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Dr. Liver: A preoperative planning system of liver graft volumetry for living donor liver transplantation

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ABSTRACT

Background and Objective: Manual tracing of the right and left liver lobes from computed tomography (CT) images for graft volumetry in preoperative surgery planning of living donor liver transplantation (LDLT) is common at most medical centers. This study aims to develop an automatic system with advanced image processing algorithms and user-friendly interfaces for liver graft volumetry and evaluate its accuracy and efficiency in comparison with a manual tracing method.

Methods: The proposed system provides a sequential procedure consisting of (1) liver segmentation, (2) blood vessel segmentation, and (3) virtual liver resection for liver graft volumetry. Automatic segmentation algorithms using histogram analysis, hybrid level-set methods, and a customized region growing method were developed. User-friendly interfaces such as sequential and hierarchical user menus, context-sensitive on-screen hotkey menus, and real-time sound and visual feedback were implemented. Blood vessels were excluded from the liver for accurate liver graft volumetry. A large sphere-based interactive method was developed for dividing the liver into left and right lobes with a customized cutting plane. The proposed system was evaluated using 50 CT datasets in terms of graft weight estimation accuracy and task completion time through comparison to the manual tracing method. The accuracy of liver graft weight estimation was assessed by absolute difference (AD) and percentage of AD (%AD) between preoperatively estimated graft weight and intraoperatively measured graft weight. Intra- and inter-observer agreements of liver graft weight estimation were assessed by intraclass correlation coefficients (ICCs) using ten cases randomly selected.

Results: The proposed system showed significantly higher accuracy and efficiency in liver graft weight estimation (AD = 21.0 ± 18.4 g; %AD = 3.1% ± 2.8%; percentage of %AD > 10% = none; task completion time = 7.3 ± 1.4 min) than the manual tracing method (AD = 70.5 ± 52.1 g; %AD = 10.2% ± 7.5%; percentage of %AD > 10% = 46%; task completion time = 37.9 ± 7.0 min). The proposed system showed slightly higher intra- and inter-observer agreements (ICC = 0.996 to 0.998) than the manual tracing method (ICC = 0.979 to 0.999).

Conclusions: The proposed system was proved accurate and efficient in liver graft volumetry for preoperative planning of LDLT.

1. Introduction

Liver graft volume needs to be accurately estimated for safety of both donors and recipients in living donor liver transplantation (LDLT). Excessive loss of liver tissue can cause a high risk of post-operative liver failure for a donor [1,2]. Schindl et al. [1] reported that serious postoperative hepatic dysfunction often occurs if the ratio of residual to total functional liver volume (TFLV = entire liver volume – tumor volume) is smaller than 26.6%. Liver graft with a proper size needs to be transplanted to a recipient to prevent post-transplant complications due to small-for-size syndrome [3-10] or large-for-size syndrome [5,11]. Kiuchi et al. [5] reported that a small-for-size graft can cause low graft survival due to enhanced parenchymal cell injury and reduced metabolic and synthetic

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capacity, while a large-for-size graft can result in an increased risk of vascular complications and immunological impairments.

Manual tracing of the right and left liver lobes from computed tomography (CT) images for graft volumetry is common at most medical centers. Using computer programs such as Rapidia (Infinitt Co., Ltd, South Korea), Voxar 3D (Toshiba Co., Japan), and syngo.via (Siemens Co., Germany), surgeons can manually trace liver regions slice by slice. Though manual tracing provides accurate results, it is subjective, cumbersome, and time-consuming ($>$ 30 min on average) and has relatively large intra- and inter- observer variations [12-14]. Besides, to estimate the volume of liver graft with high accuracy, blood vessels need to be excluded from the traced liver regions due to intraoperative drainage of blood [15]. However, it is hard to manually trace blood vessels due to their complex structures and small diameters; therefore, their volume cannot be excluded from liver graft volume, resulting in an large error in estimation of liver graft volume. Furthermore, a customized cutting plane needs to be formed for dividing the liver into left and right lobes for graft volumetry due to a large variation of vessel structures in the liver [16]. However, the manual tracing method usually generates a flat cutting plane for graft volumetry.

Systems such as Synapse Vincent (Fujifilm Co., Japan), Hepavision (MeVis, Bremen, Germany), and Philips (Eindhoven, Netherlands) liver segmentation and analysis packages have been developed for automatic segmentation of the liver. These liver surgery planning systems have been proven to be accurate and efficient in liver volumetry [17-20] and liver graft volumetry [17,18]; however, a function of liver graft weight estimation, which is important for donor candidate selection and liver surgery planning, is not available in these systems.

The present study was intended to develop a highly automatic system with advanced image processing algorithms and user-friendly interfaces for liver graft volumetry and evaluate its accuracy and efficiency compared with the manual tracing method. Blood vessels were excluded from the liver for accurate liver graft volumetry. A large sphere-based interactive method was developed for dividing the liver into left and right lobes with a customized cutting plane.

2. Methods

2.1. System development

The proposed system named Dr. Liver (Humanopia Co. Ltd, Pohang, Korea) [21] provides a sequential procedure consisting of (1) liver segmentation, (2) blood vessel segmentation, and (3) virtual liver resection for liver graft volumetry. Highly automatic segmentation algorithms using histogram analysis, hybrid level-set methods, and a customized region growing method were developed and implemented. User-friendly interfaces such as sequential and hierarchical user menus, context-sensitive on-screen hotkey menus, and real-time sound and visual feedbacks were designed. Blood vessels were excluded from the liver for accurate liver graft volumetry. A large sphere-based interactive method was developed for dividing the liver into left and right lobes with a customized cutting plane.

2.1.1. Algorithms for segmentation of liver and vessels

The liver was extracted from CT images by an automatic liver segmentation method. First, multiple seed points were automatically identified over CT images based on histogram analysis of intensity values and geometric analysis of the liver. Histogram analysis of intensity values showed that two significant maxima appear in a smoothed histogram (Fig. 1b) of which the larger maxima belongs to the liver and the other belongs to muscles [22]. The minimal and maximal intensity values of liver voxels were estimated by finding large changes in the derivatives of the histogram. A binary volume (Fig. 1c) was generated by assigning the intensity values of voxels located within the minimal and maximal liver intensity range to one and the remaining to zero. Among the objects in the binary volume, the largest object belongs to the liver; thus small objects were removed and then the remaining binary volume was eroded by five pixels so that only the liver object remained (Fig. 1d). Five to six CT slices were selected every 40 slices among the entire CT dataset as candidates for seed point identification. A 16×16 grid was generated over each of the selected slices where nodes having an intensity of one were considered as seed points (Fig. 1e) for liver extraction. After automatic identification of multiple seed points, the liver was automatically extracted from CT images by Yang et al. [23]'s hybrid liver segmentation method that incorporates a customized fast-marching level set method [24] for formation of an initial liver region and a threshold-based level set method [25,26] for detection of the actual liver region from the initial liver region.

The liver vessels including portal and hepatic veins were extracted from CT images by an automatic vessel segmentation method. First, CT images were masked (Fig. 2a) by the extracted liver region to remove the surroundings of the liver to avoid false extraction of vessels outside the liver and reduce vessel extraction time. Second, multiple seed points and vessel intensity range were automatically identified over CT images based on histogram analysis. Two significant maxima appear in the histogram of the masked CT images in which the larger maxima belongs to the vessels and the other to the liver as shown in Fig. 2b. The minimal and maximal intensity values of vessel voxels were estimated by finding large changes in the derivatives of the histogram. A binary volume (Fig. 2c) was generated by assigning the intensity values of voxels within the vessel intensity range to one and the remaining to zero. Among the objects in the binary volume, small objects were removed so that only those belonging to the major vessel branches could remain (Fig. 2d). For seed point identification 5 to 6 CT slices were selected every 40 slices among the entire CT dataset as candidates. A 32×32 grid was generated over each of the selected slices where nodes having an intensity of one were considered as seed points (Fig. 2e) for vessel extraction. Third, the liver vessels were extracted by a connected threshold region growing method implemented in ITK [27] from the identified seed points and vessel intensity range. To avoid false negative error and false positive error in the extracted vessels, five more threshold intervals around the vessel intensity range were used to provide five more extraction candidates of the vessels. An interface (Fig. 3) was provided for the user to verify and select the most appropriate vessel extraction result. Lastly, the portal and hepatic veins were separated (Fig. 4) by a connected component analysis method implemented in ITK [27]. Connected branches of the vessel trees were identified by the connected component analysis method and shown for the users to interactively select branches belonging to portal vein with an interface (Fig. 5) to separate portal vein and hepatic vein.

2.1.2. Exclusion of vessels from the liver

To avoid an estimation error of liver graft volume due to intraoperative drainage of blood, vessels were excluded from the liver. After segmentation of the liver and vessels, the intrahepatic vessels including portal and hepatic veins were subtracted from the extracted liver regions to obtain liver regions without vessels (Fig. 6).

2.1.3. Sphere-based virtual resection method

A single large sphere (Ø = 20 cm) was used multiple times [21] for dividing the liver into left and right lobes. The division was performed in the axial view of overlaid CT slices with the extracted liver regions. From the axial CT view, a circle generated by the section of the sphere over a CT slice was used to form a customized