HEMOLYSIS (ERYTHROCYTE DAMAGE) MODEL FOR PREDICTION IN TURBULENT SHEAR BLOOD FLOW

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ABSTRACT

In the development of medical fluid device, especially artificial organs and hearts, there have been problems, such as hemolysis (erythrocyte damage) and thrombosis (coagulation of blood) in the device. For hemolysis, the reason and mechanism have not been elucidated yet. There are some factors to occur the hemolysis, for example, molecular viscous shear stress, turbulent shear stress (Reynolds stress), pressure gradient, collision of red blood cells, contact with wall etc. In the recent developments, most popular type of artificial hearts is centrifugal blood pump. But in these pumps, high shear stress, which occurs at the edge of the impeller in the pump and at the lip portion separating the diffuser from the pump casing, is considered as the cause of the hemolysis. As the hemolysis in the flow has physical, biological, and chemical factors, the phenomena is too complicated to analyze.

In this study, to understand the mechanism of hemolysis by shear stress in a complicated flow such as that in a blood pump, the model for hemolysis is constructed using the pipe orifice flow to simplify configurations. In this model, it is considered that there are two methods using effects of the shear stress, and the contact with the wall of orifice including the inertia of the particle caused by differences of density to be considered.

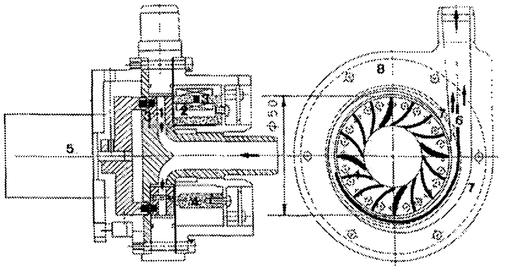


Fig.1 Typical rotary blood pump (Akamatsu 1995)

INTRODUCTION

Recently artificial organs, especially rotary blood pumps, have been developed in the worldwide (Akamatsu 1995), but in these developments hemolysis and thrombosis occur in the pumps. As for the hemolysis, it is considered to be caused by shear stress in the flow field (Croce 1977, Hashimtoto 1989, Affeld 1995). Actually, there are two kinds of shear stress in high shear flow like the flow in the rotary blood pump (Fig.1). One is molecular viscous shear stress and the other is turbulent shear stress (shear component of Reynolds stress). In this turbulent shear flow, the turbulent shear stress cannot be ignored because the turbulent shear stress is much larger than molecular shear stress. There are some papers describing predictions of hemolysis (Bludszuweit 1995)), but in the moment the agreements between the predictions and the experiments are not complete.

Hellumus et al.(1977) arranged their condition for hemolysis as shown in Fig.2. Here it is found that the threshold of hemolysis depends on the shear stress and exposure time to be worked on the shear stress field. And it

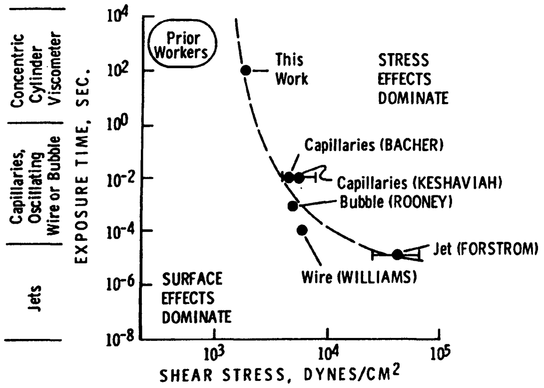


Fig. 2 The shear stress-time plane for hemolysis due to shear

is also found that there are two regions affecting the hemolysis, they are the shear stress effects dominant region and the surface effects dominant region.

We have studied about hemolysis by turbulent shear stress. In our study, considering effects of mechanical factor on hemolysis properties mainly, we deal with the orifice pipe-flow to simplify the complicated flow in the pump (Umezu 1994), and we predict the hemolysis in the pipe orifice flow to use computational fluid dynamics that is based on the low Reynolds number k- ε turbulent model for the separated flow and reattached flow. However, in our previous paper (Tamagawa 1996), the prediction has not been completed even if we deal the simple pipe orifice flow. The reason is that there are some effects such as anisotropic turbulence in the separated flow, high concentrated suspension, and the direct contact between the red blood cell and the wall as shown in Fig.2. As the fluid is high concentrated suspended flow (the Hematocrit number 40%) and interactions among the red blood cells are large, and it is too complicated and not easy to construct the model for this suspension model. And it is also difficult to get proper model coefficient from the experiments. As for anisotropicity of turbulence, the turbulent model itself should be studied and discussed. Therefore, in this study, we regard that the fluid is low concentration of particles and isotropic turbulent flow. It is necessary to make modeling for these conditions with the wall-contact and particle inertia to predict the hemolysis.

For the first step, to investigate the effects of the previous factors, we use the pipe orifice flow that we had already examined as the model for the flow near the impeller in the rotary blood pump. It is expected to get the fundamental understandings about the effects of the shear stress and the effects of the contact with the wall including inertia of particles for the hemolysis.

EXPERIMENTS FOR HEMOLYSIS

Figure 3 shows the hemolysis circuits that consists of blood pump (Bio-pump, made by Bio-Medico Co. Ltd.), reservoir bag for the blood and the orifice pipe. To decrease the effects of the differences for the blood in the each circuit, the two Bio-pumps should be used in the hemolysis circuit to fit the pressure loss.

In this study, three kinds of configurations (A, B and C) for the orifice are used and there are two directions (F: Forward and B: Backward), configurations AB, BB, CB, CF (Fig.4). These configurations can be used for the experiments to explain the effects of round for edge on the wall or the front and back of the orifice on the hemolysis. The flow rate for the pump is 5l/min according to the working conditions for the rotary blood pump, this means that Re is 3000 used by the viscosity of the blood. In addition, pressure loss is from 150 to 300 mmHg in every configuration of the orifice, and in order to keep the pressure losses in every hemolysis circuit using the variable resistance whose configuration is small and long round shaped one. In this experiment, the configuration BB is dealt as standard circuit and the pressure loss is 300mmHg in this configuration.

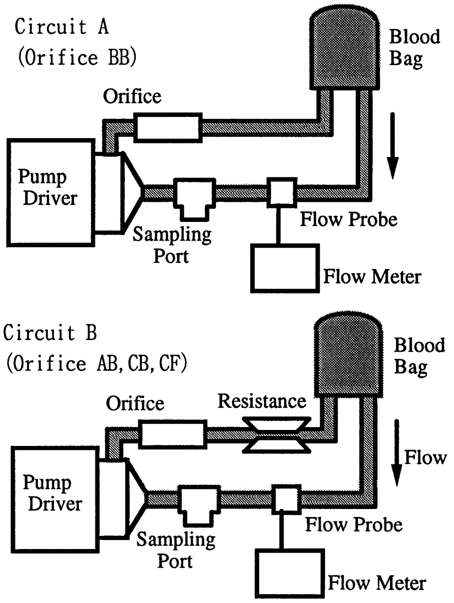


Fig.3 Hemolysis circuits (Standard BB type and other types)

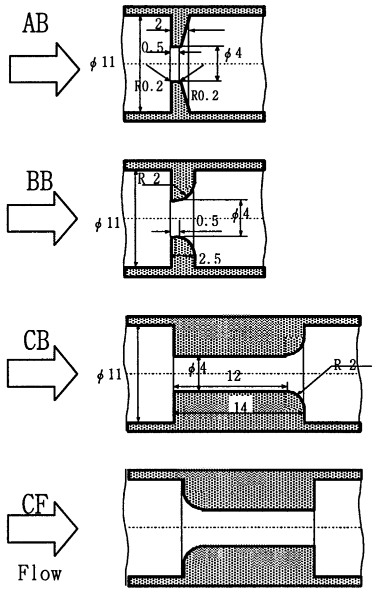


Fig.4 Various configurations for hemolysis test

As for the hemolysis test, the modified Durabkin method was used to examine free hemoglobin quantity in plasma. Although the definition, which is a kind of index for injury of red blood cells, has already been shown in the previous papers, it should be shown again here because of its special definition.

$$I.H. = \frac{(Hb(T_1) - Hb(T_0)) \times (100 - Ht) \times V}{Q \times DT} (mg/dl) \qquad (1)$$

Here I.H. means index of hemolysis, Hb (T) (mg/dl) means free hemoglobin concentration at time T, T_1 (min) means the time for getting the sample blood from the circuit, T_0 (min) means starting time for the hemolysis test, DT=T_1-T_0 (min), V (l) means the blood volume to fill the circuit, and Q (l/min) is flow rate. In this paper, relative index of hemolysis(R. I. H.) using standard circuit (Configuration BB) is defined as follows. The reason why this definition should be used is that if we use this definition the effects of the factor without physical factors are large in this test.

$$R.I.H.=\frac{I.H._{test}}{I.H._{BB}} \tag{2}$$

Figure 5 shows the relative indexes of hemolysis at each configuration (AB, BB, CB, and CF) under the condition that flow rate is 5l/min. From these results, it is found that the amount of hemolysis for the configuration CB is larger than that for the configuration BB, and the amount of AB is also a little bit large compared with that for BB. In the contrary, it is found that the hemolysis of CB is much less than that for CF.

COMPUTATIONAL METHOD FOR HEMOLYSIS PREDICTION AND RESULTS

On the other hand, this flow fields are computed by the low Reynolds number k- ε model (Abe-Nagano 1992). In this section, the momentum equations for the particles are linked to this turbulent model. Using these numerical data, the index of hemolysis is predicted. In addition, the effects of the particle's contact with the wall and inertia of particle are considered to construct the damage model.

The computational conditions are that flow rate Q=5l/min, inlet flow velocity Uin=0.877 m/s and diameter D (=11mm) is present scale. Coordinate system is cylindrical one, and x-direction is parallel to the flow direction and r-direction is radial component of the pipe. The diameter of contracted region is 4mm, and Reynolds number is 3000.

The conditions for this analytical model are supposed as follows;

(i) The number of the red blood cells is small, and there are no aggregations by mutual interactions among particles

(ii) Red blood cell is solid and spherical particle. They are moved by Stokes drag's force.

(iii) The movement of the particles is parallel motion without rotation.

(iv) Considering the particle's contact with the wall, two methods are considered as follows:

(iv-i) Reflected condition (contact condition): The particles are reflected at the wall using constant rebound coefficient.

$$e=\left|\frac{V'}{V}\right| \tag{3}$$

In this paper, these rebound coefficients are 1.0 or 0.01 in the calculation.

(iv-ii) Slip condition: Particles are moved along the wall. This definition is called "Slip".

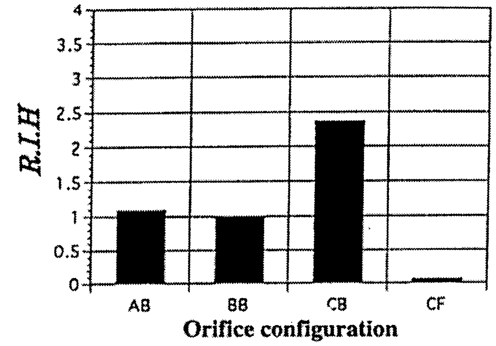


Fig. 5 Results of Hemolysis tests

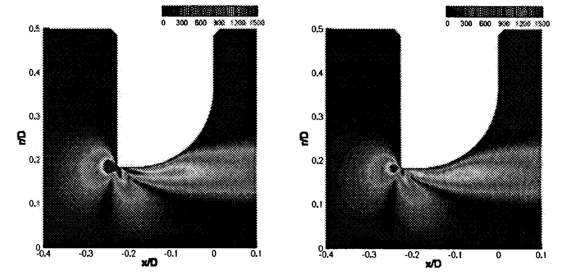


Fig.6 Turbulent shear stress ditribution without particle (left) and with particle(right)

The governing equations are continuum equation. momentum, transport equations of k, ε with low-Reynolds number k- ε model in cylindrical coordinate system and momentum equation for particles as follows:

$$\frac{\partial u}{\partial t}+u\frac{\partial u}{\partial x}+v\frac{\partial u}{\partial r}=X(x,r)-\frac{\partial p}{\partial x}+(\frac{1}{\mathrm{Re}}+v_t)\nabla^2 u +2\frac{\partial v_t}{\partial x}\frac{\partial u}{\partial x}+\frac{\partial v_t}{\partial r}(\frac{\partial u}{\partial r}+\frac{\partial v}{\partial x}) \tag{4}$$

$$\frac{\partial v}{\partial t}+u\frac{\partial v}{\partial x}+v\frac{\partial v}{\partial r}=Y(x,r)-\frac{\partial p}{\partial r}+(\frac{1}{\mathrm{Re}}+v_t)(\nabla^2 v-\frac{v}{r^2}) +2\frac{\partial v_t}{\partial r}\frac{\partial v}{\partial r}+\frac{\partial v_t}{\partial x}(\frac{\partial u}{\partial r}+\frac{\partial v}{\partial x}) \tag{5}$$

$$\begin{pmatrix} X(x,r) \\ Y(x,r) \end{pmatrix}=-3\pi\mu d_p\begin{pmatrix} u_f-u_p \\ v_f-v_p \end{pmatrix} \tag{6}$$

$$\frac{\partial k}{\partial t}+u\frac{\partial k}{\partial x}+v\frac{\partial k}{\partial r}=\frac{1}{\mathrm{Re}}\nabla^2 k+\frac{1}{\sigma_k}(\frac{\partial v_t}{\partial x}\frac{\partial k}{\partial x}+\frac{\partial v_t}{\partial r}\frac{\partial k}{\partial r}) +G-\varepsilon \tag{7}$$

$$\frac{\partial \varepsilon}{\partial t}+u\frac{\partial \varepsilon}{\partial x}+v\frac{\partial \varepsilon}{\partial r}=\frac{1}{\mathrm{Re}}\nabla^2 \varepsilon+\frac{1}{\sigma_\varepsilon}(\frac{\partial v_t}{\partial x}\frac{\partial \varepsilon}{\partial x}+\frac{\partial v_t}{\partial r}\frac{\partial \varepsilon}{\partial r}) +C_{\varepsilon 1}\frac{\varepsilon}{k}G-C_{\varepsilon 2}f_\varepsilon\frac{\varepsilon^2}{k} \tag{8}$$

$$G=v_t\left[2\left\{\left(\frac{\partial u}{\partial x}\right)^2+\left(\frac{\partial v}{\partial r}\right)^2+\left(\frac{v}{r}\right)^2\right\}+\left(\frac{\partial u}{\partial r}+\frac{\partial v}{\partial x}\right)^2\right] \tag{9}$$

$$v_t=C_\mu f_\mu\frac{k^2}{\varepsilon} \tag{10}$$

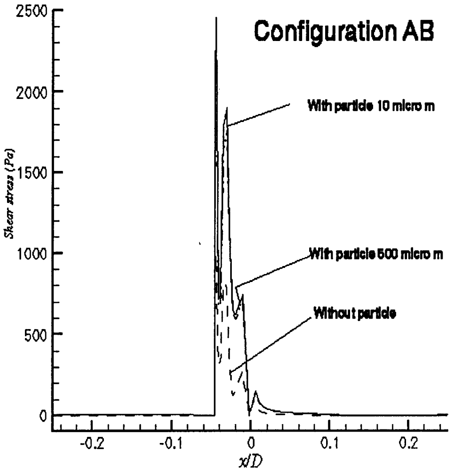


Fig.7(a) Turbulent shear stress profile along the x-axis (AB)

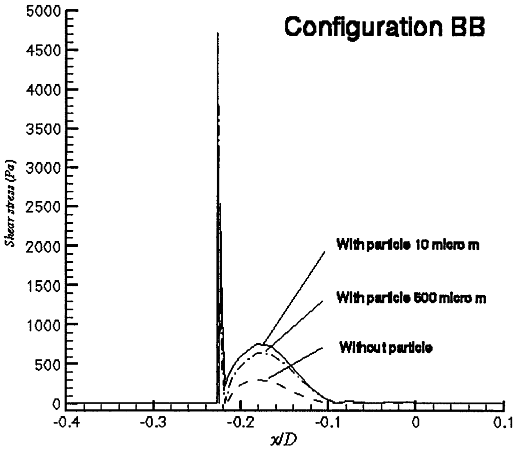


Fig.7(b) Turbulent shear stress profile along the x-axis (BB)

$$\frac{\pi}{6}d^3\rho_p\frac{dv_{p,i}}{dt}=3\pi\mu d_p(v_{f,i}-v_{p,i})-\frac{1}{2}\frac{\pi}{6}d_p{}^3\rho_f\frac{dv_{p,i}}{dt} \qquad (11)$$

where X , Y means the external force driven by particle motion.

In these equations, considering the Stokes drag force as a local term, the equations for flow fields are linked and solved at the same time. In this case, the effects of virtual mass is expressed using changing volume with constant density as the particle are dealt as point mass. Computational region is defined that 12D for the front of the orifice, 80D for the back of the orifice using 200 x 50 generalized coordinate system.

Generally diameter of the red blood cells is several micro m, but considering the inertia in the flow fields, diameter d is used to be 10,50,100,150,500 μ m. Twenty particles are located at the inlet laterally, and moved by mean flows.

Fig6 shows the turbulent shear stress distribution in case of configuration BB and figure 7(a)(b) shows the turbulent shear stress profile in case of configuration AB and BB, without particles and with particles (10,500 μ m). It is found that the larger the particle becomes the smaller the peak of the shear stress profile in spite of the differences of the configurations.

PREDICTION METHODS

In this section, the predictions for hemolysis are done using numerical data obtained from the computational fluid dynamics. The prediction method that has been developed as follows (Method 1) is used, and the other new four methods are proposed to investigate.

Method1 using Euler type

In this case, we have already proposed that the shear stress τ (molecular viscous stress + turbulent shear stress) is integrated with stream line. That is to say,

$$E_\tau = \iint \tau U \Delta S \qquad (12)$$

where U is velocity, ΔS is cross section of pipe. From this definition, it should be noticed that the contact condition is not included because this definition has only flow field information. In this case, we suppose that the red blood cells are broken when the mean component of the vortices and turbulence exceed the threshold level.

Method 2 using Lagragian type

Here we consider 4 types of prediction method when 20 numbers of 100 μ m particle flow into the main flow as if the inertia is large . In the moment, the degree of the excess of inertia is not elucidated in the experiments. Here the degree of inertia is estimated as 1000 times as that of 10 μ m particle.

(A) Prediction method A: the shear stress τ at the contact point on the wall is used for estimation.

$$E_A = \sum_{n=1}^{NP}\left[\sum_{i=1}^{M} 2\pi r_i \tau_i\right]_n \qquad (13)$$

Here M is number of contact with the wall.

(B) Prediction method B: the mean shear stress τ at the contact point on the wall is used for estimation to decrease the variance of the results.

$$E_B = \sum_{n=1}^{NP}\left[\frac{1}{M}\sum_{i=1}^{M} 2\pi r_i \tau_i\right]_n \qquad (14)$$

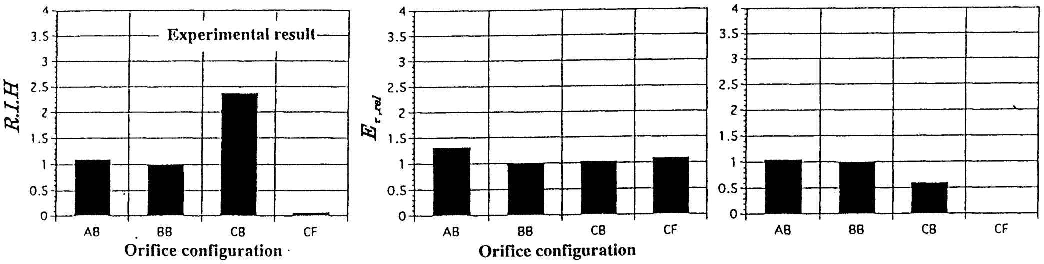
(C) Prediction method C: the products of the shear stress τ and the movement length Δ l at the contact point on the wall is used for estimation.

$$E_C = \sum_{n=1}^{NP}\left[\sum_{i=1}^{M} 2\pi r_i \tau_i \cdot \Delta l_i\right]_n \tag{15}$$

(D) Prediction method D: the mean product of the shear stress τ and the movement length $\Delta\ l$ at the contact point on the wall to decrease the variance of the results.

$$E_D = \sum_{n=1}^{NP}\left[\frac{1}{M}\left(\sum_{i=1}^{M} 2\pi r_i \tau_i \cdot \Delta l_i\right)\right]_n \tag{16}$$

Figure 8 shows the results using method 1 when the threshold is changed, figure 9 shows the results using other methods. In this figure, degree of hemolysis is presented by



(a) τ_{th} (Threshold of τ) =0 (Pa)

(b) τ_{th}=1400 (Pa)

Fig. 8 Prediction results using Method 1

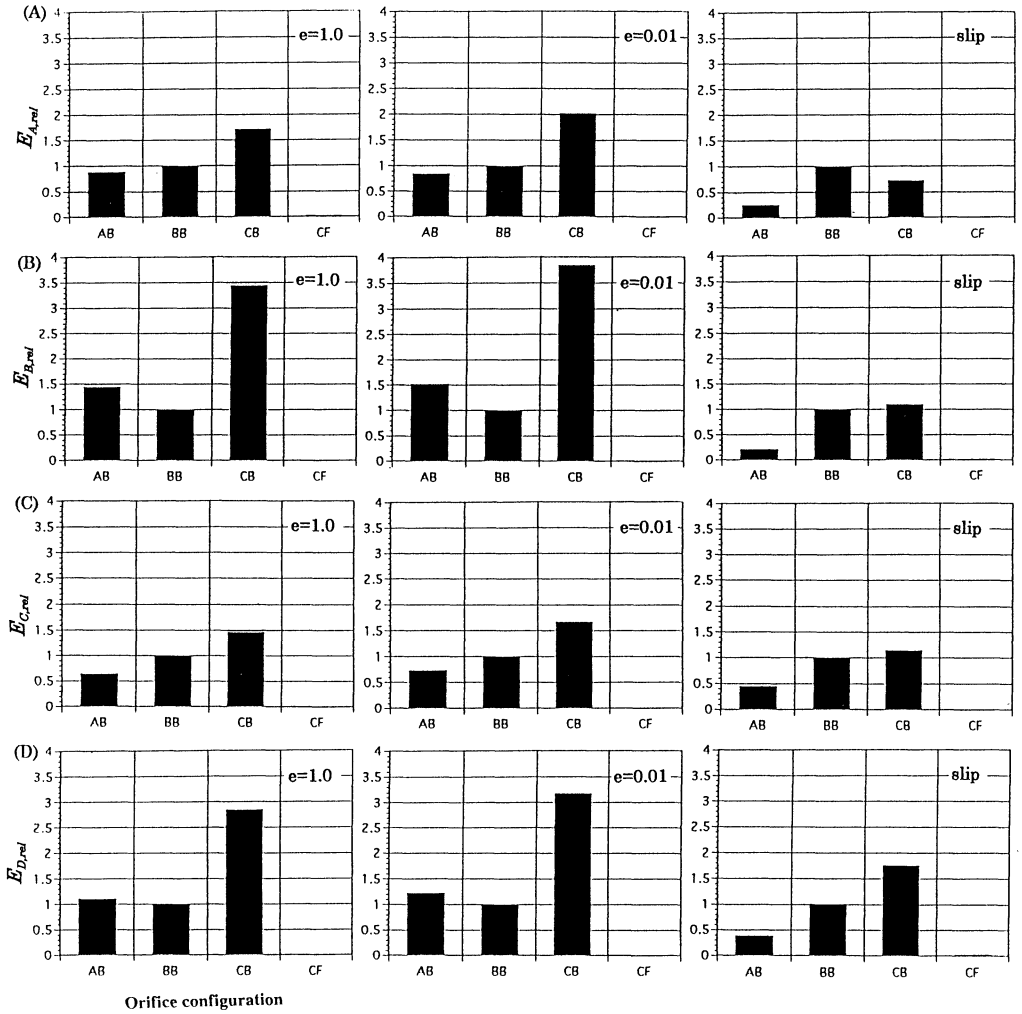


Fig. 9 Prediction results using Method 2

the relative value based on the index of hemolysis in the configuration BB. That is to say,

$$E_{x,rel} = \frac{E_x}{E_{x,BB}} \quad (17)$$

Here x indicates method A, B, C and D. There are three conditions with the rebounded coefficient e=1.0,0.01 and slip condition in the results.

From Fig.8 (method 1), the prediction doesn't agree with the experimental results even if the optimized threshold τ is used as 1400 Pa. In Fig. 9, when the results including the effects of the wall contact are considered are compared each other with the same rebound coefficient (e=1.0), the results for AB in (B) (D) agree with the experiment more than that in (A)(C). Comparing (B) with (D), the result in (B) is almost larger than that in (D). That is to say, the average of the shear stress is larger than that the degree of index of the shear stress and the contact length. Concerning about the rebound coefficient and slip in the case of e=1.0 and 0.01 in (D), when the rebound coefficient is 0.01 the relative index of hemolysis for AB and CB is estimated excessively because the particles cannot separate from the wall and remain to be near the wall. In case of considering the effect of the slip, the worse the result becomes comparing with the results considering the effects of the rebound. The reason why this difference is occurred is that this model cannot predict the actual phenomena, in which the particles separate from the edge of the orifice near the wall.

From these results, it is found that when we predict the index of hemolysis considering the effects of contact with the wall, the prediction results agree well with the experimental results because the effects of the wall shear stress and the contact length are large.

As for the ratio of estimated quantity for the effects of stress and that for the effects of contact with the wall has not been undetermined by only the experimental results yet.

ACKNOWLEDGMENTS

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CONCLUSIONS

We predict the index of hemolysis in the orifice considering the effects of the shear stress, the inertia of the particle and the contact with the wall, the followings are concluded.

(1) In the computations, the prediction only using the factor of turbulent shear stress does not agree with the experimental results.

(2) Using the method to consider averaged product of the contact with the wall and the length, the prediction agrees with the experimental results better than that with only effect of shear stress. This result means that the dominant factor for hemolysis is wall shear stress on the wall, not the shear stress itself in the flow. To predict the wall shear stress on the wall, it is necessary to use the precise turbulent model for the separated flow like pipe orifice flow.

In future, we will apply this method to the computation in the configuration of the actual rotary blood pumps, and then we will compare these results with the actual hemolysis test in developing the artificial organs in the next step.

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