Fundamental \textit{In-vitro} Hemodynamic/Hemorheologic Study for the Pathogenetic Investigation on Cardiovascular Disorder

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Abstract: - To investigate detailed hemodynamic information through a stentic lesion can provide us the fundamental pathogenetic information related to thrombosis formation which plays major role to cardiovascular disorders. Generally hemodynamic and hemorheologic features near vessel wall is well known as most important key factors for thrombosis generation. Especially, hemodynamic behavior on the stenotic lesion growth may be affected by the recirculation region of blood flow downstream through the stenosis of blood vessel and the geometrical characteristics on the blood vessel alignment. From this sense, in-vitro experiments were carried out using blood vessel models with different alignment angle made of PDMS micro-channel based on patient’s angiogram with stenotic lesion in right coronary artery. The hemodynamic feature was investigated using high resolution micro PIV technique. The red blood cells were used as tracer particles for instantaneous velocity profile measurement based on cross correlation method.

Key-Words: - Hemodynamic, Hemorheology, Cardiovascular Disorder, Stenosis

1 Introduction

Cardiovascular diseases the leading mortality factor in the westernized society is closely related with various risk factors. The flow characteristics of human blood through a stenotic throat for Coronary Artery are considered to contain important information used for the early detection of cardiovascular disorders. From this sense, recently the biophysical feature investigation of hemodynamic and hemorheologic behaviour of blood flow have received great attention. The complicated blood flow features play an important role in the development of cardiovascular diseases. Lee et al (2007) would like to provide fundamental hemodynamic features of blood flow in extraembryonic blood vessel of chicken blood using micro-PIV technique based on high speed flow visualization methods. Although extensive hemodynamic and hemorheologic studies have been conducted, there are still strong needs to reveal the relationship between fluid dynamics of blood flow and development of cardiovascular diseases. Moreover hemorheological parameters such as viscosity, hematocrit of blood, and deformation and aggregation of red blood cells (RBC) influence the blood flow in vascular networks.

Modern interdisciplinary researches have suggested that the hemodynamic and hemorheologic investigation based on fluid mechanics of blood flow play an important role in the pathogenesis and pathophysiology of vascular circulatory diseases. In general, the stenosis has been known to be generated at the arteries by LDL migration and foam cells generation. Initial stenosis generated and observed in Coronary Artery can provide very important clinical information for development of cardiovascular diseases. LDL migration generate initially, it appears in the form of foam cell formed in the coronary and carotid arteries. After removing the stenosis through a medical procedure, re-stenosis occasionally forms near the same region. Specifically, the stenosis in retina arterioles caused by diabetic symptoms on blood vessels can induce loss of eyesight and increase of blood pressure. To detect these circulatory diseases as early as possible, it is important to identify the fluid mechanical
pathogenesis of the vascular stenosis by understanding the flow characteristics of blood in the stenotic blood vessel. (Huo et al., 2006, Taylor et al., 2004, Bruce et al., 2008)

Despite the clinical importance of cardiovascular diseases, it is not easy to experimentally provide the pathogenetic information related with cardiovascular diseases based on blood flow. These in-vitro experimental results from the blood flow information at RCA (right coronary artery) with stenotic throat can provide the fundamental pathogenetic information for cardiovascular disorder. Recent studies on bio-fluidic fluid flows have employed a high resolution high speed blood flow visualization and micro-PIV (particle image velocimetry) technique as a reliable tool of velocity field measurement. (Stroud et al., 2000, Ji et al., 2007, Kiousis et al., 2007, Matsumoto et al., 2005)

In this study, we tried to get the hemodynamic and hemorheologic information of blood flow through straight micro tube to blood vessel model with stenotic throat based on real angiogram, before moving toward the practical clinical applications. The velocity fields of the blood flow through the experimental model were measured using a high-resolution micro-PIV technique. To provide more detailed hemodynamic and hemorheologic information through vessel model was also carried out. Therefore, the flow characteristics of blood flow and the transport of RBCs in the stenosis were experimentally investigated in this study.

2 Experimental Setup and Methods

Fig.1 shows the schematic diagrams of Micro-PIV system for the measurement of 2D velocity field. The various experimental models for blood flow measurement were employed in this study. To trace the particles in working fluid, the PMMA Rhodamine B particles of ranging from 1-8um in diameter were diluted in de-ionized water, low haematocrit blood flow and it is introduced into the tube and channel by syringe pump (KDS scientific) with various flow rates. The flow field was illuminated by halogen lamp (U-LH100-3) attached to the microscope (BX51) with 4X objective(UPLFL) and particle images were acquired through a high-speed camera (PCO1200hs) consecutively with speed of 1000 to 2000 fps by the condition of flow rate. The whole channel view was divided to six sections due to the limitation of view size of 7 x 5.6mm and each flow field was calculated from individual section by post-processing. Whole flow field was finally reconstructed by uniting every flow field with linear interpolation.

The high-speed CMOS camera employed to acquire temporally resolved blood flow information can capture flow images at up to 636 fps (frame per second) at a full resolution of 1,280 × 1,024 pixels. Since a continuous halogen lamp was used as the light source, the time interval (Δt) between two consecutive images was adjusted by varying the frame rate. Under these experimental conditions, the scattering of incident light was negligible, enabling the detailed evaluation of flow information in the region near the walls.

To calculate instantaneous velocity vectors from two consecutive flow images, the FFT based cross-correlation algorithm was applied. The size of the interrogation window was 16 × 16 pixels, with 50% overlap. A total of 1,000 flow images were captured for each experiment. The instantaneous velocity fields were ensemble-averaged to obtain the spatial distributions of mean velocity. The frequency characteristics of the arterial blood flow and the variation of velocity waveform were assessed by FFT analysis of the temporally resolved instantaneous velocity field data (Figs. 2).
To simulate a blood vessel model with stenotic lesion on RCA, in-vitro experimental model was made of PDMS through a micro-fabricate technique. The geometric information for blood vessel model was based on angiogram for patient with coronary artery stenotic lesion. A PDMS microchannel was used as the experimental model for the stenotic blood vessel.

3 Results and Discussions

Fig. 4 shows the DI water flow and blood flow with fluorescent particle through micro-tube with 100 μm as a diameter. In the case of DI water flow, fluorescent particles have random distribution. And in the case of blood flow, the haematocrit was controlled carefully pre-treatment. And the haematocrit was adjusted with respect to the experimental condition and the anti-aggregated fluorescent particles were put into the blood. From this experiment, averaged velocities were calculated using statistical process, and the viscosity was measured from velocity fields.

Fig. 5 shows the typical image of the RBCs of diluted blood from 5% hematocrit, which pass through a micro-stenosis. Even though some RBCs were aggregated, the biconcave shape of RBCs can be clearly observed. The size of RBCs is slightly smaller than half of the stenotic throat, so the image contains only tens of RBCs. The images of RBCs in motion through the micro-stenosis were captured with a high-speed CCD camera at a frame rate of 8000fps and with a spatial resolution of 512 X 256 pixels. In the contraction of the micro-stenosis, the moving speed of RBCs was accelerated. In Fig. 5, RBC 1 shows a counterclockwise motion while rolling along the stenotic wall. In addition to the accelerated velocity in the converging stenotic channel, the wall normal velocity component in the center region is caused by the abrupt contraction which seems to cause the rolling motion. From this, we can conjecture that the life span of RBC 1 seems to be long, and it may have been lengthened during the pre-treatment of
RBCs using the PBS solution. In general, when the life span of RBCs is longer, they tend to show rolling motion instead of tank-trading motion.

Fig. 5 shows trajectories of several RBCs throughout the micro-stenosis. The trajectories of RBCs of a sample hemodiluted as 5% hematocrit were traced using an optical flow method (Horn and Schunck, 1981). The optical flow method defined as the following equation (1) is a kind of image processing tool used for depicting motion of objects within a visual representation.

\[
\frac{dI}{dt} = \frac{\partial I}{\partial x} \frac{dx}{dt} + \frac{\partial I}{\partial y} \frac{dy}{dt} + \frac{\partial I}{\partial t}
\]

where, \(I(x,y,t)\) denotes the brightness of RBCs in two-dimensional coordinate of streamwise \(x\) direction and spanwise \(y\) direction.

To calculate the trajectories, five consecutive images were selected as a group. The outer wall of individual RBCs was edge detected by using the brightness level of RBCs. Each cell detected was identified as a tracing particle. The position and width of the traced RBCs change continuously in the microchannel as shown Fig. 5.

Blood flow in blood vessel model with a varying alignment angle simulated in RCA was optically visualized using a high resolution blood flow visualization technique. Blood flow was measured in each measurement sections and each measurement sections have overlap as shown Fig. 6. Because the RBCs’ flow has so rapid velocity passing through a stenotic throat, the observing resolution must be controlled adequately.

Fig. 6 (a) shows the averaged velocity field from experimental study with varying the vessel model alignment angle from 0° to 20° with 10° increasingly.

The steady flow rate employed in this experimental study was controlled as 5 ml/min. This velocity data was used to determine the mean velocity field of blood flow in the blood vessel model, as well as the successive instantaneous velocity fields. A total of 1,000 flow images were captured for each experiment. The instantaneous velocity fields were ensemble-averaged to obtain the spatial distributions of mean velocity.

To compare the velocity fields, numerical study was also carried out same as experimental condition for vessel alignment angle change. Fig. 6 (b) shows the averaged velocity field from numerical study with varying the vessel model alignment angle from 0 degree to 20 degree with 10 degree increasingly same as experimental condition.

As increasing the alignment angle from 0 degree to 20 degree and as going to downstream, the separation region closely related with stenotic throat development increase obviously.

The maximum velocities in each case were observed in the center region of stenotic throat. The flow rate with 5 \(\mu\)l/min in this study was controlled by using a syringe pump. As flow goes downstream, the velocity decreases rapidly. From this phenomenon, the appropriate image resolution was controlled as 6000 fps.

4 Conclusion

Flow characteristics through micro tube, sinusoidal micro-stenotic channel and a coronary artery with stenotic lesion were measured in-vitro high resolution flow visualization technique
with a high speed CMOS camera. The results were summarised as follows

(1) Measurement technique employed in this study was useful for measuring blood flow in various experimental studies. Temporally resolved velocity fields information would be useful for understanding the hemodynamics and hemorheologic feature related with pathogenetic information and the stenosis growth related with cardiovascular diseases.

(2) The separation and stagnation area of the flow in downstream grows with the increase of alignment angle and it can be expected that the separation and stagnation area would be changed to recirculation area in high flow rate and vessel various geometric case. The trajectory of peaks in velocity profiles in orthogonal section against alignment axis shows the inclined elliptical trace and its characteristic motion can be

\[ \theta = 0^\circ \]

\[ \theta = 10^\circ \]

\[ \theta = 20^\circ \]

(a) Averaged velocity fields (experimental study)  
(b) Averaged velocity fields (numerical study) 

Fig. 6 Averaged velocity vector fields according to the vessel alignment angle change 
(Comparison with experimental study and numerical study)

(3) Through anti-aggregation procedure on fluorescent particles, basic technique and concept for drug delivery may be constructed.

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