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Development of a general method for designing microvascular networks using distribution of wall shear stress

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ABSTRACT

In the present study, theoretical formulations for calculation of optimal bifurcation angle and relationship between the diameters of mother and daughter vessels using the power law model for non-Newtonian fluids are developed. The method is based on the distribution of wall shear stress in the mother and daughter vessels. Also, the effect of distribution of wall shear stress on the minimization of energy loss and flow resistance is considered. It is shown that constant wall shear stress in the mother and daughter vessels provides the minimum flow resistance and energy loss of biological flows. Moreover, the effects of different wall shear stresses in the mother and daughter branches, different lengths of daughter branches in the asymmetric bifurcations and non-Newtonian effect of biological fluid flows on the bifurcation angle and the relationship between the diameters of mother and daughter branches are considered. Using numerical simulations for non-Newtonian models such as power law and Carreau models, the effects of optimal bifurcation angle on the pressure drop and flow resistance of blood flow in the symmetric bifurcation are investigated. Numerical simulations show that optimal bifurcation angle decreases the pressure drop and flow resistance especially for bifurcations at large Reynolds number.

1. Introduction

One of the most serious problems in health care is organ failure and tissue losses. However, organ transplantation helps only 10% of the patients. Despite the numerous advances in tissue engineering, several challenges still avoid the widespread clinical application of tissue engineering products. One of the major challenges to generate vascularized tissue is lack of proper vascularization for constructing vascularized tissues that mimic natural tissues (Borenstein et al., 2002; Kaazempur-Mofrad et al., 2003). Development of a design method for vascular systems is crucial to move toward the artificial organs that mimic normal tissues.

Based on the principle of minimum work and conservation of mass, a relationship between the optimum diameter of the mother vessel and the diameters of the daughter vessels was derived by Murray (1926b). The relationship which is known in physiology as Murray law states that the cube of the radius of a mother vessel equals the sum of the cubes of the radii of the daughter vessels in a bifurcation i.e., $d_0^3 = d_1^3 + d_2^3$. An exponent of 2 instead of 3 in Murray law, $d_0^2 = d_1^2 + d_2^2$, corresponds to conservation of the area and therefore constant flow velocity in and out of the bifurcation (Beare et al., 2011). Exponents greater than 2 suggest a decrease in flow velocity downstream the bifurcation while exponents less than 2 imply an increase in flow velocity downstream the bifurcation. Therefore, applying the Murray law at the bifurcation leads to decrease of mean velocity downstream of the bifurcation. Furthermore, because of Murray law WSS remains constant throughout a vascular system.

Murray law is in agreement with small arteries of the rat cardiovascular system ($50\ \mu m < d < 500\ \mu m$) and arterioles (diameter $< 100\ \mu m$) of swine heart (Zamir et al., 1983; VanBavel and Spaan, 1992; Kaimovitz et al., 2008). The law also successfully predicts the sizing of human coronary arteries (Hahn et al., 2008). Some studies suggest that the average WSS in the mother vessel is equal to the average WSS in both the daughter vessels (LaBarbera, 1990). However, it is also reported by some investigators that the assumption of constant WSS throughout the vasculature predicted by the Murray law is not realistic and the exponent 3 in Murray law must be replaced by the different exponents (Reneman et al., 2009; Beare et al., 2011). In-vivo measurements of WSS has shown that the real exponent of Murray law is about 2 in aortic bifurcation, 2.5 to 3 in coronary, 2.9 in carotid bifurcation and about 3 in arterioles (Reneman et al., 2009; Ingebrigtsen et al., 2004; Hahn et al., 2008). Moreover, WSS and geometry of the bifurcation have been demonstrated to play vital roles in the pathogenesis of artery diseases (Malek et al., 1999; Schulz and

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Rothwell, 2001; Sitzer et al., 2003; Thomas et al., 2005). In fact, in human circulatory system WSS by affecting the endothelial wall and producing some vasoactive materials can reduce the resistance to flow and maintain blood circulation by changing the microvasculature diameter (John, 2009). In addition, blood has a non-Newtonian nature. However for most of the large arteries where shear rate is greater than 100 s^{-1}, it seems reasonable to treat blood like a Newtonian fluid. Artery wall also has compliant nature. Despite time varying blood pressure which deforms the artery walls, the effect of deformation on WSS is only 10% (Perktold and Rappitsch, 1995). Over the past decades, many studies have conducted to investigate Murray law. Nonetheless, a few have focused on bifurcation angle. The bifurcation angle also can affect hemodynamic properties. Recently, ratio of Murray law ($\alpha = D_0^3/(D_1^3 + D_2^3)$) and bifurcation angle have been measured for the chicken embryo (Lee and Lee, 2010). The mean value of bifurcation angle and the ratio of Murray law were measured $77.161^\circ \pm 26.171^\circ$ and 1.053 ± 0.188, respectively.

The objective of this study is to assess the effect of WSS on optimal design of the vascular system for both Newtonian and non-Newtonian behaviors of blood. A theoretical model for the design of vascular systems by using the WSS distribution in the cardiovascular system is developed. A novel relationship for the bifurcation angle in the asymmetric configuration is also established based on the ratio of WSS of mother to daughter conduits and the ratio of length of daughter conduits. The effect of constant WSS on minimizing global energy loss and flow resistance is discussed. Finally, the reliability of the theoretical formulation for blood flow is validated using non-Newtonian models including power law and Carreau models.

2. Methods

2.1. Newtonian and non-Newtonian behavior

In Newtonian fluids unlike non-Newtonian fluids, the shear stress is independent of shear rate. For non-Newtonian models, the constitutive equation is expressed as

$$\tau = f(\dot{\gamma}), \dot{\gamma} = -\frac{du}{dr} \tag{1}$$

where τ and $\dot{\gamma}$ are shear stress and shear rate, respectively. In this study, some common models that describe blood flow such as Newtonian, power law (Ostwald, 1925; De Waele, 1923) and Carreau et al. (1979) are considered (Johnston et al., 2004; Gijsen et al., 1999; Strony et al., 1993; Shibeshi and Collins, 2005). Models and their relations are summarized in Table 1.

2.2. Geometric configurations

The tree-shaped geometric model has been serving as an ideal simplified model to study hemodynamic phenomena both experimentally and theoretically. It has been a geometrical model of interest because in addition to its simplicity, its flow features demonstrate the most common flow behavior at arterial bifurcations. The tree-shaped bifurcation can be symmetrical or asymmetrical. In this study, an asymmetrical bifurcation with two daughter branches is selected. L_0, R_0 refer to the radius and length of mother branch, L_1, R_1 are also the length and radius of the first daughter branch and L_2, R_2 are the length and radius of the second ones, respectively. The bifurcation angle is the sum of the first and second bifurcation angles ($\theta_{1+2} = \theta_1 + \theta_2$), where θ_1 and θ_2 are the first and second bifurcation angles, respectively (see Fig. 1).

2.3. Design of vascular system using power law model

2.3.1. Volumetric flow-rate and viscous loss

Using WSS of the conduit, the flow rate (Q) and power loss due to friction in the conduit (Φ) can be calculated as

$$Q = \kappa {\tau_w}^{1/n} R^3 \tag{2}$$

$$\Phi = 2\kappa {\tau_w}^{1/n+1} R^2 L \tag{3}$$

where n is the model index and κ is constant for blood $\kappa = \mu^{-1/n}\pi/((3+1/n))$. For the Newtonian model, the index is equal to unity. For details, see Appendix A in supplementary data.

2.3.2. Optimal pattern of WSS distribution

In biological systems, usually there are two energy loss terms. The first loss, Φ, is the energy required to pump fluid through the conduit to overcome viscous loss. The second term can be related to the cost function at which energy is used up by the blood vessels by metabolism or the energy destroyed by elastic tubes (Sherman, 1981). The cost function assumed to be proportional to the volume of conduit. So the global energy loss in the conduit can be expressed as

$$E_{global} = \Phi + \Gamma(\pi R^2 L) \tag{4}$$

where Φ is power loss and Γ is metabolic rate, R and L are the radius and length of conduit, respectively. The key to achieve maximum global performance is minimizing global energy. Recently, Murray's law has been generalized to a non-Newtonian blood flow model by minimizing Eq. (4) with respect the radius of conduit (Revellin et al., 2009). A similar approach is presented here for obtaining the pattern of distribution of WSS in the vascular systems. By minimizing E_{global} with respect to the variable L, see the derivation in Appendix A in supplementary data, WSS can be written as

$$\tau_{w\_opt} = \left(n\pi\frac{\Gamma}{2\kappa}\right)^{(n/n+1)} \tag{5}$$

For the Newtonian model the result is the same but $n=1$. However, non-Newtonian effect such as shear-thinning or shear-thickening can change the value of n but for a biological fluid, the properties such as model index, viscosity and metabolic rate are known. Therefore, because of minimum energy principle, WSS is

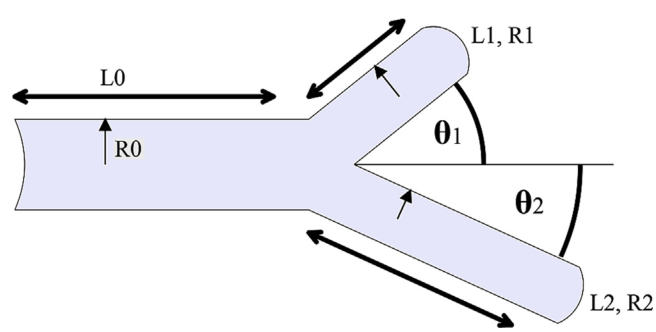

Fig. 1. The asymmetric bifurcation.

Table 1
Different rheological models for blood flow (Shibeshi and Collins 2005; Johnston et al. 2004).

Model	Formula	Symbol descriptions	Blood properties
Newtonian	$\tau(\dot{\gamma}) = \mu\dot{\gamma}$	μ is viscosity	$\mu = 0.0035$ Pa s
Power law	$\tau(\dot{\gamma}) = \mu\dot{\gamma}^n$	μ is fluid consistency	$\mu = 0.0035$ Pa s^n
		n is power law index	$n = 0.9$
Carreau	$\tau(\dot{\gamma}) = \eta\dot{\gamma}$	η is apparent viscosity	
	$\eta(\dot{\gamma}) = \mu_\infty + (\mu_0 - \mu_\infty)(1 + (\lambda\dot{\gamma})^2)^{(n-1/2)}$	μ_0 is apparent viscosity of zero shear rate	$\mu_0 = 0.056$ Pa s
		μ_∞ is apparent viscosity of infinite shear rate	$\mu_\infty = 0.0035$ Pa s
		λ is time shear relaxation factor	$\lambda = 3.313$ s
		n is the exponential constant	$n = 0.3568$