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# Magnetic microspheres for MPI and magnetic actuation

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**Abstract**

Magnetic particle imaging (MPI) systems do not only allow for the visualization of the distribution of magnetic nanoparticles, but the magnetic fields of an MPI scanner can be also used to apply a magnetic force or a torque. This enables the actuation of magnetic particles. Here, we demonstrate that magnetic microspheres (MMS) are well suitable candidates for the actuation and visualization with MPI. By means of magnetic particle spectrometer (MPS) measurements, a promising imaging performance of the MMS for MPI is confirmed. We show that MMS can be actuated by rotating focus fields of a preclinical MPI scanner. Since the used MMS can carry therapeutics, which can be released by means of hyperthermia, this approach paves the way towards an MPI monitored targeted drug delivery.

## I. Introduction

The actuation and visualization of magnetic microspheres (MMS) with an MPI scanner is of great interest for realizing targeted drug delivery monitored with MPI. For this, MMS are needed which allow for the steering by magnetic fields, the visualization with MPI and a hyperthermia induced drug release.

### I.I. Actuation with an MPI scanner

There are several ways of performing magnetic actuation by using an MPI scanner. The first possibility is to use the selection field, with which a force can be applied. Magnetic objects or particles with sufficient magnetic moment are pushed away from the field free region [1, 2, 3]. The second possibility is to generate a magnetic torque. Magnetic particles or objects tend to align with the direction of homogeneous fields, such as the focus fields of an MPI scanner. By applying sinusoidal currents to the focus field coils with a phase shift of 90° a homogeneous magnetic field with rotating field vector can be generated. This way, magnetic devices such as screws [4] or microrobots [5] can be rotated and drilled forward.

Further, the combination of magnetic actuation with MPI offers a unique possibility: the selective actuation. By superimposing the selection field forming a field free point (FFP) and a rotating focus field (see Fig. 1), objects within an ensemble can be chosen, which has been firstly demonstrated by using screws [4]. Thereafter the selective actuation and visualization was demonstrated by using magnetic nanoparticles located in spatially separated tubes [6, 7]. The observed cloud of nanoparticles showed very high traveling velocities, due to a collective rolling effect.

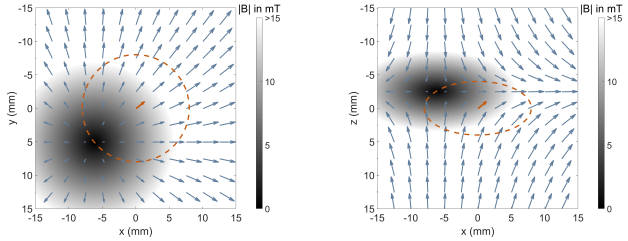


**Figure 1:** Selective actuation with an MPI scanner. By superimposing the selection field featuring an FFP and a focus field with rotating field vector, a circular trajectory (left) or an ellipsoidal trajectory (right) are formed in the xy- and xz-plane, respectively. Only objects or particles inside the FFP trajectory experience a fully rotating field vector and are therefore moving forward, while they only experience a precessing field vector outside the trajectory.

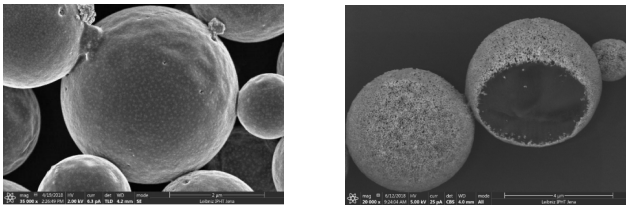

**Figure 2:** SEM images of MMS (left) and a cross-section of the MMS (right) prepared by means of a focused ion beam (FIB).

### I.II. Magnetic Microspheres

Magnetic microspheres (MMS) are very promising for magnetic drug targeting and typically consist of a polymeric matrix material loaded with magnetic nanoparticles (MNP) and a drug [8]. MMS can be magnetically guided to a target area by means of a magnetic field gradient. If the MMS are loaded with MNP showing a blocked magnetism at room/body temperature, a directed actuation due to generating a magnetic torque by exposure to a rotating magnetic field is enabled.

Once the MMS reach the targeting area, the loaded drug can be released either by degradation of the matrix or by diffusion of the drug from the matrix. Both release mechanisms can be accelerated by increasing the temperature of the MMS by means of magnetic hyperthermia [9] and thus a magnetically controlled release of the drug can be achieved [10].

## II. Material and methods

In the following we describe the synthesis and characterization of MMS as well as the experimental setups for proving the suitability for the visualization and actuation of MMS.

### II.I. Synthesis and characterization of MMS

MMS were prepared by an oil/water (o/w) emulsion evaporation method. For that, PLGA and biocompatible bisphosphonate coated multicore MNP prepared as described before [11] were dissolved/suspended in an organic solvent (o-phase) and emulsified by using a mechanical homogenizer in an aqueous PVA solution (w-phase). The obtained micro droplets were allowed to harden by evaporation of the solvent and collected using centrifugation or magnetic separation.

The MMS size was measured via static light scattering (mastersizer) and scanning electron microscopy (SEM). Magnetic properties of the MMS where investigated by means of vibrating sample magnetometry (VSM).

### II.II. MPI of MMS

For proving the ability of visualizing the MMS with MPI, measurements with a magnetic particle spectrometer (MPS) of one-dimensional excitation were performed. A 10 µl sample with a MMS concentration of 70.8 mg/ml was used. An excitation frequency of 25 kHz, an amplitude of 12 mT and 12,500 averages with a spectral resolution of 2.5 kHz were applied. To compare the signal of MMS to a typically used tracer material in MPI, a sample of 1:10 diluted Perimag (Micromod) was measured by applying the same parameters.

### II.III. Actuation of MMS

For the actuation of MMS a tube of 33 mm length and 3 mm inner diameter was filled with in water suspended MMS with a particle concentration of 141.5 mg/ml. The tube was positioned in the center of an MPI scanner (Bruker BioSpin GmbH) along the bore axis. Homogeneous focus fields with rotating field vector were applied with amplitudes ranging from 3 to 15 mT and frequencies ranging from 2 to 20 Hz. The actuation was observed with an endoscopic video camera inside the scanner bore.

## III. Results and discussion

In the following the properties of MMS will be described as well as the results from MPS measurement and actuation experiments will be shown and discussed.

### III.I. Properties of MMS

MMS with spherical shape and tunable mean diameters between 1 and 2 µm were prepared (see Fig. 2), with an inversely proportional correlation between homogenization velocity and diameter. From scanning electron microscopy images, it becomes obvious that the MNP are mainly located at the MMS surface (see Fig. 2 right).

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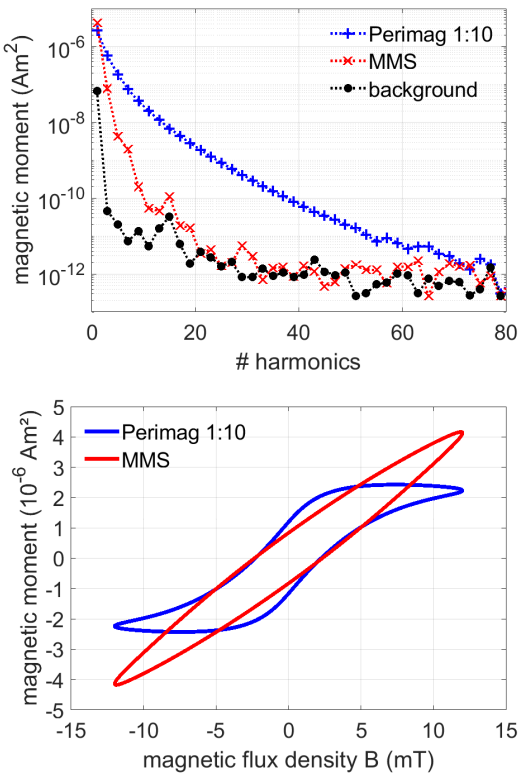


**Figure 3:** Magnetic particle spectrometry of MMS in comparison to Perimag. The amplitude spectra of the odd harmonics (top) and the dynamic magnetization curves (bottom) are shown.

The MMS show MNP concentrations of about 16 wt% with a saturation magnetization of 12 $Am^2/kg$ and a coercivity of 0.55 kA/m.

## III.II. MPI of MMS

The amplitude spectrum as well as the dynamic magnetization curve can be found in Fig. 3. Compared to Perimag the MMS show less higher harmonics and a steeper drop in the amplitude spectrum and the dynamic magnetization curve appears comparatively linear. It needs to be noted, that the signal quality of the MMS can only be qualitatively compared with the signal behavior of Perimag, since the iron concentration of the MMS has not been investigated in detail and can only be roughly estimated. Though, it can be stated that for the visualization with MPI less sensitivity and a reduced spatial resolution is expected. However, the tracking and localization of actuated MMS with MPI is expected to be feasible.

## III.III. Actuation of MMS

The actuation of MMS was demonstrated inside an MPI scanner. Snap shots of the recorded video can be seen in Fig. 4. The MMS could be steered from one side of the tube towards the other side. Due to the size distribution of the MMS different linear velocities of the MMS result, leading to a spreading of the MMS within the tube.

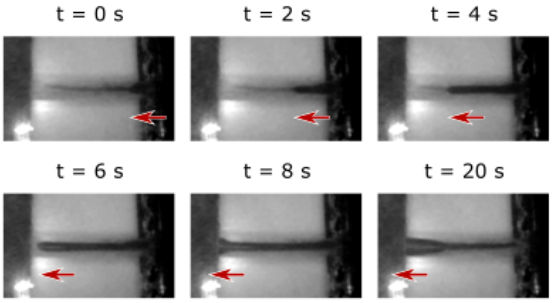


**Figure 4:** Magnetic actuation of MMS with an MPI scanner. Snapshots of a video recording are shown for different time stamps. The front of the particle cloud is indicated by the red arrow, the MMS are moving from the right side of the tube towards the left end due to rotating focus fields.

# IV. Conclusions

MMS made from PLGA with MNP were synthesized and analyzed. It has been previously shown that these MMS are suitable for a hyperthermia triggered drug release. Here, we demonstrated that the MMS are suitable to be visualized and actuated with an MPI scanner. The MPS measurement of MMS does not show an optimal signal behavior compared to a typical MPI tracer. However, as we are aiming at tracking the MMS position, we are optimistic that it is possible to determine the position of the particle cloud with MPI in future. Nevertheless, we intend to investigate the reason of the observed reduced signal, if it is e.g. because of the immobilization of MNPs inside the MMS and will optimize the signal performance. Further, we demonstrated the steerability of MMS by applying a rotating focus field of an MPI scanner. These very first experiments showed that MMS are steerable as a particle cloud, but we also observed that not all particles traveled with the same velocity. Therefore, we also intend to optimize the collective behavior of MMS moving as a particle cloud. So far, we were only using homogeneous magnetic fields with rotating field vector, but in future we want to superimpose the rotating field with the selection field of the MPI scanner in order to achieve a selective steering of MMS.

All in all, the demonstrated experiments mark the first steps towards targeted drug release, realized by actuating and monitoring the MMS by using MPI.

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## Author’s statement

Conflict of interest: Authors state no conflict of interest.

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