

Experimental Study on Capturing of Magnetic Nanoparticles Transported in an Implant Assisted Cylindrical Tube under Magnetic Field

Anurag Gaur, Nidhi, Shashi Sharma

Abstract—Targeted drug delivery is a method of delivering medication to a patient in a manner that increases the concentration of the medication in some parts of the body relative to others. Targeted drug delivery seeks to concentrate the medication in the tissues of interest while reducing the relative concentration of the medication in the remaining tissues. This improves efficacy of the while reducing side effects. In the present work, we investigate the effect of magnetic field, flow rate and particle concentration on the capturing of magnetic particles transported in a stent implanted fluidic channel. Iron oxide magnetic nanoparticles (Fe_3O_4) nanoparticles were synthesized via co-precipitation method. The synthesized Fe_3O_4 nanoparticles were added in the de-ionized (DI) water to prepare the Fe_3O_4 magnetic particle suspended fluid. This fluid is transported in a cylindrical tube of diameter 8 mm with help of a peristaltic pump at different flow rate (25-40 ml/min). A ferromagnetic coil of SS 430 has been implanted inside the cylindrical tube to enhance the capturing of magnetic nanoparticles under magnetic field. The capturing of magnetic nanoparticles was observed at different magnetic field, flow rate and particle concentration. It is observed that capture efficiency increases from 47-67% at magnetic field 2-5kG, respectively at particle concentration 0.6mg/ml and at flow rate 30 ml/min. However, the capture efficiency decreases from 65 to 44% by increasing the flow rate from 25 to 40 ml/min, respectively. Furthermore, it is observed that capture efficiency increases from 51 to 67% by increasing the particle concentration from 0.3 to 0.6 mg/ml, respectively.

Keywords—Capture efficiency, Implant assisted-Magnetic drug targeting (IA-MDT), Magnetic nanoparticles, *in vitro* study.

I. INTRODUCTION

DRUG targeting has become an active area of medical research in recent years. In this area, magnetic drug targeting (MDT) is one of the most promising drug target techniques. The targeting of drugs to a specific region of the human body can be significantly enhanced by attaching the drug to magnetic particles. Compared with traditional chemotherapy, the accumulation and retention of the magnetic drug carrier particles can be enhanced by using an external magnetic field, which is focused on the area of the tumour. Furthermore, MDT improves the effectiveness of the treatment by reducing the total dose needed to reach the therapeutic benefit, exposure of healthy tissue to the treatment

A. Gaur* and Nidhi are with the Department of Physics, National Institute of Technology, Kurukshetra-136119, Haryana, India. (*corresponding author to provide phone: +91-1744-233496; fax:+91-1744-238050; e-mail: anuragdph@gmail.com).

Shashi Sharma is with Department of Mathematics, Indian Institute of Technology, Roorkee, India

and side effects [1], [2]. This targeted technique approaches lead to using an external magnetic field source to capture and retain magnetic drug carrier particles (MDCPs) at a specific site after being injected into the body. Many studies have shown that MDT is relatively safe and effective methodology for targeting drugs to a specific site in the body [3]-[5]. However, there are some significant limitations of MDT. One limitation associated with MDT is the gradient problem, i.e., the magnetic force requires a magnetic field *gradient*. Thus it can be difficult of using external magnets *only* to target areas deep within the body, without targeting the surface more strongly [6], [7]. In general, the retention of the MDCPs is quite low due to the relatively weak nature of the magnetic force, which must overcome the hydrodynamic force. This problem is exacerbated by the fact that the strength of the magnetic field generated from a permanent magnet decreases sharply with distance. Hence, the magnetic force becomes significantly diminished as the depth of the target site increases, making sites that are more than a few centimetres deep in the body difficult to target. Nevertheless, some recent research on the MDT approaches shown that these two limitations can be circumvented by simply using a ferromagnetic implant, such as a wire or seed, in conjunction with the MDCPs and the external magnetic field source [8]–[11]. The IA-MDT concept was first reported by [5] followed by different studies using various types of implants. Chen et al. [12], [13] theoretically evaluated the IA-MDT of drug encapsulated nanoparticles using intravascular stent, while *in vitro* experiments along with theoretical approaches have evaluated the IA-MDT using ferromagnetic stents by [14]–[18]. This IA-MDT approach consists of three components: first, it uses standard magnets that provide a long-range, low-gradient magnetic field. Second, it uses an implant that creates a localized high-gradient magnetic field when it is magnetized by a low-gradient magnetic field. Third, it uses MDCPs designed to aggregate and/or collect only when and where they come across a high-gradient magnetic field.

In view of above, we investigate the effect of magnetic field, flow rate and particle concentration on the capturing of magnetic particles transported in a stent implanted fluidic channel. The obtained results show that capture efficiency increases as we increase the magnetic field and particle concentration. However, decrease in capture efficiency is observed by increasing the flow rate.

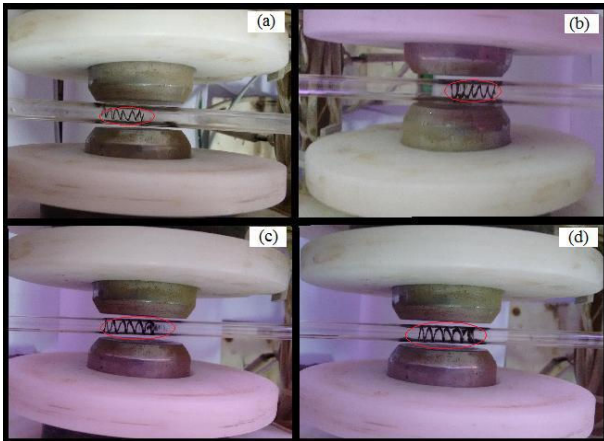


Fig. 1 Images of captured Fe_3O_4 nanoparticles at different magnetic fields: (a) 2, (b) 3, (c) 4 and (d) 5 kG at particle concentration 0.6mg/ml and at flow rate 30 ml/min an implant assisted channel

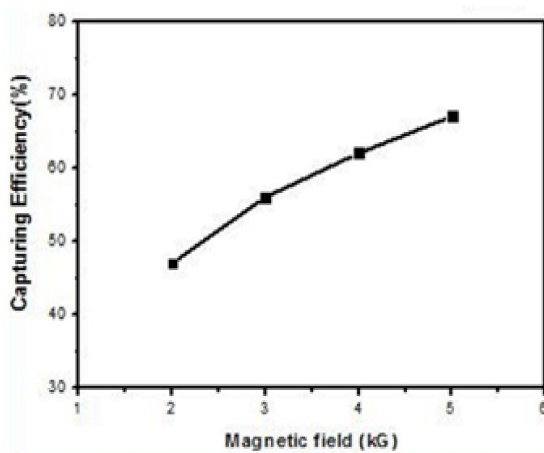


Fig. 2 Capture efficiency versus magnetic field curve of Fe_3O_4 nanoparticles of an implant assisted channel at different magnetic fields (0-5 kG)

II. EXPERIMENTAL

Iron oxide magnetic nanoparticles (Fe_3O_4) nanoparticles were synthesized via co-precipitation method and the particle size, calculated through Scherrer's formula by using XRD data, is found to be 13 nm. The saturation magnetization of Fe_3O_4 nanoparticles measured through vibrating sample magnetometer (VSM), is ~ 15.5 emu/g. The synthesized Fe_3O_4 nanoparticles were added in the de-ionized (DI) water to prepare the Fe_3O_4 magnetic particle suspended fluid. The experimental set-up consisting of a coiled wire (used as a stent) inserted into a glass tube. The coil was made-up from Kanthal wire, a ferromagnetic FeCrAl alloy and diameter of coiled wire was 5mm and length was 2cm. Then prepared fluid is transported in stent implanted cylindrical tube of diameter 8 mm with help of a peristaltic pump at different flow rate (25-40 ml/min). The weight of magnetic nanoparticles in 100 ml solution of inlet beaker was added through weighing the particles by weighing machine. The

weights of particles in outlet beaker were calculated by filtering the remaining captured particles. After that, dried this captured particles and weighed on weighing machine. The capturing of magnetic nanoparticles was observed at different magnetic fields (2-5 kG). The images of captured particles at different magnetic field, flow rate and particle concentration were recorded by a high resolution digital camera.

III. RESULTS AND DISCUSSION

Effect of Magnetic Field on Capture Efficiency

Fig. 1 shows the capturing of magnetic nanoparticles transported in a stent implanted fluidic channel under the influence of different magnetic field.

The value of capture efficiency (CE) is calculated by the ratio of weight of captured particle and total weight of particles included in the inlet beaker. The below formula is used to calculate the capture efficiency (η),

$$\eta = \frac{W_{in} - W_{out}}{W_{in}} \quad (1)$$

where W_{in} and W_{out} are the weight of particles entering and leaving the channel.

The value of capture efficiency, calculated using above formula is found to be 47, 56, 62 and 67% at magnetic field 2, 3, 4 and 5kG, respectively at particle concentration 0.6mg/ml and at flow rate 30 ml/min and shown in Fig. 2. This shows that capture efficiency increases as we increase the magnetic field. The increase in magnetic field is due to magnetophoretic force, experienced by the magnetic particles increases and also the stent was increased the gradients locally and thereby improve the magnetic force and hence CE increases. This force is attractive in nature and mainly responsible to capture or attract the magnetic particles towards magnet (targeted region) which results the enhancement in capture efficiency.

Effect of Flow Rate on Capture Efficiency

Fig. 3 shows the capturing of magnetic particles transported in a stent implanted fluidic channel at different flow rates.

The value of capture efficiency, calculated by using (1) is observed to be 65, 54, 47, and 44 % at flow rates 25, 30, 35 and 40 ml/min, respectively at particle concentration 0.6mg/ml and at magnetic field 3kG and shown in Fig. 4. This shows that capture efficiency decreases as we increase the flow rates. At the higher flow rates, the magnetic force induced by the magnets was not capable to overcome the hydrodynamic drag forces and resulting in a decreased CE. As the stent present in the glass tube, significant amounts of the MDCPs were captured at the stent surface even at the higher flow rates. Hence, the magnetic field gradient produced by the stent indeed improved the magnetic force on the MDCPs, results in higher CE.

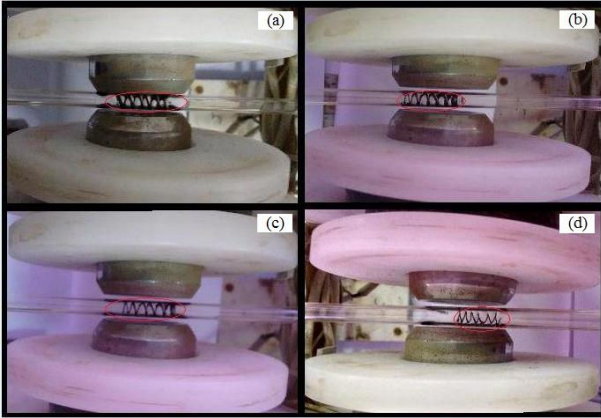


Fig. 3 Images of captured Fe_3O_4 nanoparticles at different flow rates: (a) 25, (b) 30, (c) 35 and (d) 40 ml/min at particle concentration 0.6mg/ml and at magnetic field 3kG in an implant assisted channel

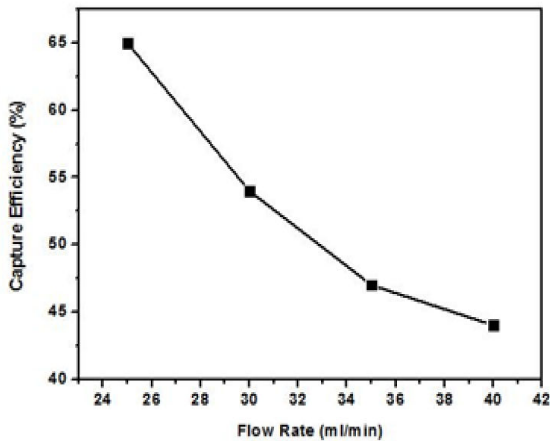


Fig. 4 Capture efficiency versus flow rate curve of Fe_3O_4 nanoparticles of an implant assisted channel at different flow rates (25-40ml/min)

Effect of Concentration of Particles on Capture Efficiency

Fig. 5 shows the capturing of magnetic nanoparticles transported in a stent implanted fluidic channel with different concentration of particles.

It is observed that the capture efficiency of magnetic particle increases as the concentration of magnetic particle in the fluid increases. The capture efficiency calculated by using (1) is found to be 51, 54, 60 and 67 % for 0.3, 0.4, 0.5 and 0.6 mg/ml particle concentration, respectively, at flow rate 30mg/ml and at magnetic field 3kG and shown in Fig. 6. By increasing the particle concentration is due to more magnetophoretic force experienced by increased number of magnetic particles and also the stent was increased the gradients locally which results the enhancement in capture efficiency.

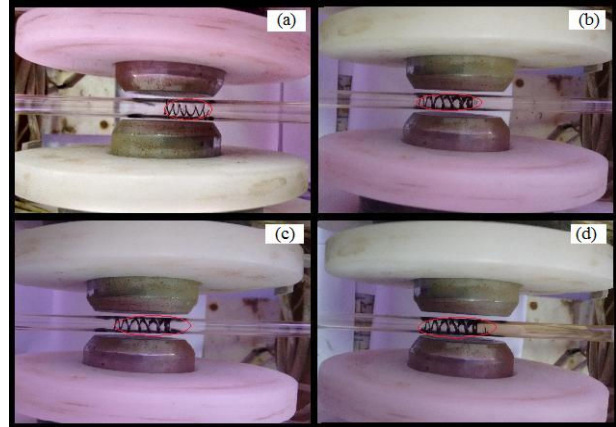


Fig. 5 Image of captured Fe_3O_4 nanoparticles at different particle concentration: (a) 0.3, (b) 0.4, (c) 0.5, and (d) 0.6 mg/ml at flow rate 30mg/ml and at magnetic field 3kG in an implant assisted channel

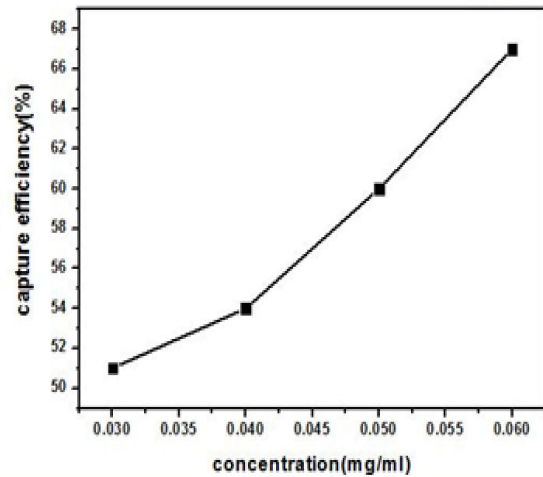


Fig. 6 Capture efficiency versus particle concentration curve of Fe_3O_4 nanoparticles of an implant assisted channel at different concentrations (0.3-0.6 mg/ml)

IV. CONCLUSIONS

In summary, the experiments were performed to study the effect of magnetic field, flow rate and particle concentration on capture efficiency of magnetic nanoparticles transported in a stent implanted cylindrical tube. The capture efficiency increases from 47-67 % at magnetic field 2-5kG, respectively at particle concentration 0.6mg/ml and at flow rate 30 ml/min. However, the capture efficiency decreases from 65 to 44 % by increasing the flow rate from 25 to 40 ml/min, respectively. Furthermore, it is observed that capture efficiency increases from 51 to 67 % by increasing the particle concentration from 0.3 to 0.6 mg/ml, respectively. Enhancement in capture efficiency by increasing the magnetic field and particle concentration is due to enhanced magnetophoretic force experienced by magnetic particles, which results the enhancement in capture efficiency.

REFERENCES

- [1] V. P. Torchilin, "Drug targeting." *Eur J. Pharm Sci*, Vol. 11, 2000, pp. 81.
- [2] D. J. A Crommelin, G. Scherphof, G. Storm, "Active targeting with particulate carrier systems in the blood compartment." *Adv drug deliver rev*, Vol. 17, 1995, pp. 49.
- [3] M. O. Avilés, A. D. Ebner, J. A. Ritter "In vitro study of magnetic particle seeding for implants assisted-magnetic drug targeting." *J. Magn. Mater.*, Vol. 320, 2008, pp. 2640.
- [4] M. O. Avilés, A. D. Ebner, J. A. Ritter "In vitro study of magnetic particle seeding for implant-assisted-magnetic drug targeting: Seed and magnetic drug carrier particle capture." *J. Magn. Mater.*, Vol. 321, 2009, pp. 1586.
- [5] J. A. Ritter, J. A. D. Ebner, K. D. Daniel, K. Stewart "Application of high gradient magnetic separation principles to magnetic drug targeting" *J. Magn. Mater.*, Vol. 280, 2004, pp. 184.
- [6] A. D. Grief, G. Richardson "Mathematical modelling of magnetically targeted drug delivery" *J. Magn. Mater.*, Vol. 293, 2005, pp. 455.
- [7] M. Babincová, D. Leszczynska, P. Sourivong, P. Babinec, "Lysis of photosensitized erythrocytes in an alternating magnetic field" *J. magn.Mater.*, Vol. 225, 2001, pp. 194.
- [8] G. H. Iacob, O. Rotariu, H. Chiriac "A possibility for local targeting of magnetic carriers" *J. Optoelectron. Adv. M*, Vol. 6, 2004, pp. 713.
- [9] G. Iacob, O. Rotariu, N. J. C Strachan, U.O. Hafeli "Magnetizable needles and wires-modeling an efficient way to target magnetic microspheres *in vivo*." *Biorheology*, Vol. 41, 2004, pp. 599.
- [10] B. B. Yellen, Z. G. Forbes, D. S. Halverson, G. Fridman, K. A. Barbee, M. Chorny, G. Friedman "Targeted drug delivery to magnetic implants for therapeutic applications." *J. magn.Mater.*, Vol. 293, 2005, pp. 647.
- [11] O. Rotariu, N. J. C. Strachan "Modelling magnetic carrier particle targeting in the tumor microvasculature for cancer treatment." *J. Magn. Mater.*, Vol. 293, 2005, pp. 639.
- [12] H. Chen, A. D. Ebner, A. J. Rosengart, M. D. Kaminski, J. A. Ritter, "Analysis of magnetic drug carrier particle capture by a magnetizable intravascular stent: 1. Parametric study with single wire correlation." *J. magn.Mater.* Vol. 284, 2004, pp. 181.
- [13] H. Chen, A. D. Ebner, A. J. Rosengart, M. D. Kaminski, J. A. Ritter "Analysis of magnetic drug carrier particle capture by a magnetizable intravascular stent—2: parametric study with multi-wire two-dimensional model." *J. magn.Mater.*, Vol. 293, 2005, pp. 616.
- [14] M. O. Avilés, A. D. Ebner, H. Chen, A. J. Rosengart, M. D. Kaminski, J. A. Ritter, "Theoretical analysis of a transdermal ferromagnetic implant for retention of magnetic drug carrier particles." *J. magn.Mater.*, Vol. 293, 2005, pp. 605.
- [15] M. O. Avilés, A. D. Ebner, J. A. Ritter "Ferromagnetic seeding for the magnetic targeting of drugs and radiation in capillary beds." *J. magn.Mater.*, Vol. 310, 2007, pp. 131
- [16] M. O. Avilés, A. D. Ebner, H. Chen, A. J. Rosengart, M. D. Kaminski, J. A. Ritter " *In vitro* study of ferromagnetic stents for implant assisted-magnetic drug targeting" *J. Magn. Mater.*, Vol. 311, 2007, pp. 306.
- [17] M. O. Avilés, J. O. Mangual, A. D. Ebner, J. A. Ritter, "Isolated swine heart ventricle perfusion model for implant assisted-magnetic drug targeting." *Int. j. pharm.*, Vol. 361, 2008, pp. 202.
- [18] Z. G. Forbes, B. B. Yellen, K. Barbee, G. Friedman "An approach to targeted drug delivery based on uniform magnetic fields." *Magnetics, IEEE Transactions on*, Vol. 39, 2003, pp. 3372.