Fundamental Design Rules for the Conception of Microdevices to be Propelled in the Blood Circulatory System through Magnetic Gradients Generated by a Clinical MRI System

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Abstract—**Magnetic Resonance Imaging (MRI) systems are widely used to gather non-invasively images of the interior of the human body but can also be used to propel and guide special microdevices in the human body to perform specific medical tasks. As such, the design of such microdevices must be suitable to operate in such an environment and within specific constraints. This paper addresses some of the fundamental design issues including but not limited to the overall dimensions of the device, the materials used, the shape of the device, biocompatibility and toxicity, and the force induced for propulsion.**

Keywords—**Microdevice, magnetic resonance, magnetic gradient, blood circulatory system, propulsion, material, biocompatibility, fluid dynamics, minimally invasive operations**

I. Introduction

In prior studies related to the MR-Sub (Magnetic Resonance Submarine) project, we showed that magnetic gradients generated from a clinical Magnetic Resonance Imaging (MRI) system could propel a ferromagnetic core in blood [1-5]. These results suggest that special microdevices could be designed to be propelled, tracked, and controlled in the human body and especially in the blood circulatory system where more sites become accessible to perform specific medical tasks.

Endoscopes and catheters are currently widely used for minimally invasive operations but many sites in the human body are still inaccessible or at high risks due mainly to possible encumbrance of the blood vessels and tissue damages caused by friction especially for complex pathways. These risks would typically still exist for any future tethered microdevices and as such, untethered microdevices may play an important complementary role in the next generation of minimally invasive tools. Already, the advantage of an untethered device has been demonstrated with the well known camera pill (11 mm × 26 mm) used for the investigation of the gastrointestinal tract and carried by the natural movement of the digestive system [6]. When such devices must be designed to operate in the human blood vessels for tasks such as highly localized drug delivery for chemotherapy, thermal treatment of tumors at selected sites, on-site delivery of MRI contrast agents, and carriers for biosensing applications, to name but a few, the constraints and design rules for the conception of such untethered devices differ significantly from wireless devices designed to operate in the gastrointestinal tract or inside other body fluids. This paper presents an introductory description that identifies some of the main fundamental design rules for the development of such microdevices.

II. Dimensions

The first fundamental design issue is certainly the overall dimensions of the microdevices. Because the human blood circulatory system has an overall length of at least ~ 96,000 km, it is of great interest as a medium to reach the various remote locations within the human body. As such, knowing that the human blood circulatory system is made of arteries, veins and capillaries, the overall size of a particular device will hence be dependent upon the diameters of the pathways being considered.

A previous analysis [5] estimates an optimal diameter ratio between the microdevices and the blood vessels of ~0.42 with an acceptable range between ~0.23-0.57, assuming a spherical shape. In a human adult, this suggests that the choice of diameters for the design of such devices may range from ~10.5 mm when operating in the aorta, down to ~2.5-4.2 µm for operation in the capillaries, with diameters of ~0.4-1.0 mm in large arteries where most of the respective volume would typically be dedicated for propulsion purpose. As explained in the following section, because the propulsion force induced on the ferromagnetic core embedded in the microdevice is proportional to its volume, the overall size must be large enough to induce sufficient force to counteract the blood flow which is typically higher in larger diameter blood vessels. If the overall volume of the ferromagnetic core is too small respective to the diameter of the blood vessel, not enough force will be induced and the control of the microdevice will be lost. Such control loss may cause a blockage in the blood

circulatory system and lead to potential catastrophic results for the patient. On the other hand, if the microdevice is too large relative to the diameter of the blood vessel, the blood flow may be constrained and potentially cause permanent damages to the patient.

III. Propulsion

Propulsion is a fundamental requirement for such microdevice. Several means of propulsion for operating within the blood vessels have been proposed. They include the use of propellers, electromagnetic and jet pumps, membrane propulsion, and active mechanisms to crawl along the surface of the blood vessels [7]. As mentioned in the preceding section, the maximum dimensions of such microdevices prevent an embedded means of propulsion, especially when issues such as the level of complexity in the implementation, the source of power, the reduction of the volume within the device for the support of a particular medical task, and reliability are considered.

As such, a technique referred to as Magnetic Resonance Propulsion* (MRP) [3] has been proposed. The MRP concept consists of applying magnetic gradients, in our particular case from a clinical MRI system, to exert a displacement force on a ferromagnetic core. This approach does not require complex mechanisms of propulsion and sources of power to be embedded onto the microdevice, making its implementation and miniaturization much easier with more volume available to implement added functionality targeted at a specific medical task.

In the context of MRP, the torque and the propulsion force on the ferromagnetic core that can be induced by the MRI system depends as shown in Eq. 1 and Eq. 2 [8] not only on the size of the ferromagnetic core but also on the choice of the ferromagnetic material and the applied magnetic gradients.

$$\vec{\tau} = \vec{m} \times \vec{B} = V_{ferro} \vec{M} \times \vec{B}, \quad (1)$$

$$\vec{F}_{magnetic} = \vec{m} \cdot \nabla \vec{B} = V_{ferro} \cdot \vec{M} \cdot \nabla \vec{B}. \quad (2)$$

In Eqs. 1 and 2, τ is the magnetic torque (N·m), $\vec{F}_{\text{magnetic}}$ is the magnetic force (N), $\vec{m}$ is the magnetic moment of the ferromagnetic body (A·m^2), $\vec{M}$ is the magnetization of the material (A/m), V_{ferro} is the volume of the ferromagnetic body (m^3), $\vec{B}$ is the magnetic induction (T), and $\nabla \vec{B}$ is the gradient or spatial variation of the magnetic induction (T/m). In the final design, the resulting induced force must be selected taking into account the size of the targeted blood vessels and the cumulative effects of maximum blood flow, drag, buoyancy, and the gravitational force or weight of the microdevice.

Based on our previous experimental results, an estimation of the magnetic field gradients that would be required to navigate a potential microdevice in the cardiovascular system is depicted in Fig. 1. It is assumed that 50% of the volume of the spherical microdevice is made of Permendur (saturation magnetization M_{Sat} = 1.9496 × 10^6 A/m) leaving 50% of the volume for the medical application. A ratio of 0.42 between the diameter of the ferromagnetic sphere and the diameter of the blood vessel is used. The applied gradient in Fig. 1 corresponds to a nominal value, i.e. that a 100 mT/m gradient with a duty cycle of 50% would be equivalent to a gradient of 50 mT/m with a duty cycle of 100%. It should be noted that the duty cycle must often be reduced to avoid overheat of the gradient coil and to adjust the propulsion force with a pulsating blood flow.

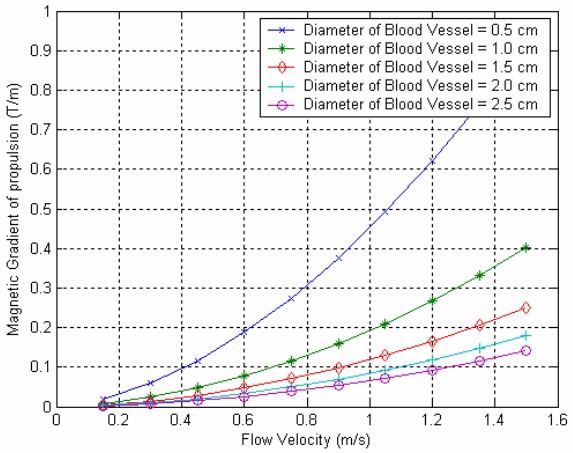

Fig.1. Optimized magnetic gradient of propulsion versus the flow velocity for various diameters of blood vessels (from [5]).

Several clinical MRI systems can generate ~40 mT/m maximum gradients. As shown in Fig. 1 and in Table 1, clinical MRI systems may be capable to propel such a device in both the ascendant and abdominal aorta according to the figures given by [9] but the gradients may be insufficient for the results provided by [10]. For large arteries, the propulsion may be problematic in some cases.

TABLE 1
Specifications of larger human blood vessels

Vessel	Diameter (cm) [9]	Min/Max Blood Velocity (cm/s) [9]	Min/Max Blood Velocity (cm/s) [10]
Aorta (ascendant)	2.0 – 3.2	0 - 63	0 - 112
Aorta (abdominal)	1.6 – 2.0	0 - 27	0 - 75
Large arteries	0.2 – 0.6	20 - 50	Not available

The designer may have a few simple options to increase the propulsion force. First, the percentage of the volume of the microdevice occupied by the ferromagnetic material may be increased beyond 50% if the volume dedicated to the medical task can be reduced accordingly. Second, the drag force can be reduced by modifying the shape of the

* Patent pending

microdevice which is discussed later in this paper. The drag force can also be reduced by modifying the blood viscosity by the injection of medication. Another option is to increase the gradients through the addition of an inner gradient coil dedicated for propulsion purpose. The gradients would have a slew rate that will not harm the patient and be synchronized with the MR imaging sequences.

The design of a microdevice to navigate in much smaller diameter blood vessels differs from larger blood vessels. In smaller diameter vessels, blood velocity decreases from more than 1 m/s in the aorta to less than 1 mm/s in the capillaries with an increase of the shear rates. Furthermore, the Reynolds number will decrease significantly from up to 10,000 in the aorta down to 0.001 in the capillaries. In smaller blood vessels, the microdevice will experience an increase of the drag coefficient. In very small vessels such as capillaries, the blood becomes inhomogeneous and as such it will operate in the presence of the Fahraeus-Lindqvist effect which tends to reduce blood viscosity. Without any doubt, clinical MRI system cannot provide sufficient gradient amplitudes to navigate a microdevice in smaller diameter vessels such as capillaries for instance, and the use of special gradient coils to upgrade the MRI system becomes essential.

III. Materials

The choice of the ferromagnetic material can also help in minimizing the overall size of the core in the microdevice. But the issues of toxicity and biocompatibility must also be considered. Table 2 provides a list of ferromagnetic materials that could be considered.

TABLE 2
Ferromagnetic materials

Material	Saturation Magnetization (T)
Fe-27%Co	2.40
Iron	2.16
Cobalt	1.72
$Nd_2Fe_{14}B$	1.61
Fe-47, 5%Ni	1.50
AISI 304L Stainless Steel	1.28
$SmCo_5$	1.05
Fe-80%Ni	1.04
Fe-50%Ni-10%Cr	0.75
Cu_2MnAl	0.70
Nickel	0.61
Fe_3O_4	0.60
$CoFe_2O_4$	0.50
Silicone MRPG	0.50
$BaFe_{12}O_{19}$	0.48
$NiFe_2O_4$	0.34
Ferrofluid of Nickel and Ferrite	0.18
$Y_3Fe_5O_{12}$	0.17
Ferrofluid with Co	0.12
Ferrofluid (Fe_3O_4)	0.07

In general and from Table 2, the materials with good magnetic properties show low biocompatibility and similarly in the best cases, materials showing good biocompatibility typically have average magnetic properties (e.g. Ferrofluid). Hence, since ferromagnetic materials resulting in sufficient induced force must be considered, biocompatibility may become an issue. Hence, techniques such as surface treatments or the deposition of a biocompatible layer can be considered to achieve biocompatibility. Nonetheless, long term biocompatibility may not be required for many applications where the microdevice is intended to operate in the human body for a relatively short period. For these particular cases, techniques such as surface treatment or the addition of a layer may not be necessary and exposing the surface of the ferromagnetic core to the blood may be acceptable for a relatively short period provided that the level of toxicity of the material is within acceptable limits.

Beside the ferromagnetic core, gravitational force may also (depending of the direction of the traveling paths of the microdevice) impede the motion of the microdevice. Hence, if it is not possible to orient the patient such as to avoid opposite gravitational force, buoyancy force may also be exploited to move the microdevice against the blood flow. As such, the addition of material with good buoyancy may also be considered in the implementation.

IV. Shapes

The shape of the microdevice is also an important aspect to consider during the design for two main reasons. First, the shape should yield a decrease of the drag force. Second, because the latency associated with closed-loop control within a clinical MRI system is relatively high, the shape must be chosen to compensate for such delay by maintaining the microdevice between the walls of the blood vessels by exploiting the blood flow pressures between the device and the walls. Furthermore, the designer should keep in mind that considering the small scale involved, simple geometries will ease the implementation of such microdevices.

Also, the pathway or trajectory of the microdevice may influence its geometry. For instance, an ellipsoidal shape would result in lower drag force and may be suitable when the induced force on the ferromagnetic core is insufficient. On the other hand, because of the presence of a strong magnetic field inside the MRI bore (1.5 T in many clinical systems), the orientation of the ferromagnetic core tends to remain constant. This means that an ellipsoidal shape would experience a low drag force in one axe but will likely experience a much larger drag force if the direction of the blood vessel varies. Therefore, such type of shapes may be considered for pathways that do not represent large variation in the direction of the movement of the microdevice. Hence, when the direction of the pathway changes significantly, a more symmetrical shape may be the best choice. A spherical shape for instance would experience the same drag force in all directions. Unfortunately, this simplicity results in an increase of the drag force compared to other shapes.

The shape of the microdevice can also be designed to experience the lowest drag force in pre-selected directions dependent upon the computed traveling pathway in the blood vessels. Another approach is to design an ellipsoidal or another low drag shape that can rotate around a spherical ferromagnetic core such as to point in the direction opposite to the direction of the blood flow at all time. Although this would be very effective, the integration of the two structures at such a scale would be very challenging.

V. Conclusions

Clinical MRI systems can generate sufficient magnetic force under specific conditions to propel a microdevice in the cardiovascular system. The propulsion force acting on the microdevice is proportional the overall size of its ferromagnetic core and the material used. The design of such microdevices must take into account the MRI system specifications and the characteristics of the human cardiovascular system. Furthermore, the design must take into account the diameters of the blood vessels used and provides a propulsion force adjusted to blood flows and angles of displacement relative to the gravitational force. Buoyancy and reduction of the drag forces are other parameters that must be considered. The delays in the closed-loop control system pose additional technical issues that must also be addressed during the design. Finally, toxicity, biocompatibility, and the type of the medical task considered are other factors that may influence the design of such microdevices.

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