Magnetic Fields and Materials for Medical Bone Reconstruction, Assisted by Advanced Finite-Element Simulations

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Abstract: We address the use of magnetic fields, forces, and materials for medical purposes. In particular, the treatment of osteochondral lesions is aimed for. To support ongoing activities in this field of research, last advances in using Finite Element Analysis (FEA) for the simulation of relevant processes, like magnetic targeting and magnetic fixation are reported. The availability of advanced multiphysics FEA software gives rise to a comprehensive descriptions of such complex scenarios both for in-vitro experiments and in-vivo applications.

Keywords: magnetic targeting, magnetic fixation, medical bone reconstruction, multiphysics finite element simulation, MAGISTER

1 Introduction

According to their fundamental role in nature, electromagnetic fields and forces are intensively used to study and influence materials properties in science. High magnetic fields have been developed to a widely used research tool for many disciplines of natural sciences. Electromagnetic forces provide unsubstitutable aid in technology and everyday life. Applications range from public transport to industrial machining purposes and also to advanced medical treatment methods such as forced diffusion of magnetic nanoparticles in blood vessels. The Forschungszentrum Dresden Rossendorf (FZD) is engaged in several research programs which exploit magnetic fields for investigations on the structure of matter, safe generation of energy, and for medical research. The Dresden High Magnetic Field Laboratory (HLD) [1] at the FZD contributes to several of these research directions. In the recent years, we have reported on our activities in the design and operation of pulsed magnets and their pulsed power supplies, works which have been essentially assisted by FEA. This has been reported in various publications [2, 3].

Here, in cooperation with our partners from Istituto Ortopedico Rizzoli and Institute of Nanostructured Materials (ISMN-CNR) in Bologna, Italy, we address activities of the recently started multidisciplinary EU-project MAGISTER [4]. In the framework of this project, scientists from 21 institutions and companies all over Europe are working on the application of magnetically assisted transport to treat bone injuries and osteochondral lesions. Here, we briefly describe the general aspects of the MAGISTER research program and present results related to FEA simulations.

2 Magnetic targeting

Magnetic targeting has been introduced as an innovative method in nanomedicine, motivated first of all for cancer treatment. It comprises that intravascularly injected magnetic nanoparticles (MNPs) loaded with a drug component are directed by magnetic fields to a certain location in the body. By this, one achieves high concentrations of the certain drug substance at the specific site.

In the framework of the EU-project MAGISTER which aims for innovative methods to treat bone and osteochondral injuries more effectively, the driving idea is the development and use of conceptually new biocompatible and bioactive magnetic scaffolds which can be manipulated *in situ* by means of magnetic forces. These scaffolds are expected to serve for multipurpose delivery in order to repair large defects and lesions of bones and cartilages. The magnetic moment of scaffolds allows for controlled deposition of tis-

sue growth factors, cells or other therapeutic agents at the cite of the injury. The latter are delivered by MNPs guided by external magnetic fields. MNPs are absorbed by the magnetic scaffold via magnetic forces, or in simple words, the scaffolds act like a fixed "station" and nanoparticles like "transport shuttles".

The presence of a magnetic scaffold modifies the local field profile and causes large local magnetic field gradients, and thus, leads to high magnetic forces and a subsequent fixation of MNPs. The motion of MNPs inside micro channels of a scaffold may be described by diffusion equations [5, 6], whereas ferrofluid dynamics may be used to describe motion of the MNPs in larger vessels [7].

3 Magnetically assisted diffusion and hydrodynamics of MNPs.

The force $\mathbf{F}_{\text{mag}}$ and torque $\mathbf{T}_{\text{mag}}$ on a particle in a magnetic field $\mathbf{B}$ are given by formulae $\mathbf{F}_{\text{mag}} = (\mathbf{m}\nabla)\mathbf{B}$ and $\mathbf{T}_{\text{mag}} = \mathbf{m} \times \mathbf{B}$, where $\mathbf{m}$ is the magnetic moment of the particle. However, magnetite particles of diameter smaller than 30 nm, as can be used for our work, are generally superparamagnetic. In this case, their magnetic moment $\mathbf{m}$ depends on the local magnetic flux density $\mathbf{B}$ and it is common to use a Langevin function to relate $\mathbf{m}$ to $\mathbf{B}$:

$$\mathbf{m} = \frac{m_{\text{sat}}\mathbf{B}}{|\mathbf{B}|} L(|\mathbf{B}|), \tag{1}$$

$$L(|\mathbf{B}|) = \coth(\varepsilon|\mathbf{B}|) - \frac{1}{\varepsilon|\mathbf{B}|}, \tag{2}$$

where $\varepsilon = m_{\text{sat}}/(k_B T)$ and m_{sat} is the saturation magnetization. For sufficiently weak fields $L(|\mathbf{B}|)$ can be linearised and the force reads than:

$$\mathbf{F}_{\text{mag}} = \frac{\varepsilon m_{\text{sat}}}{6} \nabla \mathbf{B}^2. \tag{3}$$

In case of an incompressible Newtonian liquid, the ferrohydrodynamic Bernoulli equation reads [8]:

$$\rho\left(\frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v}\nabla)\mathbf{v}\right) - \mu\nabla^2\mathbf{v} =$$

$$-\nabla p + \mu_0 \mathbf{m}\nabla\mathbf{H},$$

where ρ, μ and $\mathbf{v}$ are the blood density, velocity and dynamical viscosity respectively, $\mathbf{m}$ - the field averaged magnetization of the fluid and p and $\mathbf{H}$ stands for the pressure and magnetic field respectively.

This approach suits for the simulation of the motion of MNPs in blood vessels [7] and in bioreactors [9]. In the latter one aims to create *in vitro* a bioactive system similar to the real tissue environment. The development and use of bioreactors are very important for further successful *in vivo* experiments. FEA simulations and the use of bioreactors also allow for reducing the number of animal experiments.

On Figure 1, we show the velocity distribution of the ferrofluid near the vessel branching. The simulation has been carried out by coupling of "Magnetostatics" and "Incompressible Navier-Stokes" modules of COMSOL Multiphysics.

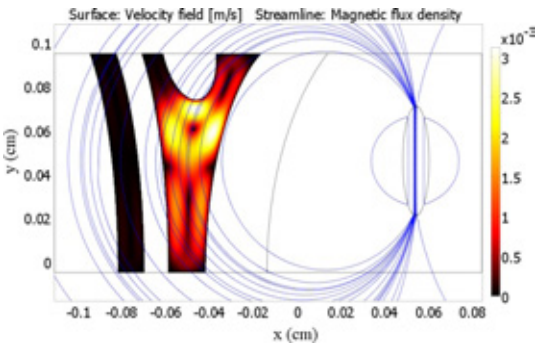

Figure 1: Velocity of the magnetic ferrofluid (blood with MNPs injected) in the vessels under the influence of a permanent magnet. The streamlines depict magnetic flux.

To simulate the penetration of MNPs into the scaffold or into the microvascular tissue one uses the diffusion approach. The diffusion equation reads

$$\frac{\partial c}{\partial t} = -\nabla(D\nabla c) - \nabla(c\mathbf{v}_{\text{mag}}), \tag{4}$$

where the first term on the right side describes the conventional Brownian diffusion, with c being the concentration of MNPs in the volume, and $D = k_B T/(6\pi\mu a)$ is the diffusion coefficient. With the dynamical viscosity $\mu = 0.001$ kg/(m $\cdot$ s) and MNP of hydrodynamic radius $a \sim 20$ nm, the diffusion coefficient at body temperature is of the order 10^{-10} m^2/s. The second term describes the flux due

to the magnetic force $\mathbf{F}_{\text{mag}}$ which gives the particle velocity $\mathbf{v}_{\text{mag}}$:

$$\mathbf{v}_{\text{mag}} = \frac{\mathbf{F}_{\text{mag}}}{6\pi\mu a}. \tag{5}$$

Here, μ is the dynamical viscosity of the fluid and a is the particle radius.

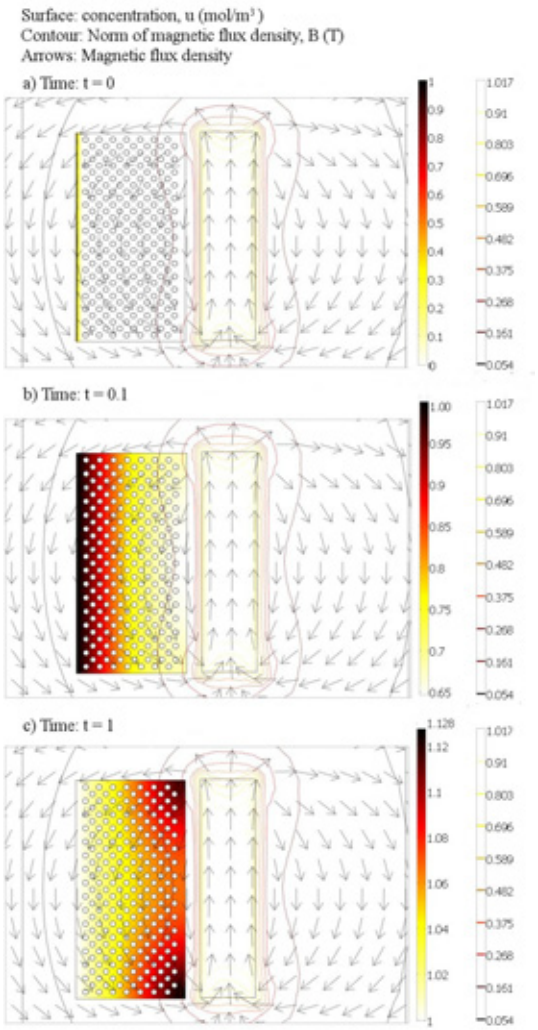

Figure 2: Distribution of magnetic particles diffused under the influence of magnetic field into the porous structure at subsequent time points t=0, 0.1, 1s.

On Figure 2, the distribution of nanoparticles in a nonmagnetic porous structure under the influence of permanent magnet is shown. For the simulation we used two Comsol modules: "Magnetostatics" and "Diffusion and Convection". The boundary conditions have been set appropriate to real conditions. From the left side of the porous structure a constant concentration is given. The simulation demonstrates the influence of magnetic field on the diffusion process. The concentration of MNPs is effectively enriched in the vicinity of an implanted magnet. Compared to free diffusion (not forced by magnetic field) where the concentration on the right boundary increases only negligibly under the same boundary conditions and during the same period of time, the presence of magnet results in a growth of 12.8% due to the additional flux caused by magnetic forces.

4 Magnetic fixation

In the MAGISTER project, the external magnetic fields serve for both, drug delivery and, additionally, fixation of the magnetic scaffolds on the site of the bone defect.

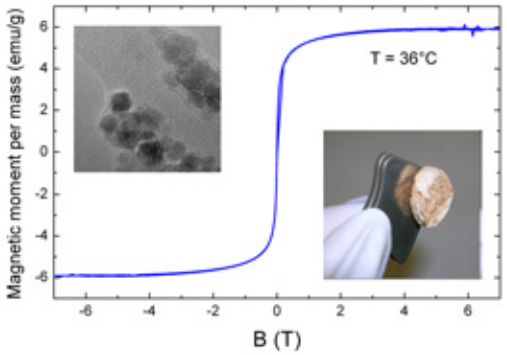

Figure 3: Magnetic properties of a scaffold doped with MNPs. The inserts show structure of a collagen-fiber pattern doped with MNPs (left) and a produced magnetic scaffold attracted by a permanent magnet.

Magnetic scaffolds are special devices made off a composite, chemically resembling the bone tissue, however, doped with magnetic nanoparticles. On Figure 3, we present magnetization data of magnetic scaffolds, produced in the MAGISTER prject. The magnetization may range up to 20 emu/g. The inserts show a collagen-fiber sample doped with the MNPs (left) and a ready-for-use magnetic scaffold magnetically fixed to a permanent magnet (right).

On Figure 4, a prototype of a fixing device is shown. It consists of two rare-earth ring-shaped magnets located in Helmholtz geometry surrounding the defect site of the bone.

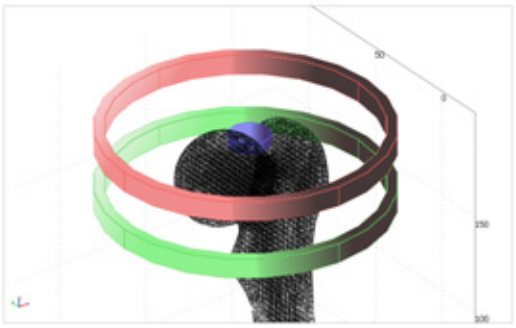

Figure 4: Scheme of the fixation of a magnetic scaffold to a defect site of a bone using external magnets.

The magnetic module of COMSOL Multiphysics has been used to calculate field distributions in such a case. On Figure 5, we show the magnetic flux in a superparamagnetic scaffold fixed with four permanent-magnet nails as shown also on Figure 6.

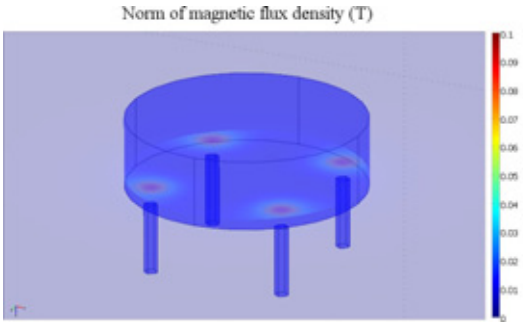

Figure 5: Magnetic field distribution in the scaffold.

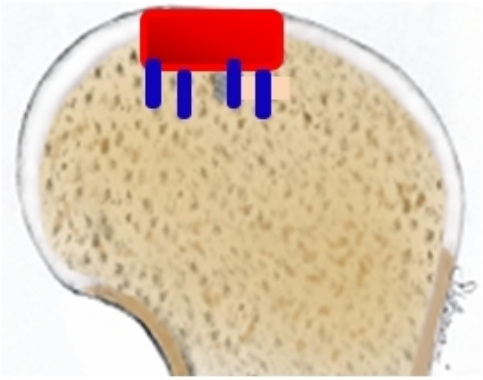

Figure 6: Magnetic scaffold fixed inside the defected bone.

5 Conclusion

FEA, in particular implemented in COMSOL-Multiphysics allows for modeling of complex processes related to tissue engineering. In conjunction with image processing data, provided *e.g.* by Simpleware® or Amira®, COMSOL can serve as a useful simulation platform for human biology and medicine. In the particular case of bone and osteochondral treatment, as investigated in the framework of MAGISTER project, it may provide a unique possibility to simulate and, thus, adjust the scaffold activity to the personal needs of the patient.

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