THE EFFECT OF SHEAR RATES ON BLOOD MATERIAL INTERACTION IN TOTAL ARTIFICIAL HEART

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INTRODUCTION

Implantable total artificial hearts(TAH) and assist devices are being developed for long-term clinical use. One of the major factors which determine their long-term implantation is thromboembolic complication. It has been generally accepted that plasma protein adsorption which is the first event at the blood-material interaction influences subsequent plate adhesion of thrombus formation. These thromboembolic events are strongly influenced by surface characteristics of materials and fluid dynamics inside of blood pump. Boretos et al. [1] and Matsuda et al. [2] worked on protein adsorption on artificial ventricular surface of the implanted devices. However, fluid dynamic effect on these phenomena has not been well-defined. From these points of view, we study the effect of shear rates on blood-material interaction, especially protein adsorption and their relationship with platelet adhesion on the blood contacted surface of the implanted TAH.

MATERIALS AND METHODS

The moving actuator type TAH[3,4] was implanted into a female calf of 95 kg weight for 7 hours. We pre-treated the surface of right ventricle (RV) by PEO-SO_3 and the surface of left ventricle (LV) by albumin immobilization. In order to find fluid dynamic condition inside of blood pump, we performed flow visualization experiment with a transparent artificial ventricle. The shear rate distribution inside of ventricle was determined by considering the directions of the major opening of the four heart valves in the implanted TAH as well as the flow pattern visualized. We sectionalized both of the blood-contacted ventricles according to the level of the shear rate after animal death. Because analysis of adsorbed protein might be influenced by the size of the ventricle segment, the number of segments was limited to 12 for each ventricle as shown in figure 1.

Platelet adhesion and its morphology were observed by SEM. For the visualization of adsorbed plasma proteins (albumin, IgG, and fibrinogen) on each segment, immunogold double antibody technique is used with SEM[5]. Adsorbed protein layer thickness and distribution are measured by immunogold method[6] under TEM. The specimens are incubated in rabbit primary antisera against each plasma protein followed by incubating in gold conjugated second antibody. Adsorbed plasma proteins of each segment are quantified by ELISA method. The specimens are soaked in 2%(w/v) SDS/PBS for two days. Released protein concentration is assessed.

We propose a model to explain the experimental data. Since the blood-contacting time of the surface is short (<7 hours), we can assume monolayer protein adsorption and no conformational change of the adsorbed protein [2]. Monolayer protein adsorption kinetics are often analyzed by the Langmuir approximation in which the adsorption rate is proportional to the fraction of uncovered surface:

$$\frac{d\Gamma}{dt} = k\left(1 - \frac{\Gamma}{\Gamma_{max}}\right) \quad \text{---------- (1)}$$

,where Γ is the surface concentration of adsorbed protein, k is the rate constant for adsorption, and Γ_{max} is a surface coverage limit. Eq. (1) can be modified to allow for desorption with rate constant k' [7]:

$$\frac{d\Gamma}{dt} = k\left(1 - \frac{\Gamma}{\Gamma_{max}}\right) - k'\Gamma \quad \text{----- (2)}$$

,where k' is the rate constant for desorption.

The average normal stress on a protrusion by fluid forces is proportional to shear rate under linear approximation of the tubular flow [8]. Therefore, we assumed the protein desorption rate is proportional to wall shear rate. The kinetic equation of the reversible protein adsorption can be modified as like eq. (3) & (4) under flow conditions.

$$\frac{d\Gamma}{dt} = k\left(1 - \frac{\Gamma}{\Gamma_{max}}\right) - k'(\gamma)\,\Gamma \quad \text{------- (3)}$$

$$k' = c\,\gamma \quad \text{------------ (4)}$$

,where c is a proportional constant between the desorption rate and the shear rate (γ).

The concentration of the plasma protein in bovine blood is high enough to neglect the effect of shear rate on the adsorption rate.

RESULTS AND DISCUSSION

Figure 2 depicts the reversible adsorption kinetics predicted by the model with an initial concentration of 0.005 mg/ml and a relatively fast surface binding rate, k, of 0.1 cm/sec. Γ_{max} was chosen to be large enough (1.0 ug/cm2) that did not limit the rate of adsorption for three different desorption rates, k'. The exact relationship between desorption rates and shear rates will be analyzed further.

Two large vortex and several separation zones are occurred in the artificial ventricle of the moving actuator type TAH at the diastolic phase. The major opening areas of the heart valves give higher shear rate than the minor ones. We categorized the

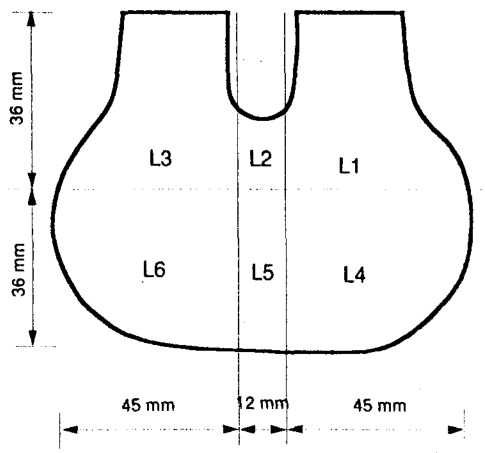

Figure 1 Left ventricle Sections, hosusing side

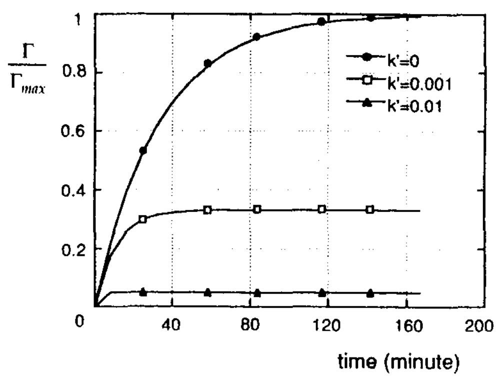

Figure 2. Comparision of Adsorbed Proteins for Different Desorption Rates (Simulation Result)

specimens of the LV into 6 groups according to the level of the shear rates. Those of the RV were also categorized into 6 groups.

For the case of PU-Alb surface of RV, we could see different degrees of platelet adhesion on segments from different groups through SEM observation. Meanwhile there was little difference for the case of PU-PEO1000-SO_3 surface of LV. To examine the distribution of adsorbed plasma proteins and their concentrations, IgG fraction of rabbit antisera against bovine fibrinogen was successfully obtained from an immunized rabbit and further analyses are presently in progress.

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