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Magnetic resonance imaging of the static magnetic field distortion caused by magnetic nanoparticles: Simulation and experimental verification

Daniel Gogola*, Oliver Štrbák, Andrej Krafčík, Martin Škrátek, Ivan Frollo

Institute of Measurement Science, Slovak Academy of Sciences, Bratislava, Slovakia

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A B S T R A C T

Magnetic nanoparticles are widely used as a contrast agent in magnetic resonance imaging (MRI). Nanoparticles in contrast agents possess a magnetic moment which generates local inhomogeneities in the static magnetic field of the MR scanner. These inhomogeneities cause a rapid loss of phase coherence which leads to the fast decay of the MR signal and thus produce a negative contrast in MR images. This article is focused on the interaction of magnetic nanoparticles aligned in a thin layer with the external homogeneous magnetic field, which changes the uniform distribution of magnetic nanoparticles in the carrier liquid. The goal of this study is to investigate the influence of the arrangement of magnetic nanoparticles on the final image contrast during MRI.

1. Introduction

Magnetic nanoparticles have been gradually gaining importance in clinical medicine as contrast agent for MRI liver diagnostics [1–3], as therapeutic agent for magnetic hyperthermia [3] or as transport agent for drug delivery to the site of interest in the human body [4,5]. Nowadays, magnetic nanoparticles have also found application in many other research areas, such as target biological entities, the magnetic separation of cells, and MRI, cancer therapy [6-10].

In general, magnetic nanoparticles consist of a solid core, most often of spherical shape. The solid core of the nanoparticle may consist of iron powder or substances containing Fe^{2+} or Fe^{3+} ions. A typical example is magnetite or maghemite. Unfortunately, the Fe^{2+} form is very toxic. Therefore, a surface treatment for each individual application is required. The surface treatment forms a chemically active coat, which can provide bindings with other molecules of interest.

For medical (in-vivo) applications the magnetic nanoparticles must be coated with biocompatible polymers such as dextran, protein, polyvinyl alcohol or polyethylene glycol. These polymers allow the binding of genes or various drugs by covalent attachment [11]. This functionality of magnetic nanoparticles allows their use for diverse applications including tumour treatment by magnetic hyperthermia [4,12], the delivery of chemotherapeutic or radioactive drugs, the improved delivery of peptides for gene transfer [12], thrombolysis, detoxification of blood, delivery of local anaesthesia or neuroblockers [13].

Another functionality which can influence the applicability of the magnetic nanoparticles is their size. Depending on their hydrodynamic diameter they can be classified into two groups, namely superparamagnetic iron oxide nanoparticle (SPION) with a diameter greater than 50 nm, or ultra-small superparamagnetic iron oxide nanoparticle (USPIO) with a diameter lower than 50 nm [1,14]. Superparamagnetism occurs when the particle is small enough to behave as a single dipole.

The shape of the hysteresis curve is in direct relation to the properties of magnetic materials such as saturation magnetization, maximum hysteresis loss and size of magnetic particles [15].

The interaction of the planar electromagnetic phantom, or the weak magnetic materials of the various shapes with homogeneous static magnetic field, was described and mathematically modelled in [16,17]. The magnetic field distribution in these articles was calculated as the superposition of elementary areas, as opposed to this study where magnetic field distribution was calculated as a superposition of individual magnetic domains.

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* Corresponding author.
E-mail address: daniel.gogola@savba.sk (D. Gogola).

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Magnetic properties of the single nanoparticle Fe$_3$O$_4$, with size 10 nm, were simulated and discussed in [18]. The magnetic field distribution of the group of nanoparticles was simulated using the equations published in [19].

The aim of this study was to investigate the influence of magnetic nanoparticle distribution in MR images, and to help understand the artefacts typical in liver or kidney MR imaging. We analysed the magnetic field of the near surroundings of the groups of magnetic nanoparticles Fe$_3$O$_4$, which are regarded as small magnetic dipoles.

2. Materials and methods

2.1. Simulations

To calculate the magnetic field of each particle in the near surroundings, a cube with the size of $20 \times a$ was selected, where a is the particle diameter, in our case 10 nm. A simulated magnetic particle is situated in the centre of each cube. The magnetic field distribution was simulated in a Matlab environment (version R2011b, Mathworks Inc., USA), using equations as described in the Appendix. In our study we used four nanoparticles, which were evenly spaced between each other. In each simulation, the distance between the particles was evenly incremented (Fig. 1). For each inter-particle distance of four nanoparticles a profile of magnetic field was observed. This profile was selected as shown in Fig. 1.

2.2. MR experiments

On the basis of the simulation we carried out the experiments on an ESAOTE Opera MR scanner. A **sensitivity test** was performed by the quantification of image intensity at ESAOTE Opera. We used a dedicated home-made phantom (Fig. 3). The phantom consisted of a series of Eppendorf tubes (1.5 ml volume), filled with the different concentrations of magnetic nanoparticles suspended in distilled water. The active substance of the phantoms was represented by water-based ferrofluid Type: EMG 607, made by FerroTec Corporation (Santa Clara, California, USA). The purpose of this test was to understand the low limit of the nanoparticle concentration which can be distinguished in the MR image.

In all cases we studied static magnetic field distribution, which was higher than the smallest induced magnetic field observable with the MR scanner. The smallest observable influence of the magnetic field is the magnetic polarization $\boldsymbol{J}$, generated by the nanoparticles placed in external field $\boldsymbol{B_0}$, which causes observable loss of the signal in MRI. Magnetic polarization of particle $\boldsymbol{J}$ can be

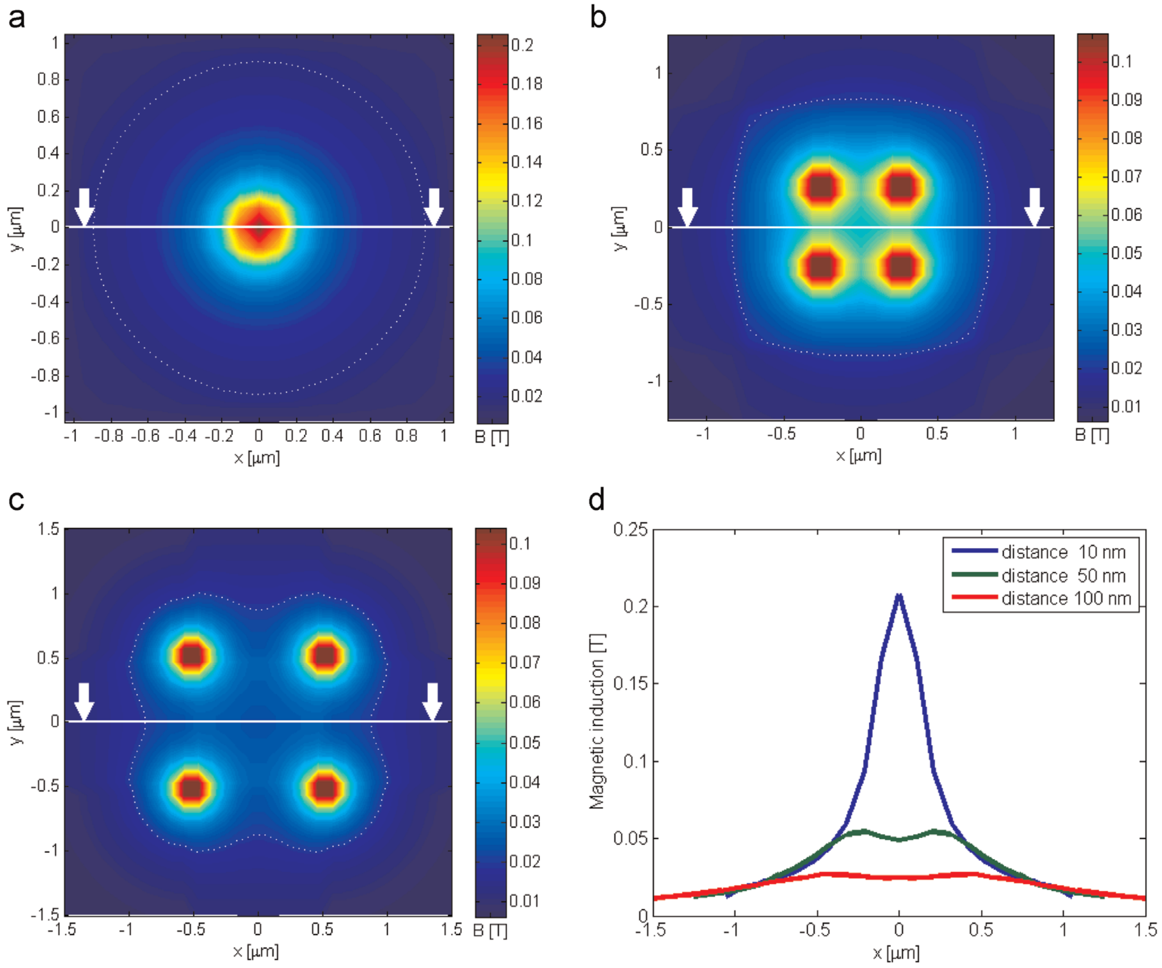

Fig. 1. Contour plot of the magnetic field of four nanoparticles. Dotted isolines define the magnetic field with value > =0.02 T. (a) The centre-to-centre distance of nanoparticles was 10 nm, what cause that individual nanoparticles cannot be distinguished. Diameter of contour with value of magnetic field 0.02 T is 170 nm. (b) The centre-to-centre distance of nanoparticles was 50 nm. Diameter of contour with value of magnetic field 0.02 T is 160.3 nm. (c) The centre-to-centre distance of nanoparticles was 100 nm. Diameter of contour with value of magnetic field 0.02 T is 168 nm. (d) Profile of magnetic field in selected line. White arrows depict the line where the profile of contour plot was measured.