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Simulation of Portal Hemodynamic Changes in a Donor After Right Hepatectomy

Remnant livers will be regenerated in live donors after a large volume resection for transplantation. How the structures and hemodynamics of portal vein will evolve with liver regeneration remains unknown. This prompts the present hemodynamic simulation for a 25 year-old man who received a right donor lobectomy. According to the magnetic resonance imaging/computed tomography images taken prior to the operation and one month after the operation, three sequential models of portal veins (pre-op, immediately after the operation, and one-month post-op) were constructed by AMIRA® *and* HYPERMESH®*, while the immediately after the operation model was generated by removing the right branch in the pre-op model. Hemodynamic equations were solved subject to the sonographically measured inlet velocity. The simulated branch velocities were compared with the measured ones. The predicted overall pressure in the portal vein after resection was found to increase to a magnitude that has not reached to an extent possibly leading to portal hypertension. As expected, blood pressure has a large change only in the vicinity of the resection region. The branches grew considerably different from the original one as the liver is regenerated. Results provide useful evidence to justify the current computer simulation.* [DOI: 10.1115/1.4000957]

Keywords: portal vein, transplantation, simulation, hemodynamics, perioperative

1 Introduction

Liver transplantation is a definite treatment modality for patients reaching their end stage of liver disease. In contrast to Western countries, the organ donation rate was considerably low in Asia. For example, in 2001 the overall deceased liver donation rate in Asia was 0.32 per million populations, as compared with the values ranging from 9 to 31 in Western societies [1]. Living donor liver transplantation (LDLT), therefore, plays an important role in Asia. When conducting LDLT, liver donor risk is always the most crucial issue. In one recent prospective study in France, though there was no donor mortality, the overall post-operative morbidity was reported to be 51% [2]. Most of the complications were the minor ones like the bile leak and mild unexplained fever. In addition, the right lobectomy has been reported to have a three-time higher risk of morbidity in comparison with the left-sided resection [2]. This prompted the necessity to make a further preoperative evaluation of the right lobectomy.

Liver regeneration will be initiated immediately after the liver donation surgery. This process involves numerous molecular events and gene expressions [3–5]. Hemodynamic changes in pressure and shear stress, for example, are also known as two of the most influential factors [6]. Moreover, donor operations also carry the risks of morbidity and mortality specifically to the hemodynamic changes of portal vein, for example, small-for-size syndrome, which involves the damage of hepatic sinusoids in small-sized liver caused by the overflow of portal vein in recipients [7]. Poor graft outcome has been reported in certain cases with the portal flow having an amount more than 260 ml/min/100 g graft [8]. The hepatic flow simulations previously carried out by Rani et al. [9] and Van der Plaats et al. [10] were mainly focused on the microcirculation and hepatic arterial side, respectively. Not much information regarding the characteristics of portal vein is currently available let alone the dramatic changes observed during the perioperative period. To the best of our knowledge, there is no numerical simulation to investigate the perioperative hemodynamic changes in live liver donation. It is therefore worthy to conduct the current computational study for gaining some knowledge about the perioperative changes in the portal vein, which supplies 75% of the blood flow to the liver, in velocity, pressure, and shear stress for a patient who underwent donor right lobectomy and compare the predicted results with the measured velocities by ultrasound. Portal vein remodeling, a term applied to this situation, was raised to colligate these situations.

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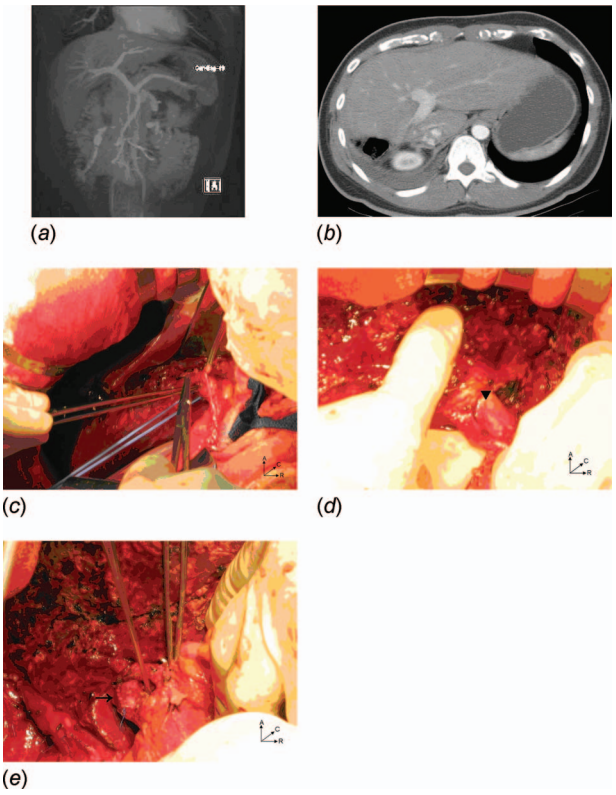

Fig. 1 Medical images versus real-life liver and portal vein. (*a*) A typical MRI angiography image of portal vein. (*b*) A cross-sectional view of the CT image. (*c*) Intraoperative view of the liver and the right branch of the portal vein (looped by a blue tape) before the liver resection. (*d*) The liver was split into the right half and the left half with the right portal vein connected in hand (▼). (*e*) The right lobe and right portal vein were removed and the cutting surface of the junction of the portal vein was sutured with stitches (→). Note also that the cutting surface of the left lobe liver was shown (A: anterior, C: cephalic, and R: right).

The rest of this paper is organized as follows. In Sec. 2, the problem under current numerical investigation will be presented. In Sec. 3, the physical model is briefly described. Then the equations of motion for the investigated incompressible blood flow, subjected to the boundary and initial conditions, will be solved numerically. Both numerical method and verification of the employed code that is applied to carry out the two-fluid simulation will be addressed. The simulated flow features are then analyzed in Sec. 4. Finally, in Sec. 5, a summary of the present study is provided.

2 Problem Description

In the present paper, a typical clinical case of living donor liver transplantation was described. A 25 year-old healthy male was admitted to proceed with a liver donor evaluation for his father who was diagnosed to reach his end stage of liver disease. The right donor lobectomy was performed smoothly. Abdominal magnetic resonance imaging (MRI) and computed tomography (CT) images were taken pre-operatively and one month post-operatively. These images were used in the reconstruction and the modeling of portal vein. Our aim is to assess the influence of living donor right lobectomy on the donor's structural and hemodynamic changes in the portal vein, which is the major blood supplier to liver. The velocity, pressure, and shear stress distributions will be computed pre- and post-operatively from a set of partial differential equations that governs the mass and momentum conservations in the blood flow.

3 Methods

3.1 Image Reconstruction and Portal Vein Model Generation. Pre-operative MRI (Signa 1.5 T, General Electric, Milwaukee, WI) examination was performed routinely at a 5 mm interval for the liver donor evaluation. Serial transverse scans of liver were taken with GE CT/T 8800 (General Electric Medical Systems, Milwaukee, WI) at a 3 mm interval one month after the operation. All the slices of liver were traced on an exact direct proportion between the weight and the area. All hepatic areas were measured with a microestimation balance and the total area of them was calculated from the proportional line. Portal phase images were then properly collected, enabling us to conduct the current computer-assisted simulation. Two representative images of portal veins, pre-operatively and one month post-operatively, were shown in Figs. 1(*a*) and 1(*b*), respectively.

Details of the image reconstruction have been previously described in Ref. [11]. Briefly, image was segmented into a number of subregions. With the aid of AMIRA® 4.0 (Mercury Computer Systems, Inc., Chelmsford), segmentation was carried out by firstly selecting proper voxels and then assigning them to a particular material in order to integrate them into a 3D structure. The invoked labels were stored in the working file as the label field. Use of the segmentation editor helps us to edit the resulting label field so as to render polygonal surfaces using the SURFACEGEN module. Three-dimensional portal vein structures were finally reconstructed by using the AMIRA® software, which is further converted to meshes by HYPERMESH®.

Of the three portal vein models investigated in the current simulation, two (the pre-op and one-month post-op) were constructed directly from the clinical images and the rest one (the immediately after the operation model) was generated directly from the right portal vein branch removed in the pre-op model. These allowed us to make a hemodynamic comparison of the changes in the investigated models: before the operation (pre-op), immediately after the resection (immediately after the operation), and one month after the resection (one-month post-op). Figures 1(*c*)–1(*e*) showed the procedures of donor right lobectomy, which involves the resection of the right portal vein branch. Our proposed models were simplified in the sense that we do not take the full peripheral branches of the portal vein into consideration as our main focus was concentrated on the macrovascular hemodynamics. The reasons will be further explained below in Secs. 3.3 and 4.1. The vessels were hypothesized to be inelastic. More precisely, liver

Table 1 The measured portal vein velocities before and one month after the operation

	Pre-op			One-month post-op	
Sonographic measurement	Main	Right branch	Left branch	Main	Remnant left branch
V_{min}(m/s)	0.097	0.118	0.070	0.185	0.285
V_{max}(m/s)	0.162	0.154	0.049	0.238	0.463
V_{avg}(m/s)	0.1295	0.136	0.0595	0.2115	0.374

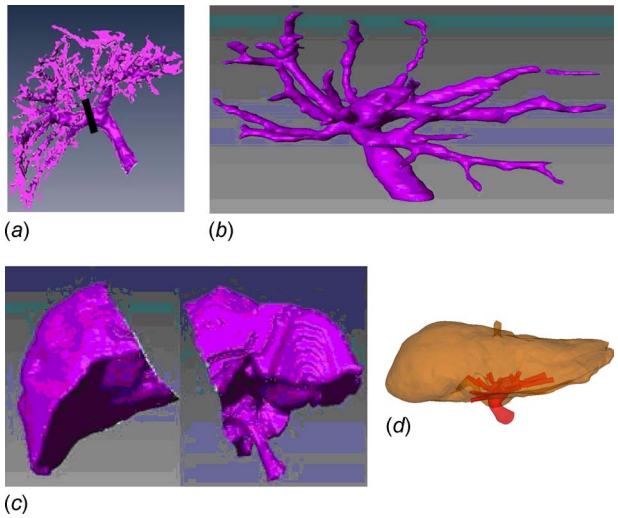

Fig. 2 The portal vessels and liver, which were reconstructed from the medical images. (*a*) Vessels before the operation. The line "—" represents the resection line. (*b*) Regenerated vessels one month after the operation. (*c*) The visualized resection for a donor's right lobectomy. (*d*) The remnant liver is regenerated one month after the operation. The vessels grew significantly different from the original vessels one month after the resection.

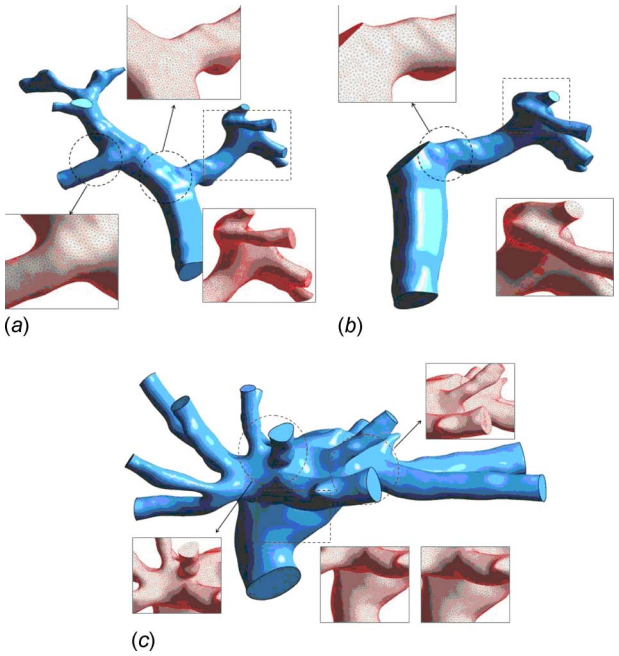

Fig. 3 The plot of three vessel models under current investigation and their detailed surface meshes. (*a*) before the operation, (*b*) immediately after the operation, and (*c*) one month after the operation.

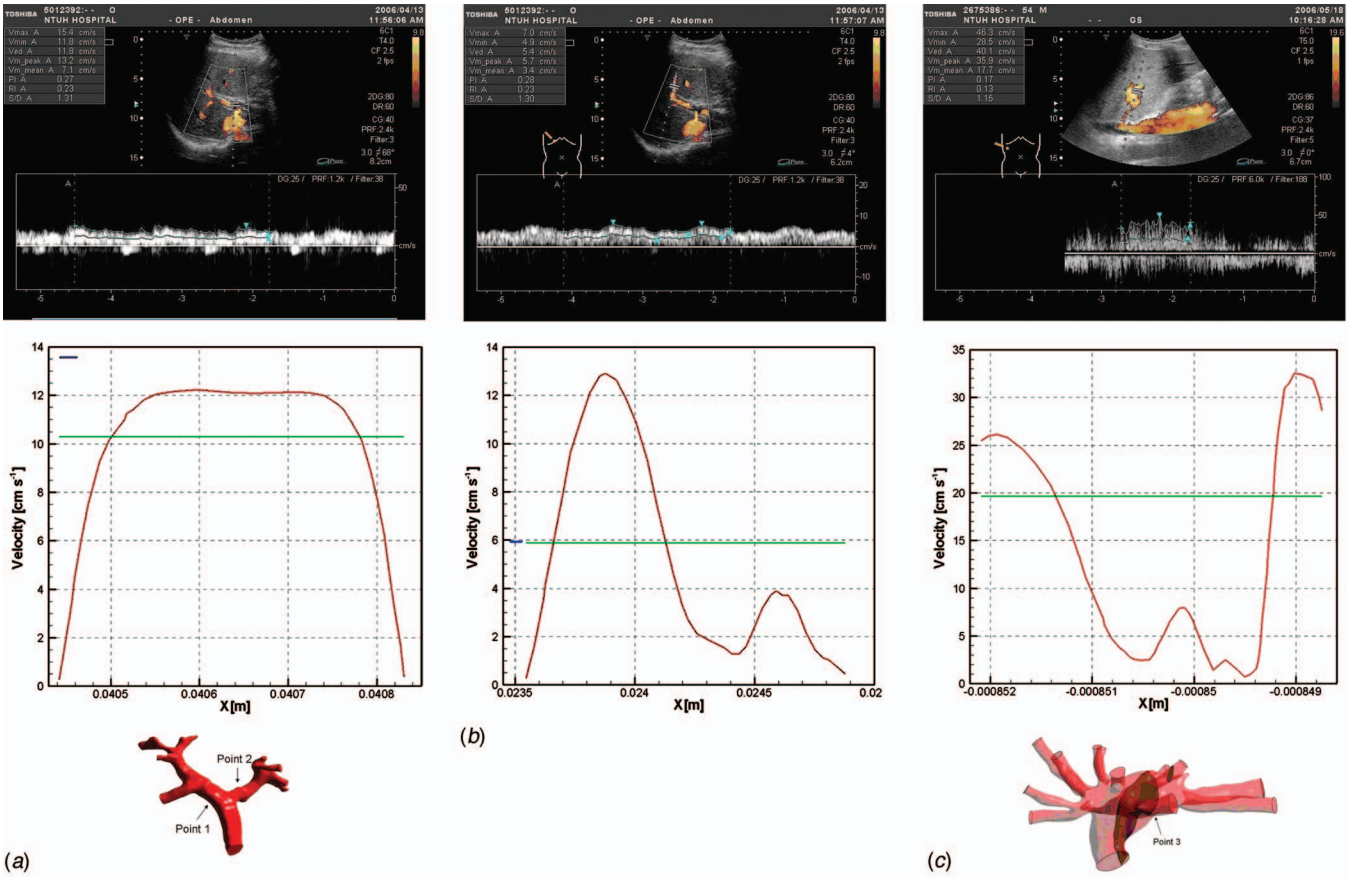

Fig. 4 Correlation of the Doppler measurement of portal vein velocity and the predicted velocity from the models. (*a*) Measured right portal vein velocities (point 1) before the operation versus the predicted results from the pre-operative model (red curve). The mean predicted velocity (green line). The averaged, measured velocity in the blue line for comparison. (*b*) Measured left portal vein velocities (point 2) before the operation versus the predicted results from the pre-operative model (red curve). The mean predicted velocity (green line). The averaged, measured velocity in the blue line for comparison. (*c*) Post-operative portal vein velocity measured one month later versus the predicted velocity at point 3 in the one-month post-operative model (red curve). The mean predicted velocity (green line). The averaged, measured velocity in the location near point 3 was 37.4 cm/s.

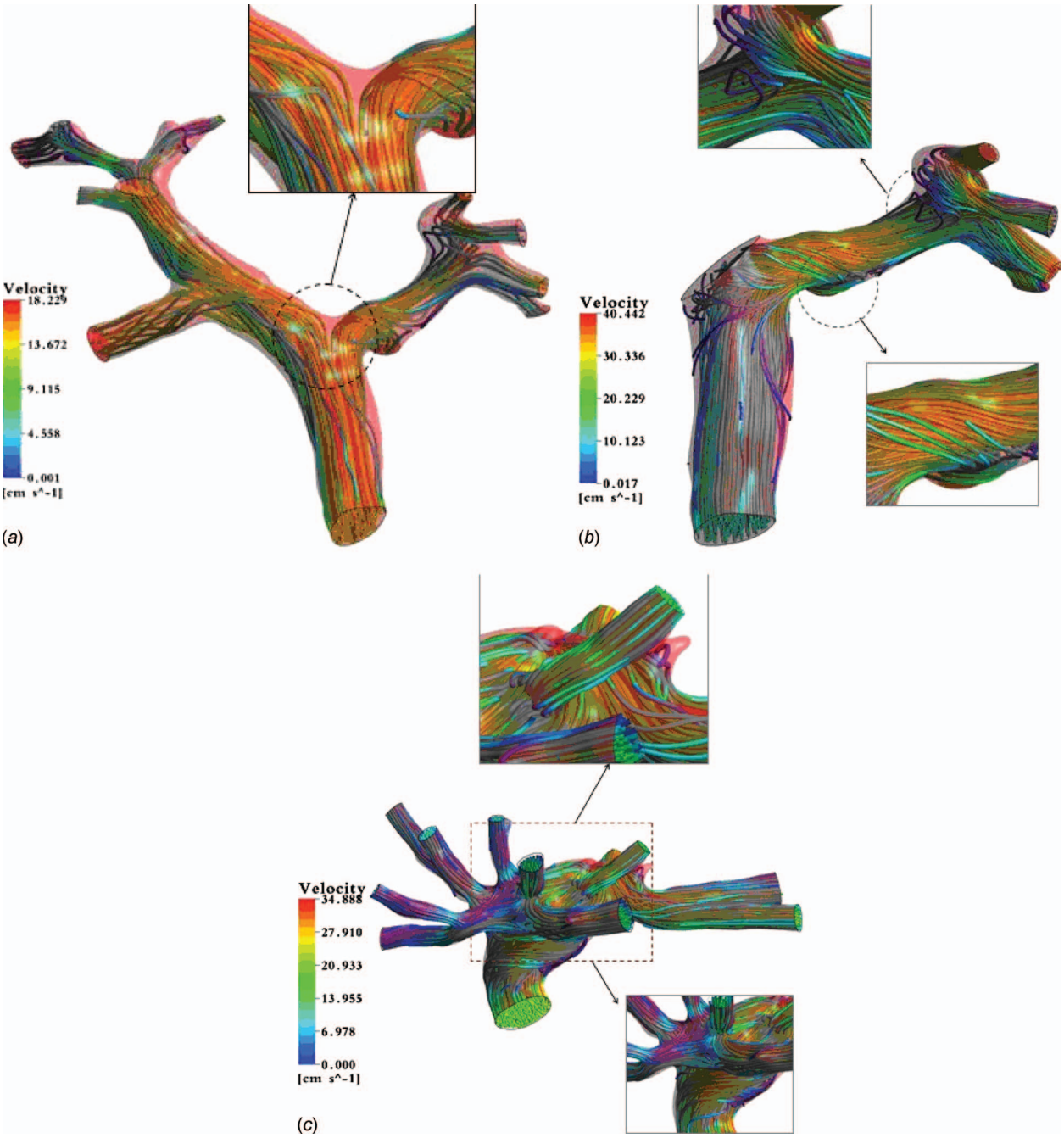

Fig. 5 The simulated particle tracers in the portal vein structures. (*a*) pre-operation, (*b*) immediately after the operation, and (*c*) one month after the operation. The streamlines, laminar in pre-op status, became more complex even at a time of one month after the operation.

parenchyma in the neighbor of blood vessels under our current investigation is not considered.

3.2 Sonographic Measurement of Portal Vein Flow Velocity. The sonographic examination was performed using the ultrasound HDI 3500 system (Advanced Technologies laboratories, Bothell, WA, USA) with a 3.75-MHz sector transducer to render a longitudinal image of portal vein. The portal vein color Doppler was recorded at an angle smaller than 50 deg. The main portal vein velocities were measured at the same time when MRI and CT were filmed, namely, before the operation and one month after the operation. The first branch velocities of portal vein, before the operation and one month later, were also measured in the current study. These measurement data were summarized in Table 1.

3.3 Governing Equations and Numerical Method. The governing equations involved in the present hemodynamic simulation were expressed as follows for the blood velocity vector $U=(u,v,w)$ and pressure p.

Continuity equation:

$$\nabla \cdot U = 0 \tag{1}$$

Momentum equation:

$$\frac{\partial U}{\partial t} + \nabla \cdot (U \otimes U) = -\nabla p + \mu \nabla^2 U \tag{2}$$

In the above, μ denotes the blood viscosity.

Calculation of the finite volume solutions for velocity components and pressure from the above fluid flow equations was car-

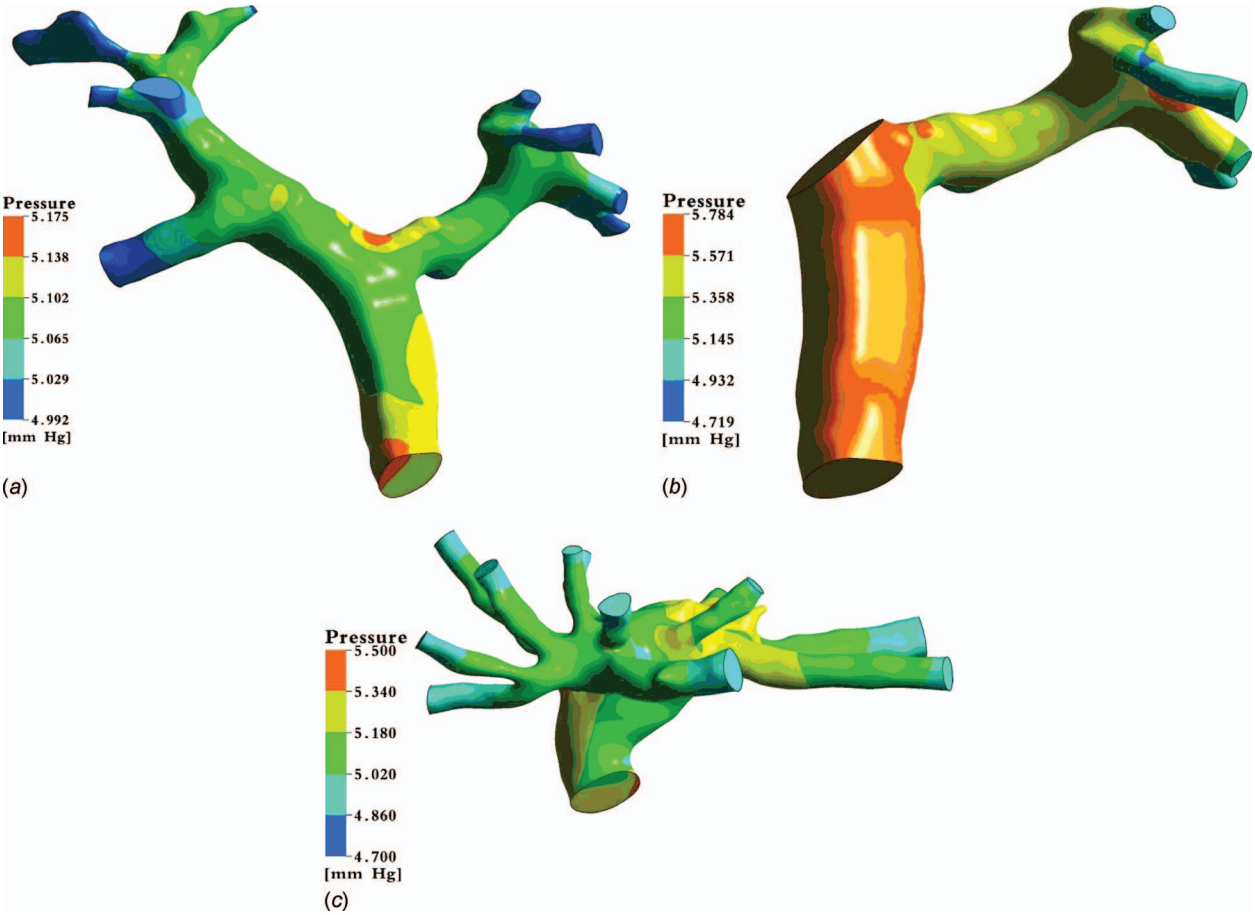

Fig. 6 The simulated pressure contours in the portal vein structures. (*a*) pre-operation, (*b*) immediately after the operation, and (*c*) one month after the operation. The increased pressure in the portal vein shaft (orange color) immediately after the operation was dropped to the pre-operative situation (green/yellow) one month later.

ried out using a user enhanced commercial program CFX-5 (ANSYS Canada Ltd.) at the centroids of the discretized control volumes. The above governing equations were integrated over a control volume along with the application of Gauss' divergence theorem to get the respective surface integrals in the co-located grid. In each time step Δt, the solution was calculated from the fully implicit discretization method and the multigrid solver, which was used together with the incomplete lower-upper (LU) factorization procedure. The transient terms were approximated by the second-order backward Euler scheme, which is robust and implicit in time. The advection term shown in Eq. (2) was approximated by the high-resolution scheme of Barth and Jespersen [12].

Blood is normally classified as a shear thinning viscoelastic fluid [13]. To simplify the analysis, the fluid flow considered in the current calculation was, however, assumed to be Newtonian. Gijsen et al. [14] pointed out that for younger individuals their characteristic shear rates are normally higher. The effect of non-Newtonian blood is normally insignificant in larger arteries, where the shear rate is high [15]. The non-Newtonian effect in venous system, for which the data are lacking, might be higher than that in arteries. However, hepatic main portal vein normally has a positive pressure in the range of 5–10 mmHg, which is much higher than those in the other veins that have been characterized as the negative-pressured, low-flow-rate vessels. The non-Newtonian effect, demonstrated in the hepatic lobule microcirculation in our previous study [9] is small for large portal vein branches, in which the macrohemodynamic changes in perioperative period are the main focus in this study. We, therefore, simulate the portal vein flow by considering it as a Newtonian fluid as did previously in the study of Van der Plaats et al. [10].

At the portal vein inlet, the mass flow rate $\dot{m}$ (for example, pre-op: 0.01479 kg/s and post-op: 0.02487 kg/s) for the blood is prescribed according to the mean measured velocity data, shown in Table 1, multiplying by the cross-sectional area of the main portal vein, measured through the clinical imaging system. Blood density and viscosity under current investigation were 1050 kg/m^3 and 0.0035 kg/m s, respectively. Zero pressure boundary condition was prescribed at each vessel outlet as the pressure drops in the continuous portal vein flow system are much smaller (5–10 mmHg to 0–2 mmHg) in unit distance when comparing them with those in the pulsatile hepatic arteries (120/100 mmHg to 0–2 mmHg) [10]. The convergent criterion set for this study is 10^{-8}. The predicted results were then visualized using the animation softwares FIELDVIEW and CFX-POST. All the calculations were performed on a Pentium-4 CPU PC with 2.0 Gbytes RAM and 250 Gbytes hard disk space.

4 Results and Discussion

4.1 Investigated Portal Vein Models. The reconstructed 3D structures of the pre-op and one-month post-op portal veins were schematic in Figs. 2(*a*) and 2(*b*), respectively. A hypothetical line of resection (thick black line in Fig. 2(*a*)) of the right portal vein was drawn for the simulation of donor right lobectomy (Fig. 2(*c*)). The left portal vein remained intact and was considered as the structure of the immediate post-op portal vein. The remnant liver was regenenerated, as shown in Fig. 2(*d*). The models and meshes of these three structures (pre-op, immediately after the operation, and one-month post-op) were plotted in Figs. 3(*a*)–3(*c*). A signifi-

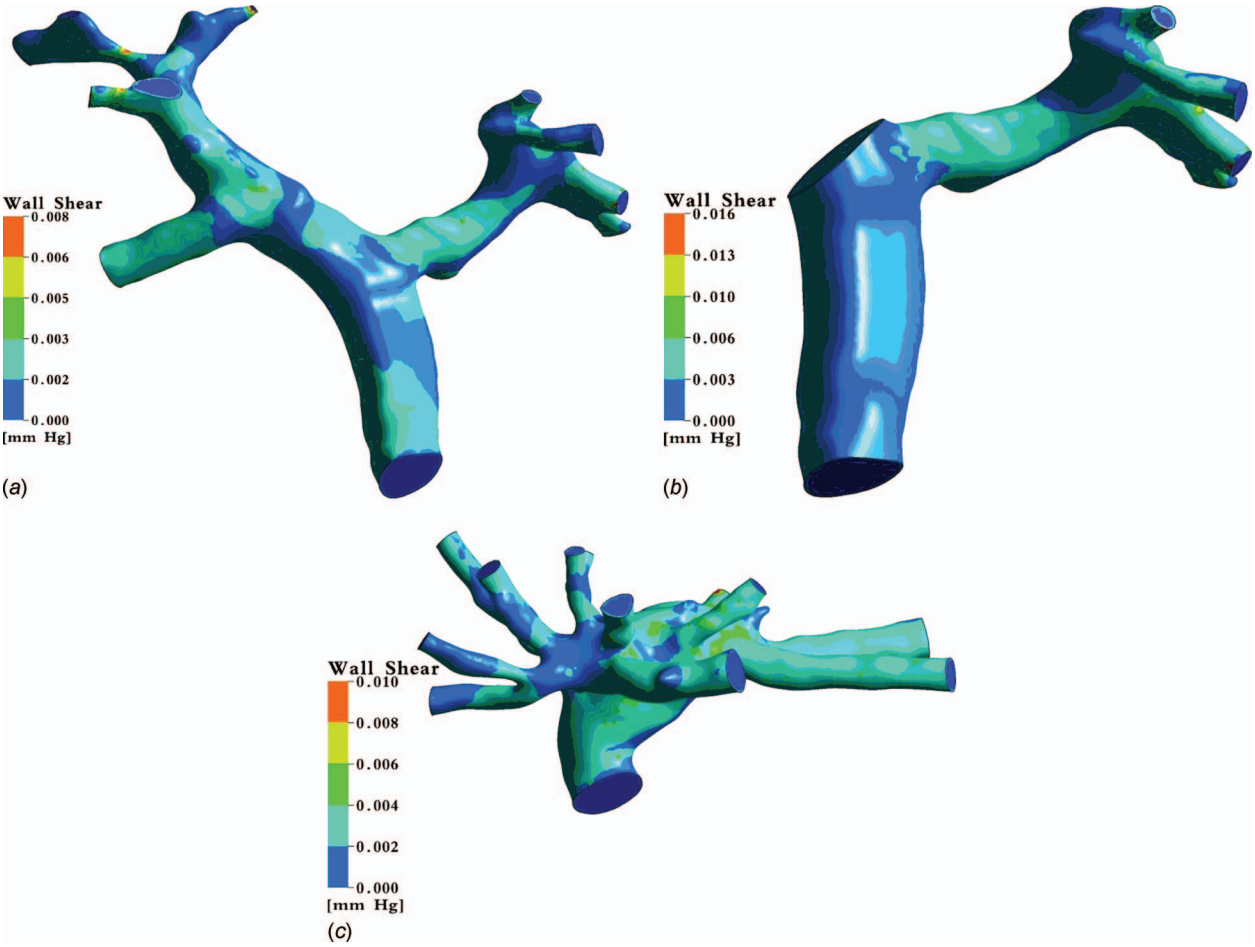

Fig. 7 The simulated shear stress contours in the portal vein structures. (*a*) pre-operation, (*b*) immediately after the operation, and (*c*) one month after the operation. The shear stress on the shaft one month after the operation is increased when comparing with that on the immediately after the operation model.

cant difference in structural pattern was seen between the immediately after the operation and one-month post-op portal veins. We called this difference a portal vein remodeling, which is accompanied by an ongoing process of liver regeneration. Other distal peripheral branches of the portal veins were discarded for the following reasons. (i) The purpose of this simulation work was to study the hemodynamic changes in larger portal vein systems, which may cause some clinical relevant surgical complications to occur if left unnoticed. (ii) The image resolution of the distal small portal veins is not high enough for us to conduct an accurate calculation. (iii) The influence of omitting distal small portal veins on the predicted accuracy is minimal.

4.2 Flow Features and Validation. For the sake of comparison, the pre-op right (point 1) and left portal vein (point 2) velocities measured by ultrasound were compared with the predicted velocities in the pre-op portal vein model (Figs. 4(*a*) and 4(*b*)). The measured velocity in the one-month post-op portal vein by ultrasound was compared with the predicted one (point 3), as shown in Fig. 4(*c*). These simulated velocities were seen to agree qualitatively with the measured results. However, certain error-prone estimation did exist when correlating the simulated velocity in one point to the measured one specifically, such as point 3 in a complex regenerating portal vein model. The hemodynamic characteristics in three models, including flow streamlines, pressure, and shear stress, were shown in Figs. 5–7, respectively. One month after the operation, the pressure in the portal vein shaft was decreased to the pre-op level in comparison with the immediately after the operation status and is distributed more homogenously toward its branches. The shear stress was also distributed more evenly at a time one month after the operation. The streamlines, laminar in pre-op status, became much complex, even at a time one month after the operation. The spiral-shaped streamlines found in the case after operation might be one of the major mechanisms that could trigger a portal vein remodeling, just as the running water keeps changing its flow passage. This causes an immediate post-op portal vein structure to turn right and thus shift toward the midline. The distal branches are also enlarged so as to accommodate a suddenly increased flow volume (Figs. 2(*a*) and 2(*b*)).

It is common to see an increased portal inlet flow after operation in both live donor partial hepatectomy and live donor liver transplantation [16]. The current study, to our knowledge, is the first attempt of theoretically predicting and estimating the portal flow hemodynamic changes in perioperative period. In recipients, portal vein flow velocity increases dramatically after reperfusion, returning to the baseline at a time three months after transplantation [16]. In donors, as healthy individuals, operations such as the right lobectomy would increase the portal vein flow as well [17]. In the same study, cardiac output and heart rate during the dissection phase became significantly larger immediately after the donor's right lobectomy (6.02 ± 1.11 v 10.28 ± 3.84 l/min; 62 ± 10 v 83 ± 9 beats/min), whereas the systemic vascular resistance tended to become smaller after operation. Not all donors, however, had such a large change. The reasons for the increased flow may be attributed to the splanchnic mediaters such as the released endotoxin during liver surgery [18]. Endotoxins can trig-

ger inflammation process by releasing cytokines and then nitric oxide, which can cause the vasodilatation and altered hemodynamics to occur [19,20]. Failure of increasing a cardiac output during and after liver surgery may even result in a likelihood of major complication [21]. It is not possible, however, to predict the extent of an altered hemodynamics in advance at the present time. We, therefore, use the measured inlet velocities as the required boundary condition to predict blood pressure and shear stress distributions in the portal vein structure for getting the trend of perioperative hemodynamic changes.

Portal vein remodeling is not a new phenomenon from the microscopic point of view. After experimentally inducing cholangiocyte proliferation in rats fed with α-naphthylisothiocyanate, both hepatic artery and portal vein undergo a marked proliferation, presumably to respond the resulting increased nutritional and functional demands of the proliferated bile ducts [22]. Following a partial portal vein ligation in rats, neovascularization was also observed using the intravital microscopy and scanning electron microscopy [23]. What we address here is the issue of portal vein remodeling from the macroscopic point of view. In response to the increased inlet flow of the portal vein, the resection-modified structure is subject to a strong turbulent flow and the tributary branches seemed to be enlarged and twisted with the regenerated liver. This phenomenon, which might be observed clinically, was not mentioned in the existing literature. The macrovascular structure modification in the perioperative period was influenced considerably by the flow-altered hemodynamics rather than by the molecular chemicals so that the modification in macrovascular structure might play an essential role in the later microvascular angiogenesis.

Doppler ultrasound is a useful and promising noninvasive monitoring tool used to measure the hemodynamic changes in liver grafts or remnant liver after liver transplantation or live donor hepatectomy when liver regeneration and early detection of vascular complications need an additional attention [24]. Pressure or shear stress, however, cannot be obtained directly through this noninvasive measurement. The computer simulation has, therefore, its proper role to play. After conducting the validation with the measured velocities by ultrasound, the numerically predicted hemodynamic parameters after operation might provide us some useful information for the surgical planning.

5 Conclusion

In this paper, an attempt has been made to conduct a hemodynamic simulation for knowing the change in flow characteristics after live donor right lobectomy. The incompressible Navier–Stokes equations were formulated under the assumption of constant fluid property. The portal vein network was reconstructed from the clinical images using the AMIRA® software. This setting enables us to study the effect of surgical resection on the remnant portal vein and the remodeling processes due to liver regeneration. It is observed that the branches grew quite differently from the liver regenerated in one month, together with the pressure relieved evenly toward the distal branches during the period. These signify that liver regeneration after donor hepatectomy involves a portal vein structure redistribution rather than just a volume increase. Some of the predicted results, such as the flow velocities, are carefully compared with the velocities measured by ultrasound in the present study. These provide us useful evidence to justify the current computer simulation, thus affording a possible avenue for the future clinical applications.

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