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ScienceDirect
Journal of Magnetism and Magnetic Materials 311 (2007) 323–329
Journal of magnetism and magnetic materials
www.elsevier.com/locate/jmmm

Modeling of magnetic bandages for drug targeting: Button vs. Halbach arrays

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Available online 13 December 2006

Abstract

Magnetic targeting of drugs to diseased tissues, such as non-healing wounds or skin tumors, is a promising clinical use of magnetic microspheres. For successful magnetic targeting, a magnet must be placed in close proximity to the target tissue. In this work the forces exerted on magnetic microspheres by different arrangements of magnets including a simple square magnet, a number of button magnet arrays, and a Halbach array were simulated and compared. Magnetic bandages utilizing a Halbach array configuration were found to yield the best trapping characteristics (large and uniform force distributions) for magnetic targeting applications close to a surface.

Keywords: Halbach array; Magnetic bandage; Magnetic microspheres; Skin ulcer; Modeling; Magnetic drug targeting

1. Introduction

Magnetic targeting involves the delivery and concentration of drugs bound to a magnetic carrier to a target organ or tissue using a carefully chosen interplay of magnetic forces and blood flow [1,2]. The highest probability of success is reached by injecting the magnetic carriers into the arterial vessels leading to the target region. For example, by using direct intra-arterial injection, Gallo and Hassan reached a 3.5 × higher brain uptake in the magnetically targeted brain hemisphere compared to the opposite untargeted hemisphere [3]. In large animals and patients, magnetic targeting of liver tumors after injection into the hepatic artery allowed more than 90% to be retained in distinct liver areas [4]. Other investigations in rabbit tumors have also confirmed that intraarterial injections lead to much higher particle uptake in the target region compared to targeting after intravenous injection [5,6].

Magnetic carriers for in vivo magnetic targeting are generally made from magnetite particles coated with polymers or other biocompatible materials [2]. In order to maximize the trapping efficiency, the force exerted by a magnet must exceed the thermodynamic forces generated by Brownian motion [7] and the hydrodynamic forces from blood flow [8]. Hence, large magnetic microspheres must be used in magnetic targeting. From a biophysical perspective, however, the particles should be smaller than red blood cells so as not to embolize the capillaries. Magnetic particles of around 1 μm diameter seem to represent a workable compromise between these two competing requirements.

The forces for magnetic targeting have been generally produced by strong external magnets, such as rare earth neodymium–iron–boron (NdFeB) or samarium–cobalt (SmCo) magnets [9]. Alternatively, the force can be generated using conventional or superconducting electromagnets [10–12]. A third method involves magnetizable implants that are able to produce localized regions of large attractive magnetic forces deep within the body [13–16].

We are interested in optimizing the use of permanent rare earth magnets for targeting diseases relatively near the surface of the body (within 1–2 cm). This way, skin tumors could be treated with chemotherapeutic drugs or radioactive isotopes, and non-healing wounds could be treated with growth factors. For these applications, a magnetic bandage consisting of thin and light-weight magnet arrays

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doi:10.1016/j.jmmm.2006.10.1152

seems appealing, as it could be worn by a patient for extended periods of time (days). The attractive force between the magnetic bandage and magnetic particles will hold the latter stationary within the capillaries. This would, for example, be useful for the slow release of drugs from the magnetic particles and would lead to prolonged treatment of the desired area. For successful therapy, it is desirable (1) to maximize the trapping efficiency for magnetic particles of a certain size and magnetic susceptibility and (2) to maximize the uniformity of the distribution of the magnetic particles throughout the target region. Reaching these aims through design of the magnetic bandage is the intent of this paper.

2. Magnetic force modeling

A three-step procedure was used to obtain an estimate of the force that would be exerted on a single microsphere placed in the vicinity of various magnetic bandages. In the first step, the magnetic field $\vec{B}$ was calculated using the commercial finite-element modeling software package Opera-3d v10.5 (Vector Fields, Aurora, IL, USA). It was assumed that each magnet or magnet array comprising the magnetic bandage was composed of uniformly magnetized NdFeB rare earth magnets with a maximum energy product (grade) of 44 MGOe (megaGauss–oersted) and a residual magnetic induction B_r of 1.35 T. A uniform Cartesian mesh with 0.1 cm increments was used for all of the work reported here. In the second step, the calculated magnetic flux density data were extracted from the modeling software and imported into the graphing and data analysis software package Origin v7.0 (OriginLabs, Northampton, MA, USA). Numerical partial derivatives of the flux density were then calculated using standard three-point Lagrange interpolation formulae [17] . Finally, the force $\vec{F}$ that would be exerted on a magnetic microsphere with magnetic moment m was determined using the relationship $\vec{F} = m\nabla|\vec{B}|$ [8]. For the sake of argument, calculations were performed for 1 μm diameter microspheres consisting of 30 wt% magnetite and 70 wt% poly(lactic-co-glycolic acid) (= PLGA) with densities of 5.2 and 1.0 g/cm^3, respectively. The magnetite was assumed to be present in the form of a uniform distribution of superparamagnetic grains 10 nm in diameter possessing a volume saturation magnetization of 484 emu/cm^3, allowing us to model the field dependence of m using a Langevin function [8].

3. Magnet geometries

The force that would be exerted on the microsphere described above if it were placed in the vicinity of various magnet arrays was calculated for five distinct geometries. In each case the same total volume of magnetized material was used to construct the bandage. The first bandage (Fig. 1) corresponds to a single square magnet (3.75 cm on each side and 0.20 cm thick) magnetized perpendicular to the large faces. The next three bandages correspond to button arrays, each comprised of four cylindrical magnets (1.50 cm in diameter and 0.40 cm thick) arranged on the corners of a square with 2.25 cm sides. The maximum lateral extent of these arrays was chosen so that they would

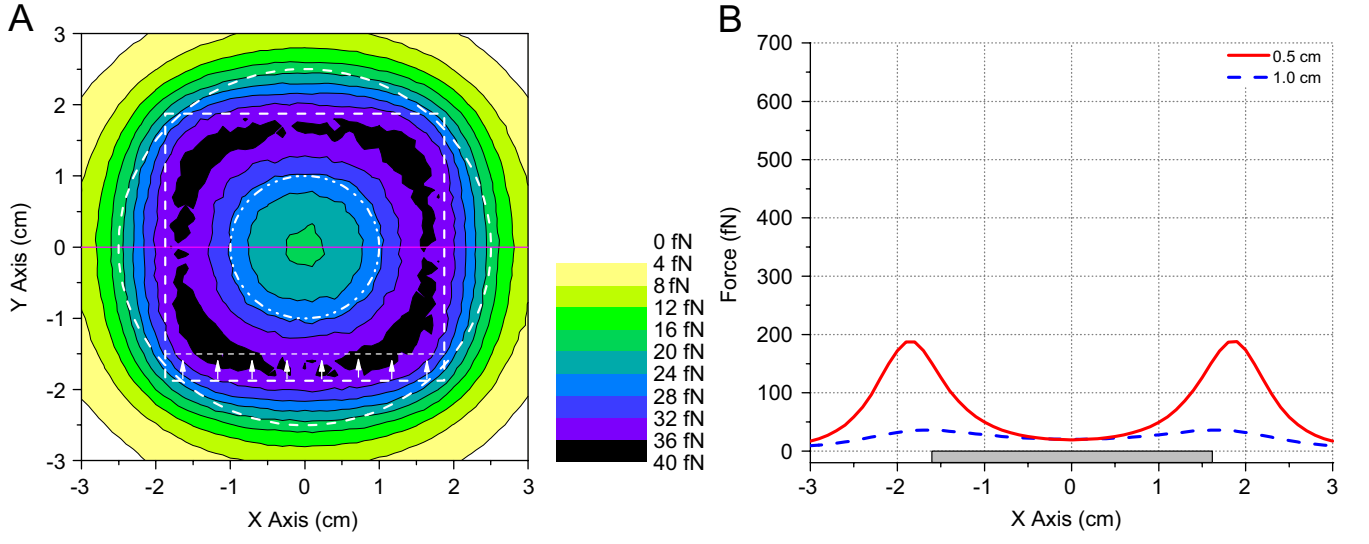

Fig. 1. Square magnet. (A) Contour plot for the magnitude of the force experienced by a single microsphere located 1 cm from the magnet surface. Here and in subsequent figures a dashed-and-dotted 2 cm diameter circle centered on the magnet (or array) is drawn to represent a loosely defined target area for the magnetic delivery of drugs. A dashed 5 cm diameter circle is also shown, and is used to demarcate a peripheral region, which one would also expect to entrap some of the magnetic particles. The white dashed outline indicates the magnet geometry, with the white arrows giving the magnetization direction. Summary statistics for the force distribution in both regions are given in Table 1 and (B) magnitude of the force at 0.5 and 1.0 cm distances from the array face. The magnet position is indicated by the gray bar.