Computational Simulations on Drug Particle Transport in a Clotted Channel for Biomedical Applications

Prativendra Singh, Shashi Sharma, Anurag Gaur, Paras Ram

***Abstract*—**The present work reports the computer simulations performed to study the effect of drug particle transport within a fluid on velocity and pressure profile in a clotted channel. The fluid along with drug particles is flowing in a clotted channel, which is considered as a simulated blood vessel. The fluid flow is defined using Navier-Stokes equation and particle motion through Newton's second law equation. The governing nonlinear partial differential equations are solved using COMSOL software based on finite element method. Results illustrate that the velocity and pressure changes significantly when drug particles strike on the clot present in the channel. It is observed that velocity and pressure both decrease as particles move ahead from the clotted region in the channel.

***Keywords*—**Computer simulation, Drug delivery, Particle transport, Velocity and pressure profile.

I. Introduction

One of the main problems of chemotherapy is often not the lack of efficient drugs, but the inability to precisely deliver and concentrate these drugs in affected areas. Cancer is one of the most insidious and potentially fatal diseases in human being. Many evidences indicate that progressive tumor growth is dependent on angiogenesis which is the process in which new blood vessels develop from an existing vasculature through endothelial cell sprouting, proliferation and fusion [1]. New blood vessels provide nutrients to proliferating cancer cells, which is in favour of tumor growth. Tumor cells need an adequate blood supply in order to perform vital cellular functions. The degree of disturbance of blood flow is thus a good predictor of the course of the disease, and hence regional blood flow measure can permit earlier cancer detection. The modern-day approach to cancer treatment is a multidisciplinary one involving varying combination of surgery, radiation therapy, chemotherapy, and targeted therapies. In drug therapies, a medication or drug is controlled to target a specific pathway in the growth and development of a tumor [2]. Understanding the flow of blood and drug in the microchannel is very important for investigating the efficiency of drug treatment as they pass from parent blood vessel to tumor surface via an associated channel [3-4]. In the past years, a number of mathematical models for blood and particle flow in arteries and channel networks have been developed [5-13]. For targeted drug delivery, drug has to be bound with small biocompatible magnetic particles and their transport could be controlled outside the body.

In general, blood is pushed under high pressure and velocity away from the heart, initially along the main artery and the aorta. In the aorta, the blood travels at 30 cm/sec and then blood flows into the arteries and arterioles and ultimately to the capillaries. As it reaches the capillaries, the rate of flow is dramatically (one-thousand times) slower than the rate of flow in the aorta. While the diameter of each individual arteriole and capillary is far narrower than the diameter of the aorta, the rate is actually slower due to the overall diameter of all the combined capillaries being far greater than the diameter of the individual aorta. Moreover, the transport of drugs within blood also significantly affects the flow parameters. Mirza et al. [14] studied the flow of blood with heat transfer in the presence of a stenosis and reported that increase in the height of the constriction, increases the velocity of blood, wall shear stress, pressure and temperature. Gitter et al. [15] studied the experimental investigation on a branched tube model in magnetic drug targeting. Morega et al. [16] studied the flow interaction in drug delivery through an arterial system.

In view of the above, the study of drug particle transport in a channel along with their effect on flow parameters is interesting and important for biomedical applications. Therefore, in the present work, we have studied the effect of drug particle transport within a fluid in a clotted channel by using the below parameters as shown in Table 1. The governing nonlinear Navier-Stokes equations for fluid flow and Newton's second law equation for particles transport are introduced and solved using finite element based COMSOL software. The observed results are analysed to understand the drug particle transport effect on velocity and pressure profile.

II. MODEL PARAMETERS

Table I: Fluid parameters used in the simulation:

Name	Value	Unit
Dynamic viscosity	3e-3	Pa*s

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Name	Value	Unit
Density	1060	kg/m^3
Inlet Velocity	0.004	m/sec
Pressure	13332.23	Pa
Temperature	27	^{0}C

III. BASIC EQUATION USED IN SIMULATION

A. *Equations for Fluid flow*

$$\rho(u.\nabla u) = \nabla.\left[-pI + \mu(\nabla u + (\nabla u)^T) - \frac{2}{3}\mu(\nabla u)I\right] + F \quad \text{..... (1)}$$

$$\nabla(\rho u) = 0 \quad \text{..... (2)}$$

Walls equation

$$u = 0 \ (no\ slip\ condition) \quad \text{..... (3)}$$

Inlet equation:

$$u = -u_0 n \quad \text{..... (4)}$$

Outlet equation:

$$[-pI + \mu(\nabla u + (\nabla u)^T)]n = -\hat{p}_0 n \quad \text{..... (5)}$$

$$\hat{p}_0 \leq p_0 \quad \text{..... (6)}$$

B. *Equation for particle transport*

$$\frac{d(m_p v)}{dt} = F_t \quad \text{..... (7)}$$

Wall equation:

$$v = v_c - 2(n.v_c)n \quad \text{..... (8)}$$

where v_c is the particle velocity when particle strikes at the wall of channel.

The Drag coefficients are defined as:

$$C_D = \frac{2F_D}{\rho U_{mean}^2 L} \quad \text{..... (9)}$$

where F_D is the drag force, ρ is the fluid's density
U_{mean} is the mean velocity and L is the length of channel.

Drag Force Equation

$$F = \frac{1}{\tau_p} m_p (u - v) \quad \text{..... (10)}$$

$$\tau_p = \frac{\rho_p d_p^2}{18\mu} \quad \text{..... (11)}$$

Inlet equation:

$$q = q_0 \, , v = v_0 \quad \text{..... (12)}$$

Outlet Equation:

$$v = v_c \quad \text{..... (13)}$$

where, v_c is the particle velocity when particle strikes at the wall of the channel.

IV. RESULTS AND DISCUSSIONS

The meshing used in the present model for transport of drug particles in a clotted channel is shown in the Fig. 1. The meshing around the geometry was 10 μm to obtain precise velocity and pressure profiles.

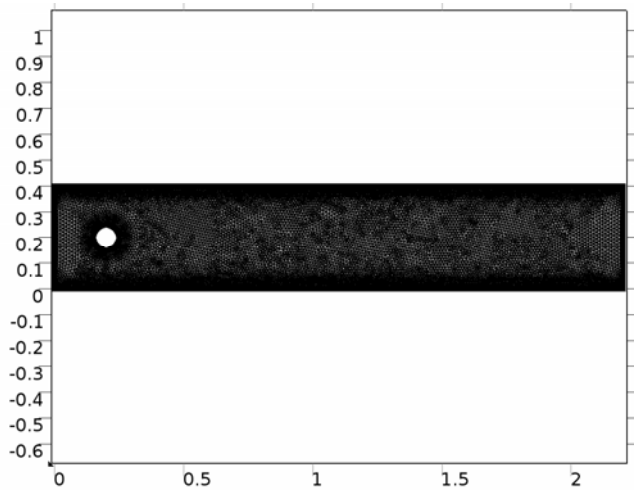

Fig. 1: The meshing used in the present model for transport of drug particles in a clotted channel**.**

Fig. 2 shows the variations in pressure profile during drug particles transport within a fluid in a clotted microchannel at different timings: (a) t=3.7, (b) t=4.1, (c) t=4.5, (d) t=4.9, (e) t=5.7 and (f) t=6.9. The clot has been inserted in the microchannel as a circular ball at a fix position (2 mm from the beginning of the channel) to study the clotting effect in arteries due to cholesterol deposition.

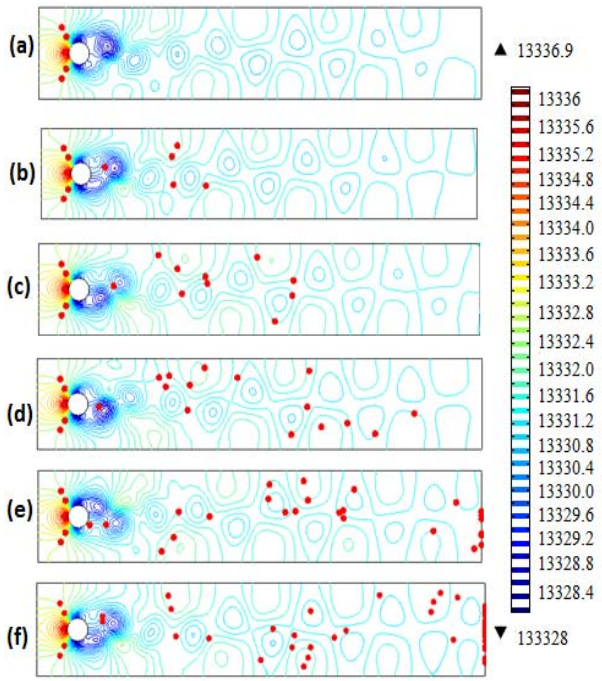

Fig. 2: Pressure profile (Pa) of drug particle transport within a fluid flowing in a clotted microchannel at different timings: (a) t=3.7, (b) t=4.1, (c) t=4.5, (d) t=4.9, (e) t=5.7 and (f) t=6.9.

It is observed through pressure profile that pressure contours become dense as the particle density increases within the fluid, which indicate the enhancement in pressure by increasing the particle concentration. Moreover, it can also be noticed that pressure increases sharply as drug particle strike with obstacle (circular clot in the present case) and then decreases as particle moves ahead in the channel.

The change in pressure profile with arc length (0-1) at different positions of the channel from origin: (a) x = 0.3 (b) x = 0.6 (c) x = 0.9 and (d) x= 1.2 mm is shown in Fig. 3. Arc-length is representing the distance along the diameter of the clotted channel. Fig. 3(a) represents the pressure profile at the 0.3 mm distance from the origin of the channel and clot is situated at 0.2 mm. It is observed by these figures that the pressure is increased at the clotted region and it decreases as the fluid with particle moves away from the clotted area. Further, it re-gains the same pressure as in a uniform channel as particles move away from the clotted region. The maximum pressure inside the clotted blood vessel also depends over the size of the clot.

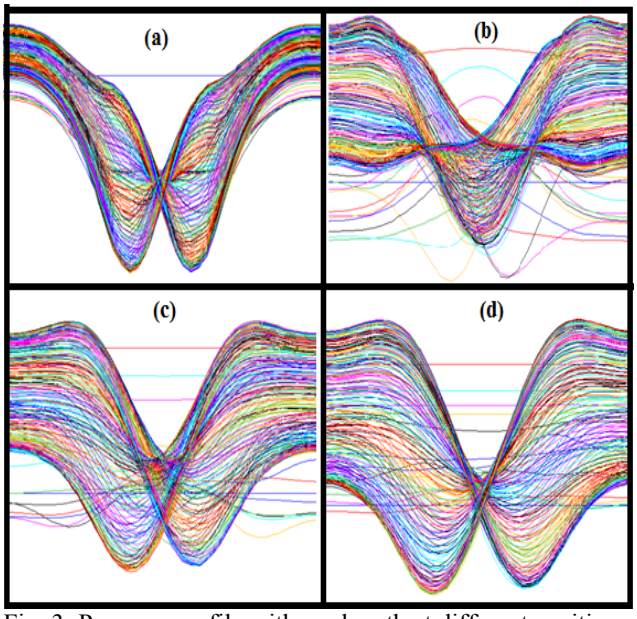

Fig. 3: Pressure profile with arc length at different positions of the channel from origin: (a) x = 0.3 (b) x = 0.6 (c) x = 0.9 (d) x= 1.2 mm.

Fig. 4 represents the variations in velocity profile during drug particle transport within a fluid in a clotted microchannel at different timings: (a) t=3.7, (b) t=4.1, (c) t=4.5, (d) t=4.9, (e) t=5.7 and (f) t=6.9. It can also be observed through images that the velocity increases significantly when particle strike at obstacle (circular clot in the present case). Furthermore, the velocity decreases with distance after striking the obstacle.

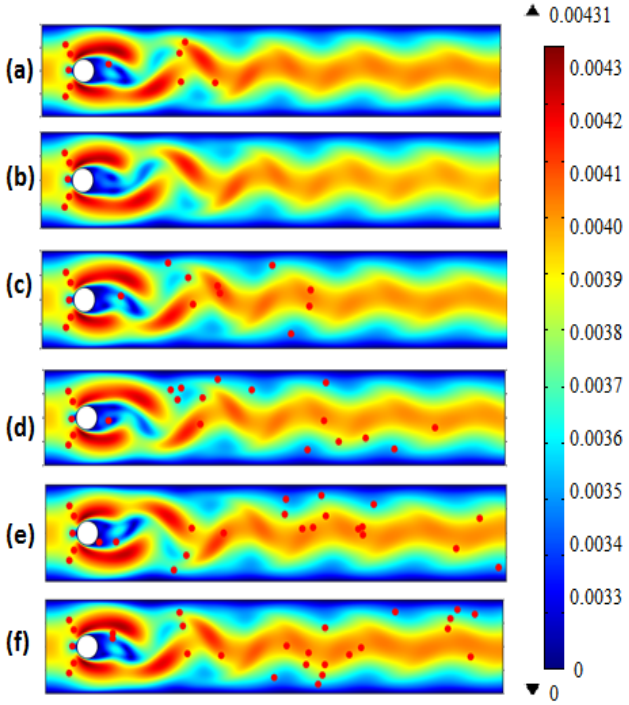

Fig. 4: Velocity profile (m/sec) of drug particles transport within a fluid flowing in a clotted microchannel at different timings: (a) t=3.7, (b) t=4.1, (c) t=4.5, (d) t=4.9, (e) t=5.7 and (f) t=6.9.

Fig. 5 shows the velocity profile with arc length (0-1) at different positions of the channel from origin: (a) x = 0.3 (b) x = 0.6 (c) x = 0.9 and (d) x= 1.2 mm. It is observed that velocity of particles is majorly affected near the clot in the channel (at x=0.3) due to turbulence as the nature of velocity profile is completely deviate from its parabolic nature, which is observed for the laminar flow. Further, as the particles move away to the clot (for x=0.6, 0.9 and 1.2 mm), the parabolic nature of velocity profile regains. This is also supported by the analysis of Fig. 4 that the maximum change in the velocity is observed near the clot present in the channel.

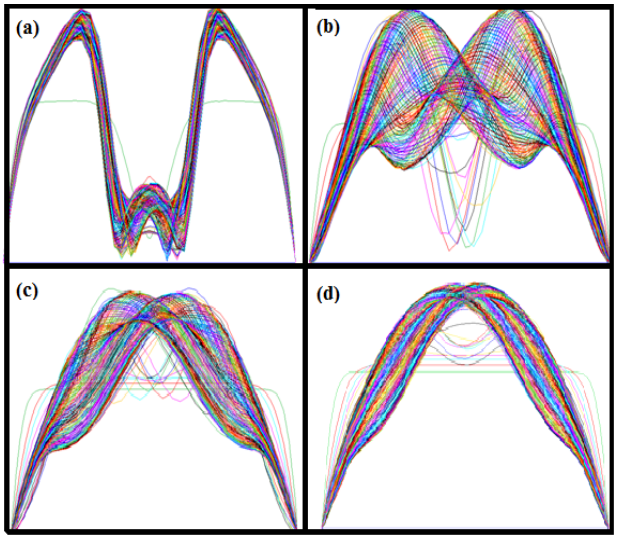

Fig. 5: Velocity profile with arc length at different positions of the channel (a) x = 0.3 (b) x = 0.6 (c) x = 0.9 (d) x= 1.2 mm.

The combined effect of pressure and velocity during drug particle transport within a fluid in a channel at different timings: (a) t=3.7, (b) t=4.1, (c) t=4.5, (d) t=4.9, (e) t=5.7 and (f) t=6.9 is shown in Fig. 6.

As discussed above, the same trend has been observed that maximum changes in velocity as well as pressure are observed during striking the particle with circular clot. Further, velocity and pressure both decrease as particles move away from the clotted area in the channel.

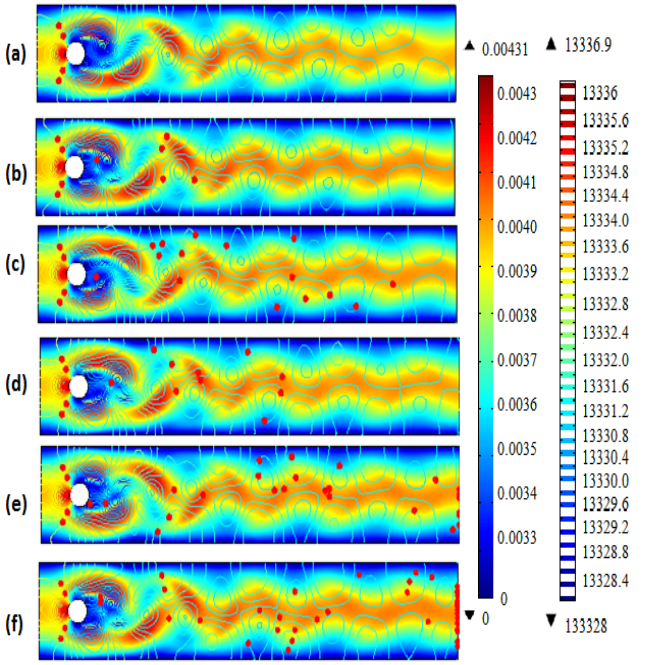

Fig. 6: Combined velocity (m/sec) and pressure (Pa) profile of drug particles transport within a fluid flowing in a clotted microchannel at different timings: (a) t=3.7, (b) t=4.1, (c) t=4.5, (d) t=4.9, (e) t=5.7 and (f) t=6.9.

V. CONCLUSIONS

In summary, the effect of drug particle transport within a fluid on velocity and pressure profile in a clotted channel has been studied through computational simulations. The coupled nonlinear partial differential Navier-Stokes equations for fluid floe and Newton's second law equation for particle transport are solved using finite element method based COMSOL software. Results demonstrate that the velocity and pressure changes significantly during the strike of drug particles on the clot present in the channel. Further, as particle move away from the clot region, their velocity and pressure being normalised.

REFERENCES

[1] W. Risau, Mechanisms of angiogenesis, *Nature*, vol. 386, 1997, pp. 671.

[2] S. Kayal, D. Bandhopadhyay, T. K. Mandal, R. V. Ramanujan, "The flow of magnetic nanoparticles in magnetic drug targeting". *RSC Adv.*, vol. 1, 2011, pp. 238.

[3] S. Kayal and R. V. Ramanujan, J. Nanosci. Nanotechnol., 2010, 10, 5527.

[4] F. Carapau, A. Sequeira, 1D Models for Blood Flow in Small Vessels Using the Cosserat Theory, *WSEAS Transactions on Mathematics*, vol. 5, 2006, pp. 54.

[5] S. R. McDougall, A. R. A. Anderson, M. A. J. Chaplian, J. A. Sherratt, Mathematical modeling of flow through vascular networks: implications for tumour-induced angiogenesis and chemotherapy strategies *Bulletin of Mathematical Biology*, vol. 64, 2002, pp. 673.

[6] T. Alarcon, H. Byrne, P. Maini, A cellular automaton model for tumour growth in inhomogeneous environment, *Journal of Theoretical Biology*, vol. 225, 2003, pp. 257.

[7] A. Stephanou, S. R. McDougall, A. R. A. Anderson, M. A. J. Chaplain, Mathematical modeling of the influence of blood rheological properties

upon adaptive tumour-induced angiogenesis, *Mathematical and Computer Modelling*, vol. 41, 2005, pp. 1137.

[8] A. D. Haitao Chen, H. Ebner, A. J. Chen, M. D. Rosengart, J. A. Ritter, Analysis of magnetic drug carrier particle capture by a magnetizableintravascular stent 2: Parametric study with single wire correlation, *Journal of Magnetism and Magnetic Materials*, vol. 284, 2005, pp. 181.

[9] O. Rotariu, N. J. C. Strachan, Modelling magnetic carrier particle targeting in the tumor microvasculature for cancer treatment, *Journal of Magnetism and Magnetic Materials*, vol. 293, 2005, pp. 639.

[10] E. P. Furlani, K. C. Ng, Analytical model of magnetic nanoparticle transport and capture in the microvasculature, Physical Review E, vol.73, 2006, pp. 061919.

[11] E. J. Furlani, E. P. Furlani, A model for predicting magnetic targeting of multifunctional particles in the microvasculature *Journal of Magnetism and Magnetic Materials,* vol. 312, 2007, pp.187.

[12] B. Wiwatanapataphee, K. Chayantrakom, Y. H. Wu, Mathematical Modelling and Numerical Simulation of Fluid-Magnetic Particle Flow in a Small Vessel, *International Journal of Mathematical models and methods in Applied Sciences*, vol. 1, 2007, pp. 209.

[13] P. Ruengsakulrach, A.K. Joshi, S. Fremes, S. Foster, Wall Shear Stress and Atherosclerosis: Numerical Blood Flow Simulations in the Mouse Aortic Arch, *WSEAS Transactions on Fluid Mechanics*, vol. 3, 2008, pp. 90.

[14] A. Mirza, A. R. Ansari, A. M. Siddiqui, T. Haroon, On the steady two-dimensional flow of blood with heat transfer in the presence of a stenosis, *WSEAS Transactions on Fluid Mechanics*, vol. 8, 2013, pp. 149.

[15] K. Gitter, S. Odenbach, Experimental investigation on a branched tube model in magnetic drug targeting, *J. Magn. Magn. Mater.,* vol. 323, 2011, pp. 1413.

[16] A. M. Morega, A. A. Dobre, M. Morega, Magnetic field: flow interaction in drug delivery through an arterial system, *Rev. Roum. Sci. Techn.– Électrotechn. et Énerg.,* vol. 56, 2011, pp. 199.