Proceedings of the 15th Czech and Slovak Conference on Magnetism, Košice, Slovakia, June 17–21 2013

Biogenic Magnetite Nanoparticle Ensemble Use in MRI Diagnostics

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We present a simple analytical tool, which allows the calculation of the MRI diagnostics feasibility of the biogenic magnetite nanoparticles. Elevated levels of these particles are usually linked to the pathological processes, especially to neurodegenerative disorders. We showed theoretically that the biogenic magnetite itself is not sufficient for the non-invasive diagnostics and must be extended with the total iron incorporated in other biological structures.

DOI: 10.12693/APhysPolA.126.388

PACS: 75.50.Gg, 75.50.Tt, 87.61.-c

1. Introduction

The magnetite nanoparticles are in a wide range of interest of the various biomedical applications due to their unique superparamagnetic properties. However the magnetite nanoparticles were also found in the human brain tissue [1] and their elevated levels are usually connected with the neurodegenerative processes [2]. Magnetic properties of these particles make them "visible" by the magnetic resonance imaging (MRI) and open the question of possibility to become a biomarker for the non-invasive diagnostics of the neurodegenerative disorders [3]. However, there still remain unresolved questions. The most important is, at what concentration and spatial distribution are these particles able to alter the MRI signal sufficiently for the detection by the clinical tomographs. We bring a simple simulation method, which provides the theoretical determination of the biogenic magnetite quantitative imaging feasibility in clinical practice.

2. Methods

Our simulations are focused only on the nanoparticles in the single domain size range, which were found in the human brain tissue [1]. Magnetic moment of particles is derived from the "Cell unit" (CU) approach which represents cube model approximation [4]. The nanoparticle magnetic field was calculated with the use of the analytical expressions for the magnetic field of a current loop, adjusted to the cube particle [5]:

$$B_x = xz\frac{\mu_0\boldsymbol{\mu}_{mag}}{12\pi a^2}C_1, \quad B_y = yz\frac{\mu_0\boldsymbol{\mu}_{mag}}{12\pi a^2}C_1,$$
$$B_z = \frac{\mu_0\boldsymbol{\mu}_{mag}}{12\pi a^2}C_2, \tag{1}$$

where $\boldsymbol{\mu}_{mag}$ is the particle magnetic moment, μ_0 is the permeability, a is the particle size, and $C_{1,2}$ represent geometrical substitutions. Simulations were performed in Matlab R2011b. For each point of the selected cube with the size of $20a$ (with nanoparticle in the centre) we determined the total magnetic flux density $\boldsymbol{B}_{mag}$.

The effective volume V_{eff}, represented by the space distribution of protons affected by the nanoparticle magnetic field, was calculated as follows. Magnetic flux density value $\boldsymbol{B}_{mag}$ in each point of rectangular grid in selected cube was compared with the magnitude of standard MRI tomograph field $\boldsymbol{B}_0$. If the point of rectangular grid was outside the particle volume V_a and $\boldsymbol{B}_{mag} \geq 0.5\boldsymbol{B}_0$, it was counted, otherwise it wasn't. Total number of such points ($N_{B_{mag}\geq 0.5B_0}$) relative to total number of all points in the cube (N_{cube}), with the exception of the ones inside particle volume (N_a) multiplied by the volume of examined cube (V_{cube}) and reduced by particle volume, results in V_{eff}:

$$V_{eff} = \frac{N_{B_{mag}\geq 0.5B_0}}{N_{cube} - N_a}\left(V_{cube} - V_a\right). \tag{2}$$

Two approximations have been used during simulations: (i) we looked at particles as non-interacting ($d \gg a$, where d is distance between particles), (ii) we counted only excess protons which were affected by the particle magnetic field $\boldsymbol{B}_{mag}$ in the range $\boldsymbol{B}_{mag} \geq 0.5\boldsymbol{B}_0$.

To determine the possibility of the magnetite nanoparticle quantitative magnetic resonance imaging we have defined the number of the total excess protons in one voxel, which are affected by the condition $\boldsymbol{B} \geq 0.5\boldsymbol{B}_0$:

$$N_{eff} = KN_{mag}N_pV_{eff}V_{vox}, \tag{3}$$

where $K = 5.35\times 10^{22}$ protons per volume, N_{mag} – number of magnetite nanoparticles per volume, N_p – number of excess protons ($N_p = 4.94$ ppm at $\boldsymbol{B}_0 = 1.5$ T), and V_{vox} – voxel volume.

3. Results

In Fig.1 the simulated magnetic field is pictured in the proximity of the single magnetite nanoparticle with the size of 35 nm. Magnetic moment of particle points toward the z-axis. Except for the ring plane and a narrow tube along the z-axis, the $\boldsymbol{B}_{mag}$ values are defined by the sharp exponential decrease with distance. Along the z-axis the magnetic field logarithmically increases up to the end of the simulated space. The maximum values are located

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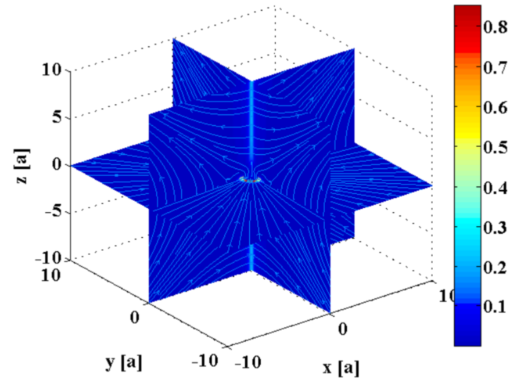

Fig. 1. Magnetite nanoparticle (black cube in the centre, $a = 35$ nm) magnetic field visualization. Central planes define the values of the nanoparticle magnetic flux density in Tesla unit.

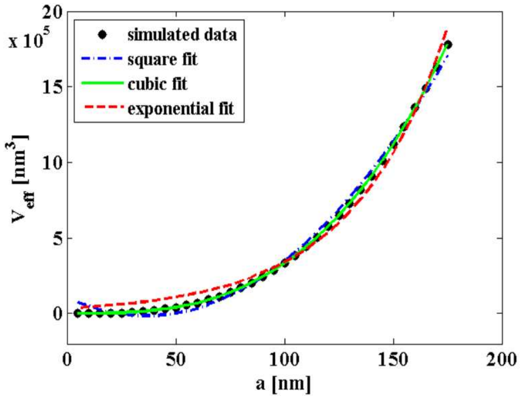

Fig. 2. Effective volume vs. size of magnetite nanoparticles for excess protons, affected by the condition $\boldsymbol{B}_{mag} \geq 0.5\boldsymbol{B}_0$, including various fit comparison.

in the thin ring around the particle in the xy plane and rapidly fall to a minimum from the distance $1.5a$.

Figure 2 demonstrates the effective volume V_{eff} enlargement with the increase of particle size a. The fit comparison shows cubic expansion of the V_{eff}.

The dependence between the number of the effective protons N_{eff} and the number and size of the magnetite nanoparticles is shown in Fig. 3. The data were simulated for the voxel size $V_{vox} = 1$ ml and main field strength of $\boldsymbol{B}_0 = 1.5$ T.

4. Discussion

The simulation has shown that regions effective for the practical applications are located only in the thin ring around the particle, perpendicular to the particle magnetic moment, and in the narrow tube along the orientation of the magnetic moment (Fig. 1). With the particle size increase the effective volume V_{eff} expands cubically in simulated range (Fig. 2). The maximum number of the effective protons in one voxel, which are affected by the nanoparticle magnetic field is in the order of 10^6 for the condition $\boldsymbol{B} \geq 0.5\boldsymbol{B}_0$ (Fig. 3). In case of 100% B_0, it is 10^5, and 10% B affects 10^7 protons. In comparison with the number of the total excess protons in one

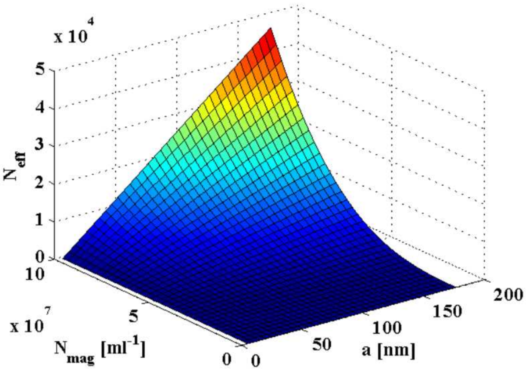

Fig. 3. The number of the effective protons in one voxel, affected by the nanoparticle field, vs. the size and the number of the magnetite nanoparticles.

voxel, $\approx 10^{17}$, it is quite a small number, and may be not sufficient for the desired MRI signal alteration. However, it counts only the iron incorporated in magnetite nanoparticles. According to Schenck and Zimmerman the total iron concentration in wet brain tissue is sufficient for high field MRI [3]. Therefore in the next step the simulation will be adjusted with the iron included in the other biological structures like ferritin, hemosiderin, etc. Of course, firstly the experiment is needed to clear this issue.

5. Conclusions

We showed that only specific regions of the magnetite nanoparticle magnetic field are able to affect the excess protons during the MRI. The volume of the effective region cubically expands with the particle size increase. The concentration of the biogenic magnetite nanoparticles themselves, according to our simulation, is theoretically not sufficient for the desired signal alteration in MRI and must be extended with the total iron incorporated in the other biological structures, as a result of the disrupted iron homeostasis in neurodegenerative processes.

Acknowledgments

This work was supported by the Slovak Research and Development Agency APVV-0431-12, Slovak Scientific Grant Agency VEGA 2/0090/11, 2/0043/13, 2/0045/13, and by the European Structural Funds, Projects No. 26110230061, 26220120021.

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