NONLINEAR MAGNETIZATION EFFECTS OF MAGNETIC NANOPARTICLES FOR IMPLANT BASED HYPERTHERMIA TUMOR THERAPY

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***Abstract* – In this study, we investigate the nonlinear magnetization effects of hybrid materials consisting of polypropylene with incorporated magnetic nanoparticles (MNP), which are used for the fabrication of implants, such as stents. Because of their nonlinear magnetic relaxation effects in an alternating magnetic field, these implants can generate heat, which is applied in hyperthermia tumor therapy. We show that the magnetization of the implant base material (hybrid compounds) as well as of the final implant material (hybrid fiber) is not influenced by different production steps. Furthermore, we show that the hyperthermia performance decreases by approx. 40 % for MNP incorporated in compounds and in fibers compared to the one of as-synthesized MNP. This is attributed to the blocking of MNP physical rotation in the direction of the magnetic field influencing their overall magnetic relaxation behaviour.**

I. INTRODICTION

Hollow organ occlusion arising from endoluminal tumors (e. g. trachea carcinoma, esophagus adenocarcimoma or bile duct Klatskin tumor) can be treated by implanting metallic stents to widen the occluded endoluminal site. However, tumor tissue ingrowth, so-called restenosis, often causes a re-closure of the hollow organ. In order to overcome this problem, we develop hybrid stents made of polypropylene (PP) fibers with incorporated magnetic nanoparticles (MNP) to perform local hyperthermia treatment and destroy the tumor tissue. By applying an alternating magnetic field (AFM) heat will be generated in close vicinity of the stent leading to cell death for temperatures about 43 °C, for which healthy tissue remains unharmed [1].

Inductive heating of metallic stents leads to cell necrosis, which usually leads to higher risks of developing inflammation and damage of healthy cells. Further, metallic stents lack the ability of controlling the saturation temperature and showed too small energy uptake [2].

In this study, we investigate the effects of different implant production steps on MNP magnetization and MNP magnetic heating properties. For this, we characterize as-synthesized MNP, MNP incorporated in PP compounds and in PP fibers.

II. MATERIAL AND METHODS

The compounds were produced by melt spinning of PP granulate with 4 wt% freeze dried MNP. In a second melt spinning process, fibers were produced using the compounds as base material. The MNP had a core diameter of (10.2 ± 2.4) nm and were coated with lauric acid as described in literature [3]. The MNP concentration inside the compounds and the fibers was investigated by thermogravimetric analysis (TGA).

The size distribution and morphology of as-synthesized MNP as well as the MNP incorporated in compounds and fibers were characterized by transmission electron microscopy (TEM) using a Zeiss LEO 906 microscope (Carl Zeiss GmbH, Germany).

The magnetic properties of the samples were measured with a SQUID magnetometer MPMS 5S (LOT Quantum Design, USA). Magnetization measurements were performed at 295 K varying the field strength from - $4 \cdot 10^6$ A/m to $4 \cdot 10^6$ A/m.

The magnetic heating properties were investigated using a custom-built hyperthermia setup (Trumpf Hüttinger, Germany). For the measurements, in water dispersed MNP as well as in agarose gel (1.5 wt%) embedded PP compounds and PP fibers were exposed to an AMF at = 40 kA/m and f = 270 kHz for 30 min. These settings match the best combination between field parameters and particle properties to achieve a good heating performance and is based on experience.

The specific loss power (SLP) value was calculated using the following expression:

$$SLP = \frac{c}{\rho} \cdot \frac{dT}{dt}\Big|_{t \to 0} \qquad (1)$$

where c = 4.187 J g^{-1} K^{-1} is the specific heat capacity of water, ρ the MNP weight fraction, T the temperature and t the measurement time.

III. RESULTS AND DISCUSSION

TGA measurements yield an MNP concentration of (1.88 ± 0.01) wt% and (2.25 ± 0.14) wt% for the PP compounds and the PP fibers, respectively. Fig.1 shows the magnetization curves for all samples normalized to the saturation magnetization values. The curves nearly overlap for all samples and show no remanence magnetization.

Fig. 2 shows the SLP values for the as-synthesized MNP dispersed in water as well as for MNP incorporated in PP compounds and PP fibers. The highest value SLP of (211.8 ±10.6) W/g(Fe) is achieved for the dispersed MNP. The SLP values of MNP incorporated in PP compounds and PP fibers are approx. 40 % lower than the ones of dispersed MNP.

The dispersed MNP and both, compounds and fibers, show superparamagnetic behavior indicated by the absence of the remanence magnetization. The overlapping magnetization curves indicate that the magnetic properties during the production process of PP compounds and PP fibers remain

unaffected. These findings are confirmed by the hyperthermia measurements showing no difference in SLP value of MNP in PP compounds and PP fibers. The significant decrease in SLP by approx. 40 % for MNP incorporated in PP compounds and PP fibers compared to the dispersed MNP is attributed to the blocking of MNP physical rotation. The MNP immobilization in the polymer matrix inhibits the contribution of Brownian relaxation to the overall magnetic relaxation process. Such a decrease was recently demonstrated for immobilized MNP inside hydrogels [4].

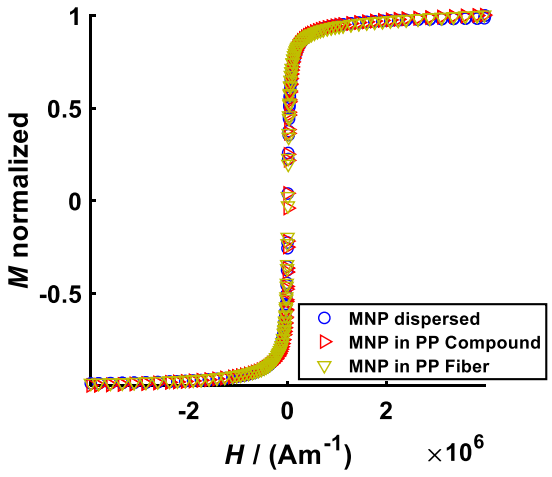

Fig.1. Magnetization curves of as-synthesized MNP dispersed in water, MNP incorporated in PP compounds and in PP fibers.

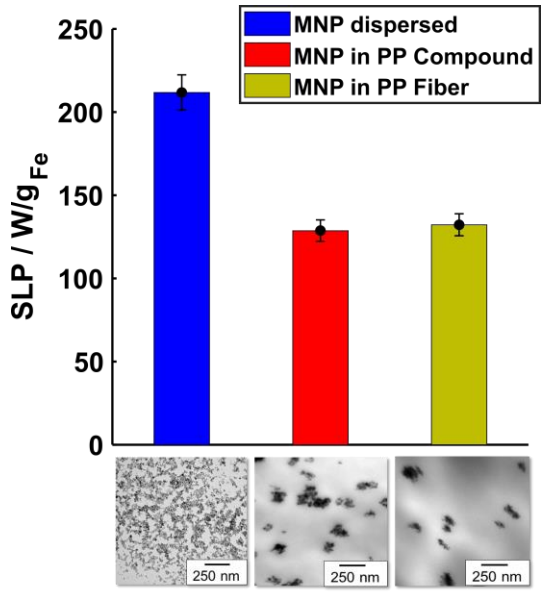

Fig.2. SLP values and exemplary TEM images of dispersed as-synthesized MNP, MNP incorporated in PP compounds and in PP fibers.

The TEM images (see Fig. 2) show homogenously distributed as-synthesized MNP and MNP agglomerates of approx. 100 nm incorporated in PP compounds and PP fibers. The formation of small MNP agglomerations might lead to dipolar particle-particle interactions changing the magnetization properties. Since no big difference can be observed in the agglomerate size and distribution within the PP compounds or PP fibers, this effect is expected to be in the same range for both PP compounds and PP fibers.

III. CONCLUSIONS

The magnetization and hyperthermia performance of hybrid implants with incorporated MNP were investigated with respect to changes that may arise during their production process. For this, dispersed as-synthesize MNP, MNP in PP compounds and in PP fibers are compared. The results show that the hyperthermia performance of both, MNP incorporated inside PP compounds and PP fibers, decrease by approx. 40 % compared to the one of dispersed MNP. This is clearly attributed to the MNP immobilization leading to the blocking of Brownian magnetic relaxation. Comparing PP compounds and PP fibers, no significant change in magnetization and hyperthermia performance was observed indicating no deterioration of magnetic properties during the production process.

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