



Sequestration of Blood-Borne Magnetic Drug Carrier Particles Using Magnetizable Intravascular Stents

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INTRODUCTION

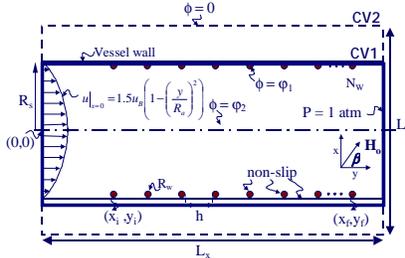
- The ability to effectively target a specific area in the body is one of the major concerns of current drug administration research.
- Acceptable therapeutic levels at the desired site require large doses of the drug to be given; but with current procedures, only a fraction of the dose will actually reach the intended organ or disease site. In fact, much of the drug causes undesirable toxic side effects at non-target organs or is naturally deactivated in the body.
- One solution to this problem is to incorporate magnetic particles into drug carrier vesicles and use an externally applied magnetic field to physically direct them to a site.
- However, it has been shown that an externally applied magnetic field alone may not be capable of retaining a sufficient number of drug carrier particles to justify its use.

OBJECTIVE

- High gradient magnetic separation (HGMS) principles via the implantation of a ferromagnetic element of large curvature in a tissue or blood vessel is a relatively new way to magnetically target drugs to a site in the body.¹
- In this work, the possibility of using HGMS-assisted magnetic drug targeting (MDT) in collecting magnetic drug carrier particles (MDCPs) via a magnetizable intravascular stent (MIS) made of a ferromagnetic material is investigated.
- This MIS is placed in a large artery or vein adjacent to the target tissue or organ, while an external magnetic field is used to energize the MIS to collect the MDCPs at the site.
- The MIS is also used to expand the vessel from radius R_v to that of the radius R_e of the expanded MIS to slow down the high velocities typically found in arteries, as shown in the figure above. The velocity of the unexpanded vessel $u_{b,0}$ is fixed at 0.8 m/s (which is typical of systolic conditions).
- The variables investigated in the MDCP capture efficiency (CE) of the MIS are the radius ($R_e = 0.5 - 20 \mu\text{m}$) and weight fraction of ferromagnetic material ($x_{m,p} = 0.2 - 0.8$) of the MDCPs, the ferromagnetic material of the MIS (409 SS and Ni) and in the MDCPs (Fe and magnetite), and the radii of the MIS ($R_s = 1.5$ and 2.5 mm) and of its wires ($R_w = 125 - 250 \mu\text{m}$).

SCHEMATIC OF THE MIS

Figure 1: 2-D representation of the magnetizable intravascular stent (MIS). The MIS of radius R_e , consisting of N_w loops of ferromagnetic wires of radius R_w and interspatial separation h is modeled with the 2-D representation as depicted. The blood vessel walls and the loops are assumed to consist of two parallel planes and two sets of N_w parallel wires, respectively, with both being set perpendicular to the plane of the figure. The blood, which transports the MDCPs to the MIS, moves from left to right, and enters the region with a velocity that is defined by a parabolic profile with u_b as its average. u_b reflects the change of blood velocity $u_{b,0}$ as a consequence of the expansion of the blood vessel from a radius of R_v to R_e . Finally, the magnetic field H_0 rests in the plane of the figure and its direction is defined by the angle β as depicted. The figure also depicts the two control volumes (CV) that are used to determine the MIS performance. CV1, which is defined by the thick inner continuous box, is used to determine the x-y components of the blood velocity by solving the Navier-Stokes and mass continuity equations. Non-slip conditions are used at every solid-liquid interface. CV2, which is defined by the outer discontinuous box, is used to solve Maxwell's continuity equation for the magnetic flux Φ . This flux is redefined in terms of a scalar magnetic potential ϕ , which is set to zero at the CV2 boundaries.

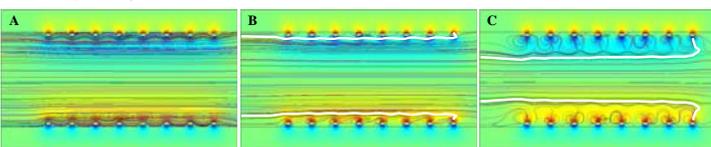


ASSUMPTIONS

- The model accounts for only magnetic and drag forces acting on the MDCPs. For simplicity, wall, lift and interparticle magnetic forces are not considered, while both the gravitational and inertial forces are assumed to be negligible at the flow conditions investigated in this study.
- Additional assumptions include the blood to be a homogeneous, incompressible Newtonian fluid flowing at a constant, non-pulsating velocity.

TYPICAL SIMULATION RESULTS

Figure 2: Dynamic simulations of the MDCPs through the MIS (below). The streamlines of the MDCPs moving past the MIS (409 SS, $R_w = 125 \mu\text{m}$, $R_s = 2.5 \text{ mm}$, $h = 8R_w$, and $N_w = 8$) under a magnetic field $\mu_0 H_0$ of 1.0 T ($\beta = \pi/2$) are obtained using FEMLAB. Because the radius R_v of the unexpanded blood vessel is 0.5 mm , the average velocity u_b entering in each of the figures is 3.2 cm/s . The streamlines correspond to those of A) blood, B) single non-porous ($\epsilon_p = 0.0$) MDCPs ($R_p = 2.0 \text{ mm}$, magnetite content, $x_{m,p} = 50 \text{ wt\%}$) and C) porous ($\epsilon_p = 0.4$) agglomerated MDCPs ($R_p = 20.0 \text{ mm}$, magnetite content, $x_{m,p} = 50 \text{ wt\%}$). The fraction of the streamlines captured by the MIS represents its collection efficiency (CE), which is determined via visual inspection. The CEs for cases B and C are 20.9% and 57.9%, respectively.



COLLECTION EFFICIENCY RESULTS

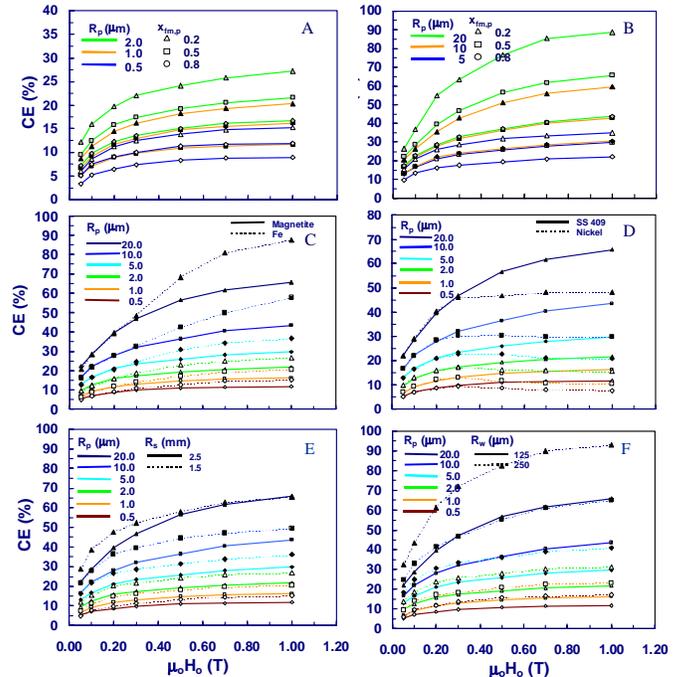


Figure 3: Parametric study on the CE of the MIS (above). The CEs are all plotted as a function of the magnetic field strength $\mu_0 H_0$ with A) for small MDCP radii R_p and B) for large MDCP radii R_p , and both for different magnetic material contents $x_{m,p}$ in the MDCPs, C) different ferromagnetic materials in the MDCPs, D) different ferromagnetic materials in the MIS, E) stent radii R_s , and F) individual wire radii R_w . Unless specified in the graph, the conditions used to generate these plots are: $x_{m,p} = 0.5$, $R_s = 2.5 \text{ mm}$, $R_w = 125 \mu\text{m}$, and magnetite and 409 SS as the ferromagnetic materials in the MDCPs and MIS, respectively. The rest of the parameters are $u_{b,0} = 0.8 \text{ m/s}$, $h = 8R_w$, $N_w = 8$, $R_e = 0.5 \text{ mm}$ and $\beta = 0$.

COMMENTS AND CONCLUSIONS

- The results in Figure 3 provide sufficient evidence in support of HGMS-assisted MDT via a MIS.
- Despite the adverse systolic conditions used in these plots, the use of a MIS shows considerable promise in collecting MDCPs for a wide range of feasible conditions, with CEs varying from 5 to almost 100%. Furthermore, the short recirculation periods of the circulatory system should grant further collections of the MDCPs not collected during the first pass through the MIS.
- The results depend heavily on the existence of magnetic agglomeration between the MDCPs, a phenomenon that is known to occur and currently under investigation.
- The results suggest that large contents of ferromagnetic material in the MDCPs (A, B) and magnetic fields (A-F) are not at all critical for the success of the proposed technique.
 - MDCPs with $x_{m,p}$ as little as 0.2 (~ 4 vol%) can provide plenty of volume for the drug (which is usually in liquid form) and still allow for large CEs to be realized.
 - Contrary to common understanding, large magnetic fields are also not required, since the magnetic materials being used are ferromagnetic and saturate at fields of around 1.0 T or less. In fact, under conditions where all the ferromagnetic materials involved are magnetically saturated, the CEs may even decrease with increasing magnetic field strengths as is the case with the nickel MIS (D).
- It is noteworthy that the CEs do not differ significantly with the ferromagnetic material being used, even when the saturation magnetization of the materials differ by a factor of 4 (C and D).
- More significant than reducing the blood velocity, the results indicate that CEs are improved if the ratio between the stent radius R_s and the wire radii R_w is reduced. This is the case when either R_s is reduced (E) or R_w is increased (F).
- Clearly, using a MIS as a drug targeting platform, the MDCPs as a drug targeting delivery vehicle, and an external magnetic field as the energy source provides a very new and innovative means of periodically bringing drugs to various disease sites in the body.

ACKNOWLEDGEMENTS

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REFERENCE

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