Biomed Tech 2013; 58 (Suppl. 1) © 2013 by Walter de Gruyter · Berlin · Boston. DOI 10.1515/bmt-2013-4039

SIMULATION OF MAGNETIC NANOPARTICLES IN BLOOD FLOW FOR MAGNETIC DRUG TARGETING APPLICATIONS

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Abstract: *A new magnetic drug targeting model of placing an array of permanent magnets and coils inside hollow organs of the body was developed. This gives the possibility to target e. g. prostate carcinoma, oesophagus adenocarcinoma or bile duct Klatskin tumours with drugs bounded to magnetic nanoparticles. The targeting model uses FEM based simulations and describes the interaction of an external magnetic field with single suspended superparamagnetic iron oxide (SPIO) nanoparticles in blood flow, thereby, quantifying the amount of the accumulated SPIO at a vessel wall.*

Keywords: *SPIO, FEM, magnetic drug targeting*

Introduction

The interaction of magnetic fields with single suspended superparamagnetic iron oxides (SPIO) nanoparticles in blood flow is described in a new magnetic targeting simulation model. Based on FEM simulations, this model traces the SPIO in a vessel and counts the number of SPIO that are adsorbed at the vessel wall facilitating a quantification of the efficiency of the targeting system. It has been constructed for endoluminal tumours (e. g. prostate carcinoma, oesophagus adenocarcinoma or bile duct Klatskin tumours) which permit a minimally invasive endoscopic insertion of permanent magnets and coils very close to the tumour site where a strong magnetic field and a high magnetic field gradient are achieved. The simulation model was applied to the respective physical and chemical properties of SPIO, the blood flow properties and different magnetic field configurations generated by coils and permanent magnets.

Methods

For the FEM simulations, which were performed with the COMSOL Multiphysics (Stockholm, Sweden) code system, the Navier-Stokes equation of a non-Newtonian fluid including the magnetic force acting on the SPIO was used [1,2]:

$$\rho \frac{D\vec{v}}{Dt} = \nabla \bullet (\eta(\gamma') \bullet (\nabla \vec{v} + (\nabla \vec{v})^T) + \nabla \vec{p}_{tot} \bullet \vec{I} + \mu_0 M \nabla \vec{H} \tag{1}$$

where

$$\frac{D}{Dt} = \frac{\partial}{\partial t} + \vec{v} \bullet \nabla \ , \tag{2}$$

$$\gamma' = \frac{dv}{dx} \ . \tag{3}$$

Here, v is the velocity, p_{tot} is the hydrostatic pressure, γ is the shear rate, η is the dynamic viscosity, ρ is the density, H is the magnetic field, M is the magnetization and μ_0 is the vacuum permeability.
In Tab. 1 the parameters used for the simulation of a capillary model are listed.

Table 1: Parameters used to simulate the capillary model.

Parameter	Value	Unit
Blood density	1060	kg/m^3
Dynamic viscosity	1.2	mPa·s
Capillary diameter	40	µm
Blood velocity	0.03	cm/s
Magnetic field	0.3	T
Magnet diameter	6	mm
Magnet height	12	mm
SPIO saturation magnetisation	256	kA/m
SPIO susceptibility	5.2	-
SPIO core diameter	11.5	nm
SPIO hydrodynamic diameter	40	nm

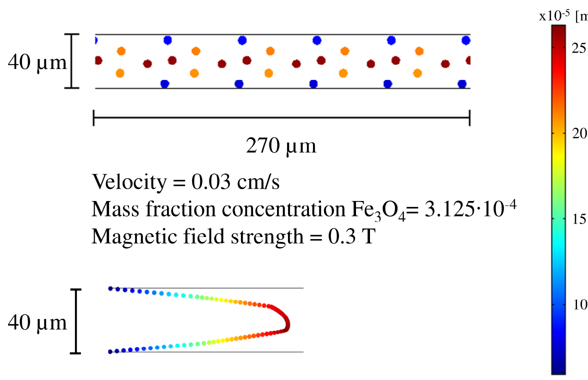

Figure 1: Simulation of the capillary model with single suspended SPIO (Fe_3O_4). The colours of the SPIO indicate their velocity value according to the velocity profile shown in the bottom of the picture, see text.

Fig. 1 displays the capillary simulation model. A short part of a capillary (270 µm in length) is shown. Beneath the capillary, a permanent magnet was placed in a distance of 350 µm to the capillary's wall (not shown in this picture, the properties of the magnet system are listed in Tab. 1). Due to the interaction with the magnetic field the

SPIO are attracted to the vessel wall where they are adsorbed. The colours of the SPIO indicate their velocity value according to the velocity profile shown in the bottom of the picture.

The influence of the geometry of the applied magnetic field was investigated by changing the setting of the permanent magnet at different angles and with coils.

The model was applied in animal trials with pigs in which an amount of SPIO equivalent to the simulations was injected intravenously. Various in-house assembled arrays of magnets and coils were inserted into the bile duct. After a circulation time of 60 min, the pigs were euthanized and the arrays were removed. In this way, further particle transport due to blood circulation or magnetic field attraction could be avoided in order not to falsify the results of the subsequent investigations. Then, magnetic resonance imaging was performed to identify regions where the magnetic nanoparticles were accumulated. Tissue samples were extracted and cryopreserved for a magnetic behaviour investigation with a Superconducting Quantum Interference Device (SQUID).

Results

For the parameters listed in Tab. 1, a total iron adsorption of 5.5×10^{-4} mg to the vessel wall within one hour was calculated for a SPIO mass fraction of 3.125×10^{-4}. In this way, 10.7 % of the total amount of SPIO could be accumulated at the vessel wall.

SQUID measurements of the extracted tissues from the animal experiments confirmed the accumulation of SPIO at the target site, where the magnetic behaviour of tissues changed from diamagnetic to paramagnetic (Fig. 2).

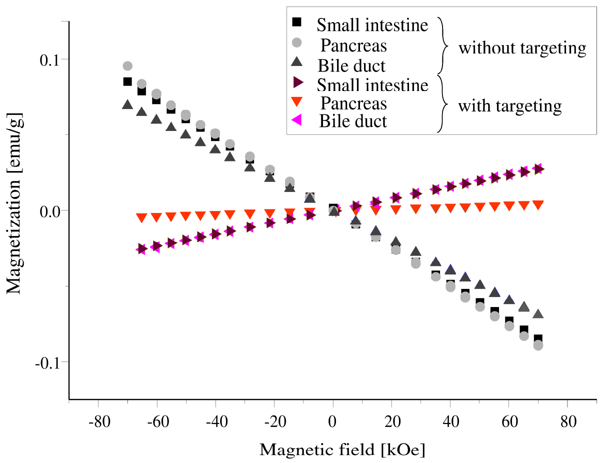

Figure 2: Magnetisation measurements on tissues with and without previous targeting. The diamagnetic behaviour (negative slope) of the sample changes to a paramagnetic behaviour (positive slope) after targeting procedures.

Discussion

A novel simulation model for magnetic drug targeting was presented and applied in animal experiments. The theoretical results predict approximately the strength and orientation of the magnetic field necessary for the adsorption of SPIO to a vessel wall of a capillary. The mathematical characterisation proved to be suitable for further investigation with advanced geometries and consideration of more factors of influence, e. g. the particles interaction.

The experimental study described the local accumulation of SPIO in the bile duct and the surrounding tissue after application of the targeting system and confirmed the results of the simulations. Due to the big significance of the geometry of the magnetic field for an efficient accumulation of SPIO at a target site, various permanent magnet and coil configurations were simulated in order to estimate their capabilities to match the targeting requirements. In this way, the targeting efficiency could be enhanced.

The simulations show a way for prediction of the delivery rate of drug targeting systems which can help to tremendously improve the efficacy of current treatment.

Bibliography

[1] R. E. Rosensweig et al., *Ferrohydrodynamics*, New York: Dover Publications, (1997).

[2] S. Odenbach, *Magnetoviscous Effects in Ferrofluids*, Berlin: Springer, (2002).