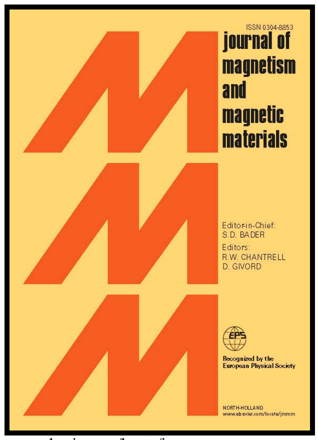

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Development of a real time imaging-based guidance system of magnetic nanoparticles for targeted drug delivery

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Abstract

Targeted drug delivery using magnetic nanoparticles is an efficient technique as molecules can be directed toward specific tissues inside a human body. For the first time, we implemented a real-time imaging-based guidance system of nanoparticles using untethered electro-magnetic devices for simultaneous guiding and tracking. In this paper a low-amplitude-excitation-field magnetic particle imaging (MPI) is introduced. Based on this imaging technology, a hybrid system comprised of an electromagnetic actuator and MPI was used to navigate nanoparticles in a non-invasive way. The real-time low-amplitude-excitation-field MPI and electromagnetic actuator of this navigation system are achieved by applying a time-division multiplexing scheme to the coil topology. A one dimensional nanoparticle navigation system was built to demonstrate the feasibility of the proposed approach and it could achieve a 2Hz navigation update rate with the field gradient of 3.5T/m during the imaging mode and 8.75T/m during the actuation mode. Particles with both 90nm and 5nm diameters could be successfully manipulated and monitored in a tube through the proposed system, which can significantly enhance targeting efficiency and allow precise analysis in a real drug delivery.

Keyword: Magnetic particle imaging; Nanoparticles; Electromagnetic actuator; Guidance system; Targeted drug delivery

1. Introduction

In biological interactions, magnetic nanoparticles can function at both the cellular and molecular level [1], making them suitable for use as contrast agents in magnetic particle imaging (MPI)[2] and as carriers for targeted drug delivery. In the first human trials of this drug targeting technique, drugs were attached to 100nm diameter iron-core particles and then concentrated by an external magnet field to treat tumors [3]. Our previous work demonstrated the delivery of 770nm magnetic particles using an electromagnetic actuator into the brains of mice based on an open-loop control approach using extensive simulations [4, 13]. These magnetic nanoparticles contain a fluorophore and have been engineered to enable tracking of their locations even after introduction in the body through blood. However, a guidance system capable of performing both actuation and monitoring of nanoparticles would be extremely useful to precisely steer the nanoparticles and track the nanoparticles in real-time through a feedback control. Several methods have been suggested to develop the targeting scheme with feedback control such as using an ultrasound for the locations of solid micro-size particles [5], or using microscope to track the visible particles [6]. Magnetic resonance navigation is the most efficient method for feedback control of targeted drug delivery. Magnetic resonance navigation is mainly based on magnetic nanoparticles embedded in micro carriers, which are controlled and tracked by Magnetic Resonance Imaging systems [7-8]. However, the major challenges faced in a targeting system are generating high gradient fields to steer the nanoparticles and tracking nanoparticles in real-time to enable precise targeting [9].

Magnetic Particle Imaging is a new tracer imaging modality that is gaining significant interest from Nuclear Magnetic Resonance Imaging researchers [10]. MPI scanners can achieve fast and high-sensitivity with millimeter-scale resolutions, and it has high potentials to revolutionize the biomedical imaging field. Tracer nanoparticles in MPI can provide the spatial information and it can be used as drug carrier particles. In MPI, the detection threshold of magnetic tracers is less limited by background