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Numerical study of nanofluid transport in tumors during nanofluid infusion for magnetic nanoparticle hyperthermia treatment

Di Su, Ronghui Ma, and Liang Zhu

Department of Mechanical Engineering
University of Maryland, Baltimore County
1000 Hilltop Circle, Baltimore MD 21250

INTRODUCTION

The application of nanostructures in hyperthermia treatment of cancer has attracted growing research interest due to the fact that magnetic nanoparticles are able to generate impressive levels of heat when excited by an external magnetic field [1-3]. Various types of nanoparticles such as magnetite and superparamagentic iron oxide nanoparticles have demonstrated great potentials in hyperthermia treatment; however many challenges need to be addressed for future applications of this method in clinical studies. One leading issue is the limited knowledge of nanoparticle distribution in tumors. Since the temperature elevation is induced as the result of the heat generation by the nanoparticles, the concentration distributions of the particles in a tumor play a critical role in determining the efficacy of the treatment. The lack of control of the nanoparticle distribution may lead to inadequacy in killing tumor cells and/or damage to the healthy tissue.

Intratumoral infusion is an important technique to deliver a variety of nanostructures in tumors by continuous injection of a nanofluid under a positive pressure gradient [2]. Previous study [3, 4] of the injection of a ferrofluid in semi-transparent agarose gels suggests a non-uniform nanoparticle distribution with a high nanoparticle concentration near the needle tip. However, the underlying mechanisms that govern the transport of nanofluids in tissues during an infusion are poorly understood. Specifically, it remains unclear to what extent the deformation of the tissue affects the nanoparticle transport in tumors.

The objective of the current study is to investigate the interrelated mechanisms of nanofluid transport in tumors. Presented in this paper is a multi-scale model that considers fluid flow and deformation of tumoral tissues during an infusion process, particle interaction with the cellular structure, and nanoparticle advection and deposition in tumors. The integration of the three components allows the study of the nanoparticle transport behavior during an infusion process. The influence of the deformation-induced backflow and change in porosity on particle distribution was quantified for various infusion rates.

MATHEMATICAL MODEL AND SIMULATION SETUP

The behavior of nanoparticle transport in biological tissues stems from the complex chemicophysical processes occurring on largely disparate temporal and spatial scales. In this study, a multi-scale model that consists of three major components is developed to describe an intratumoral infusion of nanofluids: (a) a poroelastic model for fluid flow through a tumor and tumor deformation; (b) nanoparticle convection, diffusion, and deposition in a tumor; and (c) a particle trajectory tracking model for particle interactions with the cell surface. The integrated model enables one to predict the distributions of nanoparticle concentration in tumors under a variety of infusion parameters. The simulations of nanofluid injection in tumors are performed in a configuration depicted in Fig. 1, where a spherical tumor of 10 mm in diameter is embedded in 20 mm thick normal tissue. A needle is inserted at the center of the tumor. A commercially available multiphysics software COMSOL® is used to solve the equations. A total number of 22792 triangular elements with quadratic Lagrange shape functions are used in the simulation.

RESULTS AND DISCUSSIONS

A baseline case with the infusion rate of 5 µl/min, the needle size of 26 gauge, and the Young's modulus E of 0.5 MPa is simulated first. The predicted nanoparticle distribution in a tumor is shown in Fig. 2a. It can be seen that the particle distribution is not spherically symmetric due to the formation of 6 mm long backflow.

The effect of the infusion rate on the tissue deformation and particle distribution is studied by changing the infusion rate while holding other parameters prescribed in the baseline case constant. Shown in Figs. 2b is the particle distribution for a higher infusion rate of 10 µl/min. In addition to a longer backflow length, the elevated infusion rate yields a

larger tissue porosity and lower particle concentration near the injection site. The variations of porosity and nanoparticle concentration along the injection direction (A-A line) for different infusion rates are shown in Figs. 3a and 3b respectively. For both infusion rates, tissue porosity and nanoparticle concentration decrease monotonously in the radial direction from the injection site. A higher infusion rate causes a deeper particle penetration depth and lower nanoparticle concentration at the needle tip.

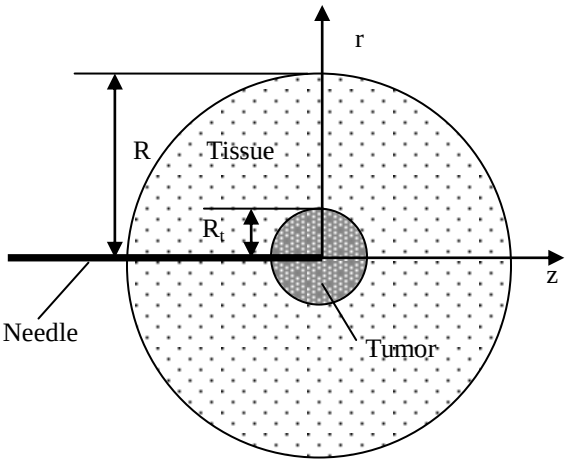
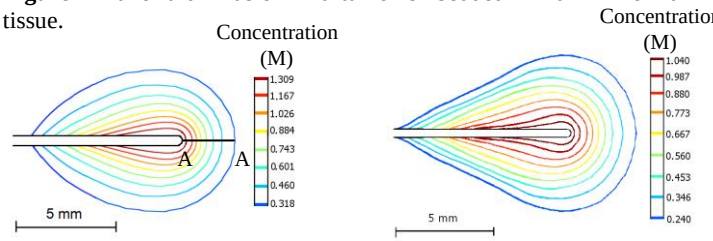


Figure 1 Nanofluid infusion in a tumor embedded in 20-mm-normal tissue.



a) Back flow length = 6mm (b) Back flow length =11mm

Figure 2 Distributions of nanoparticle concentration for (a) the baseline case with infusion rate of 5µl/min, E = 0.5 MPa, and 26 gauge needle, (b) infusion rate of 10 µl/min.

A higher infusion rate yields three consequences: a longer backflow length and the spreading of the particles along the needle track, a lower deposition rate coefficient, and a larger tissue porosity near the needle tip. All these contribute to a reduced particle deposition at the needle tip, leading to deeper particle penetrations and lower particle concentrations at the injection site. The relationship of the particle penetration depth to the infusion rates observed in this study is consistent with previous micro-CT imagining results and *SAR* measurements in gels and tissues.

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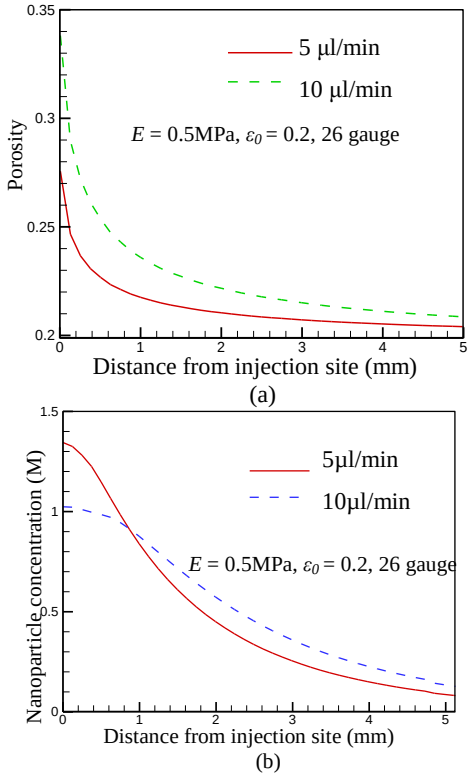

Figure 3 Variations of (a) porosity and (b) particle distribution along the injection direction for various infusion rates (E = 0.5MPa, ε_0 = 0.2, 26 gauge needle)

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