image series were performed using the Extended Brilliance Workspace environment (EBW version 5, Philips Healthcare, Cleveland, OH) employing a commercially available CT Volume Viewer software package (version 5.0.10778.0) as well as the PortalLiver volumetry (version 5.0.0.0022) application. All quantitative volumetric evaluations were performed in consensus decision by two radiologists, (G.F.) and (D.T.B.), with one and seven years' experience in image data post-processing, respectively. Volumetry duration was timed; all manual and automated liver volumetry was repeated 3 times with more than one-month interval between individual repetitions.

Manual Liver Volumetry

In-vivo patient (747 ± 57 axial slices, range 593 – 877) volumetric datasets were loaded by the CT Volume Viewer application and made available in axial, sagittal, and coronal reformations. A seed pointer was centrally placed over internal portions of the liver, with an interactively controlled growing color-overlay region-of-interest (ROI) visible to the radiologists; region growing speed (100 mL/sec), seed size (20 mm^2) and sensitivity to attenuation differences (sensitivity 5, range 1 – 10) were standardized for the in-vitro phantom and in-vivo patient datasets. If color-overlay ROIs were noticed outside of the liver on axial, sagittal, and coronal reformations, an eraser tool with identical settings was utilized. This was performed until the radiologists deemed the volumetric assessment appropriate. The CT Volume Viewer application was then prompted to provide volumetric calculation of the hepatic ROI, resulting in the whole-organ volume of the in-vitro and in-vivo livers.

Manual lobar segmentation performed in the in-vivo patient population was based on whole-organ volumetry with additional manual tracing of the middle hepatic vein from confluence to the periphery as well as location of the gallbladder fossa. This manual tracing defined a cut-plane separating the right hepatic lobe (Couinaud segments V, VI, VII and VIII) from the left hepatic lobe and caudate lobe (Couinaud segments II, III, IV, and I, respectively).[12] The CT Volume Viewer application was analogously prompted to calculate the volumes of right as well as left and caudate lobes.

Automated Liver Volumetry

Phantom and patient volumetric datasets were loaded into the PortalLiver volumetry application; whole-organ segmentation started without any further user input. The liver volumetry process employed by the PortalLiver application using contrast-enhanced MDCT image series belongs to the family of variational approaches algorithms. These algorithms rely on deformation processes of population-based meshes guided by Hounsfield attenuation differences as well as surrounding anatomical structures. Here, variational approaches algorithms are composed of four sequential steps:

1. Anatomical structures in the imaged field-of-view are coarsely segmented to provide spatial context information using high-pass filtration
2. Region of interest with high likelihood to be located inside the liver are defined
3. Liver tissue likelihood within the region of interest is estimated and refined as the mesh evolves
4. Mesh evolution is based on likelihood of and proximity to surrounding structures.

Subsequently, two-seed lobar segmentation commenced after the operator confirmed location of two seed points located at the confluence of the middle hepatic vein and the inferior vena cava (IVC) as well as 2 cm distal into the middle hepatic vein lumen.

Statistical Analysis

Reproducibility of the three in-vivo patient liver measurement repetition results utilizing the manual and automated whole-organ and lobar segmentation tools were evaluated by determining the intra-observer kappa-values and PANOVA p-values.

Consistency of volumetric results achieved with manual and automated segmentation approaches were evaluated by determining the inter-class correlation coefficient and PANOVA methodology. Graphical analyses of intra-observer and inter-class correlation was performed using the Bland-Altman methodology.

Comparison of processing times for each measurement performed with manual and automated segmentation tools was analogously performed with PANOVA methodology.

Results

Performance of the Manual and Automated Segmentation Applications

Reproducibility of Measurement repetitions performed with the automated volumetry application resulted in identical values for the whole-organ assessment, Figure 1. Significantly reproducible whole-organ volumetry was achieved with the manual segmentation application, PANOVA 0.98, Figure 2a and Table 1. Automated volumetry utilized to perform lobar segmentation improved reproducibility over manual segmentation approaches in particular for left lobe segmentation, without detecting significant measurement variations in repetitions for either approach, PANOVA 0.95 - 0.99, Figures 3, 4a and 4c as well as Table 2.

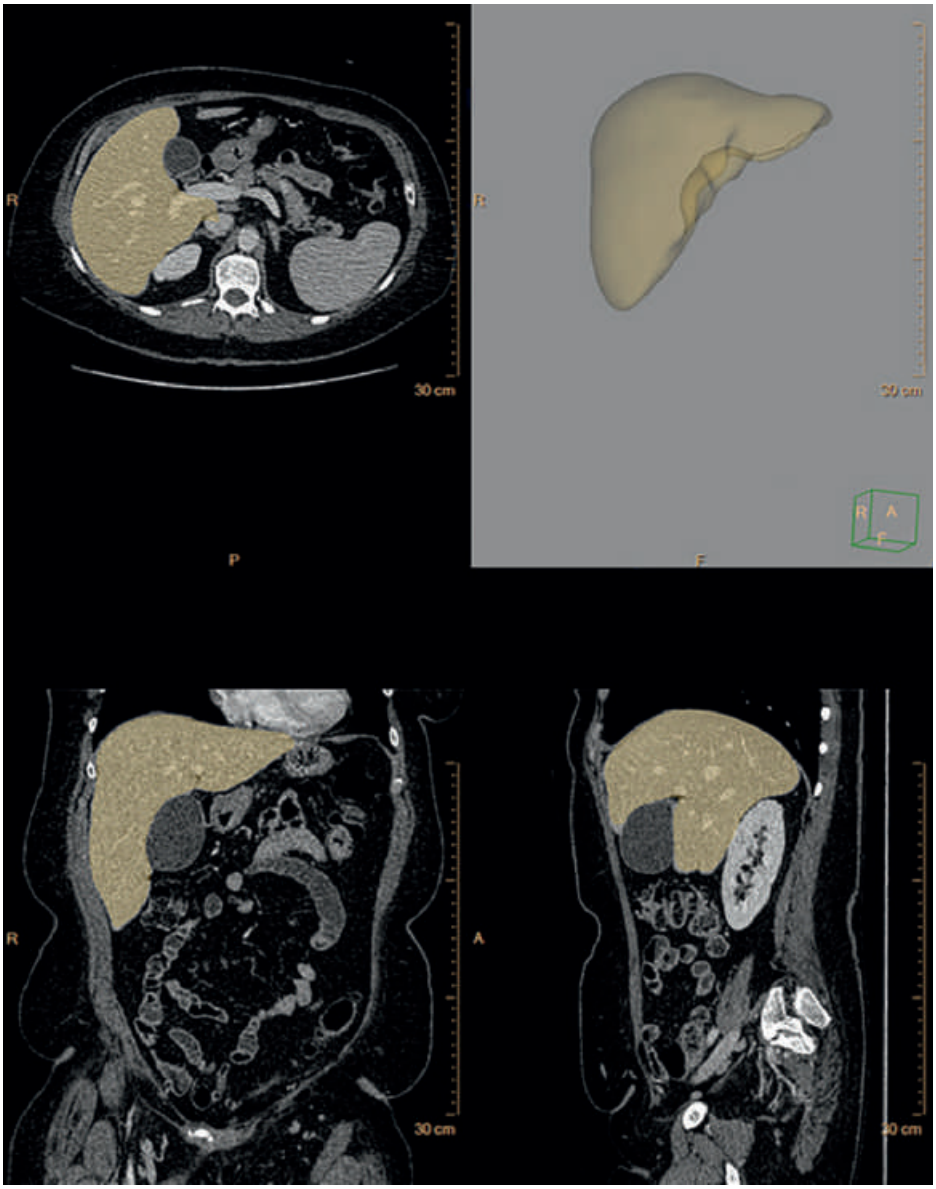

Figure 1: PortalLiver volumetry application showing whole-liver volumetry as color-overlay on axial, coronal and sagittal reformations as well as volume-rendering.

Consistency between Manual and Automated Segmentation

Comparisons of volumetric whole-organ results achieved with manual and automated segmentation solutions showed no significant differences between the two methods with significant inter-class correlation, Table 1. Notably, the spectrum of measurement variations observed in repetitions utilizing the manual technique appears greater than the mean variation seen in a direct comparison between manual and automated segmentation tools, Figure 2b.

Analogously, no significant differences between manual and automated lobar segmentation, however, significant inter-class correlation was observed, Table 2. The variation between manual and automated lobar segmentation was greater in the left lobe compared to the right lobe, Figures 4b and 4d. Similarly, the spectra of measurement variations observed in right and left lobar repetitions utilizing the manual technique appears greater than the mean variation seen in a direct comparison between manual and automated segmentation tools.

Duration of Manual and Automated Segmentation

Automation of whole-organ and segmental volumetry accelerated volumetric post-processing significantly, compared to manual approaches, PANOVA < 0.001 and, simultaneously, decreased the spectrum of different durations for this post-processing task, Table 1.

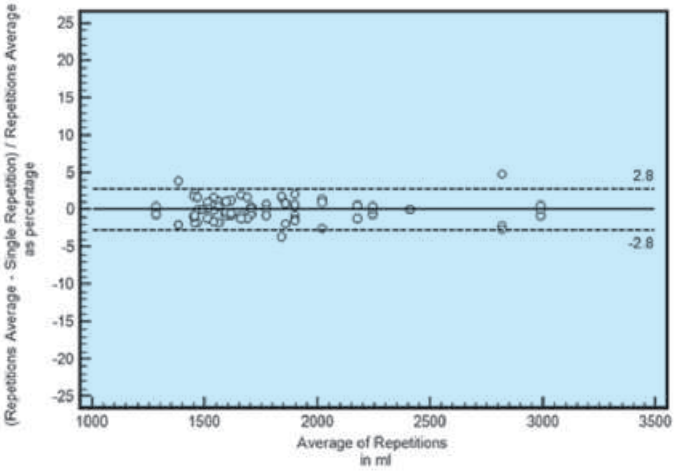

Figure 2a: Bland-Altman plots evaluating whole-organ hepatic volumetry. Graphical analyses of intra-observer manual (a) and inter-class correlation between manual and automated approaches (b). Note that the spectrum of measurement variations observed in repetitions (a) appears greater than the mean variation seen in a direct comparison between manual and automated segmentation tools (b).

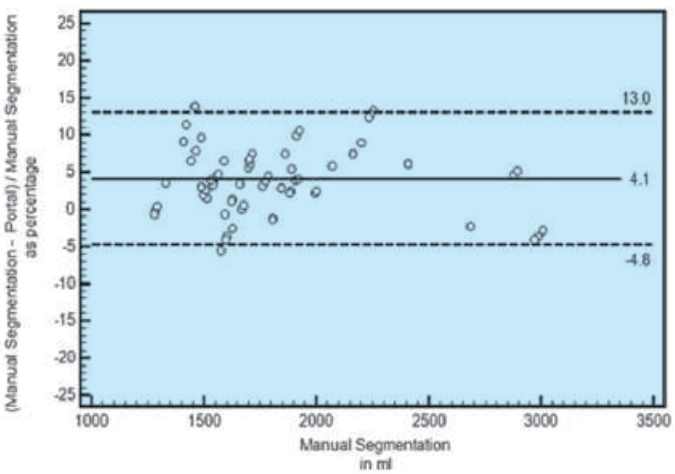

Figure 2b: Bland-Altman plots evaluating whole-organ hepatic volumetry. Graphical analyses of intra-observer manual (a) and inter-class correlation between manual and automated approaches (b). Note that the spectrum of measurement variations observed in repetitions (a) appears greater than the mean variation seen in a direct comparison between manual and automated segmentation tools (b).

Discussion

The practice of using MDCT datasets for liver volumetry has been supported by evidence of substantial congruity between manual assessments of liver volumetry comparing MDCT and ex-vivo liver volume determination results; however, the use of conversion factors to improve measurement correlation was still advocated by various studies.[7,8,9,10] More recently, newer techniques have emerged that automatically assess whole-liver volumes and have shown promising accuracy with substantial decrease in post-processing times.[5] However, whenever locoregional therapies such as external beam radiation or selective radioembolization have been considered in clinical scenarios, whole-organ volumetry is insufficient to precisely determine appropriate dosages.[13,14] Subsequently, the previously proposed automated techniques have limitations in their clinical utility, since segmental volumetry has not been incorporated yet.

This evaluation showed that the automated software systems demonstrate close approximation of whole-organ and lobar volumes with that generated through the manual interactive approach. Interestingly, automated approaches resulted in insignificant underestimation of whole-organ and lobar volumetry in the majority of clinical cases, averaging ~4.1%. Bland-Altman plots revealed that repetitive manual left lobe segmentations resulted in greater intraobserver variability, the detected overall differences in measurement variation between manual and automated left lobar segmentations, however, averaged to ~0.2%. In contrast, right lobar segmentation achieved substantially better intraobserver variability, however, resulted in overall mean differences in measurement variation between manual and automated approaches approximating ~5.7%. Few studies have evaluated lobar volumetry; a recent study confirmed our findings that the right hepatic lobe shows less variation in volumetric results than the left for automated systems.[15]

Generation of whole-liver and lobar volumes can often be cumbersome, either when using the manual or interactive approaches. Automated tools can prove to be of use in rapidly extracting clinically reliable whole-liver volumes, as evident by significantly shortened processing time of automated compared to manual approaches. Knowledge that greater variations occur mostly in the left hepatic lobe can help in focusing the radiologist to this portion of the liver when validating the automatically generated volume. While whole-liver volumes are useful, there is substantially added benefit in being able to generate automated lobar and possibly segmental volumes.

This evaluation showed that fully-automated whole-liver segmentation can be achieved with high precision in in-vivo patient populations; dual-seed lobar segmentation showed slight tendencies for underestimating the right hepatic lobe and greater variability in edge detection for the left hepatic lobe.

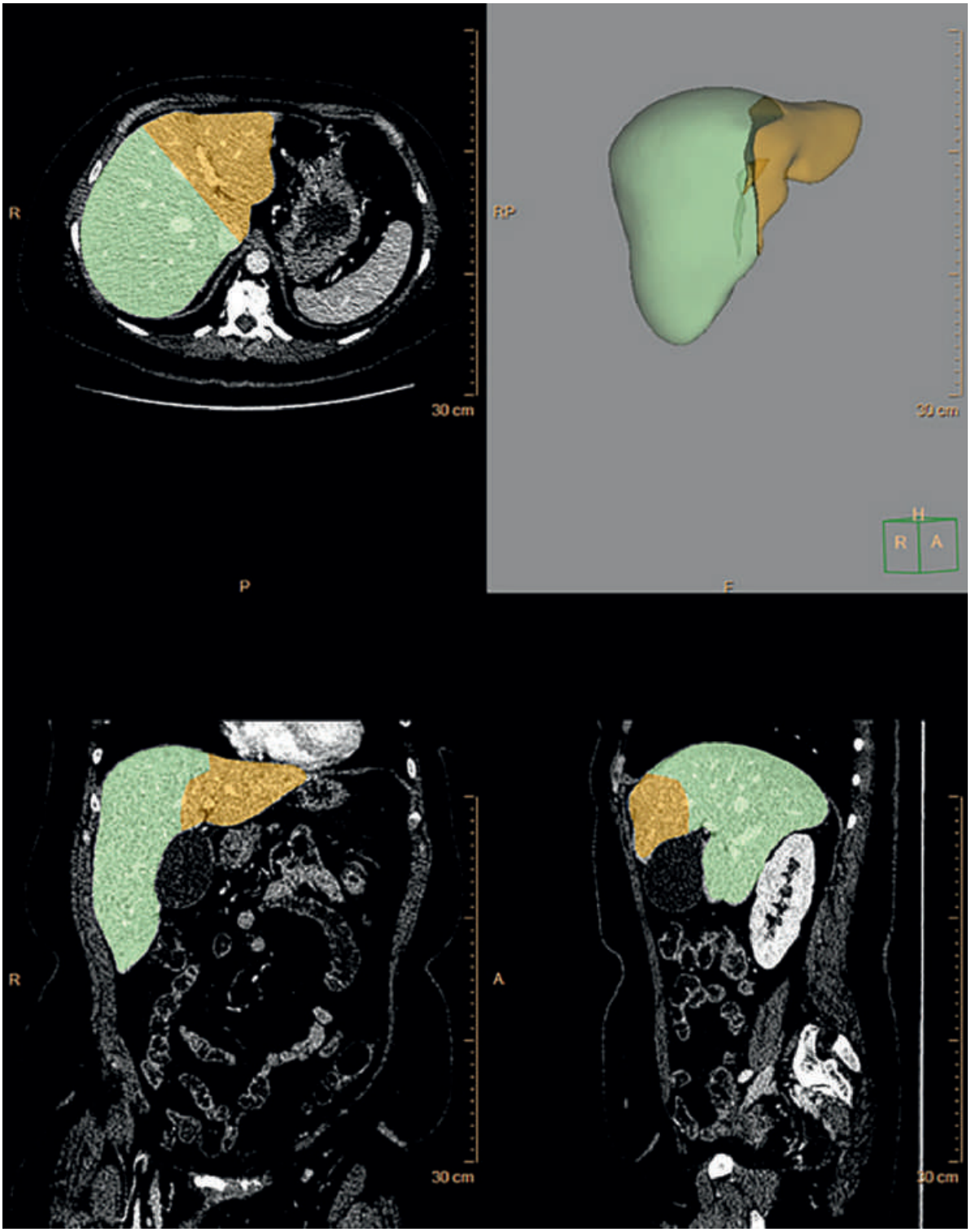

Figure 3: PortalLiver volumetry application showing lobar volumetry as color-overlay on axial, coronal and sagittal reformations as well as volume-rendering.

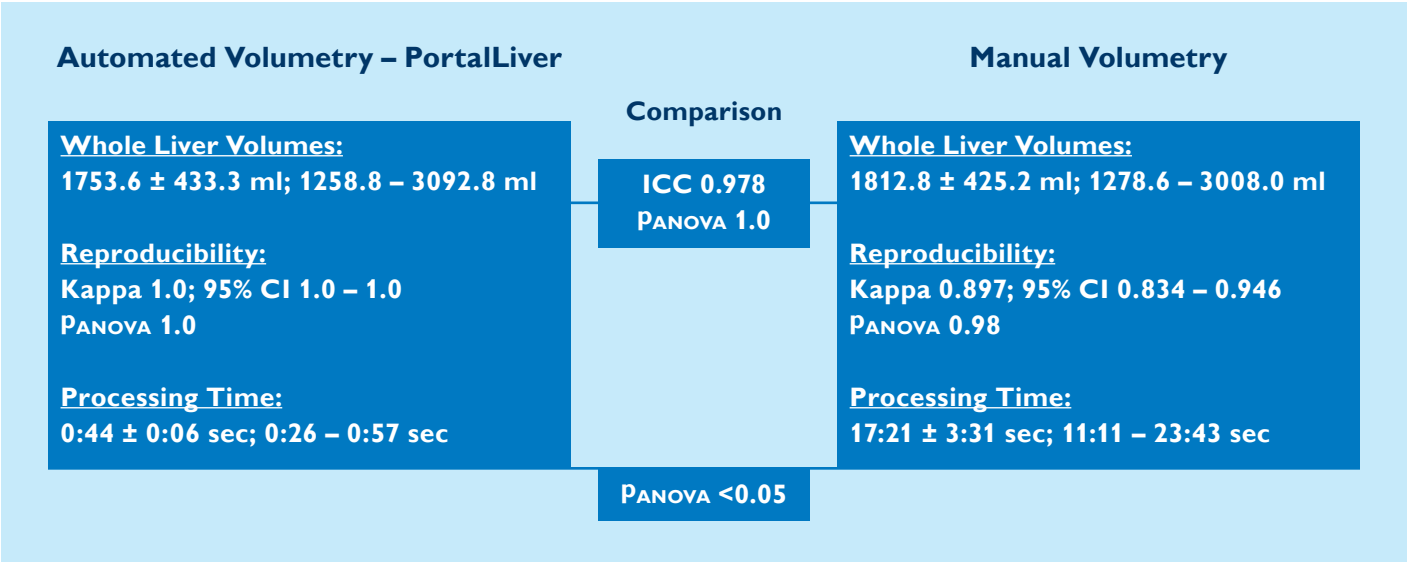

Table 1: Performance of the manual and automated whole-organ segmentation.

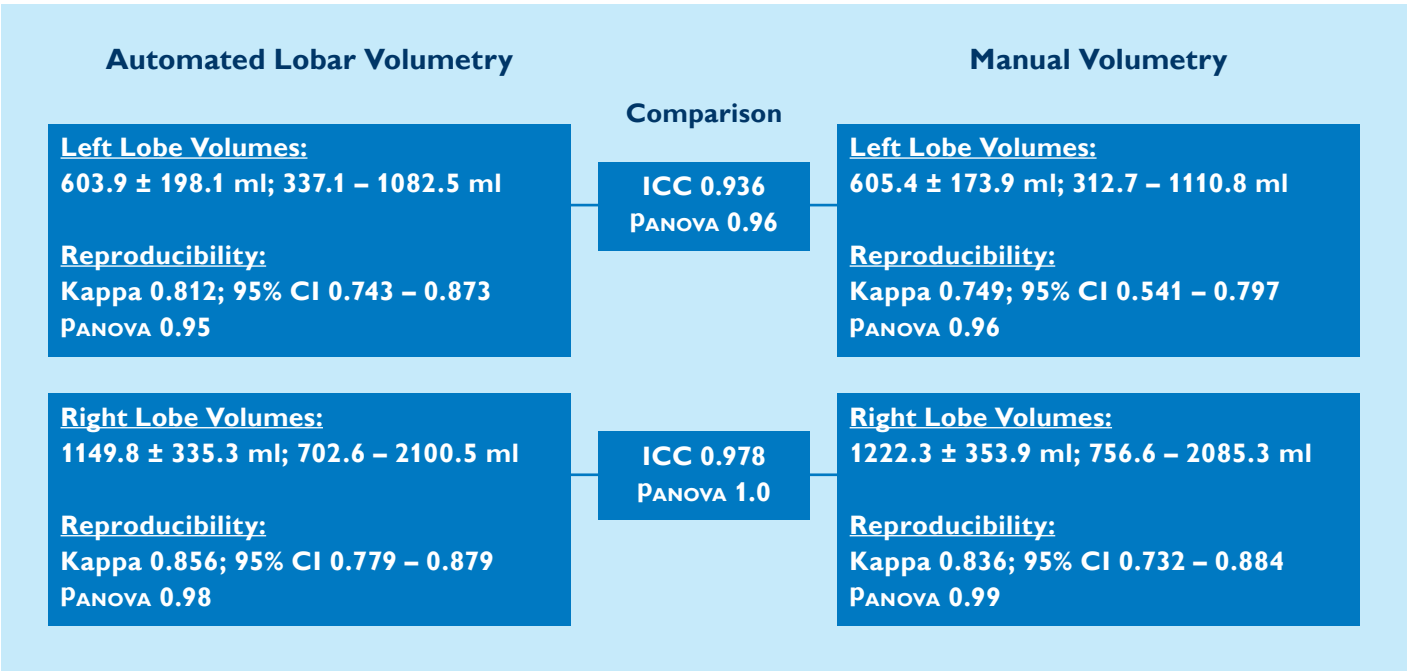

Table 2: Performance of the manual and automated lobar segmentation.

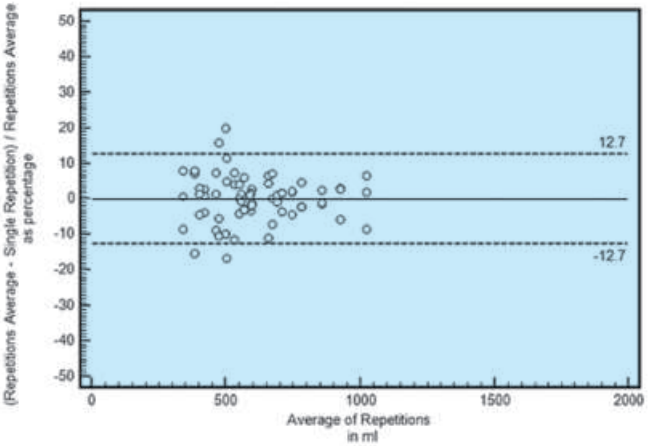

Figure 4a: Bland-Altman plots evaluating lobar volumetry assessing the left (a and b) and right (c and d) hepatic lobes. Graphical analyses of intra-observer manual (a and c) and inter-class correlation between manual and automated approaches (b and d). Note that the spectrum of measurement variations observed in repetitions (a and c) appears greater than the mean variation seen in a direct comparison between manual and automated segmentation tools (b and d).

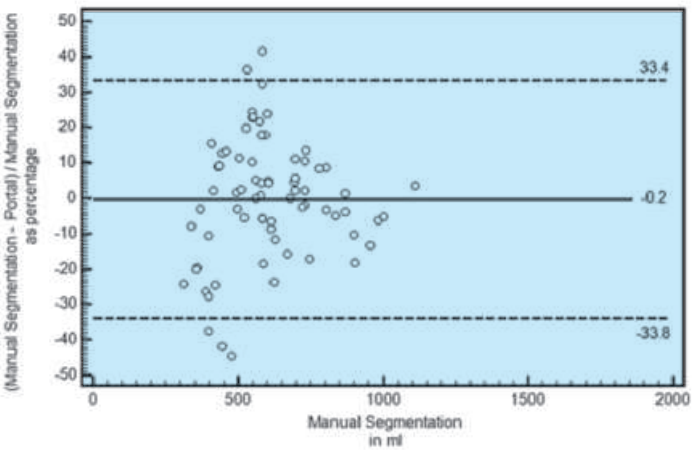

Figure 4b: Bland-Altman plots evaluating lobar volumetry assessing the left (a and b) and right (c and d) hepatic lobes. Graphical analyses of intra-observer manual (a and c) and inter-class correlation between manual and automated approaches (b and d). Note that the spectrum of measurement variations observed in repetitions (a and c) appears greater than the mean variation seen in a direct comparison between manual and automated segmentation tools (b and d).

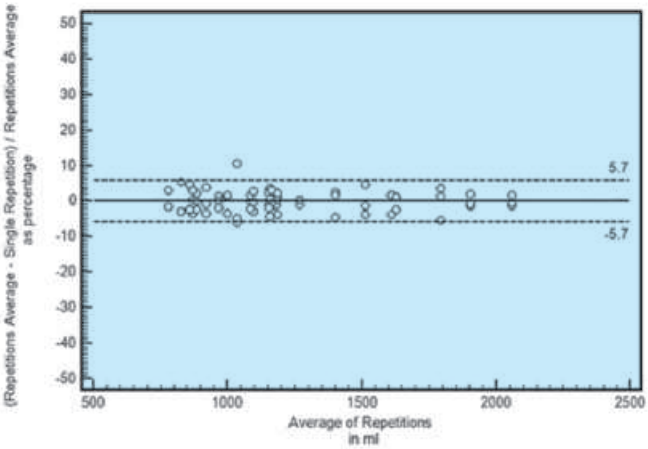

Figure 4c: Bland-Altman plots evaluating lobar volumetry assessing the left (a and b) and right (c and d) hepatic lobes. Graphical analyses of intra-observer manual (a and c) and inter-class correlation between manual and automated approaches (b and d). Note that the spectrum of measurement variations observed in repetitions (a and c) appears greater than the mean variation seen in a direct comparison between manual and automated segmentation tools (b and d).

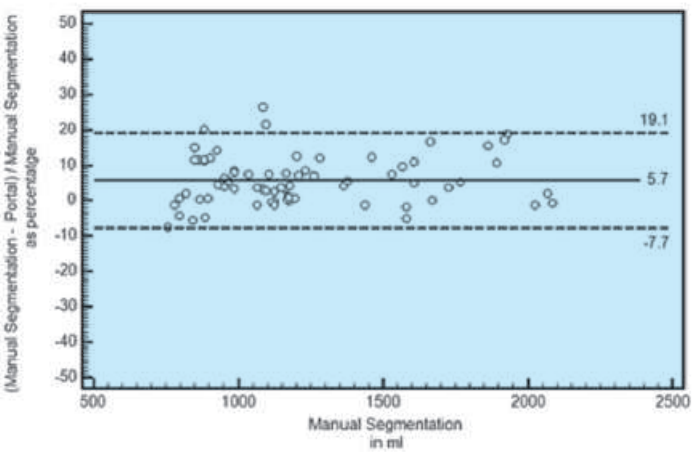

Figure 4d: Bland-Altman plots evaluating lobar volumetry assessing the left (a and b) and right (c and d) hepatic lobes. Graphical analyses of intra-observer manual (a and c) and inter-class correlation between manual and automated approaches (b and d). Note that the spectrum of measurement variations observed in repetitions (a and c) appears greater than the mean variation seen in a direct comparison between manual and automated segmentation tools (b and d).

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