Analysis of Drug Behavior in Abdominal Aortic Aneurysm by Considering Random Force and Pulsation

Takuya Tajima, Marie Oshima, Katsuyuki Hoshina, Yutaka Miura, and Nobuhiko Mukai

***Abstract*—In this study, a physical simulation using the MPS (Moving Particle Semi-implicit) method is applied to the analysis of the drug behavior. The conventional MPS method, however, cannot be applied to mesoscopic scale simulations, where the random force causing the Brownian motion and pulsation are dominant. Therefore, we propose a method that introduces the random force into the MPS method and the model considering pulsation.**

I. Introduction

The mortality rate caused by the Rupture of an abdominal aortic aneurysm (AAA) is more than 90% [1]. The risk of the AAA rupture increases along the size of the aneurysm, and the aneurysm which size is larger than 55 [mm] in diameter needs surgical treatments. However, since 90% of the diagnosed AAA is less than 55 [mm] in diameter [2], medical therapies using drug delivery system (DDS) can reduce the mortality rate by suppressing the enlargement of the mass and can decrease the risk of the potential rupture.

DDS needs the development of the micelle that encapsulates hydrophobic drugs in a hydrophilic outer shell, and the retention of the micelles in the aneurysm can inhibit AAA expansion in diameter. However, the mechanism by which the micelles are retained on the vessel wall is unknown and needs to be analyzed by simulations. In this paper, we report the micelle behavior in the AAA and the influence of pulsation by the simulation using our proposed method.

II. Methods

F The Newtonian's equation of motion is described as follows.

$$\nabla \cdot \boldsymbol{u} = 0, \tag{1}$$

$$\frac{d\boldsymbol{u}}{dt} = -\frac{1}{\rho}\nabla p + \nu\nabla^2\boldsymbol{u} + \frac{1}{\rho dV}\sqrt{2\gamma k_B T}R(t), \tag{2}$$

$$\langle R(t)\rangle = 0, \ \ \langle R(t)R(t')\rangle = \delta(t-t') \tag{3}$$

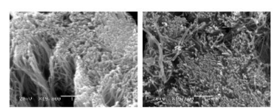
where, $\boldsymbol{u}$ is velocity, t is time, ρ is density, p is pressure, ν is kinematic viscosity, dV is unit volume, $\sqrt{2\gamma k_B T}R(t)$ is random force causing the Brownian motion, γ is coefficient of friction, k_B is the Boltzmann constant, T is absolute temperature, $R(t)$ is random variable which follows a normal distribution, $\langle R(t)\rangle$ is average of $R(t)$, $\langle R(t)R(t')\rangle$ is dispersion of $R(t)$, and $\delta(\,)$ is the delta function.

The variables are too small in the mesoscopic scale, and the range of the distance is 1.0×10^{-8}~1.0×10^{-6} [m]. Then, the dimensionless is needed to the variables in Eqs. (1), (2), and (3). The dimensionless equations can be described in the following.

$$\frac{d\hat{\boldsymbol{u}}}{dt} = -\nabla\hat{p} + \frac{\nu T}{L^2}\nabla^2\hat{\boldsymbol{u}} + \hat{\boldsymbol{f}}, \tag{4}$$

$$\hat{\boldsymbol{x}} = \frac{\boldsymbol{x}}{L},\ \hat{t} = \frac{t}{T}, \hat{\boldsymbol{u}} = \frac{\boldsymbol{u}}{U}, \hat{p} = \frac{p}{P}, \hat{\boldsymbol{f}} = \frac{\boldsymbol{f}}{F}, P = \frac{\rho UL}{T},\ \mathrm{F} = \frac{\rho UL^3}{T} \tag{5}$$

where, $\boldsymbol{f}$ is $\sqrt{2\gamma k_B T}R(t)$ in Eq. (2), L, T, U, P, and F are representative scale. These equations are introduced into the MPS method for the simulation.



(a) Control (b) AAA

Fig.1 Images of abdomen

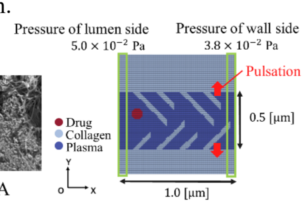


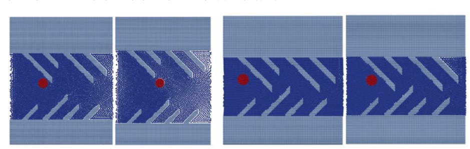
Fig.2 Simulation model

III. Model

Fig.1 shows the images of abdomen. AAA has bigger holes and more complex structure than control. These are many collagens to prevent the progress of micelles and the pulsation makes the hole bigger. Thus we use the simulation model shown in Fig.2.

IV. Simulation Results

ig.3 shows two simulation results with and without the pulsation. The micelle flew out with the pulsation, while it did not without it. Then, it has found that the pulsation has the influence for micelles to flow out.



(a) With pulsation (b) Without pulsation

Fig.3 Simulation results

Takuya Tajima is with Graduate School of Integrative Science and Engineering, Tokyo City University, 1-28-1, Tamazutsumi, Setagaya, Tokyo 158-8557 Japan (e-mail: tajima@vgl.cs.tcu.ac.jp).

Marie Oshima is with Institute of Industrial Science, The University of Tokyo, 4-6-1, Komaba, Meguro-ku, Tokyo, 153-8505 Japan (email: marie@iis.u-tokyo.ac.jp)

Katsuyuki Hoshina is with Vascular Surgery, The University of Tokyo, 7-3-1, Hongo, Bunkyo, Tokyo, 113-8655 Japan (email: traruba@gmail.com)

Yutaka Miura is with Institute of Innovative Research, Tokyo Institute of Technology, 4259, Nagatsuta-cho, Midori-ku, Yokohama, Kanagawa, 226-8503 Japan (e-mail: miura.y.ai@m.titech.ac.jp)

Nobuhiko Mukai is with Graduate School of Integrative Science and Engineering, Tokyo City University, 1-28-1, Tamazutsumi, Setagaya, Tokyo 158-8557 Japan (e-mail: nmukai@tcu.ac.jp)

References

[1] K. Salata et al., "Statins reduce abdominal aortic aneurysm growth, rupture, and perioperative mortality: a systematic review and meta-analysis", *Journal of the American Heart Association*, Vol. 7, No. 19, p. e008657, 2018.

[2] B. T. Baxter et al., "Medical management of small abdominal aortic aneurysms", *Circulation*, Vol. 117, No. 14, pp. 1883–1889, 2008.