Acta Technica 62 No. 4B/2017, 1–8

Numerical modeling of the dynamic behavior of a gaseous plug in treatment of the cancerous tumors by embolism

B. Farzaneh[1], M. T. Shervani-Tabar[1,3], R. Ahrabi[2], S. E. Razavi[1]

Abstract. Embolism is a well-known and wide used technique for treatment of the cancerous tumors. In the conventional embolism technique, the solid materials are used for preventing the blood flow to the targeted tissues. The proposed numerical modeling of the problem is capable for simulation of the dynamic behavior of the gaseous plug inside the vein during its growth and partially collapse phases and predicts the lifetime of the gaseous plug for preventing the blood flow to the targeted tissues. This numerical model also offers three different thermodynamic processes for the growth and partially collapse phases of the gaseous plug. In the first thermodynamic process for the gaseous plug growth and partially collapse phases, it is assumed that the gaseous plug contains a constant pressure vapor. In the second thermodynamic process of the gaseous plug growth and partially collapse phases, it is assumed that the gaseous plug contains an ideal gas which undergoes a classical thermodynamic process. In the third case, a mathematical-experimental model has been employed for the simulation of the growth and partially collapse phases of the gaseous plug. Numerical results for the three different thermodynamic processes of the gaseous plug growth and partially collapse phases have been illustrated and discussed.

Key words. Embolotherapy, thermodynamic of bubble, cancerous tumors, liquid drug DDFP
.

1. Introduction

Non-invasive treatment of the damaged or cancerous tissues in medicine is of significant importance. One of the most important treatment methods for the cancerous tissues is embolism. In the conventional methods of embolism, the solid materials are used in the macro and micro scales [1–4]. Recently a revolutionary technique is proposed by Professor Bull at the University of Michigan, Ann Arbor [5], which uses

[1]Department of Mechanical Engineering, University of Tabriz, Tabriz, Iran
[2]Department of Interventional Radiology, Alinasab Hospital, Tabriz, Iran
[3]Corresponding author; e-mail: msherv@tabrizu.ac.ir

the lipid coated spheres inside an emulsion containing a liquid drug for delivering the drug to the veins. In this method, the liquid drug inside the very small lipid coated spheres release inside the veins due to the emission of the ultrasound waves and its consequent rupturing of the lipid coating of the microspheres. The liquid drug then converts to the vapor or superheat gas at the body temperature. This superheat gas constructs a gaseous plug inside the veins and prevents the blood flow to the targeted cancerous tumors.

In this paper, a numerical model has been proposed for simulation of the dynamic behavior of the gaseous plug inside the vein by employing the boundary integral equation method Finally, a mathematical-experimental model which uses the thermodynamic tabulated data of the liquid drug DDFP has been employed for offering the third option. In the third option, the pressure and temperature of the gaseous content of the plug inside the vein have been calculated from the experimental tabulated thermodynamic data of the liquid drug DDFP at every time step. The initial idea of this mathematical-experimental model has been proposed by Soh [6] and Soh and Shervani [7] for more realistic modeling.

2. Geometrical and physical discretization

The boundary integral equation method has been employed for the numerical solution of the problem under investigation. The surface of the vapor bubble has been divided by the cubic spline elements and the internal surface of the rigid wall of the horizontal cylinder has been divided by the linear segments (see Fig. 1). The physical functions which are the velocity potentials and the normal derivatives of the velocity potentials in the directions normal to the surfaces of the liquid domain have been assumed to be constant and are located at the midpoints of the boundary elements.

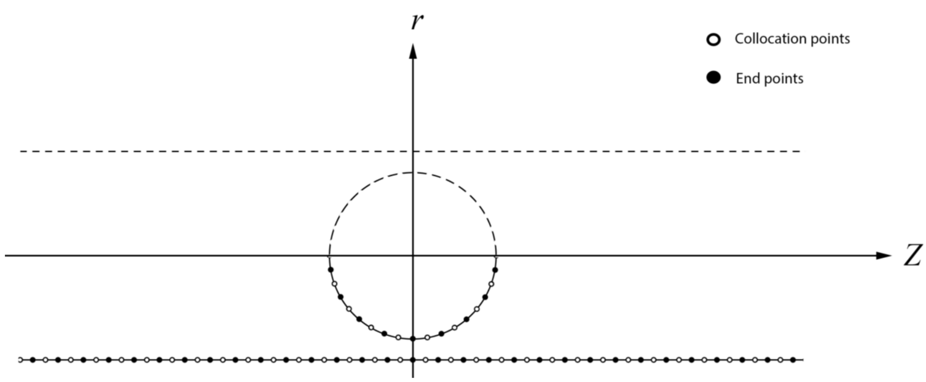

Fig. 1. Discretization of the geometry and physical functions of the problem

3. Mathematical-Experimental modeling of a real vapor bubble

In the mathematical-experimental model of real vapor bubble instead of using the classical thermodynamic process for evaluating mass and volume of the gaseous plug a mathematical-experimental approach which has been proposed in [6–7] is employed. In this model, the pressure of the gaseous contents of the plug at every time step has been estimated from the tabulated data of the thermodynamic properties of the liquid drug under the investigation which leads to the most realistic evaluation of the pressure of the plug gaseous contents.

As is reported by Soh [6] and Soh and Shervani-Tabar [7] a formulation for obtaining the initial condition for a real vapor bubble growing from its initial minimum volume has been constructed on the basis of conservation law as follows:

$$P_{\mathrm{b}} + \frac{a}{b+1} = \left(\frac{a}{b+1} + P_i\right)\left(\frac{V_i}{V}\right)^{\frac{b+1}{b}}, \tag{1}$$

where P_{v} is the pressure inside the vapor bubble at every time step, P_i is the initial pressure of the vapor bubble when its initial volume is V_i and a and b are constants.

The Rayleigh equation describing the motion of a cavitation bubble in an infinite fluid has been employed as

$$R\ddot{R} + \frac{3}{2}\dot{R}^2 + \frac{\Delta P}{\rho} = 0\,, \tag{2}$$

where $\Delta P = P_{\mathrm{c}} - P_{\infty}$ (the pressure difference from the current point to the final point) and R is the radius of the bubble, with dots denoting time derivatives.

Equation (2) is non-dimensionalised by multiplying both sides of the equation by $\frac{\rho}{\Delta P}$. Then the non-dimensional form of equation (2) will be

$$R\ddot{R} + \frac{3}{2}\dot{R}^2 + \frac{P_{\infty} - P_{\mathrm{b}}}{P_{\infty} - P_{\mathrm{c}}} = 0\,. \tag{3}$$

where P_{b} is the interior pressure of the real vapor bubble and has been given by equation (1). Therefore, by considering the value of the pressure inside a real vapor bubble equation becomes

$$R\ddot{R} + \frac{3}{2}\dot{R}^2 + \frac{P_{\infty} - \left(\frac{a}{b+1} + P_i\right)\left(\frac{V_i}{V}\right)^{\frac{b+1}{b}}}{P_{\infty} - P_{\mathrm{c}}} = 0\,. \tag{4}$$

Equation (4) can be written as

$$R\ddot{R} + \frac{3}{2}\dot{R}^2 = \varepsilon_2\left(\frac{R_i}{R}\right)^{3\gamma} - \varepsilon_1\,. \tag{5}$$

For integrating equation (5) we use $R\ddot{R} = R\frac{\mathrm{d}\dot{R}}{\mathrm{d}R}\dot{R}$ and $\dot{R} = y$, so that

$$y^2 = 2R^{-3}\left[\frac{\varepsilon_2 R_0^{3\gamma}}{3(1-\gamma)}R^{3-3\gamma} - \frac{\varepsilon_1}{3}R^3 + C\right]. \tag{6}$$

Here, $\varepsilon_1 = P_\infty/DeltaP$ and $\varepsilon_2 = P_0/DeltaP$, where P_0 is the initial pressure and P_∞ is the final pressure and γ is the convenience ratio. By considering that the velocity of the bubble boundary at its maximum volume is equal to zero, C in equation (6) becomes

$$C = \frac{\varepsilon_1}{3} - \frac{\varepsilon_2 R_0^{3\gamma}}{3(1-\gamma)}R^{-3\gamma} \tag{7}$$

and consequently

$$\dot{R}^2 = \frac{-2\varepsilon_2 R_0^{3\gamma}}{3(\gamma-1)}(R^{-3} - R^{-3\gamma}) + \frac{2\varepsilon_1}{3}\left(R^{-3} - 1\right). \tag{8}$$

4. Results and discussion

4.1. Numerical results by assuming a constant pressure vapor bubble

By assuming the vapor bubble undergoing as a constant pressure vapor bubble which represents a cavitation bubble generated by the emission of the ultrasound waves and by employing the boundary integral equation method for computational simulation of such a bubble gives the results of Figs. 3–5. Figure 2 illustrates the explosive growth of a constant pressure vapor a bubble inside a vein. As it is shown in Fig. 3, the liquid drug inside the lipid coated micro spheres release inside the vein due to the rapturing of the lipid shells. The lipid shells rapturing is in turn consequence of emissions of the ultrasound waves which are focused on a specified point in the targeted vein. The five growth stages of a constant pressure vapor bubble inside a vein have been illustrated in Fig. 2.

The fifth stage of the bubble growth phase represents its stable maximum volume. As time goes on, the volume of this stable bubble which acts as a gaseous plug and prevents the blood flow to the ill tissue decreases due to the mass transfer from the vein's wall.

Figure 3 illustrates the ratio of volume of the constraint pressure vapor bubble to its minimum volume with respect to the non-dimensional time during its growth and partially collapse phase.

Figure 4 shows the non-dimensional velocity of the bubble boundary on the axis of symmetry with respect to the non-dimensional time during its explosive growth and partially collapse phases. As it is shown in Fig. 4 the non-dimensional velocities of the bubble boundary with the negative magnitudes indicate the growth phase of the bubble. Whereas the non-dimensional velocities of the bubble boundary with the positive magnitudes indicate it is partially collapse phase. It should be noted

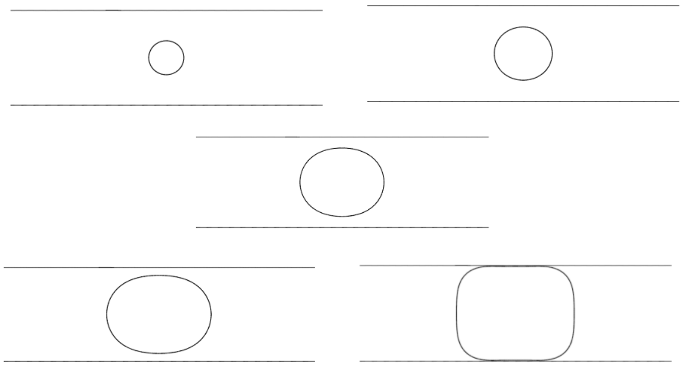

Fig. 2. Explosive growth of a constant pressure vapor bubble inside a vein

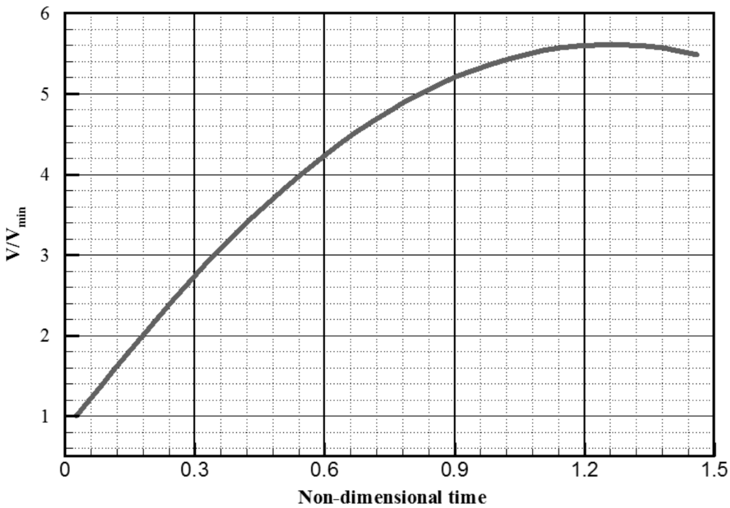

Fig. 3. Ratio of volume of the constant pressure vapor bubble to its minimum volume

that at the end of partially collapse phase of the bubble, it reaches to its maximum stable volume. After reaching of the bubble to its maximum stable volume, it acts as a gaseous plug which prevents to blood flow to the ill tissues. Then due to the mass transfer from the gaseous plug inside the vein through the vein's wall, the volume of the gaseous plug gradually decreases and finally vanished at the end of lifetime of the plug.

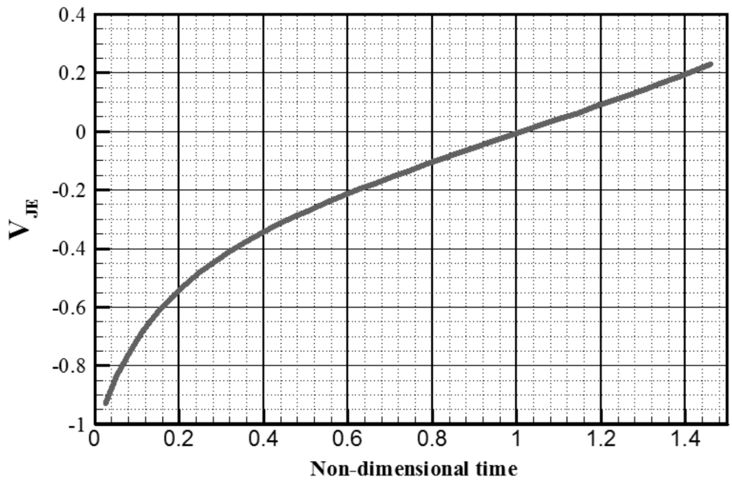

Fig. 4. The non-dimensional velocity of the bubble on the axis of symmetry

4.2. Comparisons between the results of the three different models of the vapor bubble

Figures 5 and 6 shows comparisons between the velocities of the gaseous bubble boundary on the axis of symmetry and the relative volume of the gaseous bubble with respect to the non-dimensional time. As it can be seen in Fig. 5 the gaseous bubble volume during its explosive growth and partially collapse phases in the case of a constant pressure vapor bubble expands to a relatively smaller maximum volume and it life time is relative shorter. Also Fig. 5 shows that the gaseous bubble during its explosive growth and partially collapse phases in the case of a real vapor bubble expands to a relatively larger maximum volume and its life time is relatively longer. As it is illustrate in Fig. 5 the maximum volume of an ideal gaseous bubble at the end of it explosive growth phase and its life time are between the case of a constant pressure vapor gaseous bubble and a real vapor gaseous bubble.

5. Conclusion

In this paper the novel idea of professor Bull for generating a gaseous plug, inside a vein by using the encapsulated liquid drug DDFP inside the micro lipid coated spheres, and preventing of the blood flow to the cancerous and damaged tissue for the purpose of killing or deactivating of the ill tissues has been investigated by assuming three different thermodynamic processes for the explosive growth and partially collapse phase of the gaseous bubble. In the first case the vapor pressure inside the gaseous vapor bubble during its explosive growth and partially collapse phases remains constant. In the second case the pressure of the gas inside the gaseous bubble during its explosive growth and partially collapse phases varies according to

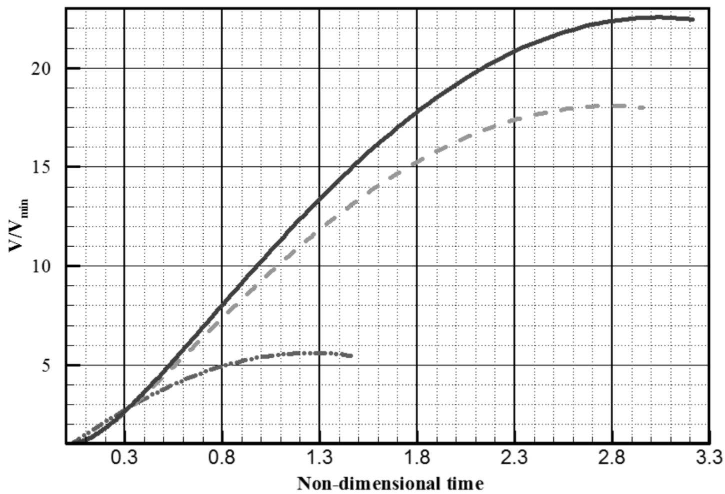

Fig. 5. Ratio of the bubble volume a–constant pressure vapor bubble, b–ideal gas bubble and c–real vapor bubble

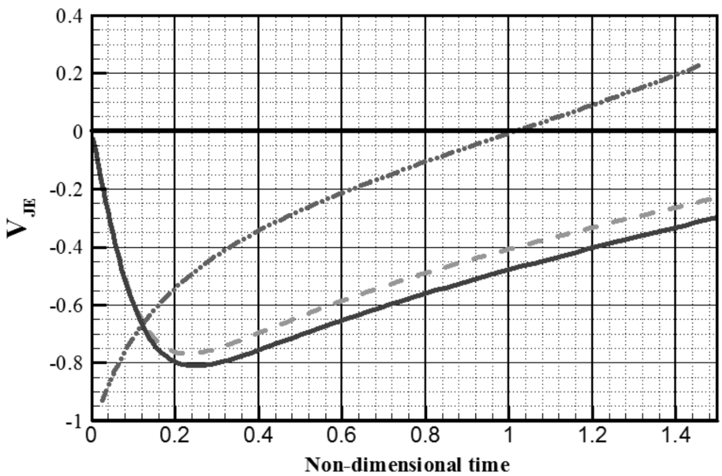

Fig. 6. Non-dimensional velocity a–constant pressure vapor bubble, b–ideal gas bubble and c–real vapor bubble

the classical ideal gas process. At the end of the explosive growth phase of the gaseous vapor bubble and its consequent partially collapse phase, a gaseous stable bubble generates inside the targeted vein which behaves as a plug and presents the blood flow towards the cancerous or damaged tissue. The required time for killing or deactivating of a cancerous or damaged tissue has been assumed to be eight hours. Then the permeability of any vein wall in any part of a human body and the required time for the killing or deactivating of a cancerous or damaged tissue specifies the volume of the gaseous plug inside a any vein in any part of a human body and consequently specifies the required dose of the liquid drug DDFP which should be released inside the targeted vein due to the emission of ultrasound waves.

References

[1] T. Ye, J. L. Bull: *Direct numerical simulations of microbubble expansion in gas embolotherapy.* Journal of Biomechanical Engineering *126* (2005), No. 6, 745–759.

[2] A. Qamar, Z. Z. Wong, J. B. Fowlkes, J. L. Bull: *Dynamics of acoustic droplet vaporization in gas embolotherapy.* Applied Physics Letters *96* (2010), No. 14, paper 143702.

[3] A. J. Calderon, J. B. Fowlkes, J. L. Bull: *Bubble splitting in bifurcating tubes: A model study of cardiovascular gas emboli transport.* Journal of Applied Physiology *99* (2005), No. 2, 479–487.

[4] A. Qamar, Z. Z. Wong, J. B. Fowlkes, J. L. Bull: *Evolution of acoustically vaporized microdroplets in gas embolotherapy.* Journal of Biomechanical Engineering *134* (2012), No. 3, paper 031010.

[5] J. Bull: *Cardiovascular bubble dynamics*: Critical Reviews in Biomedical Engineering *33* (2005), No. 4, 299–346.

[6] W. K. Soh: *On the thermodynamic process of a pulsating vapour bubble.* Applied Mathematical Modelling *18* (1994), No. 12, 685–690.

[7] W. K. Soh, M. T. Shervani-Tabar: *Dynamics of acoustic droplet vaporization in gas embolotherapy.* Conferece of Computational Methods in Engineering: Advances and Applications (ICCME), 11–13 November 1992, Singapore, Conference Proceedings (1992), 529–534.

Received October 31, 2017