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Design of a High Field Gradient Electromagnet for Magnetic Drug Delivery to a Mouse Brain

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Abstract: The application of nanoparticles coupled with medical agents to brain tumors remains one of the biggest obstacles in neuro scientific researches (1) (2). This work explores an optimal design of an electromagnet to overcome the blood-brain barrier by means of an intensive external magnetic field gradient. It is found that the field gradients depend strongly on the design of the magnet tip. The model consists of an optimized coil and magnet system to focally target the brain of a small animal.

Computations concerning the heating of the coil are presented as well as its simulation using COMSOL Multiphysics.

Moreover, we performed a heating analysis of the used coil to determine the maximum application duration allowed, before a given critical temperature of 65 °C is reached.

Many forms of tips have been implemented and compared in order to finally obtain the perfect design to assure the availability of a minimum magnetic flux density of 200 mT and a field gradient of 10 T/m in the targeted volume.

Future tests are intended using experimental mice or rats and should certify the accuracy of the simulative predictions and the ease of use of the conceived magnetic system (6) (7) (8).

Keywords: Magnetic Drug Targeting, Blood-Brain Barrier, Brain Tumor, Electromagnet, Coil.

1. Introduction

Magnetic drug delivery has gained importance in the last years. It is a new therapy technique that consists in magnetically directing medical agents, combined with paramagnetic nanoparticles, to certain areas of the body without affecting healthy organs and tissue. Applying this to brain tumors necessitates the overcoming of the blood-brain barrier that automatically acts to protect the inner parts of the skull from chemical substances in the blood. We have been able to experimentally determine the needed magnetic force to drag nanoparticles into the brain and therefore the necessary magnetic flux density and relatively high magnetic field gradient to perform this, according to the formula $F_{magnetic} \sim B \cdot \mathrm{grad}(B)$.

In this work, we designed an electromagnet that produces these necessary magnetic field properties in an active volume of 2x2x2 cm³, which covers the whole volume of the brain of a laboratory mouse. We conceived the entire system in a way to be manageable and of small size.

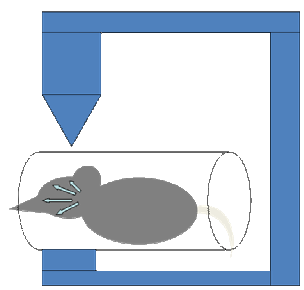

Figure 1. A draft of the intended experimental setup to overcome the blood-brain barrier in laboratory mice skulls. The arrows show the direction of the needed forces to drag nanoparticles into the cranium.

2. Theory

To compute and plot the magnetic flux density around the system tip, the model of the electromagnet was implemented in 2D as well as in 3D. Since the problem is symmetric to the z-axis, it was adequate to use the 2D axial symmetric mode in order to reduce complexity and processing time. For better understanding and future manufacturing of the geometry, a 3D model has also been revolved out of the 2D outline.

The paramagnetic nanoparticles experience a magnetic force according to $F_{mag} = \mu \cdot \nabla B$, where μ is the magnetic moment of a given particle and

∇B is the gradient of the magnetic field. In order to drag and hold the particles in the desired region the magnetic flux density of 200 mT and a field gradient in the range of 8 T/m to 10 T/m are required. Furthermore it is assumed that the needed penetration depth is 1-2 cm into the brain, to assure an efficient drug delivery (3) (4).

3. Equations

The involved Maxwell equations are: $\nabla \times H = J$ and $\nabla B = 0$, with the constitutive relation $B = \mu_0 \mu_r H$. The magnetic vector potential A produces the governing equation of the Magnetostatics mode. $\nabla \times (\mu^{-1} \nabla \times A - M) = J$.

Hence the basic input parameters are the relative permeability of the magnet and the external current density. Tables 1 and 2 show the important magnetic constants and boundary conditions.

Table 1: Magnetic Constants

Magnetic Constants	Value
Relative permeability (μ_r)	4e3 (Iron)
External current density ($J_0\varphi$)	1.79e6 A/m^2

Table 2: Magnetostatic Equations

Magnetostatic Equations	Value
Magnetic Insulation	$A_\varphi = 0$
Continuity	$n \times (H_1 - H_2) = 0$
Relative Permeability	Isotropic in each subdomain

3. Results

3.1 Concept of the Magnet

The electromagnet consists of an iron core, a yoke and a coil (copper). The iron yoke is necessary to enforce the magnetic flux density. The figures below show the drafts for the core and the yoke. A screw thread in the upper part of the yoke permits the adjustment of the tip level and makes the variation of the air gap from 3 to 7 cm possible.

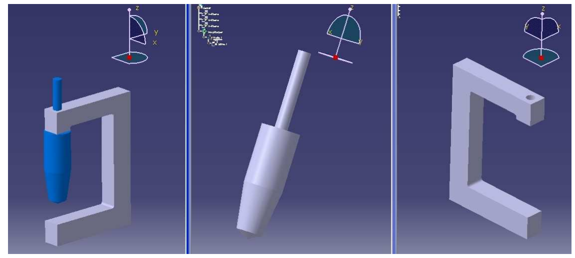

Figure 2. Design of the iron core and the iron yoke.

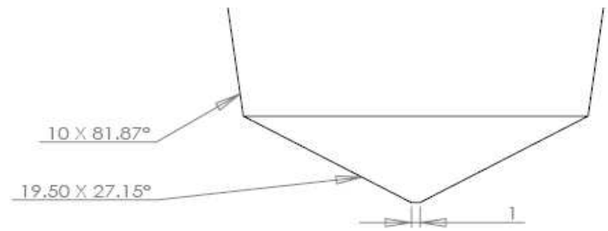

Figure 3. Dimensioning of the magnet tip.

3.2 Calculation of the Coil

The external current density was determined to 1.79e6 A/m². Hence table 3 indicates further parameters. For the wire wound coil a copper wire with an external diameter of 1.2 mm is used.

Table 3: Parameters of the coil

Diameter of the copper wire	d = 1.2 mm
Cross-section of the wire	A_L = 1.13 mm^2
Average length of the winding	l_m = 34.56 cm
Number of windings	N = 3714
Length of the coil	l = 1283.56 m
Mass of the coil	m = 12.95 kg
External current density	J = 1.79e6 A/m²
Output voltage	U = 41.12 V
Output current	I = 2.04 A
Power loss	P = 83.71 W
Adiabatic heating	$\Delta\theta$ = 40.3 K

The adiabatic heating of the coil is given by the formula $\Delta\theta = \frac{P \cdot t}{m \cdot c_{Cu}}$ where

P power loss
t operating time (assumed to 40 min.)
m mass of the coil
c_{CU} specific heat capacity

3.3 FEM Calculations

An ideal magnetic field results from the form of the magnet. Therefore COMSOL Multiphysics has been used to study and test multiple possible magnet forms to optimize the magnetic force. The result of our magnet tip is shown in figures 4-6. A maximum B-field of 1.43 T could be reached. The magnetic flux density directly under the magnet tip is 588 mT. With the distance from the tip the flux density falls then rapidly. The field gradient ranges from 27.08 T/m for z = 1 mm to 10.37 T/m at a distance of 2 cm from the magnet surface.

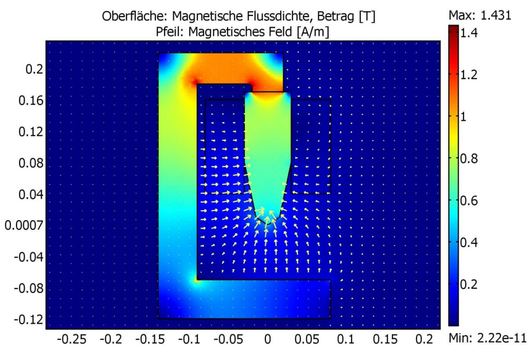

Figure 4. Magnetic flux density.

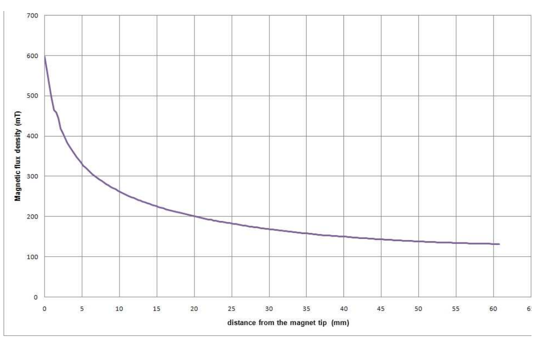

Figure 5. Decay of the magnetic flux density.

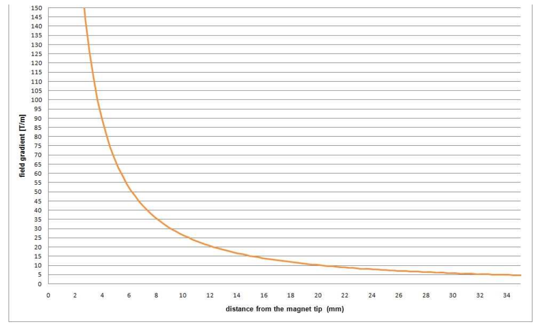

Figure 6. Magnetic field gradient

3.4 Heating of the magnet

Using the electro-thermal interaction module, we could also study the thermal aspect of the conceived magnet.

According to the FEM calculations the highest amount of heat is found at the exterior of the winding. The simulation in COMSOL does not consider the copper filling factor. Hence the real heating result is about 70% of the simulated outcome.

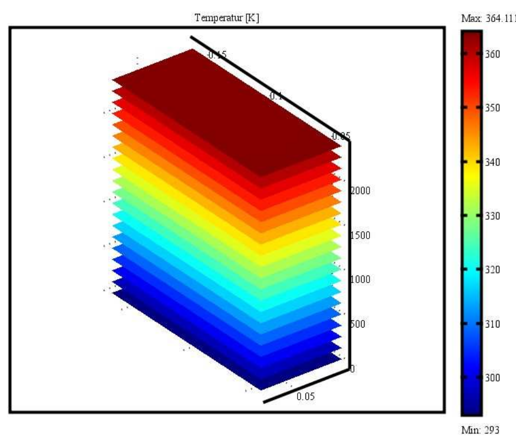

Figure 7. Heating of the copper winding after 40 minutes operation time.

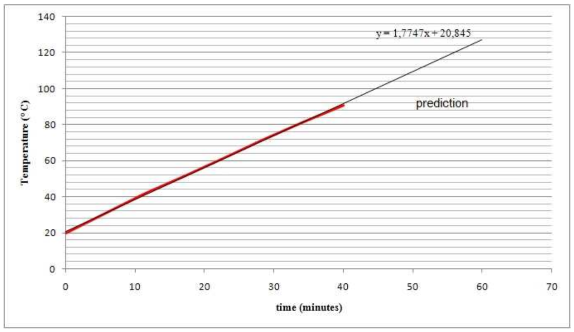

Figure 8. Analytically determined increase of the heating, in comparison to the simulated values (5)

4. Conclusions

In this model, Comsol has been used to determine the optimal geometry that assures the necessary magnetic field properties to let magnetic nanoparticles overcome the blood-brain barrier of a laboratory mouse.

This model will be manufactured and is expected to prove the feasibility of locally targeting vascular defects in the brain.

Comsol also allowed a prediction of the heating behavior of the conceived magnet and the necessity of an additional cooling system after a certain operation time.

5. References

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