Available online at www.sciencedirect.com
ScienceDirect
Journal of Magnetism and Magnetic Materials 310 (2007) 2883–2885
Journal of magnetism and magnetic materials
www.elsevier.com/locate/jmmm

Development of control system for magnetically targeted drug delivery

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Available online 28 November 2006

Abstract

In this paper, we described the development of control system using multiple magnets for magnetically targeting drug delivery. Our previous study has investigated the navigation and accumulation of the magnetic particles in the Y-shaped glass tube with single branching point. Here, we extended the previous study towards much more realistic system of blood vessel and considered the feasibility and efficiency of the navigation and accumulation of the magnetic particles. For the experimental work in more realistic model, connected Y-shaped glass tube with multiple branching points was used to understand the behavior of magnetically targeted delivery when we optimize the magnetic control system. To avoid or reduce the interaction effect between magnetic particles and inner surface of glass tube, it was finally found that adjustment of the on-and-off interval of applying the magnet force could be one promising answer.

PACS: 47.63.mh; 85.70.kh; 87.50.Mn

Keywords: Magnetic drug targeting; Magnetic particle; Magnetic control system

1. Introduction

In conventional systemic drug delivery method, the drug is administered by intravenous injection; it then travels to the heart from where it is pumped to all regions of the body. When the drug is aimed at a small target region, this method is extremely inefficient and leads to require much larger doses than those being necessary. In order to overcome this problem, a number of targeted drug delivery methods have been developed. One of these, magnetically targeted drug delivery system (MT-DDS) will be a promising way, which involves binding a drug to small biocompatible magnetic particles, injecting these into the blood stream and using a high-gradient magnetic field to pull them out of suspension in the target region. In the present work, we describe an in vitro experimental work and a theoretical analysis for MT-DDS with emphasis on the modified navigation method aiming at the improvement of the navigation efficiency to the desired site. In the previous paper [1,2], it was found that the navigation efficiency reached only 54%, and 27% of the magnetic particles were retained onto the inner surface of the tube before going to the branching point. In the present paper, we report that proper adjustment of the on-and-off interval of applying the magnet force is one of the promising ways to improve the navigation efficiency, because the position of the particles before going to the first branching point is one of the dominant factors to decide the final position of the particles in the circulatory system.

2. Analysis technique and result of model flow system

Computational fluid dynamics analysis using ANSYS 9.0 was performed for the Y-shaped model flow system of blood vessel where the flow averaged velocity is 400 mm/s, inner diameter of flow vessel is 2 mm, and the flow lengths both between inlet and branching point, and branching point and outlet is 50 mm (schematic in shown Fig. 1). These velocity and geometry correspond to those of artery in the human circulatory system. The analysis result shows that the property of this flow demonstrates the laminar flow, and the flow velocity reached the maximum value of 250 mm/s at the front part of the branching point. The calculated streamline in the Y-shaped model flow system was shown in Fig. 1. Since the flow region with the same

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0304-8853/$ - see front matter
doi:10.1016/j.jmmm.2006.11.124

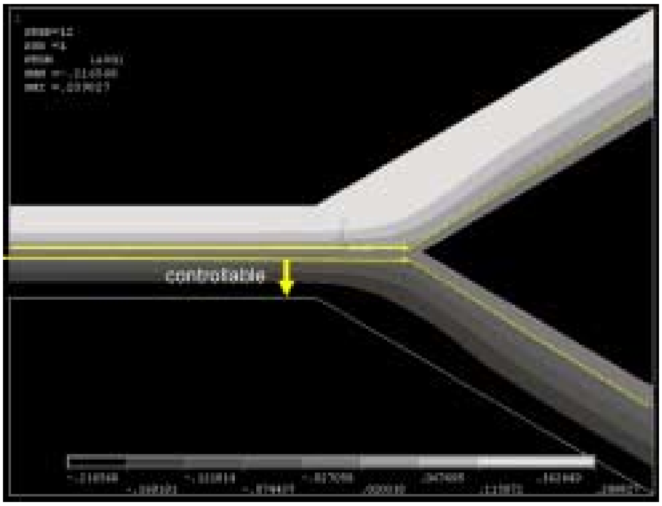

Fig. 1. Analysis of streamline.

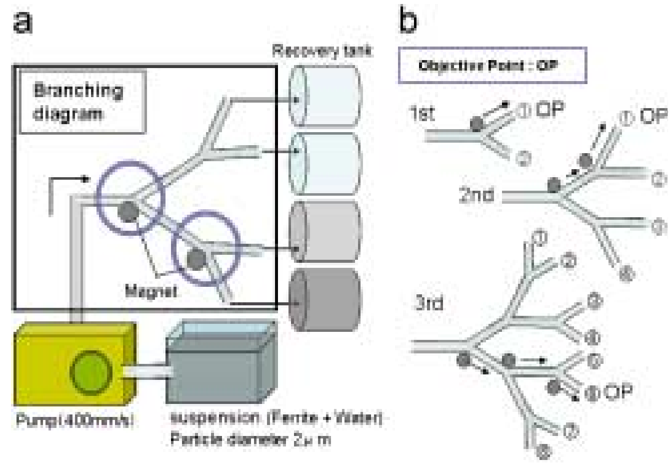

Fig. 2. Schematic illustration of set up.

direction was depicted in the same color, the particles floating in upper region (white region in this figure) of the tube go to the upper part of the tube after the branching point (only white color was seen in the upper part of the tube). If we want to navigate the magnetic particles into the lower part of the tube after branching point, the particles should be attracted to the lower half of the tube before going to the branching point. Once particles are attracted to the lower part of the tube prior to the branching point, they naturally go to the lower part unless particles are retained at the very close point to the inlet of the tube (left part of Fig. 1). Furthermore, in order to effectively navigate the particles to the desired part of the tube with multiple branching points, interaction between the magnetic fields generated by the magnet placed at the next branching point should be taken into account. To avoid or reduce the interaction effect, adjustment of the on-and-off interval of applying the magnetic force could be one promising answer.

3. Navigation test procedure and its result

In order to properly estimate the navigation efficiency and thus design the improved methodology of the navigation, the model flow system was designed and constructed as shown in Fig. 2-a. The flow averaged velocity, inner diameter of flow vessel, and the flow lengths are all the same as the system for the computational fluid dynamics analysis. The employed magnetic particle and permanent magnet were Mn–Zn ferrite with the size of $2\,\mu m$ and neodymium magnet (magnetic flux density: 0.25 T, gradient: 26 T/m). To improve the navigation efficiency, adjustment of the on-and-off interval of applying the magnet force was made in such manner as follows: 30 s is ON and gradually OFF for the subsequent 10 s at the first branching point, 30 s ON just after passing the first branching point. After the navigation, navigation efficiency was estimated by ICP-AES for the collected particles at the final position after thoroughly dissolving the particles.

Navigation efficiency of the magnetic particles under the model flow system was summarized in Table 1. The obtained values were calculated results of the accumulated fraction of the magnetic particle at the final part of the tube for the each Y-shaped tube with different branching points. The navigation efficiency for ferromagnetic particle is calculated using

$$\text{navigation efficiency (\%)} = \frac{\text{quantity of the ferromagnetic particle at the final part of the branch tube (outlet)}}{\text{concentration of all the injected ferromagnetic (inlet)}} \times 100. \quad (1)$$

The circled numbers from 1 to 8 correspond to the final part of the tube shown in Fig. 2(b).

When no magnet was placed at the branching point, it was found that the fraction of the accumulated magnetic particles is the same. For instance, when we try the navigation test using the tube with eight final parts, the navigation efficiency without magnet is 12.5%. It can be concluded from the Table 1 that experimentally obtained navigation efficiency reached about 80%, because the efficiency shows 85% after one branching point, 70% after two branching points ($0.80 \times 0.80 = 64\%$), and 50% after three branching points ($0.80 \times 0.80 \times 0.80 = 51\%$). When optimization of the magnet position was solely employed as the magnetically navigation method, the navigation efficiency reached 54%, and 27% of the magnetic particles

Table 1
Navigation efficiency at each outlet (numbers 1–8)

1st	1: (objective point: OP) 85.5%				2 14.5%			
2nd	1: (OP) 69.4%		2 5.4%		3 13.6%		4 11.6%	
3rd	1 6.3%	2 5.9%	3 4.3%	4: (OP) 8.6%	5 13.8%	6 49.3%	7 8.8%	8 3.0%

were retained onto the inner surface of the tube before going to the branching point. This result indicated that adjustment of the on-and-off interval of applying the magnet force is one of the promising ways to improve the navigation efficiency.

4. Summary

By performing the computational fluid dynamics analysis using ANSYS 9.0, it was found that once particles are attracted to the lower part of the tube prior to the branching point, they naturally go to the lower part unless particles are retained at the very close point to the inlet of the tube. It was also concluded that proper adjustment of the on-and-off interval of applying the magnet force is one of the promising ways to improve the navigation efficiency.

References

[1] F. Mishima, S. Takeda, Y. Izumi, S. Nishijima, IEEE Trans. Appl. Supercond. 16 (2006) 1539–1542.
[2] S. Takeda, F. Mishima, B. Terazono, Y. Izumi, S. Nishijima, IEEE Trans. Appl. Supercond. 16 (2006) 1543–1546.