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Numerical Analysis of Motion and Stress Distribution of Circulating Tumor Cells in Micro Vessels

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Abstract: The motion of circulating tumor cells (CTCs) in microcirculatory system is one of the critical steps during cancer metastasis. The moving behavior and stress distribution of circulating tumor cells under different geometry and flow conditions are important basis for studying the adhesion between circulating tumor cells and vessel walls. In the present work, the motion and deformation of circulating tumor cells in capillary tubes are numerically studied using the immersed boundary method (IBM). The membrane stress distribution of CTCs in confined tubes are investigated with under vessel diameters, hematocrit (H_t) values and capillary numbers (Ca). The results show that the vessel diameter, Ca and H_t has profound effects on membrane stress of CTCs.

Keywords: Immersed boundary method; fluid-membrane interaction; circulating tumor cell; hemodynamics

1 Introduction

Motion and stress distribution of circulating tumor cells (CTCs) under interaction with red blood cells (RBC) in micro-vessels are crucial for their efficient adhesion to the vascular endothelium. But it is difficult to investigate CTCs *in vivo* because of their extremely low concentrations in blood. It is also impossible to measure the stress distribution on the membrane of CTCs when CTCs flow in microvessels with RBCs. Since the effect of the interactions between the flowing cells on the rolling and adhesion of CTCs is unclear, investigation of the mechanisms of motion and stress distribution of CTCs with numerical method are valuable which may help for the development of new therapeutic strategy to reduce metastasis. In this study, the effects of hematocrit on CTCs were studied. The effects of vessel diameters, hematocrit, CTCs stiffness and shear rate on stress distribution of CTCs in microvessels were investigated.

2 Methods

The fluid-structure interaction is solved based on the immersed boundary method (IBM), which in brief is implemented by projecting membrane forces onto the fluid and then updating the membrane configuration according to the flow field. The main advantages of this approach are that the fluid flow problem can be solved by standard numerical schemes over a fixed Eulerian mesh and the interfaces are treated in terms of Lagrangian marker. The IBM can be readily combined with a variety of computational fluid dynamics formulations (e.g., finite volume method, finite difference method). In our research, we employ the marker and cell (MAC) method as the Navier-Stokes solver. To get the second order accuracy, inertial terms are treated explicitly using the second-order Adams-Bashforth method, viscous term are treated semi-implicitly using the second-order Crank-Nicolson method [Gong et al. (2009)]. The capsule membrane is treated as an infinitely thin hyperelastic surface and assumed to follow the Skalak model [Skalak, Tozeren, Zarda et al. (1973)]. We complete the mathematical formulation by adopting a linear constitutive equation for the bending moment. The finite-element method (FEM) is used to calculate the membrane stress. The RBCs are modeled as biconcave capsules with an effective radius of 2.82 μm and

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CTCs are modeled as spherical capsules with a radius of 6 μm. The density of cytoplasm is assumed to be equal to the density of plasma. The microvessels are modeled as a cylindrical channel, and periodic boundary conditions are employed. The no-slip boundary condition is applied both on the cells membranes and the vessel walls.

3 Results

The simulation results show that the diameters of the vessels, hematocrit (H_t) values, CTCs stiffness and shear rate have profound effects both on motion and membrane stress of CTCs. As the H_t increased, the distance between CTCs and vessel wall decreased, and the stress on the CTCs membranes would increase with the effect of inter-cellular interactions. It is also found that the interaction between CTCs, RBCs and vascular wall is the major factor to the stress on CTCs membrane when the diameter of blood vessel is less than 20 μm, and the shear rate of flow field is major factor to the stress on CTCs membrane when the diameter of blood vessel is larger than 20 μm with H_t = 10%. In addition, larger CTCs membrane stiffness and shear rate leads to larger stress on the CTCs membranes. The effect of shear modules on stress is more significant than that of bending modulus. The present study provides fundamentals for further researches on the viability, transformation of the phenotype and the extravasation of CTCs under metastasis.

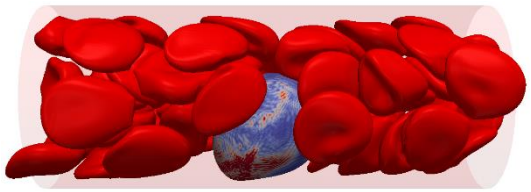

Figure 1: Simulation snapshots of the flow in a microvessel of diameter D = 20 μm, hematocrit H_t = 30%.

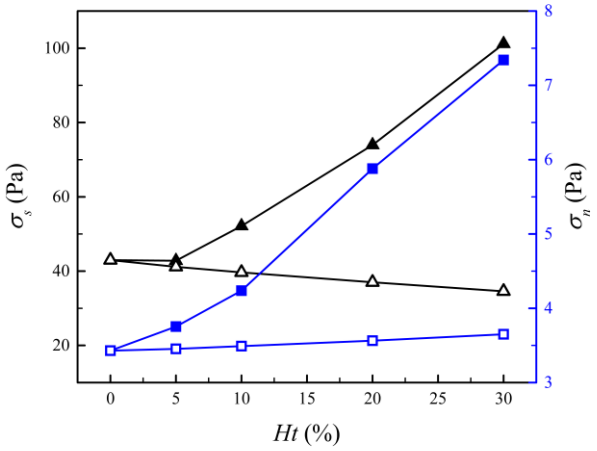

Figure 2: Averaged stress in the tangential (σ_s, triangle) and normal (σ_n, square) direction on the membrane of CTC for various H_t values. The opened symbol show homogeneous blood models without RBCs, and the plasma viscosity is equal to the apparent viscosity for corresponding H_t value.

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References

1. Gong X, Sugiyama K, Takagi S, Matsumoto Y. The deformation behavior of multiple red blood cells in a capillary vessel. *ASME Journal of Biomechanical Engineering* **2009**, 131(7): 074504.
2. Skalak R, Tozeren A, Zarda PR, Chien S. Strain energy function of red blood cell membranes. *Biophysical Journal* **1973**, 13(3): 245-264.