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Liver volumetric and anatomic assessment in living donor liver transplantation: The role of modern imaging and artificial intelligence

Mayara Machry, Luis Fernando Ferreira, Angelica Maria Lucchese, Antonio Nocchi Kalil, Flavia Heinz Feier

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Abstract

The shortage of deceased donor organs has prompted the development of alternative liver grafts for transplantation. Living-donor liver transplantation (LDLT) has emerged as a viable option, expanding the donor pool and enabling timely transplantation with favorable graft function and improved long-term outcomes. An accurate evaluation of the donor liver's volumetry (LV) and anatomical study is crucial to ensure adequate future liver remnant, graft volume and precise liver resection. Thus, ensuring donor safety and an appropriate graft-to-recipient weight ratio. Manual LV (MLV) using computed tomography has traditionally been considered the gold standard for assessing liver volume. However, the method has been limited by cost, subjectivity, and variability. Automated LV techniques employing advanced segmentation algorithms offer improved reproducibility, reduced variability, and enhanced efficiency compared to manual measurements. However, the accuracy of automated LV requires further investigation. The study provides a comprehensive review of traditional and emerging LV methods, including semi-automated image processing, automated LV techniques, and machine learning-based approaches. Additionally, the study discusses the respective strengths and weaknesses of each of the aforementioned techniques. The use of artificial intelligence (AI) technologies, including machine learning and deep learning, is expected to become a routine part of surgical planning in the near future. The implementation of AI is expected to enable faster and more accurate image study interpretations, improve workflow efficiency, and enhance the safety, speed, and cost-effectiveness of the procedures. Accurate preoperative assessment of the liver plays a crucial role in

ensuring safe donor selection and improved outcomes in LDLT. MLV has inherent limitations that have led to the adoption of semi-automated and automated software solutions. Moreover, AI has tremendous potential for LV and segmentation; however, its widespread use is hindered by cost and availability. Therefore, the integration of multiple specialties is necessary to embrace technology and explore its possibilities, ranging from patient counseling to intraoperative decision-making through automation and AI.

Key Words: Liver transplantation; Living-donor; Diagnostic imaging; Artificial intelligence; Machine learning; Deep learning

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Core Tip: Accurate liver's volumetry (LV) is imperative for successful living-donor liver transplantation to ensure adequate future liver remnant and graft volumes. Manual computed tomography scan delineation conventionally serves as the standard approach; however, it is constrained by factors such as cost, subjectivity, and variability. In contrast, automated LV techniques utilizing advanced segmentation algorithms present superior reproducibility, reduced variability, and enhanced efficiency compared with manual measurements. However, the accuracy of automated LV requires further investigation. The study comprehensively reviewed both traditional and emerging LV methods, including semi-automated image processing, automated LV techniques, and machine learning-based approaches, while analyzing their respective strengths and weaknesses.

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INTRODUCTION

Liver transplantation is the first-line treatment for patients with terminal liver disease. Deceased donor organ shortage and cultural barriers have led to the development of alternative graft types. Living-donor liver transplantation (LDLT) has emerged as an extension of the *ex-situ* graft transection concept, encompassing reduced-size and split-liver techniques. By enabling the expansion of the donor pool, LDLT offers the advantage of timely transplantation and holds the potential for excellent graft function and improved long-term outcomes[1-6]. Moreover, LDLT reduces waiting list mortality.

An adequate preoperative evaluation of the donor is essential for successful LDLT. Sufficient future liver remnant (FLR) and graft volume must be ensured through liver's volumetry (LV) studies[7,8]. An FLR of 30% to 35% of the original liver volume is required for donor safety, whereas at least 4% of the standard liver volume or more than 0.8 and less than 3–3.5 of the graft recipient weight ratio (estimated before the surgery through imaging and confirmed after the graft is weighted) is required to meet the recipient's needs[9,10]. Small grafts are associated with cellular damage due to excessive portal flow, leading to "small-for-size syndrome," whereas large grafts may receive inadequate portal flow, resulting in "large-for-size syndrome"[11-17].

Manual liver volumetry (MLV) conducted on portal venous phase multidetector computed tomography (CT) scans with intravenous contrast is conventionally considered the standard method for measuring LV[7,18,19]. However, it can be costly, time-consuming, subjective, and prone to inter- and intra-observer variabilities. The process entails manual tracing of the liver borders using specialized software, necessitating the expertise of an experienced radiologist, often without the input of the surgeon. The percentage of error (PE) may vary significantly, ranging from 2% to 20%, which can have a dramatic effect on the final graft volume and transplantation outcomes[20-24].

Advancements in medical imaging, computational algorithms, and artificial intelligence (AI) have set the stage for the development and application of automated LV techniques. Automated LV holds significant promise in the evaluation of LDLT, as it utilizes sophisticated segmentation algorithms to delineate liver boundaries from CT or magnetic resonance imaging (MRI) scans. Therefore, enabling volumetric calculations and comprehensive volumetric analysis and allowing for the assessment of lobe-specific volumes, segmental volumes, and overall liver volume. Such automated approaches offer advantages over manual measurements, including enhanced reproducibility, reduced intra- and interobserver variability, and improved efficiency. However, the accuracy of automated LV techniques is yet to be conclusively determined[25-28].

The study aimed to provide a comprehensive review of the literature, presenting both traditional and emerging methods of LV and anatomical liver assessment, while discussing their respective strengths and weaknesses. By examining the current state of LV techniques, the review aimed to contribute to the advancement and optimization of liver transplantation outcomes.

MANUAL LIVER VOLUMETRY

The introduction of multiphasic CT and MRI techniques has led to the widespread adoption of MLV as the standard practice in liver transplant centers to estimate liver volume before accepting a living-donor as a suitable candidate. During the donor evaluation, a complete anatomical analysis of the hepatic veins, portal vein and hepatic arteries is provided by multiphasic CT and MRI. Bile duct anatomy is evaluated in cholangio MRI studies, specially, in left lobe and right lobe donors.

If the donor's anatomy is suitable for the planned procedure, LV is carried out. The procedure involves manual delineation of the liver borders using sequential image slices to determine the overall liver volume. Subsequently, a transection plane is selected based on the specific type of liver graft and the inclusion of the middle hepatic vein (MHV) [25,29-31] (Figure 1).

Limitations include reliance on operator expertise and medical specialty, leading to discrepancies between the analyses performed by radiologists and surgeons, potentially related to the transection line. Furthermore, the inclusion of blood vessels and bile ducts in the final volume calculation can lead to overestimations[32]. Additionally, the LV procedure itself is time-consuming, typically requiring approximately 20-40 min to complete, which significantly affects the daily workflow of both radiologists and surgeons[19,33]. In terms of accuracy, PE ranges from 5% to 36% when comparing the estimated volume with the actual graft weight (AGW)[34]. It is important to note that errors can occur in both directions, resulting in overestimation and underestimations[8].

It is routinely considered that the density of the liver is equivalent to the density of water; therefore, the AGW is representative of the graft volume[35]. However, studies measuring AGW have identified the necessity of correction factors when estimating graft volume, as highlighted in Table 1. Recently, Lemke *et al*[36], measured the mean physical density of 16 transplanted liver lobes to be 1.1157 g/mL, asserting that the conversion factor was, on average, 12% higher than expected. Tongyoo *et al*[32] demonstrated that the AGW of a right lobe donor liver graft (RLDG) was approximately 91% of the estimated right lobe liver volume. The 9% volume reduction was attributed to intrahepatic blood flushed out of the liver by the preservation solution during back-table preparation[9,31,37]. Other inaccuracies may have been due to the inclusion of the MHV and/or the caudate lobe[38].

SEMI-AUTOMATED IMAGE PROCESSING

Semi-automated methods have been developed to address observer-related issues associated with manual measurements and to enhance the efficiency of LV and hepatic segmentation. An example of such a method is the MeVis Liver Analyzer (MeVis Medical Solutions AG, Bremen, Germany), which is a computer-assisted software that operates on CT images. Moreover, the software employs a modified live-wire algorithm to automatically determine the contours between user-defined boundary points based on the CT values and gradients. The algorithm parameters were tailored to each CT phase, including the venous (V), arterial (HA), and native (N) phases. To ensure accurate liver segmentation, manual correction of automatically delineated contours and manual drawing of the contour parts were performed. Live-wire contours were interactively determined on 3 mm axial two-dimensional (2D) CT slices. The software automatically interpolates and optimizes the contours of intermediate slices, with final adjustments made by the operator through manual corrections, if necessary (Figure 2).

Volumetric calculations, expressed in milliliters (mL), were performed by adding the areas of all segmented regions. Surrounding structures such as major extrahepatic vessels (portal vein, hepatic artery, and inferior vena cava) and the gallbladder fossa were excluded from the volume calculations (Figure 3).

Goja *et al*[39] discovered that semiautomated software tools exhibited the highest correlation ($r = 0.82$) for measuring right lobe grafts. However, left lobe grafts tend to be overestimated, whereas left lateral segment (LLS) grafts are often underestimated, with an underestimation of approximately 66% of the total LLS grafts. One possible explanation for the underestimation of LLS grafts is that CT scans typically underestimate the volume because the actual surgical plane of transection is approximately 1 cm to the right of the falciform ligament, whereas the radiological plane of transection is exactly at the falciform ligament. Other studies have addressed the accuracy of semi-automated image processing (SAIP), and their results are presented in Table 2.

AUTOMATED LIVER VOLUMETRY TECHNIQUES

Automated LV relies on advanced image-processing techniques and algorithms to accurately segment the liver from CT or MRI scans. The principles and algorithms vary depending on the approach employed. However, some common techniques and concepts are involved.

Image preprocessing

Before liver segmentation, image preprocessing techniques may be applied to enhance the image quality, reduce noise, and improve the contrast between the liver and surrounding structures. These techniques include filtering, intensity normalization, and image enhancement methods.

Table 1 Formulas to estimate liver volumetry by computerized tomography

Ref.	Formula	Research place
Poovathumkadavil <i>et al</i> [22], 2010	$LV = 12.26 \times BW(\text{kg}) + 555.65$	Saudi Arabia
Noda <i>et al</i> [21], 1997	$LV = 0.05012 \times BW^{0.78}$	Japan
Johnson <i>et al</i> [20], 2005	$LV = 0.722 \times BSA^{1.176}$	North America
Yuan <i>et al</i> [24], 2008	$LV = 949.7 \times BSA (\text{m}^2) - 48.3 \times \text{age} - 247.4$	China
Yoshizumi <i>et al</i> [23], 2003	$LV = (0.772 \times BSA)/1.08$	North America

LV: Liver volume; BW: Body weight; BSA: Body surface area.

Table 2 Results of semi-automated image processing in different analysis

Ref.	Software and comparison	Reports
Pomposelli <i>et al</i> [47], 2012	Software MeVis Compared right lobe graft volumes estimated by SAIP with actual graft weights measured during LDLT	A nonsignificant volume difference of approximately 17.5 mL and a low percentage error of approximately 2.8%
Çelik <i>et al</i> [34], 2023	CT Liver Analysis, Philips Healthcare-RLDG volumes by manual and SA were compared to AGW	Both manual and SA overestimated the graft weight (manual: 893 ± 155 mL <i>vs</i> AGW: 787 ± 128 g, $P < 0.001$, SA: 879 ± 143 mL <i>vs</i> AGW, $P < 0.001$). The mean interaction time was 27.3 \pm 14.2 min for manual and 6.8 \pm 1.4 min for SAIP ($P < 0.001$)
Mohapatra <i>et al</i> [31], 2020	Myrian XP Liver 3D software (France)-RLDG, LLDG and LLSDG volumes by manual and SA were compared to AGW	Both manual and SA showed strong correlation with AGW ($r = 0.834$ and 0.856 , respectively). The mean percentage error for manual and SA was $14.2 \pm 12.5\%$ and $12.2 \pm 11.8\%$, respectively. The overall accuracy improved using SA ($P = 0.015$)
Kalshabay <i>et al</i> [25], 2023	Vitrea software, including two different applications for manual segmentation (Volume analysis) and automated segmentation (CT liver analysis) SA software (OsiriX MD) RLDG	The manual method correlated better with AGW ($r = 0.730$) in comparison with the SA ($r = 0.685$) and the automated ($r = 0.699$) methods ($P < 0.001$). The mean error ratio in volume estimation by each application was $12.7 \pm 16.6\%$ for manual, $17.1 \pm 17.3\%$ for SA, $14.7 \pm 16.8\%$ for automated methods
Goja <i>et al</i> [39], 2018	AW Volume share 6 (GE Healthcare; Chicago, Illinois, United States) RLDG, LLDG and LLSDG volumes by SA were compared to AGW	RLDGt: There was no statistically significant difference between mean SA and AGW in RL (722 ± 134 <i>vs</i> 717 ± 126 gm; $P = 0.06$). LLDG: Correlated strongly ($r = 0.81$, $P < 0.001$), mean SA was significantly high as compared to mean of AGW (460 ± 118 <i>vs</i> 433 ± 102 gm; $P = 0.003$). LLSDG: Mean SA was significantly low as compared to mean of AGW (203 ± 48 <i>vs</i> 254 ± 49 gm; $P < 0.001$)

CT: Computerized tomography; SA: Semi-automated; AGW: Actual graft weight, RLDG: Right lobe donor graft; LLDG: Left lobe donor graft; LLSDG: Left lateral segment donor graft.

Segmentation algorithms

Segmentation algorithms were used to delineate the liver region of interest from the remaining images. Additionally, such algorithms aim to accurately identify the liver boundaries. Commonly used algorithms include threshold-based methods, region growing, active contours (or snakes), level sets, graph cuts, and machine-learning-based techniques.

Threshold-based methods

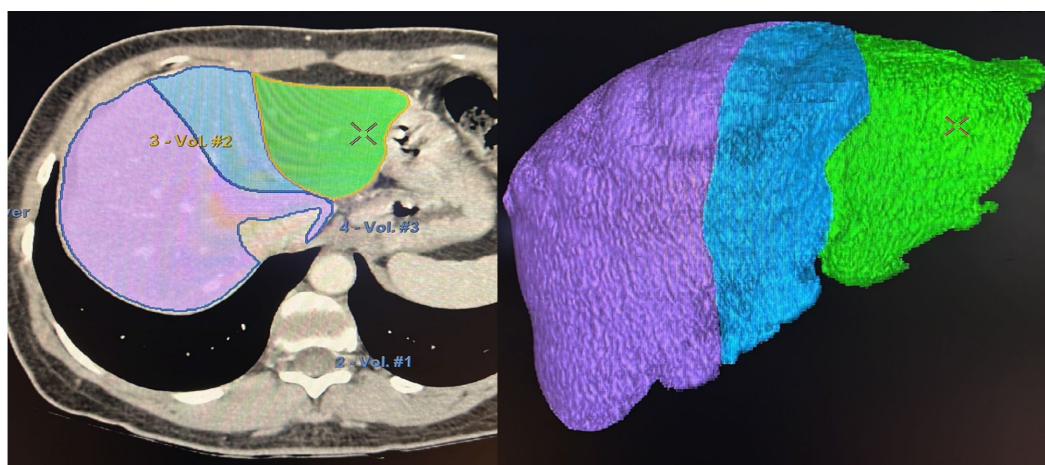
Threshold-based methods involve setting intensity thresholds to separate the liver from the background or other organs. The liver is segmented based on predefined intensity ranges or statistical measures such as the mean intensity or intensity distribution.

Region growing

Region-growing algorithms start from a seed point within the liver and iteratively develop the region by including pixels with similar characteristics (*e.g.*, intensity, texture, or gradient) until a stopping criterion is met. The method is particularly useful when the liver has a distinct intensity pattern compared to the surrounding tissues.

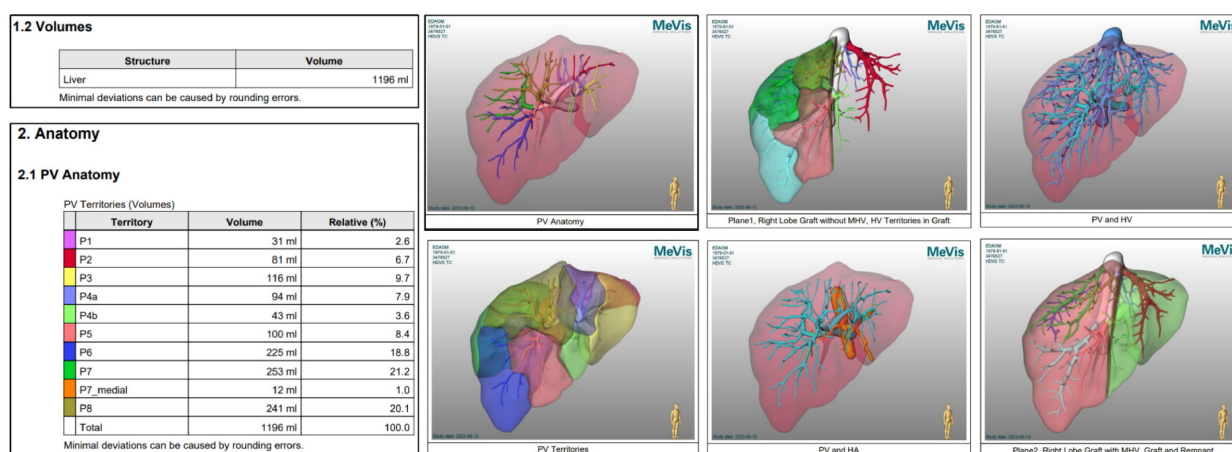
Active contours (snakes)

Active contour models, also known as snakes, use an energy-optimization approach to iteratively deform a contour to fit the liver boundary. The contour was attracted to the image edges or intensity gradients, ensuring accurate delineation of the liver boundaries.



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Figure 1 Manual volumetric study performed in our institution for pre-operative living-donor evaluation (Hepatic VCAR-GE Healthcare).



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Figure 2 MeVis software images and tables output: The software returns multiple images and tables. PV: Peripheral vein; MHV: Middle hepatic vein; HA: Hepatic artery.

Level sets

Level-set methods are mathematical techniques used to evolve a curve or surface over time to delineate the liver boundaries. The methods use the concept of level sets, which represent the evolving contour as a zero-level set of a higher-dimensional function.

Graph cuts

Graph cut algorithms model the liver segmentation problem as an optimization task in a graph framework. The graph is constructed using image features, and the segmentation is achieved by identifying the minimum energy cut that separates the liver from the background.

Machine learning-based techniques and deep learning

Machine learning algorithms, such as random forests, support vector machines, and deep learning models, can be trained on annotated liver images to automatically segment the liver. Such algorithms learn the patterns and features that distinguish the liver from other structures and can provide accurate and robust segmentation results[40].

Most software tools employ a combination of techniques or advanced algorithms that are specific to their methodology. The choice of algorithm depends on factors such as image quality, complexity of liver structures, computational efficiency, and specific requirements of the application. Each algorithm has its advantages, limitations, and parameter settings, which must be carefully considered and optimized for accurate LV. A combination of techniques can be used to improve accuracy and robustness[41].

For example, the initial segmentation can be obtained using thresholding or region growth, followed by refinement using active contours or graph cuts. Hybrid approaches that combine multiple algorithms can leverage the strength of each technique to achieve more accurate LV. Additionally, the validation and evaluation of the automated LV results against the ground truth or manual segmentations are critical for assessing the algorithm's performance and reliability.

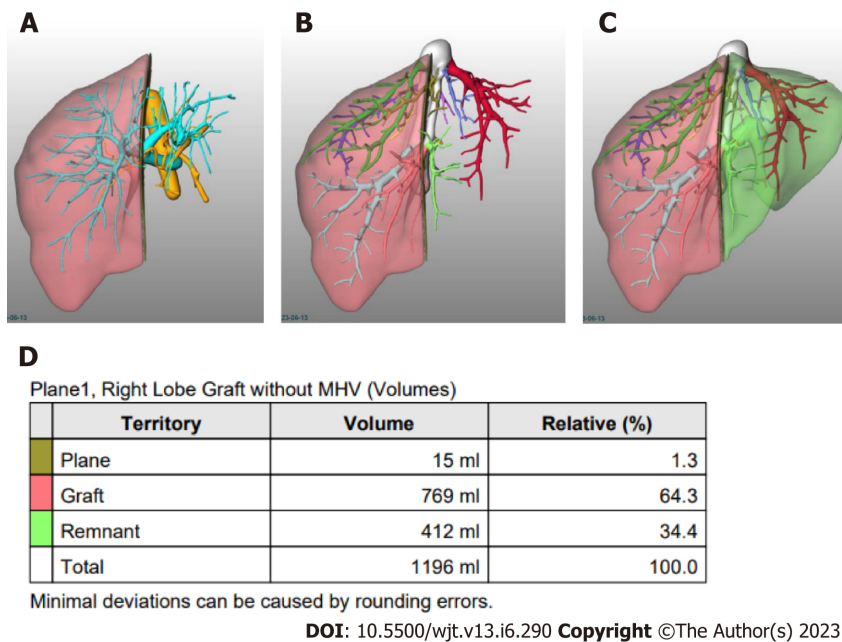


Figure 3 Resection planes volumetric estimation using MeVis. A: Right Lobe Graft without middle hepatic vein (MHV), peripheral vein and hepatic artery; B: Right Lobe Graft without MHV, HV; C: Right Lobe Graft without MHV, Graft and Remnant; D: Table showing total, plane, graft and remnant liver volumes. MHV: Middle hepatic vein.

[42].

Most computer aided diagnostics used in clinical practice use conventional machine learning approaches, in which the effectiveness depends on the domain expertise of the developers. So, the limitations of conventional learning are linked to the limitations of the human developer. Manual and semi-automated volumetry is dependent on conventional machine learning. Deep learning has emerged as a state-of-the-art machine-learning method for many applications. Deep learning is a type of representation learning method in which a complex multilayer neural network architecture learns representations of data automatically by transforming the input information into multiple levels of abstraction[43].

Deep convolutional neural networks (DCNN) are widely used in image pattern recognition. They can automatically extract relevant features from training samples by adjusting their weights through backpropagation. In contrast to manual feature design, the DCNN learns feature representations during training. When trained with a large and representative dataset, the DCNN features outperformed the hand-engineered features by being highly selective and invariant. The automated deep learning process enables the analysis of numerous cases, surpassing human capabilities. Deep learning proves robust in handling variations across different classes, as long as the training set is diverse and extensive [40-43].

ACCURACY AND RELIABILITY

Automated LV and deep machine learning for LDLT has gained attention in recent years. There has been an increase in the number and quality of AI and machine learning studies in the medical field, mainly those focused on automating the interpretation of 2D image tests (MRI, CT, and radiographs), assembling three-dimensional models of organs and tissues, and volumetric calculations, including virtual segmentation of the liver. In liver resection and liver transplantation, most studies have a small number of cases, focusing on adult liver transplantation and RLDG, with very few studies on left lobe donor graft and left lateral segment donor graft[26-28,42-44]. The higher risk of the small-for-size syndrome in adult liver transplantation justifies the intense volumetric and anatomical studies on RLDG. Usually, for pediatric recipients (< 10 kg), an inaccurate volumetric assessment will rarely lead to insufficient liver volume; in contrast, the risk of the large-for-size syndrome is higher compared to the small-for-size syndrome. In such cases, the surgeon usually reduces the graft on the back table or converts it into a mono-segmental graft before implantation[45].

Automated software allows the surgeon to choose the transection plane; some studies have compared the correlation of these measurements for RLDG when performed by the surgeon using automated software with the manual measurements performed by radiologists. Moreover, both measurements had a good correlation with the AGW ($r > 0.80$), along with no significant difference between measurements by the surgeon and the radiologist[29].

As it is of paramount importance that the surgeon who is going to perform the procedure to perform the anatomical assessment and to choose the adequate liver segmentation plane, new softwares, focusing on the surgeon's interaction are being developed. A more user-friendly automated platform was developed by a group from the Republic of Korea[46], which they referred to as Dr. Liver. They validated the method in 50 RLDG and compared it to MLV. The correlation with AGW was better for the automated Dr. Liver ($r = 0.98$) than for the MLV ($r = 0.92$), although they were both good correlations. However, the percentage of absolute difference (%AD) from AGW of Dr. Liver ($3.1\% \pm 2.8\%$) was significantly

smaller than that of the MLV ($10.2\% \pm 7.5\%$). None of the Dr. Liver measurements percentages of %AD was $> 10\%$, while they were 46% for MLV measurements. Evaluation of %AD is very important in clinical practice because an error percentage of more than 10% can result in a small-for-size boundary graft volume. Also, the total time for task completion was shorter for Dr. Liver *vs* MLV (7.3 ± 1.4 min *vs* 37.9 ± 7.0 min).

CONCLUSION

Accurate preoperative assessment of the liver plays a critical role in ensuring the selection of suitable donors and improving recipient outcomes after LDLT. MLV initially emerged as the gold standard for accurate assessment. However, the time-consuming nature of the manual analysis, reliance on operator expertise, and high variability in PE have prompted the adoption of SAIP software tools, and more recently, automated software solutions. AI represents the future of LV and segmentation and offers immense potential in the field, leading to a future fully automated liver segmentation and volumetry based on deep-learning. However, the widespread adoption and daily application of AI are hindered by cost and accessibility limitations. We are responsible for embracing technology and fostering interdisciplinary collaborations in the fields of radiology, engineering, informatics, and surgery. The possibilities afforded by AI are limitless, ranging from patient counseling and education to intraoperative decision-making facilitated by automation and AI assistance.

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