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Linear structures of magnetic nanoparticles in hyperthermia and magnetic particle imaging

M. Schoenen[a] · S. Schober[a] · B. Bauer[b] · B. Mues[a] · T. Gries[b] · E. Buhl[c] · T. Schmitz-Rode[a] · I. Slabu[a,*]

[a]Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany
[b]Institut für Textiltechnik, RWTH Aachen University, Germany
[c]Institute of Pathology, Electron Microscopy Facility, RWTH University Hospital Aachen, Germany
[*]Corresponding author, email: slabu@ame.rwth-aachen.de

Abstract

The development of theranostic devices combining magnetic particle imaging (MPI) and magnetic hyperthermia opens new possibilities for clinical applications of magnetic nanoparticles (MNP), e.g., hyperthermia-mediated drug delivery. Enhancing MNP performance for such applications can be achieved by using linear structures of MNP (i.e. chains, elongated clusters) instead of randomly distributed MNP. Here, we investigate the hyperthermia and MPI performance of two types of MNP linear structures: one generated by exposing MNP to a static magnetic field inside a hydrogel and the other by extruding a mixture of polypropylene and MNP to hybrid fibers. For both types of linear structures, an increase in heating efficiency and MPI signal was observed when the linear structure orientation is in the direction of the excitation field. In summary, the generation of MNP linear structures is a promising approach to increase their performance in MPI and magnetic hyperthermia. For MPI image reconstruction, the orientation of the linear structures relative to the drive field direction should be considered.

I. Introduction

Hybrid fiber-based implants with incorporated magnetic nanoparticles (MNP) are of great interest for applications in magnetic particle imaging (MPI) and magnetic hyperthermia. A promising therapeutic approach is hyperthermia-triggered drug release from biodegradable fiber-based scaffolds in tumor and cardiovascular therapies. The degradation state of the implants and the effectiveness of the drug release is tracked via MPI. Compared to magnetic drug targeting, the application of hybrid implants has the advantage of providing high local concentrations of MNP to achieve the necessary heating output. During the manufacturing process by extrusion of the hybrid fibers, MNP form linear structures, which was shown to increase the performance of MNP in magnetic hyperthermia and MPI compared to randomly distributed MNP [1,2].

In this study, we investigate the impact of MNP aligned inside a hydrogel on magnetic hyperthermia efficiency and MPI signal and compare it with the performance of MNP linear structures formed inside hybrid fibers. These investigations enable deeper insights into the effects of MNP linear structures on magnetic relaxation and demonstrate the promising characteristics of these structures for theranostic applications.

I.I. Material and Methods

The hybrid fibers were produced by extruding a mixture of polypropylene and MNP as described in [3,4]. To generate linear structures of MNP inside an acrylamide hydrogel, the MNP were added to hydrogel and during gel polymerization the mixture was exposed to a magnetic

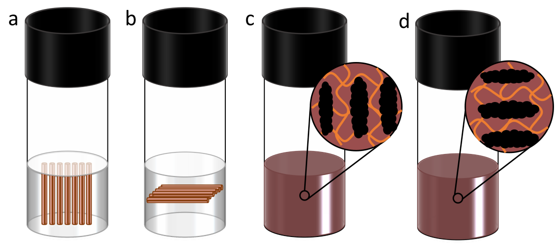

Figure 1: Sketches of fibers samples for hyperthermia measurements orientated in (a) z-direction (parallel to the excitation field), (b) in the xy-plane (orthogonal to the excitation field) and of hydrogel samples containing MNP linear structures oriented in (c) z-direction and (d) the xy-plane. The zoom-ins in (c) and (d) show three exemplary MNP linear structures embedded inside the hydrogel.

field (see Figure 1d, $H_S = 90$ kA/m). In this way, the MNP linear structures could be preserved allowing for investigation of the effects of their orientation relative to the direction of different magnetic fields on magnetic hyperthermia and MPI performance. The hydrogel preparation was performed as described in [5]. All hydrogel samples were prepared with an iron concentration of 1 mg/ml and a volume of 1 ml. The MNP have a a lauric acid coating and a magnetite core with a diameter of $d_C = (10.2 \pm 2.4)$ nm, a saturation magnetization of $M_S = (72.0 \pm 0.6)$ Am^2/kg (bulk magnetite: 92 Am^2/kg [6]). Further information on MNP properties is given in [7].

Hyperthermia measurements were performed using a custom-built setup. The alternating magnetic field had an amplitude of $H_0 = 40$ kA/m and a frequency of $f = 270$ kHz. A set of fibers were arranged in 1 cm^2 squares and placed in x, y and z-orientation of the hyperthermia setup as depicted in Figure 1a-c. To keep this orientation during the measurement, the fibers were embedded in 2 ml of 2 wt% agarose hydrogel. For the acquisition of the heating curves a fiberoptic thermometer was placed directly next to the center of the fiber square and in the center of the hydrogel containing the MNP linear structures.

The MPI measurements were performed with a Bruker MPI (MPI 25/20 FF, Bruker BioSpin MRI GmbH, Ettlingen, Germany). System matrices with a field of view (FOV) of (23 x 23 x 12) mm^3 were acquired. The excitation amplitude was set to $H_E = 11$ kA/m and the field gradient to $G = 2000$ kA/m^2. For signal acquisition in y and z the built-in coils were used, while for the x-axis a dedicated 1D RX coil insert from Bruker was used. For the measurements, the hydrogel samples were prepared as described above inside a container with a volume $V_S = 16$ µl.

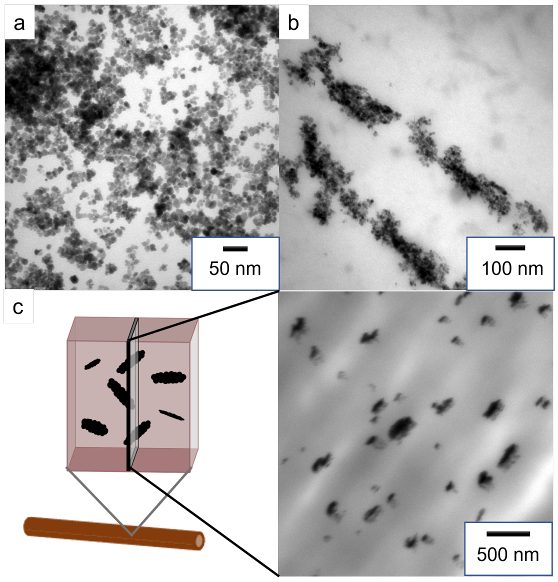

Figure 2: TEM images of the MNP (a) randomly distributed, (b) exposed to a static magnetic field ($H_S = 90$ kA/m) in acrylamide hydrogel. (c) Left: Sketch of the MNP structure and orientation immobilized in a fiber indicating the orientation of the TEM image. Right: TEM image.

I.II. Results and discussion

The TEM images in Figure 2a and b display the effects of the static magnetic field exposure to MNP inside a hydrogel: Linear structures of MNP are oriented parallel to the applied field direction (Figure 2b). Elongated MNP agglomerates are displayed in the TEM image of a hybrid fiber (Figure 2c). The agglomerates are mainly oriented along the axis of the fiber (see sketch in Figure 2c).

As shown in Figure 3 the highest hyperthermia heating output is achieved for fibers orientated parallel to excitation field direction. After a measurement time of 900 s a maximum temperature difference of ca. 2 °C between the parallelly and orthogonally oriented fibers is observed. Likewise, a difference in temperature increase of ca. 4 °C is observed for the linear structures in the acrylamide hydrogel oriented parallelly to the direction of the excitation field compared to the orthogonally orientated ones (see Figure 3). This is consistent with the results of parallelly orientated elongated MNP agglomerates inside the fibers along the symmetry axis. The linear structures in the acrylamide hydrogel are larger, which might explain the higher increase in temperature.

Hyperthermia and MPI both rely on the nonlinear magnetization response of MNP to alternating magnetic fields [8,9]. Thus, an effect on the MPI signal of differently orientated linear structures relative to the direction of the excitation field is expected. Figure 4 shows the results of the MPI system matrix acquisition for the hydrogel samples (cf. Figure 1 c,d). Here, a shift in the SNR peak positions in the frequency spectra can be ob-

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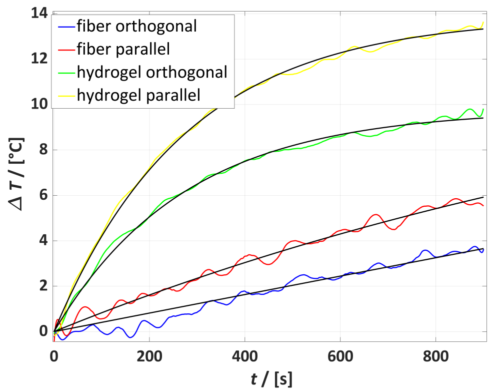

Figure 3: Magnetic hyperthermia heating curves including their fits (black lines) for fibers and hydrogel samples oriented parallel and orthogonal to the direction of the excitation field (see settings in Figure 1).

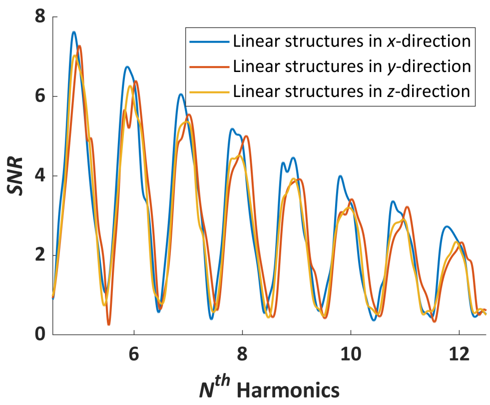

Figure 4: x-channel frequency spectra envelop (5^{th} to 12^{th} harmonic) of MNP linear structures inside an acrylamide hydrogel. Linear structures are oriented along the x-, y- and z-direction of drive field.

served depending on how the MNP linear structures are oriented relative to x-, y- and z-direction of the drive field of the MPI device. This is consistent to the results previously reported for differently oriented fibers [10]. In both cases, linear structures in hydrogel and inside fibers, the origin of this effect is attributed to differing magnetic response of the linear structures to the three different drive field directions. During excitation, MNP linear structures are exposed to a drive field, which has the same field amplitude ($H_E = 11$ kA/m) and slightly different frequencies ($f_x = 24.51$ kHz, $f_y = 26.04$ kHz, $f_z = 25.25$ kHz) in x-, y- and z-direction. Depending on the orientation of the MNP linear structures (set prior to the measurement in x-, y- or z-direction), SNR peak positions in the frequency spectra show specific shifts changing their position relative to each other. In Figure 4, this is exemplarily shown for the x-direction of the drive field (x-channel). For all three orientations of the linear structures different peak positions are visible. Additionally, for the linear structures oriented in x-direction an increase in signal strength is observed. The shifts and the differences in strength of the SNR for the different orientations can be explained by magnetic dipole-dipole interactions between the MNP inside the structures altering the dynamic relaxation processes of the individual MNP. This may explain the increase in MPI signal when the drive field direction (respectively channel direction, in Figure 4 x-direction) coincides with the MNP linear structures orientation. For more pronounced chain structures, Tay et al. [1] observed an even stronger increase in MPI performance.

II. Conclusions

This work demonstrated the dependency of magnetic hyperthermia performance and MPI signal on the presence and orientation of linear MNP structures relative to the direction of an applied excitation field. The best heating performance could be achieved for fibers and MNP oriented inside a hydrogel parallel to the direction of the excitation field. MPI system matrices data showed a shift of the frequency spectrum peak positions depending on the orientation of the linear structures relative to the drive field directions of the MPI. Consequently, for the reconstruction of fiber-based implants, the dependency of the MPI signal on the orientation of MNP linear structures inside the fibers with respect to the direction of the drive field must be taken into account. This can be realized in the future e.g. with a multi-channel technique [11]. A preorientation of the MNP linear structures inside the fibers with a static magnetic field during production might be favorable.

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Author's statement

Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent has been obtained from all individuals included in this study. Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration, and has been approved by the

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authors' institutional review board or equivalent committee.

References

[1] Z. W. Tay, *Superferromagnetic Nanoparticles Enable Order-of-Magnitude Resolution & Sensitivity Gain in Magnetic Particle Imaging*, Small methods, vol. 5, 2021, No. 2100796

[2] D. Serantes, *Multiplying Magnetic Hyperthermia Response by Nanoparticle Assembling*, J. Phys. Chem. C, vol. 118, 2014, pp. 5927-34.

[3] B. Mues, *Nanomagnetic Actuation of Hybrid Stents for Hyperthermia Treatment of Hollow Organ Tumors*, Nanomaterials, vol. 37, 2020, pp. 1-21.

[4] B. Mues, *Assessing hyperthermia performance of hybrid textile filaments: The impact of different heating agents*, Journal of Magnetism and Magnetic Materials, vol. 419, 2021, No. 167486

[5] U. Engelmann, *Heating efficiency of magnetic nanoparticles decreases with gradual immobilization in hydrogels*, Journal of Magnetism and Magnetic Materials, vol. 471, 2019, pp. 486-494.

[6] M. S. Mascolo, *Room Temperature Co-Precipitation Synthesis of Magnetite Nanoparticles in a Large pH Window with Different Bases*, Materials, vol. 6, 2013, pp. 5549-5567.

[7] B. Mues, *Towards optimized MRI contrast agents for implant engineering: Clustering and immobilization effects of magnetic nanoparticles*, J. Magn. Magn. Mater, vol. 471, 2019, pp. 432-438.

[8] Y. Lu, *Combining magnetic particle imaging and magnetic fluid hyperthermia for localized and image-guided treatment*, International Journal of Hyperthermia, vol. 618, 2021, pp. 141-154.

[9] C. Shasha, *Nonequilibrium Dynamics of Magnetic Nanoparticles with Applications in Biomedicine*, Advanced Materials, vol. 33, 2021, No. 1904131

[10] B. Mues, *MPI visualization of hybrid implant fibers using different system matrices.* International Journal on Magnetic Particle Imaging, vol. 8, 2022, No. 1

[11] M. Möddel, Estimating orientation using multi-contrast MPI, International Journal on Magnetic Particle Imaging, vol. 6, 2020, pp. 1-3.

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