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Volumetric aspects of the extensive liver resections planning

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Abstract

Introduction: The reasonability of routine volumetry prior to liver transplantation is unquestionable. However, there is a lack of clear recommendations for this procedure in the cohort of patients with planned liver resection.

Objectives: Analysis of the results of own experience and recent literature data on precise determination of optimal approach for volumetry implementation for liver resection. The volume of future liver remnant is a critical factor of hepato-biliary surgery as it represents potential risk factors of acute liver failure (ALF) in postoperative period. Such a questions like safe minimal parenchyma volume of future liver remnant (FLR) and selection of the modality of its volume calculation remain to be unclear.

Results: The median of total liver volume was 1784.1±72, 1763.3±94 and 1799.9±81 mm^3 while used Philips Workstation, Onis 2.5 and Varian Eclipse, respectively ($p = 0.54$). The median of FLR volume was 375.4±115, 368.7±111 and 397.9±110 mm^3 with mentioned above programs, respectively, ($p = 0.73$). We emphasize that preoperative calculation of FLR volume, precise examination of variant vascular and biliary liver anatomy are critical for reduction of surgical complications rate, especially when extensive resections are planned.

Conclusions: Analysis of own results and literature data demonstrate importance of carried out studies and indicate reliable correlation between manual and semi-automatic methods of volumetric measurements of liver and its separate segments/sections. We demonstrate that volumetry of liver and its separate anatomic structures in case of "major" resections is a necessary stage in preoperative examination in terms of calculation of minimally permissible tissue volume in such patients. MRI and CT images are equivalent, self-sufficient and high informative methods for liver volumetry implementation. Analysis of radiological images demonstrates that manual volumetry with independent software application allows prediction of the future volume of FLR and ALF risks in postoperative period.

Keywords: volumetry, major liver resections, acute liver failure

Introduction

Growing knowledge in the field of liver anatomy and function, development of new surgical and anestesiological technologies, chemotherapy method improvement allowed to achieve significant success in immediate surgical results, leaded to the reduction of postoperative mortality rate after resections to ≤ 5%. In addition, in majority of specialized surgical centers extensive or "major" (>3 segments) hemihepatectomy became routine practice [1]. Preoperative liver volumetry became a fundamental examination method in hepato-biliary surgery [2]. It is well known that the volume of future residual LR is an independent risk factor for ALF development in postoperative period. Volume of future residual LR is a factor predisposing postoperative complications rate and duration of patient recovery.

Accordingly to recent consensus statements ALF after liver resection is a loss of liver ability to realize its energetic, synthetic, excretory and detoxication functions with increase of total bilirubin concentration in blood serum on day ≥5 of postoperative period. The rate of ALF development varies in the range 1.2 – 32% and it depends on criteria of patients' selection and operative intervention scope [3]. As mentioned above, the mortality in postoperative period in such patients is within the range from 0 to 5%, whereas the ALF remains to be the a main trigger [4].

The factors that might affect the ALF course can be divided into 3 groups: patient-dependent factors (age, diabetes, obesity); parenchyma-dependent factors (cirrhosis, cholestasis, steatosis, toxic chemotherapy effects); surgery-dependent factors (bleeding, oxidation-induced injures, resulting from ischemia-reperfusion, sepsis, insufficient FLR volume) [5]. It is known that after the liver resection the reduction on the amount of functioning parenchyma occurs. In residual hepatocytes enhanced rates of regeneration, apoptosis and necrosis have place. One of the goal through the surgery is to minimize the processes of apoptosis and necrosis in the liver tissue

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which stump is formed in order to preserve adequate synthetic function [6]. However, nowadays we do not have unified concern about the adequate individual volume of liver parenchyma that can be safely resected in these patients. Based on our own experience and on literature (data of Guglielmi *et al.*) [7] we concluded that for patients with conditionally "healthy liver" (absence of chronic virus diseases, normal functional values) the limit for residual LR is within 20-30%. In livers with concomitant diseases (cirrhosis, cholestasis, steatosis) it is critically important to increase residual LR volume up to 30-40%.

Volumetric principles. Over the last 5 years we carried out a number of studies and tested out novel modalities for volumetric measurements of LR and a liver as a whole. Kitajima and others [8] published the data about the possibility of liver volumetry using conventional ultrasound examination (US). Authors achieved good correlation relationships with actual volume of liver parenchyma specimens after resection. This procedure did not appear to be wide usage. Application of the modern methods (i.e. MRI, CT) for the planning of extensive resections, liver transplantation and "major" hepatectomies demonstrated high precision and specificity for calculation of transplant volume [9] and for precise quantification of whole organ volume before planned resections as well [10]. CT-volumetry allows determining the correspondence between volumetric measures of future liver remnant and total liver volume (TLV) before and after resection. This approach plays a key role in monitoring of hypertrophy signs and determination of the 2-nd stage terms for liver resection when two-stage and in situ-split liver resections planned.

Vienne and others [11] demonstrated that CT-volumetry makes able to estimate the efficacy of the extrahepatic bile ducts drainage after the endoscopic stenting; as a result liver volume reduction for more than 50% is a good prognostic factor. Kalkmann and others [12] proposed CT-volumetry application for the assessment of effectiveness of chemotherapy given to patients with advanced metastatic process in liver. They claim that disease progression characterized by increase of liver volume median but not by stabilization and regression.

Numminen and others [13] show that 3D liver models, based on MRI data reconstruction, help surgeons to get much more reliable information on liver anatomy which, in turn, makes surgical interventions predictable and safe. Use of the regression analysis for the obtained results demonstrated high correlation between CT-volumetry and water displacement method ($r = 0.985$). It was found that CT-volumetry results over-exceeded volume by 13% as compared to water displacement measurement of the organ ($P<0.0001$). The only explanation for this difference may be blood reperfusion in the organ.

For this reason some authors proposed application of conversion factors that allow volumetry adaptation and makes it much more realistic [14]. In particular, Tongyoo and others proposed formula used for donors screening for the purpose of liver graft selection and assessment of its dimensions. This approach deals with portal veins diameter assessment according to sonography data and CT liver volumetry [15]. Sakei and others [16] introduced another formula purposed to calculate standard liver volume in children with planned liver transplantation (standard liver volume = 689.9 x body surface area – 24.7). Li and others proposed to use the equation (intraoperative weight = 0.844 x liver volume according to CT-volumetry + 5.271) that may be useful for prediction of future graft weigh ($r = 0.885$). Ribero and others [17] reported that application of TLV measurements that were calculated basing on the formula with body surface consideration (-794.41+1267.28 × human body surface) allowed to determine about 11% of patients with mistakenly underestimated assessment of risk of acute liver failure in postoperative period at CT-volumetry. Chun and others confirmed the feasibility to apply the formula of FLR volume calculation by standardized CT-volumetric measurements and surface area or patient's body mass index, demonstrating their strong correlation ($r = 0.98$). In their work Vauthey and others demonstrated that calculation of future residual LR volume using formula (liver volume = 706 x body surface area + 2.4) based on SCT data can possesses adequate LR assessment before resection. Such calculation may be useful in calculations of residual LR after portal vein embolization. Müller and others [18] examined different algorithms of residual LR calculation and determined that 3D analysis of SCT-volumetry demonstrated good correlation between the actual and the calculated liver volumes in all examined algorithms of different authors. The algorithm from Heidelberg demonstrated the reduction of deviation in calculations that was only 1.2%. Kayashima and others developed a formula that includes the age adjustment. They applied regression model for the analysis of 167 donors. Results show 70.767 + (0.703 × graft volume according to 3D CT-volumetry data) + (1.298 × donor's age). The median error at application of the formula with indication of age was 9.6% that almost twice less than at standard calculations.

The results of own studies. *Material and methods* the survey included 15 cases whom volumetry performed retrospectively by radiologists with ≥ 7 years of experience in abdominal CT/MRI. All patients were those who underwent "major" liver resections due to liver malignancies or its metastatic injuries during the period March, 2014 –December, 2015 in the clinic of National Cancer Institute. Calculation of the liver and its sections/segments volume has been done using operational CT stations and specialized software (Extended Brilliance Workstation, Philips, Eindhoven, the Netherlands; Onis 2.5 (http://www.onis-viewer.com/ProductInfo.aspx?id =19) and Varian Eclipse) from the facilities of Institute. Inclusion criteria for the study were anatomic nature of liver resection, CT and MRI performance using facilities of the Institute with the identical scanning protocol application.

Statistical analysis done with the package STATISTICA 6.0 (StatSoft, USA, 2001). Normality of variables distribution was checked with Shapiro-Wilk test. The value $p = 0.05$ assumed as a critical level of significance at statistical hypotheses checking. For comparison of independent samples with abnormal distribution Whitney-Mann test was applied. The value $p = 0.05$ was accepted as a critical significance level at statistical hypotheses checking.

The majority of the examined patients underwent liver surgery due to metastatic disease as a complication of the colorectal cancer -12 (80%). Most of them had synchronous metastases - 7 (46.6%), whereas metachronous liver metastases were registered in 5 cases (33.3%). Hepatocellular and cholangio-cellular liver carcinomas were operated in 2 (13.3%) and 1 (6.6%) clinical cases, respectively. Among the analyzed patients there were 2 times more females than males (10 and 5, respectively), age median was 55.5±0.76 years (Table 1). In the majority of cases volumetric calculations were performed, basing on CT images - 9 (60%).

Table 1: Patients' characteristics

Characteristics	n	%
Age (median±SD)	55.5±0.76	-
Gender distribution (male/female)	5/10	33.3/66.7
SCT/MRI	9/6	60/40
Morbidity:	-	-
HCC	2	13.3
CCC	1	6.6
Synchronous metastases of CRC	7	46.6
Metachronous metastases of CRC	5	33.3
Total:	15	100.0

Note: HCC – hepatocellular carcinoma; CCC – cholangiocellular carcinoma; CRC – colorectal cancer.

Table 2: Measurements of TLV and FLR

Variables	Philips	Onis	Varian Eclipse	p value
TLV(median±SD)	1784.1±72	1763.3±94	1799.9±81	0.54
FLR (Seg. 2,3 – left lateral section), (median±SD)	375.4±115	368.7±111	397.9±110	0.73
Duration of volumetry performance, min. (median±SD)	42±12	51±8	29±5	0.83

Note: TLV – total liver volume; FLR – future liver remnant.

CT and MRI liver images analyzed with three specialized software (Extended Brilliance Workstation, Philips, Eindhoven, the Netherlands; Onis 2.5 and Varian Eclipse). We examined both TLV and volume of FLR to evaluate minimally permissible tissue volume capable to ensure organism's demands. Radiologist performed volumetry did not have access to information about the operative intervention volume and patient's disease course throughout the early postoperative period.

Analysis of the results demonstrate strong linear correlation between applied computer programs (Table 2). The median of TLV was 1784.1±72; 1763.3±94 and 1799.9±81 mm^3 when Philips Workstation, Onis 2.5 and Varian Eclipse used, respectively (p = 0.54). FLR median was 375.4±115; 368.7±111 and 397.9±110 mm^3 with mentioned above programs, respectively (p = 0.73). Interestingly, we did not find any significant difference in duration of TLV and FLR volumes calculations (p=0.83). We should emphasize that the manual volumetry was the most time-consuming both with Philips Workstation (42±12 min.), and in Onis 2.5 (51±8 min.), whereas the semi-automatic method (Varian Eclipse) subjectively allowed to save radiologist's time and it comprised 29±5min.

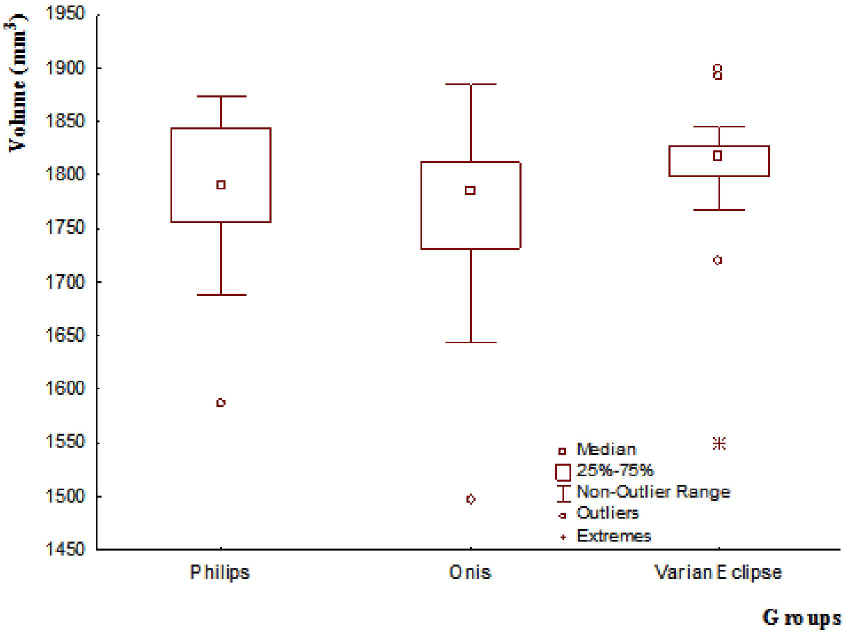


Fig 1: Graphic representation (2D Box Plots) of median and standard deviation of TLV, depending on the procedure of MRI and CT scans processing (Extended Brilliance Workstation, Philips; Onis 2.5 and Varian Eclipse).

We documented a trend in TLV increase when volumetry performed using computer program Varian Eclipse. Calculations with programs from Onis and Philips demonstrate slightly lower TLV values (Fig. 1), that might be explained by the principles of programs work. In particular, while working with Onis 2.5, radiologist manually determines liver contours, considering own experience and knowledge of anatomy that likely allows to perform more accurate analysis. Whereas semi-automatic computer program (Varian Eclipse) may have biased calculations due to unclear liver contours and many other factors.

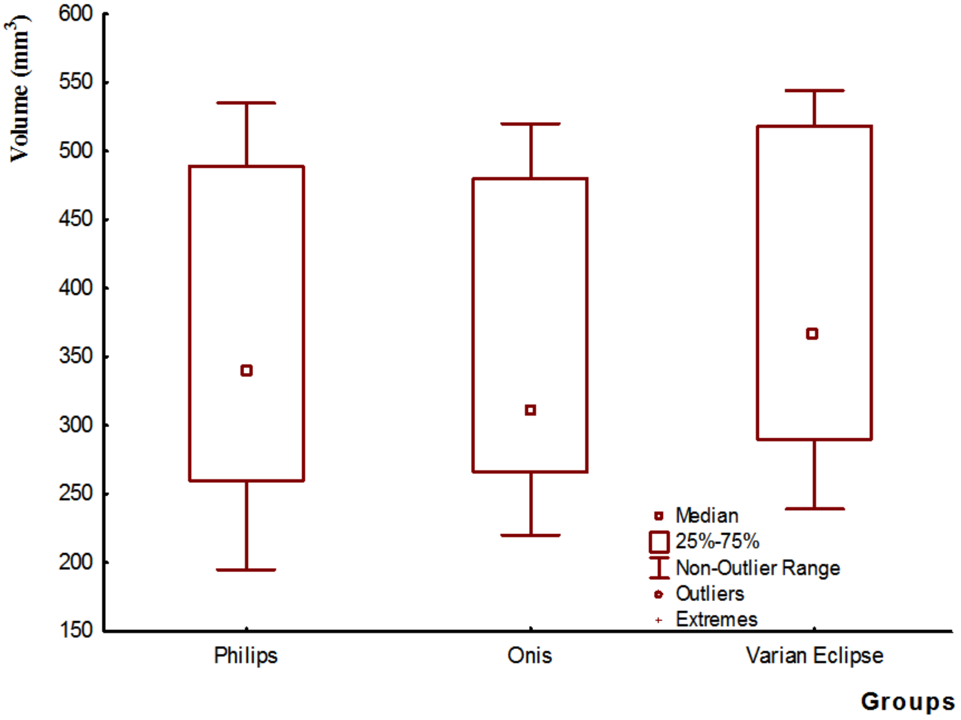
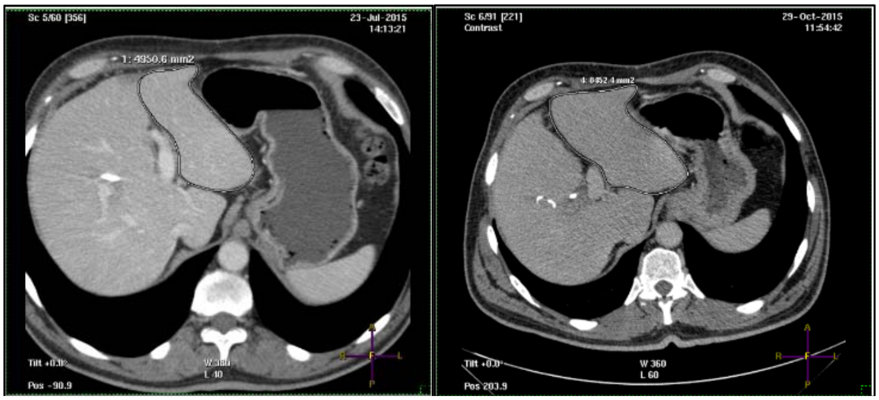


Fig 2: Graphic representation (2D Box Plots) of median and standard deviation of FLR volumes (Seg. 2,3), depending on approaches of MRI and CT scans processing (Extended Brilliance Workstation, Philips; Onis 2.5 and Varian Eclipse).

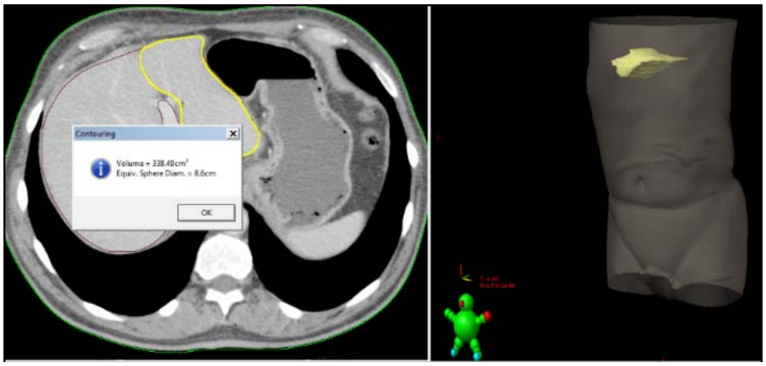
Similar trend registered also out of analysis of the calculations results of FLR volumes (Fig. 2). In that part of study using the Onis 2.5 software radiologist obtained statistically insignificant lower FLR median ($p = 0.73$). However, relatively larger standard deviation (368.7±111) as compared to other programs documented (Fig. 2).

Clinical case Patient M., 54 years *Main diagnosis*: Cancer of extrahepatic bile ducts bifurcation $cT_{2b}N_0M_0$ II stage II, Bismuth-Corlette stage IIIA. Portal veins embolization (PVE) Seg 4-8 with further Seg. 2,3 hypertrophy (33,5%). *Complications***:** mechanical jaundice (endoscopic hepatico-choledoch stenting before embolization).



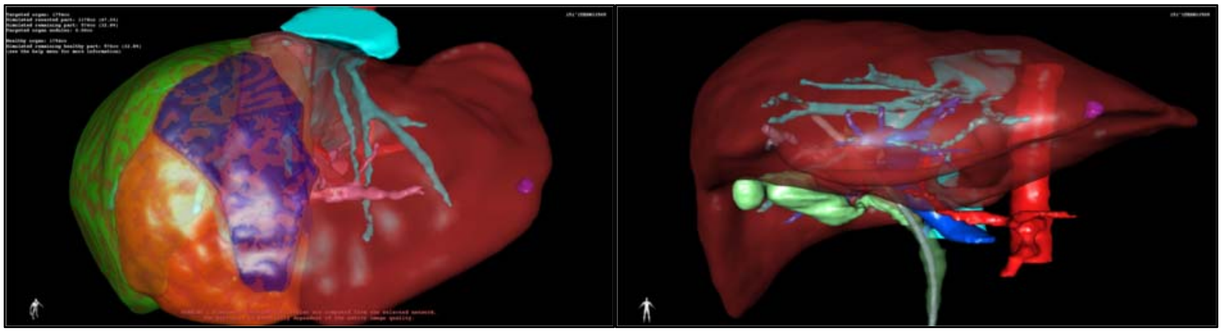
A

B



Volume = 338.49cm³
Equiv. Sphere Diam. = 8.6cm

C



D

Fig 3: Software processing of CT images in 2D and 3D modes during volumetric measurements of TLV and FLR volume. A – Extended Brilliance Workstation, Philips, Eindhoven, the Netherlands; B - Onis 2.5; C – Varian Eclipse; D – VP Planing.

CT-volumetry of this case before and after PVE was performed using three types of computer programs mentioned above. This set was additionally analyzed by independent radiologists group in IRCAD, Paris with the software from VP Planning (https://www.visiblepatient.com/planning/). Examples of patient's images processing given in Fig. 3

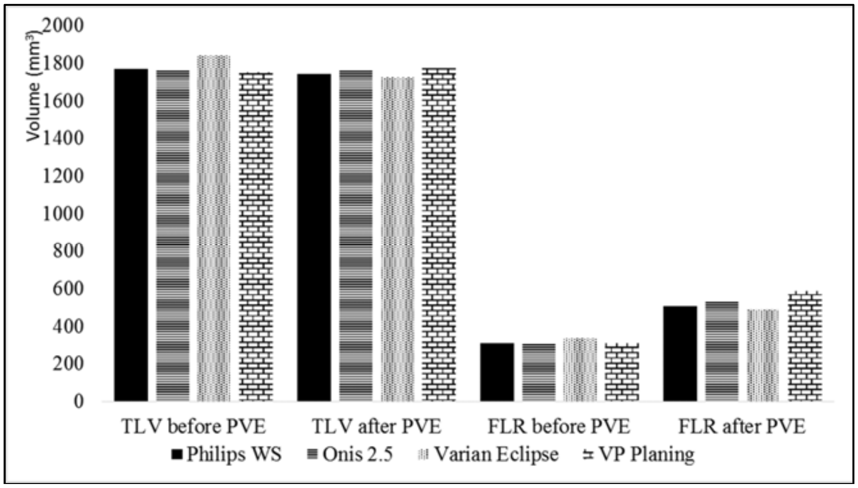


Fig 4: TLV and FLR data of the patient M., obtained before and after PVE with application of: Extended Brilliance Workstation, Philips, Eindhoven, the Netherlands; Onis 2.5; Varian Eclipse; VP Planing.

Discussion. Over the last few years a number of methods of liver volume calculation, using CT/MRI visualization data, has been developed and introduced. Manual volumetric method was one of the pioneers. However, due to its long-term performance the procedure is not widely used but still remains relevant. Suzuki and others [19] developed automated scheme of the CT images calculations and wrote a specialized computer program for automated liver volumetry that is now considered as a standard.

Interestingly, results obtained using an automatic, interactive and manual volumetric measurements in single patient were equivalent (coefficient of correlation between the procedures was 0.94 and 0.96). Automatic volumetry required < 1 min/clinical case; manual – 40 min/clinical case, whereas interactive – about 30 min/clinical case. Nakayama and others [20] proposed automatic method of liver volumetry implementation based on the analysis of CT data that demonstrated good correlation with in vivo values ($r = 0.792$), the study was carried out in patients awaiting transplantation. Soyer and others determined strong correlation relation between liver height and volume ($r=0.767$, $P<0.001$), thereby claiming that liver height measurements can allow rapid calculation of liver volume, thereby reducing time spent on manual segmentation of CT data.

Suzuki and others [21] introduced approaches of the of CT/MRI images segmentation, using for this purpose anisotropic diffusion filter to reduce the level of images noise, specific scale of filter magnitude gradient to increase resolution of liver contours, algorithm for rapid determination of organ margins and a number of other adjustment approaches. Such approach of computer liver volumetry became the "golden standard", and its measurements demonstrated excellent correlations with the manual method (intragroup correlation coefficient 0.94 and 0.98, respectively) thereby reducing radiologist's time spent on manual segmentation of SCT data.

Currently application of independent software for the analysis of digital images from CT or MRI during liver volumetry on personal computer is widely practiced. Dello and others [22] compared the effectiveness of the programs ImageJ (http://rsb.info.nih.gov/ij/download.html) and OsiriX (http://www.osirix-viewer.com) in retrospective volumetry of CT data in patients that underwent "major" liver resections. The authors determined significant correlation between direct examination of the volume of liver sections that were removed in vivo and the volume that was obtained with Image J and OsiriX on personal computer (r=0.89 and r=0.83, respectively).

Conclusions. Analysis of obtained results and literature data demonstrate high importance of the carried out studies and indicate reliable correlation between manual and semi-automatic methods of volumetric measurements of liver and its separate segments/sections. It was demonstrated that volumetry of liver and its separate anatomic structures on the stage of "major" resections planning is a necessary point in preoperative examination of the calculation of minimally permissible tissue volume in these patients. MRI and CT images are equivalent and self-sufficient in informativity at liver volumetry implementation. Analysis of radiological images demonstrate that manual volumetry with independent software application allows effective prediction of the future volume of FLR and also ALF risks in postoperative period.

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