DISTRIBUTION OF THE FLUID SHEAR STRESS ON THE MEMBRANE OF LEUKOCYTES IN MICROVESSELS

Masako Sugihara-Seki (1), Geert W Schmid-Schönbein (2)

(1) Faculty of Engineering
Kansai University
Suita, Osaka
JAPAN

(2) Department of Bioengineering
The Whitaker Institute for Bioengineering
University of California, San Diego
La Jolla, CA

INTRODUCTION

Recent evidence suggests that circulating leukocytes not only influence the flow plasma and circulating cells in the microcirculation but fluid stresses in the plasma also control the biology and the cell mechanics of circulating leukocytes. Several biological activities can be controlled by fluid shear stress, such as retraction of pseudopods by actin polymerization on migrating leukocytes [1], their cytoplasmic stiffness and integrin [1,2], and so on. In contrast to endothelial cells which have been subject to extensive studies, so far only few details are known about the fluid shear response in leukocytes and the fluid shear distribution on the membrane of leukocytes encountered *in vivo*.

During passage through capillaries and venules, leukocytes make their first contact with the endothelial membrane in small postcapillary venules (about 8 to 12 μm in diameter) [3]. In this report, we will focus on the membrane fluid shear stress distribution on a leukocyte in such a microvessel. We will numerically examine the membrane fluid shear stress on a leukocyte as it passes unattached from the center stream to an off center position with rotation, and finally to a point of attachment on the endothelium. The fluid shear stress was determined by solution of the Stokes approximation of the equations of motion for plasma at constant viscosity assuming a spherical shape for the leukocyte in a cylindrical microvessel.

FORMULATION AND METHODS

As a model for a leukocyte, consider a rigid sphere with radius a in a microvessel with radius R. We neglect the cell deformation [4] and study two cases:

(i) a sphere freely suspended in a circular cylindrical tube (Figure 1(a)),
(ii) a sphere attached to or rolling along the wall of a tube(Figure 1(b)).

In case (i), the translational velocity of the sphere parallel to the tube centerline is denoted as U and its angular velocity with respect to the center of the particle as Ω, and their values are determined as a part of the solution simultaneously with the flow field of the fluid. In case (ii), we assume that the sphere rolls along the tube wall without slip, so that its rolling velocity U_r and angular velocity with respect to the center of the sphere Ω_r are $U_r = a\,\Omega_r$. These values are prescribed in the current model. The case $U_r = a\,\Omega_r = 0$ represents the particle attached stationary to the tube wall.

In both cases (i) and (ii), we assume that the motion of the fluid obeys the Stokes equation and the continuity equation, and the resultant force and torque acting on the particle vanish in case (i). We adopt the no-slip boundary condition on the wall of the tube and the particle surface, and assume that the velocity profile of the fluid approaches that of the Poiseuille flow far upstream and downstream from the particle. The flow fields around a spherical particle are solved numerically by a three-dimensional finite element method [5,6]. The shear stresses exerted on its surface are computed explicitly.

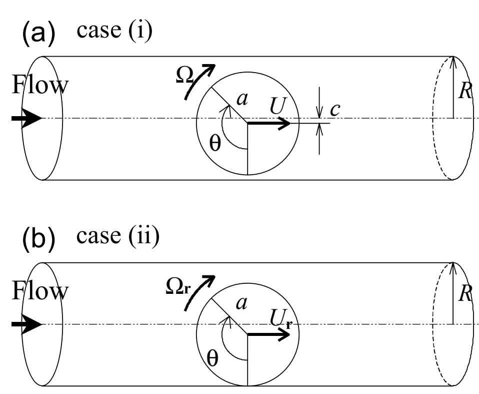


Figure 1. (a) geometry for a freely suspended sphere in a vessel, and (b) geometry for a sphere adherent to or rolling along the vessel wall.

RESULTS AND DISCUSSION

In case (i), the shear stresses exerted on the surface of a freely suspended sphere are computed for various size ratios a/R and radial positions of the sphere c/R. Figure 2(a) shows the distribution of the shear stress on the surface, for $a/R = 0.8$ and $c/R = 0.15$. In this case, the sphere translates with the velocity U/V = 1.22, and rotates clockwise with the angular velocity $R\Omega/V$ = 0.24, where V represents the mean velocity of the fluid over the cross-section of the vessel. It is apparent from Figure 2(a) that the shear stress varies its direction and magnitude over the surface. A large shear stress acts on a part close to the tube wall, which points in the direction opposite to the undisturbed flow velocity.

In case (ii), the shear stresses acting on an attached or rolling sphere are calculated for various preselected values of the rolling velocity U_r (= $a\Omega_r$). As a representative example, Figure 2(b) shows the distribution of the shear stress on the surface of an adherent sphere ($U_r = a\Omega_r = 0$) with a/R = 0.8. The shear stress attains its maximum near the top portion of the particle surface, while it is relatively small near the tube wall. Note that the scale of each arrow in Figure 2(b) is one-third of that in Figure 2(a).

Figures 2(a) and (b) indicate that the shear stresses exerted on the surface of the sphere are considerably non-uniform in both cases, and their variations are most significant along the circumference in a plane containing the center of the sphere and the tube centerline. The distributions of the shear stress around this circumference in cases (i) and (ii) are plotted as a function of the azimuth angle θ (Figure 1) for a/R = 0.8 in Figures 3. The shear stress is normalized by the undisturbed shear stress on the wall $\tau_w = 4\mu V/R$. The curves (a)-(d) represent the results of case (i) for c/R=0, 0.05, 0.1, and 0.15, respectively. The curves (e)-(g) represent case (ii) for U_r/V = 0, 0.1 and 0.2, respectively.

The curves (a)-(d) show that a freely flowing sphere experiences both positive and negative shear stresses, and the amplitude of the shear stress increases as the particle approaches the vessel wall. Since a sphere placed off-center rotates, this indicates that every point on this circumference experiences periodically varying shear stresses. The curves (e)-(g) show that the peak shear stress on the surface of an adherent or rolling sphere is near the highest point ($\theta = \pi$), and this peak value decreases gradually as the rolling velocity increases. A comparison between curves (a)-(d) and (e)-(g) clearly suggests that much larger fluid stresses are exerted on the surface of an adherent or rolling cell compared to a freely suspended cell.

CONCLUSIONS

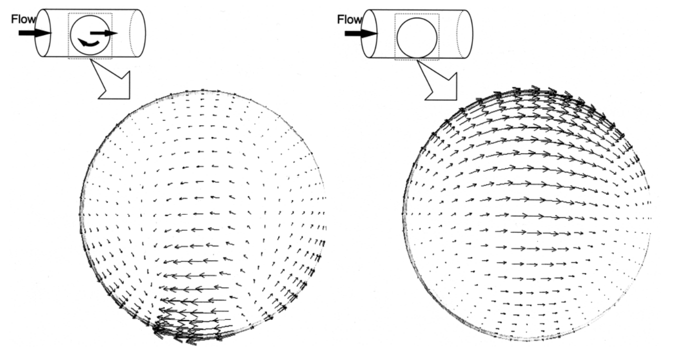
Assuming a rigid spherical particle as a model for the leukocyte, we examined the distributions of the shear stress exerted on its surface when it is freely suspended, or when it is attached to or rolling on the microvessel wall. The present study suggests that once a leukocyte makes attachment with the vessel wall, a dramatic increase in shear stress occurs both for rolling and adherent cells. The magnitude of the shear stress on the surface of a freely suspended cell is estimated to be several times larger than the wall shear stress produced by an undisturbed Poiseuille flow, when the radius ratio of the cell to the vessel is 0.8. For a typical in-vivo wall shear stress of 10-20 dyn/cm^2 for postcapillary venules [7], we assess the shear stress acting on freely flowing leukocytes of order of several 10 dyn/cm^2. For the same radius ratio, on the other hand, adherent or rolling leukocytes experience higher membrane shear stresses of order of 100 dyn/cm^2.

ACKNOLEDGEMENTS

This work was supported by a Grant-in-Aid for Scientific Research (C), Japan, and by grant HL 43026 from the NHLBI.

REFERENCES

1. Moazzam, F., DeLano, F. A., Zweifach, B. W., and Schmid-Schönbein, G. W., 1997, “The Leukocyte Response to Fluid Stress,” *Proc. Nat. Acad. Sci*. USA**,** 94, pp.5338-5343.
2. Fukuda, S., and Schmid-Schönbein, G.W., 2000, “Regulation of CD18 Expression on Neutrophils in Response to Fluid Shear Stress,” *FASEB J*., 14, A1.
3. Schmid-Schönbein, G.W., Usami, S., Skalak, R., and Chien, S., 1980, “The Interaction of Leukocytes and Erythrocytes in Capillary and Postcapillary Vessels,” *Microvasc. Res*. 19, pp.45-70.
4. Dong, C., Cao, J., Struble, E.J. and Lipowsky, H.H., 1999, “Mechanics of Leukocyte Deformation and Adhesion to Endothelium in Shear Flow,” *Ann. Biomed. Eng*., 27, pp.298-312.
5. Sugihara-Seki, M., 1996, “The Motion of an Ellipsoid in Tube Flow at Low Reynolds Numbers,” *J. Fluid Mech.*, 324, pp.287-308.
6. Sugihara-Seki, M., 2000, “Flow around Cells Adhered to a Microvessel Wall,” *Biorheology*, 37, pp.341-359.
7. Lipowsky, H.H., 1995, “Shear Stress in the Circulation,” in *Flow Dependent Regulation of Vascular Function*, Bevan, J.A., Kaley, G. and Rubanyi, G.M. eds. pp. 28-45, Oxford University Press.



(a) **(b)**

Figure 2. Shear stress distributions on the particle surface: (a) freely suspended sphere with *a/R*=0.8 and *c/R*=0.15, and (b) adherent sphere with *a/R*=0.8. The scale of each arrow in (b) is one-third of that in (a).

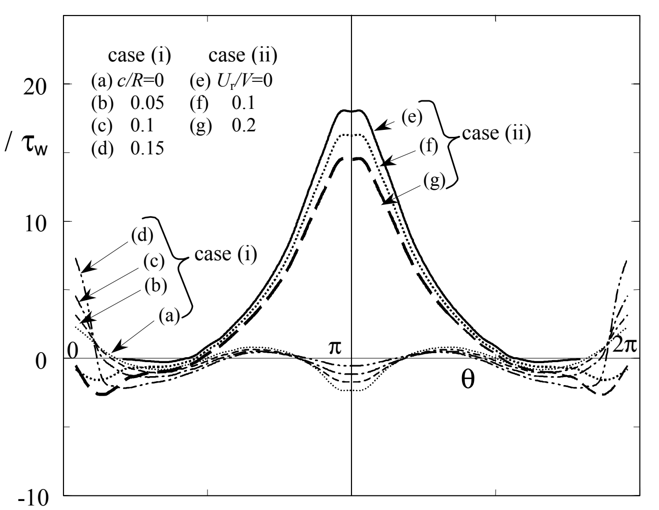


Figure 3. Shear stress distributions on the surface of a sphere along a circumference in the plane containing the center of the sphere and the vessel centerline.