Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Magnetic Steering of Iron Oxide Microparticles Using Propulsion Gradient Coils in MRI

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***Abstract*—Steering micro-carriers being tracked by an MRI system may be very attractive in oncology. Here, Iron Oxide microparticles have been steered in a Y-shaped microchannel placed between a Maxwell pair (*dB/dz* = 443 mT/m) located in the center of an MRI bore. A suspension of 10.82 μm Iron Oxide particles was injected into the channel and a magnetic gradient generated by the Maxwell pair was used to deflect their trajectory. The experimental results based on the percentage of particles retrieved at the targeted outlet during the experiments show that magnetic gradient steering in the human cardiovascular system within an MRI bore can be envisioned.**

Index Terms—**Magnetic resonance imaging, Iron Oxide microparticles, magnetic steering, Maxwell pair, microvascular channel**

I. Introduction

Recent experimental results demonstrated that Magnetic Resonance Imaging (MRI) gradient coils found in clinical MRI systems can be used to induce sufficient magnetic force on a magnetized material [1] to consider it for medical interventions. Hence, these results open new possibilities for the development of new MRI-based medical interventions relying on magnetic cores or carriers being propelled or steered in the blood vessels. In this context, micro- and nanoparticles are also of special interests for improving targeting efficacy for chemotherapy or chemo-embolization, to name but only two applications. Nevertheless, clinical MRI gradient coils are designed with imaging constraints in mind such that their requirement for a low rise time does not allow the amplitude of the gradient to exceed a typical maximum strength of 40 mT/m, hence constraining flexibility for the 3D control and navigation of magnetic particles in the cardiovascular system.

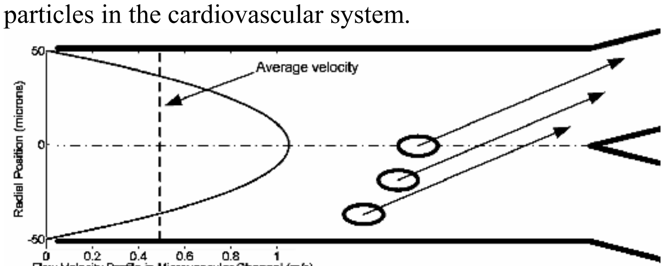

Fig. 1. Schematic of the semi-empirical steering criterion applied to the flow and diameter of the microvascular channel used in the experiments

This project is supported in part by a Canada Research Chair (CRC) in Micro/Nanosystem Development, Fabrication and Validation, the Canada Foundation for Innovation (CFI), the National Sciences and Engineering Research Council of Canada (NSERC), and the Government of Québec.
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As such, additional steering coils providing higher gradient strengths must be installed in the MRI bore and operate synchronously in a time-multiplexed fashion with the MR-imaging coils. A first step towards the development of such steering coils calls for a validation of the gradient strength required for improving targeting efficacy of microparticles. A criterion used to model magnetic steering of magnetic particles by external magnets is the magnetic gradient required to bring a particle past the centerline of a given blood vessel before the next symmetric bifurcation (Fig. 1). Even though magnetite nanoparticles require gradients as high as several T/m for efficient steering in mice blood vessels [2], a few hundreds mT/m would theoretically be sufficient to steer microparticles according to the steering criterion (Fig. 2). The development of steering gradient coils for microparticles would be limited here to a few hundreds mT/m due to constraints related to the size of the human body, the space available within a clinical MRI bore, and cooling issues. Unlike imaging coils, steering gradient coils emphasize gradient strength over inductance and linearity. The imaging coils would still be used for tracking purposes. Once tracking is performed, the steering coils would be powered in order to apply a magnetic force computed from the previous acquired tracking information. Here, smaller scale experimental one-dimensional steering gradient coils based on a Maxwell pair is used to steer microparticles inside a micro-channel to gather experimental data in order to validate our steering models and to set the required gradient amplitude before future larger-scale designs and fabrications of 3D steering coils are undertaken.

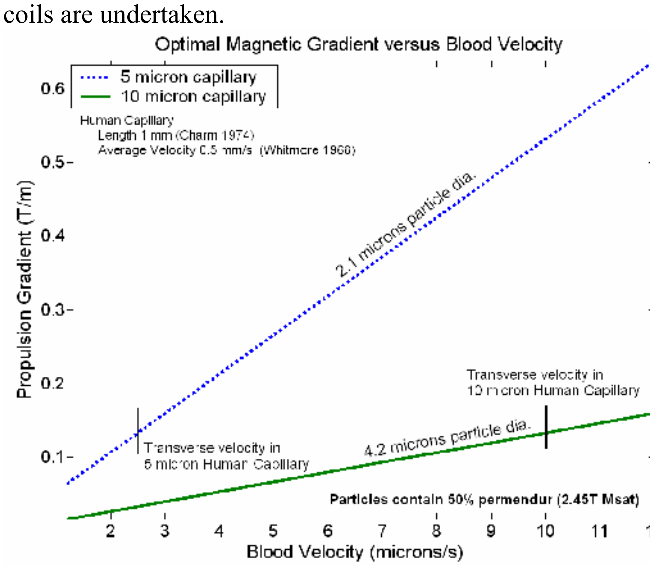

Fig. 2. Steering gradients for 2.1 and 4.2 micrometer diameter 50% volume Permendur sphere in human capillaries with diameters of 5 and 10 micrometers (physiological specifications from [3]). According to the steering criterion, approximately 100 mT/m gradients are required for steering of 2.1 and 4.2 micron particles in such capillaries.

II. Materials and Methods

A. Steering Platform

The magnetic steering set-up or platform relies on a Y-shaped microchannel emulating a microvascular channel in which a magnetite microparticles suspension is injected. A magnetic force is applied on the particles in order to deflect their trajectory towards a preferred outlet in a manner similar to the method used in [4].

The magnetic force in Newtons is given by

$$\vec{F}_{mag} = \mu_0 . (\vec{m}.\nabla)\vec{H}, \qquad (1)$$

where, μ_0 is the vacuum permeability, m ($A.m^2$) is the magnetic moment of the particle, and H (A/m) is the magnetic field.

The magnetic moment m of a material is related to the magnetic field in which it is placed and its magnetization. In our case, the strong magnetic field ($B_0 = \mu_0 H_0 = 1.5$ T) of the MRI system forces the magnetic material to reach its saturation magnetization. Hence, the combination of an adequate magnetic material combined with the MRI B_0 field provides the m term of Eq.1.

As shown and validated in [1], the field gradient term of Eq.1 can be provided by standard MRI imaging gradient coils but only to propel millimeter-size particles in larger vessels. For microparticles in smaller vessels, the drag force becomes comparatively stronger. For operations at such a smaller scale, a Maxwell pair has been built to generate a field gradient of sufficient amplitude for these steering experiments.

To our knowledge, this is a first attempt to steer magnetic microparticles inside a clinical MRI system. A simple schematic of the experimental set-up is depicted in Fig. 3.

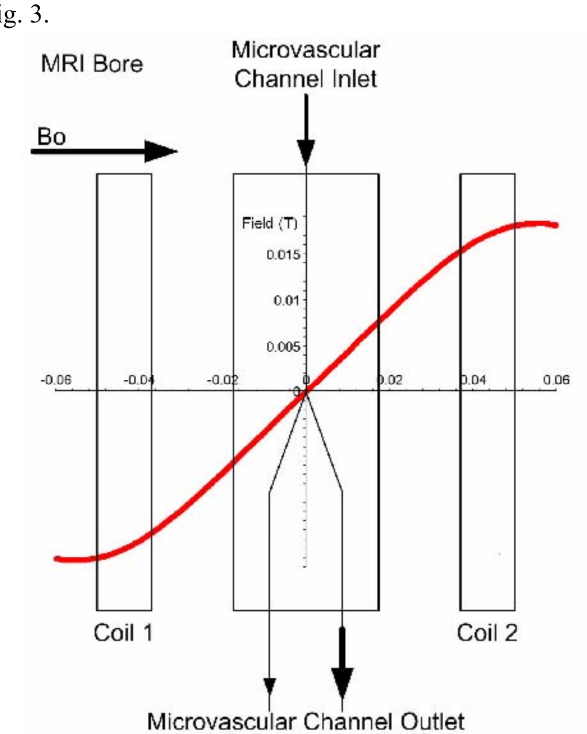

Fig. 3. Schematic of the experimental set-up.

B. Maxwell Pair

For the Maxwell pair specially developed in the context of this experiment (Fig. 4), the longitudinal component of the magnetic field and magnetic field gradient produced by two electrical current loops are given by Eqs. 2 and 3 respectively.

$$B(z) = \frac{50\,\mu\, i\, a^2}{\left(\left(\frac{1}{2}d - z\right)^2 + a^2\right)^{(3/2)}} + \frac{50\,\mu\, i\, a^2}{\left(\left(\frac{1}{2}d + z\right)^2 + a^2\right)^{(3/2)}} \qquad (2)$$

$$\frac{dB(z)}{dz} = - \frac{75\,\mu\, i\, a^2\,(-d + 2\,z)}{\left(\left(\frac{1}{2}d - z\right)^2 + a^2\right)^{(5/2)}} - \frac{75\,\mu\, i\, a^2\,(d + 2\,z)}{\left(\left(\frac{1}{2}d + z\right)^2 + a^2\right)^{(5/2)}} \qquad (3)$$

In the above equations, a is the radius of the current loop, μ is the vacuum permeability, i is the electrical current, d is the distance between the coils, and z is the position along the longitudinal axis of the loops. A Maxwell pair is an arrangement of two coils separated by a distance $a*3^{1/2}$ and supplied with equal but opposed current. This type of arrangement is used to generate a linear magnetic field gradient between the coils since they minimize all but the linear longitudinal term of the field (Fig.5). Table I lists the main specifications of our Maxwell pair. A TTI TSX 1820P DC power supply was used [5].

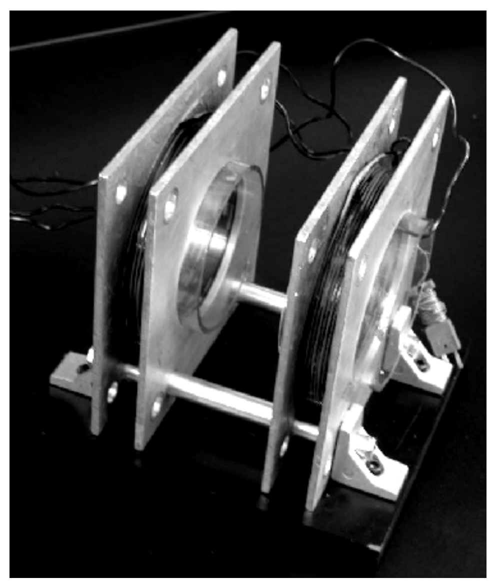

Fig. 4. Photograph of the Maxwell pair developed for the experiments

TABLE I
Specifications of the Maxwell Pair.

Wire	Cu wire, AWG 13, square section, high temperature insulation, supplied by MWS wire industries http://www.mwswire.com/
Maximum current	20 A
Maximum Gradient (20 A)	0.443 T/m
Winding	100 turns
Radius	0,0603 m

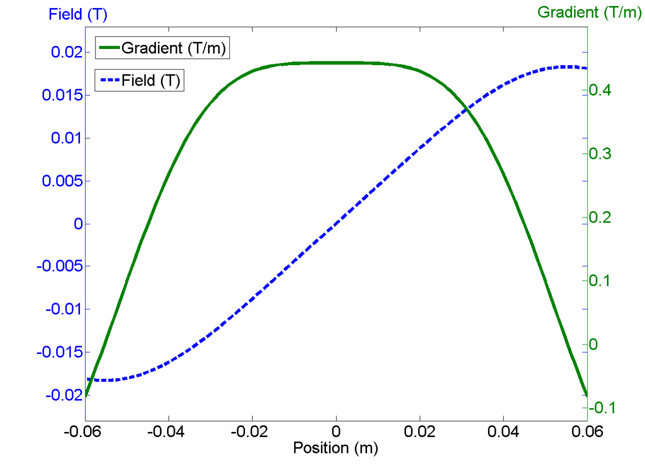

Fig. 5. Magnetic field and gradient of the Maxwell pair (I=20A)

C. Iron Oxide Suspension

The magnetic suspension was purchased from Bangs Laboratories [6]. It is an Iron Oxide magnetic particles suspension in distilled water with average size particles of 10.82 µm. For magnetite, M_{sat} = 92 emu/g (i.e. one gram of magnetite has a magnetic moment of 92 emu inside the MRI). The magnetite weigh fraction inside the particles is above 90%, corresponding to a minimum particle magnetic moment of 82.8 emu/g. Theoretical particle terminal velocity is calculated from the equilibrium of forces between magnetic force and Stokes law of fluid friction weighted by a wall effect correlation [7-9]. With a gradient of 443 mT/m induced in 10.82 µm particles with magnetic moment m = 82.8 emu/g inside a 100 µm cylindrical channel, the theoretical terminal velocity is 956 µm/s.

D. Microvascular Channel

A 100 µm diameter microvascular channel was fabricated by direct-write assembly [10] (Fig. 6). The layout of the microvascular channel is a straight 5.5 cm inlet channel branching towards two outlet channels. Since the microvascular channel is placed between the Maxwell pair inside the MRI bore, a magnetic force can be applied at will on the magnetic particles in the suspension. For this experiment, the magnetic particles suspension is first injected through the inlet of the microvascular channel, then deflected prior to the Y-intersection by the magnetic gradient generated by the Maxwell pair, causing a difference in the quantity of suspension being collected at each of the two outlets. The channel towards which the particles are deflected is defined here as the positive outlet for convenience.

The aim of the experiment is to compare the fraction or percentage of the Iron Oxide particles driven towards the positive outlet channel when the Maxwell pair is *'on'* versus *'off'*. This approach is an attempt to characterize targeting efficacy with a larger percentage of the particles reaching the positive outlet.

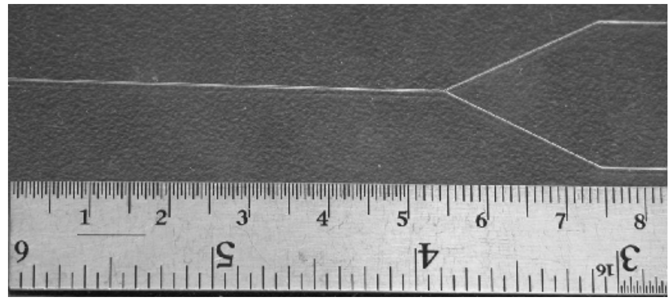

Fig. 6. Y-shaped microvascular channel fabricated by direct write assembly

The fluid velocity was set to 1.05 m/s so that the deflection of the particles submitted to the gradient strength would be half the radius of the channel (in 0.052 second) during a travel of 5.5 cm corresponding to the length of the inlet channel. In order to obtain a maximum velocity of 1.05m/s on the centerline of the channel [11], the flow was set to 0.248 ml/min using a New Era NE-1000 programmable syringe pump [12] located outside the bore of the MRI system.

E. Measurements

A volume of 1.5 ml of suspension was injected in the microvascular channel and collected inside sealed capsules before the gradient was applied. These sample pairs correspond to the control values and are referred to as *'off'* samples. Then, a 443 mT/m gradient was applied while 1.5 ml of suspension is injected and collected in new sealed capsules. These sample pairs are referred to as *'on'* samples. Finally, another 1.5 ml of suspension was injected and collected in two other capsules without any gradient applied.

This protocol was run twice for each gradient polarity (+443mT/m and -443mT/m), N = 4 for the positive outlets. The fraction of the volume of magnetic particles of each sample was measured by light absorption using a Varian Cary 50 Bio UV Visible spectrophotometer [13]. Volume fraction differences were computed between the positive and the negative outlet for each sample pair.

III. Results and Discussion

As shown in Fig. 7, a Maxwell pair providing a 443 mT/m gradient can be used to steer magnetite microparticles inside a microvascular channel. The ratio of particles is consistent with the direction towards which the magnetic force points. Nevertheless, although the method is validated, a percentage higher than 60% would be suitable in the positive outlet within the constraints imposed by clinical MRI systems. Although 85% fraction was achieved in [4], their experimental conditions differ too much from ours to allow any direct comparison. The diameter of the microvascular channel was chosen to emulate a human arteriole. Its length was maximized within the radius of the coils in order to increase steering efficiency. Nevertheless, the fluid velocity inside the channel is much higher than stated in physiological data charts and is closer to arterial flow.

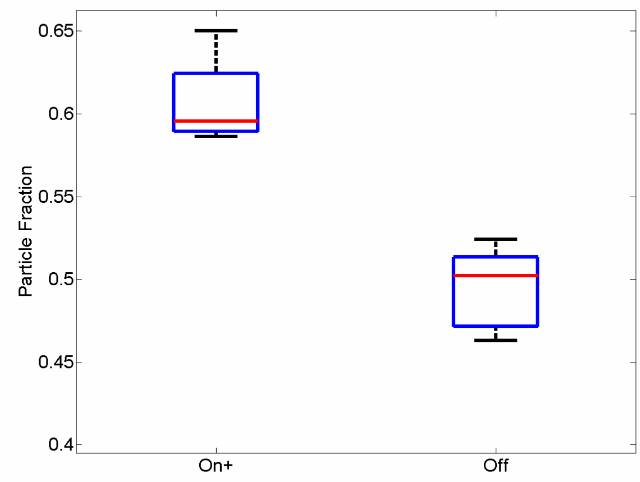

Figure 7. Box plot of the ratio of particles at the positive outlet. The 'On+' box shows the particle fraction when the gradient coil is applied (average = 0.61), the 'Off' box shows the particle fraction when the gradient coil is not applied (average = 0.48).

This decision was made in order to reduce the duration of each individual trial during the experiments and to increase the number of samples *N*. Hence, a larger proportion of particles reaching the positive outlet would be expected in physiological flow conditions.

Several more channel diameters, flow rates, and gradient amplitudes need to be tested in order to validate our models and hypotheses further.

Magnetic targeting applications are the long term motivation for the MRI-based microcirculatory navigation platform proposed here. But the same platform could be used in a shorter term to navigate macroparticles or untethered millimeter-scale magnetic devices for usage in sinuous arteries that are out-of-reach or at high risks for catheters. The same approach can also be adapted to steer a soft magnet tipped catheter or a ferrofluid filled angioplasty balloon catheter where a proof-of-concept has already be done by our group. Further works are being done to embed these applications within our Magnetic Resonance Propulsion (MRP) platform described in [14].

The next step towards these goals is systematic data gathering with the set-up described in this paper in order to set the requirements for the design and fabrication of a complete human-compatible multilayer gradient coils system [15-17].

ACKNOWLEDGMENT

The authors acknowledge support from Pr. Daniel Therriault and from Jean-François Dufresne for their support in the design and fabrication of the Microvascular Networks and Mahmood Mohammadi for his support with the light absorption measurements.

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