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Analysis of magnetic drug carrier particle capture by a magnetizable intravascular stent—2: Parametric study with multi-wire two-dimensional model

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Abstract

A 2-D mathematical model was developed and used to examine the capture of magnetic drug carrier particles (MDCPs) by a magnetizable intravascular stent (MIS). The roles of both non-stent system parameters, i.e., the blood flow rate, magnetic field strength and direction and MDCP properties, and stent design parameters, i.e., the MIS radius, its wire radius, number of MIS loops, interwire loop spacing and MIS ferromagnetic material were evaluated over a wide range of plausible conditions. The results showed that the MIS could be a very effective magnetic drug targeting tool with many possible applications.

Keywords: Magnetic drug targeting; Stent; Drug delivery; Magnetic drug delivery; Magnetic microspheres; High-gradient magnetic separation; Magnetic fields; Circulatory system; Blood flow; Magnetic implant; Simulation

1. Introduction

The inclusion of magnetic elements into biocompatible materials is becoming quite popular in the medical research community. In fact, the use of magnetically doped polymeric particles as carriers of chemo- and radio-therapeutic agents for drug tracking and targeting is showing considerable potential for treating a wide variety of diseases from cancer to cardiovascular problems [1]. However, when it comes to magnetic drug targeting (MDT) the current approach of using only an external magnet faces several challenges [2].

One problem is associated with the high blood velocities, typically varying between 0.1 and 1.0 m/s in large arteries and veins, imposing adverse

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hydrodynamic conditions on the magnetic collection of magnetic drug carrier particles (MDCPs) at the target site. Also, because the magnetic field intensity decreases abruptly with distance, another problem with the use of an external magnet alone is that MDT may be limited to only a couple of centimeters deep in the body. With the force exerted on a MDCP ($\mathbf{F}_m$) being proportional to both $\mathbf{H}$ and $\nabla\mathbf{H}$ [3], i.e.,

$$\mathbf{F}_m \propto \mathbf{H} \cdot \nabla\mathbf{H} \tag{1}$$

a larger, more powerful magnet may not improve matters very much because its $\nabla\mathbf{H}$ would necessarily be small. For this reason, the application of high-gradient magnetic separation (HGMS) principles has been proposed recently to assist MDT [2,4–6].

These works collectively consider the use of an insertable or implantable ferromagnetic element, such as a wire, needle, catheter or stent, to locally increase the force $\mathbf{F}_m$ on a MDCP at the target site by necessarily increasing $\nabla\mathbf{H}$ in the region of the element. In particular, the recent study presented in Part 1 of this series on the use of a magnetizable intravascular stent (MIS) to assist MDT showed considerable promise even under high-velocity conditions typically found in large arteries [6]. In that work [6], the effect of both non-stent system and stent design parameters on the MDCP capture efficiencies of a single stent wire using a simple single wire HGMS correlation [7] was investigated.

The objective of this work, i.e., Part 2 of the series, is to elucidate the effects of both non-stent system and stent design parameters on the MDCP capture efficiency of the MIS using a more rigorous and hence more realistic 2-D mathematical analysis [2]. The non-stent system parameters include the blood flow rate, the properties of the MDCPs, and the magnetic field strength and direction. The stent design parameters include the MIS radius, its wire radius, the number of MIS loops, the interwire loop spacing, and the MIS ferromagnetic material. The results from a detailed parametric study, carried out over a wide range of physically plausible conditions that are typical of the circulatory system, are provided and discussed.

2. System description and model development

A schematic of the control volume (CV) utilized for modeling the magnetic capture of MDCPs by the MIS is depicted in Fig. 1. This MDT system consists of a stent of radius R_s with N_w wire loops placed in an expanded blood vessel, originally with upstream radius R_v and average velocity $u_{B,u,avg}$. The loops ideally consist of parallel rings of wires each with radius R_w, a surface-to-surface interwire spacing h, and all facing perpendicular to the blood flow. Because the model is 2-D, the loops are represented here by two sets of N_w parallel wires placed perpendicular to the plane of the figure and along each side of the vessel (i.e., next to the top and bottom vessel walls). The vessel walls are assumed to be two parallel planes also placed perpendicular to the plane of the figure, as shown. Since the loops are parallel to themselves and perpendicular to the blood flow, the upper and lower sets of wires are symmetric with respect to the horizontal line located in the middle of the vessel (i.e., at $y = 0$). The relative location of the MIS in this vessel is arbitrarily chosen with the coordinates of the left most lower wire being at $x_i = 21R_w$ and $y_i = -R_s + 0.3R_w$. The horizontal length L_x of the CV is chosen so that its distance x_f from the right most loop wire is identical to the distance between two consecutive wires (i.e., $L_x - x_f = 2R_w + h$). The blood and hence the MDCPs to be captured by the MIS wires enter the MIS from the left at an average upstream velocity $u_{B,u,avg}$. The blood and MDCPs are then slowed to $u_{B,o,avg}$ due to expansion by the MIS. Finally, the MIS-MDT is subjected to a homogeneous magnetic field H_o positioned at angle β relative to the flow of blood.

The aim is to predict the trajectories of the MDCPs as they travel with the blood into and through the CV while under the influence of both hydrodynamic and magnetic forces. Then, by visual inspection, the fractions of them that lead to the MIS wires are evaluated because these trajectories indicate magnetic retention or MDCP capture. Hence, the performance of the MIS-MDT system shown in Fig. 1 is determined by its capture or collection efficiency (CE), which is defined as the fraction of MDCP trajectories that enter