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Computational Investigation of the Effect of Adhesion between Cancer Cells and Vessel Walls on the Movement of the Cells in Blood Vessels

A. Khorram, B. Vahidi* , Z. Mollahoseini

Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran

ABSTRACT: Cancer is a disease that causes mortality in the world. Despite of improvements in medicine, there is not still sufficient knowledge of cancer. Therefore, there is a strong need for engineering modeling to understand it. The motion and adhesion of cancer cells in a blood vessel during metastasis is a complex mechanism that occurs in body. A two-dimensional model of the movement of cancer cells has been developed that is solved in two different modes in a straight line in a blood vessel. These modes are related to presence and absence of adhesion between cancer cell and blood vessel wall in presence of adhesion between cancer cell and white blood cell. The analysis is performed using FEM and FSI equations. It is assumed that the properties of blood and cells are homogeneous and fluid is incompressible and Newtonian. Cancer cell is modeled as a rigid body and white blood cell is assumed as linear elastic. The analysis shows that the influence of adhesion between the cell and the vessel wall is more important from cell-cell adhesion. Through consideration in the adhesion charts along with medical issues such as drug delivery to patients can affect the treatment or prevention of metastasis.

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1. Introduction

Cancer is one of the diseases caused by excessive and uncontrolled growth of the cells and their spreading into various parts of the body [1]. Cancer metastasis is the same as the tumor cells spreading from the primary tumor to the secondary tumors, which is the main cause of many deaths due to cancer [2].

Although different models have been investigated with different geometries and conditions of cancer, it has often been studied in tumor dimensions. In fact, few studies have been conducted at cell level on cancer, including Hoskins's study [3] which has investigated the adhesion and collision of cancer cells and leukocytes, in which the cancer cells and leukocytes bonds have been considered, while the effect of the adhesion between the cancer cells and the vessel wall has not been studied.

Establishing the cancer cells and the vessel wall bonds is the most important factor in the cancer cells movement from the vessel wall which completes the metastasis process. This phenomenon has never been investigated in any research. The study of this phenomenon is necessary in order to understand cancer disease, cells movement in the blood and its development effects on the speed of the movement. The next stage of the study, which is biologically based and requires a lot of time and effort, is to examine strategies for reducing or increasing the rate of cancer cells in the blood to eliminate these cells and prevent the completion of the metastatic process. The aim of the present study is to evaluate the effect of the adhesion between cancer cells and the wall of the vessel on their movement in the bloodstream.

*Corresponding author's email: vahidi@ut.ac.ir

2. Methodology

In this study, two different analyzes are performed, such that a cancer cell travels in a straight path and passes through the leukocyte which is adhered to the floor of the vessel. Considering the vessel wall bonds is the difference between the analyzes.

In this study, based on empirical observations, the cancer cell and leukocyte are, respectively, considered as a rigid circle [3-4] and a simple deformable model with linear elastic rigidity. To model cell-cell adhesion, the linear spring has been used [5]. Each bond is modeled as a linear spring, and this bond creates an equal force f. These forces arrive at a point at the lowest distance between the two cells on the cancer cell, which is perpendicular to the cancer cell surface. Note that the inverse forces of these forces, which must also be applied to leukocytes, are negligible in investigations in comparison to other fluid forces and vessel surface adhesions [3].

The Monte Carlo method is used to calculate the number of bonds as well as the exact location of F forces. In the proposed method, most of the relationships and constants are computed empirically and statistically estimates the number of bonds [6].

The Eq. (1) is the probability of the formation or breakdown of the bonds which is calculated at each time step [3]:

$$P = 1 - exp\left(-k\,\Delta t\right) \tag{1}$$

Where P is the probability of the formation or breakdown of the bonds, Δt is the t, step and k , calculated and used in two modes, K_{on} or $K_{off,}$ is defined in Eq. (2) and (3) [3]:

$$k_{on} = A_L(n_L - n_B)k_{on}^0 \exp\left(\frac{-s_{ts}(\mathrm{d}-\lambda)^2}{2k_bT}\right) \tag{2}$$

$$k_{off} = k_{off}^0 \exp\left(\frac{(s-s_{ts})(\mathrm{d}-\lambda)^2}{2k_bT}\right) \tag{3}$$

In the above equations, k_{on0} and k_{off0} are, respectively, the formation and breaking rates of the bonds in equilibrium conditions. The number of ligands and receptors are respectively shown by n_L and n_B. s, s_{ts} and A_L are respectively the linear spring constant of the bond and the adhesion molecules and surface of the cells exposed to the bonding. Also, d is the length of the spring and λ is the length of the spring in equilibrium, while k_b and T are respectively the Boltzmann constant and the absolute temperature.

For the Fluid-Solid-Interaction (FSI) analysis, the COSMOL 5.2 has been used. But, calculating forces with COMSOL requires a lot of time and cost. In order to resolve this limitation, the use of programming software is recommended. Therefore, the Monte Carlo equation coding has been done in MATLAB directly and coupled with COMSOL.

3. Results and Discussion

Fig.1 is a comparison of the horizontal velocity of the cancer cell and Fig. 2 is a comparison of velocities in the vertical direction. Looking at the graphs, one can see the high effect of adhesion to the wall of the vessel in the cancer cell movement. The amount of time needed to reach to the leukocyte is about 3.0 seconds in cell-cell adhesion, while it rises to about 42.0 in complete adhesion. Also, the velocity graph in complete adhesion state significantly reduced.

The next comparison is a comparison of the location of the cell in terms of time. Fig. 3 shows how adhesion to the wall causes the movement of the cell to occur more slowly and later to reach the desired location. For example, the distance between 520 and 560 microns in cell-cell adhesion takes place in 0.07 seconds, while this time for complete adhesion is about 0.17 seconds.

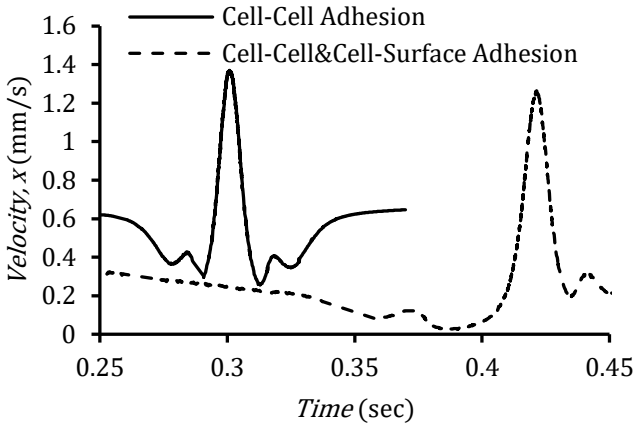

Fig. 1. Cancer cell horizontal velocity comparison

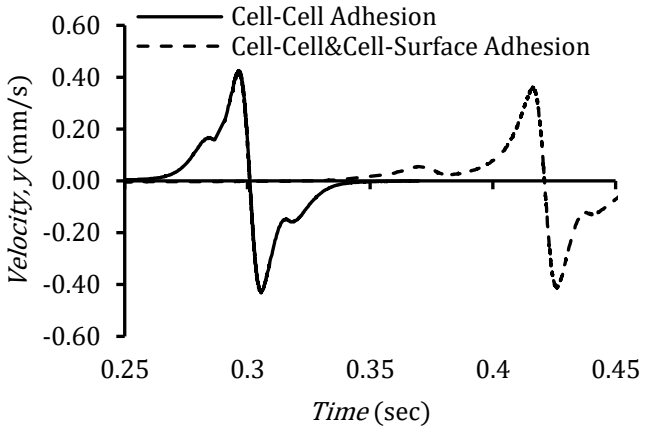

Fig. 2. Cancer cell vertical velocity comparison.

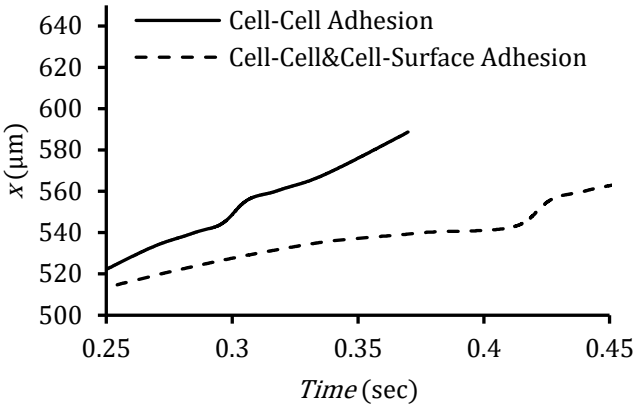

Fig. 3. Cancer cell horizontal location comparison.

4. Conclusions

In this research, the movement of the cancer cell in the bloodstream was investigated to evaluate, both, the cellular motion by FSI method, and the adhesion of the cancer cell to the leukocyte and to the wall of the vessel.

Comparison of cancer cell velocity and its separation distance with leukocyte has shown that the cell - wall adhesion has a significant effect on the movement of cancer cells, to the extent that up to 50% of the cellular movement becomes slower.

In line with this analysis, for the continuation of this study, the cancer tumor model could be considered more precisely in terms of geometry or mechanical properties, or the effects of the flow on the leukocyte. More importantly, MATLAB code discussions and functions are simplified, which requires much more computational cost in order to increase the accuracy of the solution. Also, 3D modeling of vessels and cells will lead to more accurate results.

References

[1] J. Gabriel, The biology of cancer, Whurr publishers London and Philadelphia, 2004.

[2] E.B. J. Massague, R. R.Gomis, Understanding the molecular mechanisms driving metastasis, Molcular Oncology, 11 (2017).

[3] R.F.K. M.H. Hoskins, J. Bistline, C. Dong, Coupled flow-structure-biochemistry simulations of dynamic systems of blood cells using an adaptive surface tracking method, Journal of Fluids and Structure, 25(5) (2009) 936-953.

[4] M.S. S. Liang, C. Dong, Shear stress and shear rate differentially affect the multi-step process of leukocyte-facilitated melanoma adhesion, Experimental Cell Research, 310(2) (2005) 282-292.

[5] D.T. M. Dembo, K. Saxaman, D. Hammer, The reaction-limited kinetics of membrane-to-surface adhesion and detachment, The Royal Society of London, 234(1274) (1988) 55-83.

[6] S.M.A. D.A. Hammer, Simulation of cell rolling and adhesion on surfaces in shear flow: general results and analysis of selectin- mediated neutrophil adhesio, Biophysical Journal, 63(1) (1992) 35-57.