Thin Film Magnetic Nanoparticles with disruptive Properties

The biomedical potential for 3d-imaging and localized hyperthermia using magnetic particles with performance-optimized properties is explored. Industrial-scale fabrication permits obtaining sufficient particles to open new frontiers in diagnostics and therapy with disruptive potential. This research activity profits from established collaborations with Prof. Dr. Dieter Suess (University of Vienna) for micromagnetic modeling [1-5], Prof. Dr. Inge K. Herrmann (ETHZ & Empa) and Dr. Peter Wick (Empa, Particles-Biology Interaction Lab) [6-10] for biochemical functionalization and in-vitro testing, Prof. Dr. Samuel Huber Lindenberger (OST) [11,12] for microfabrication and industrial partners for high-throughput sputter-deposition and microfabrication.

Executive Summary

Non-invasive imaging technologies have significantly advanced our abilities to detect and diagnose diseases. Especially in cancer medicine, early detection and imaged-based guiding of surgical interventions are imperative. However, current imaging technologies are still limited, with potentially severe consequences, such as micro-metastases going unnoticed. Because magnetic fields can penetrate the body, magnetic nanoparticles (MNPs) have significant appeal for medical imaging technology, advanced diagnostics and localized therapy (Fig. 1).

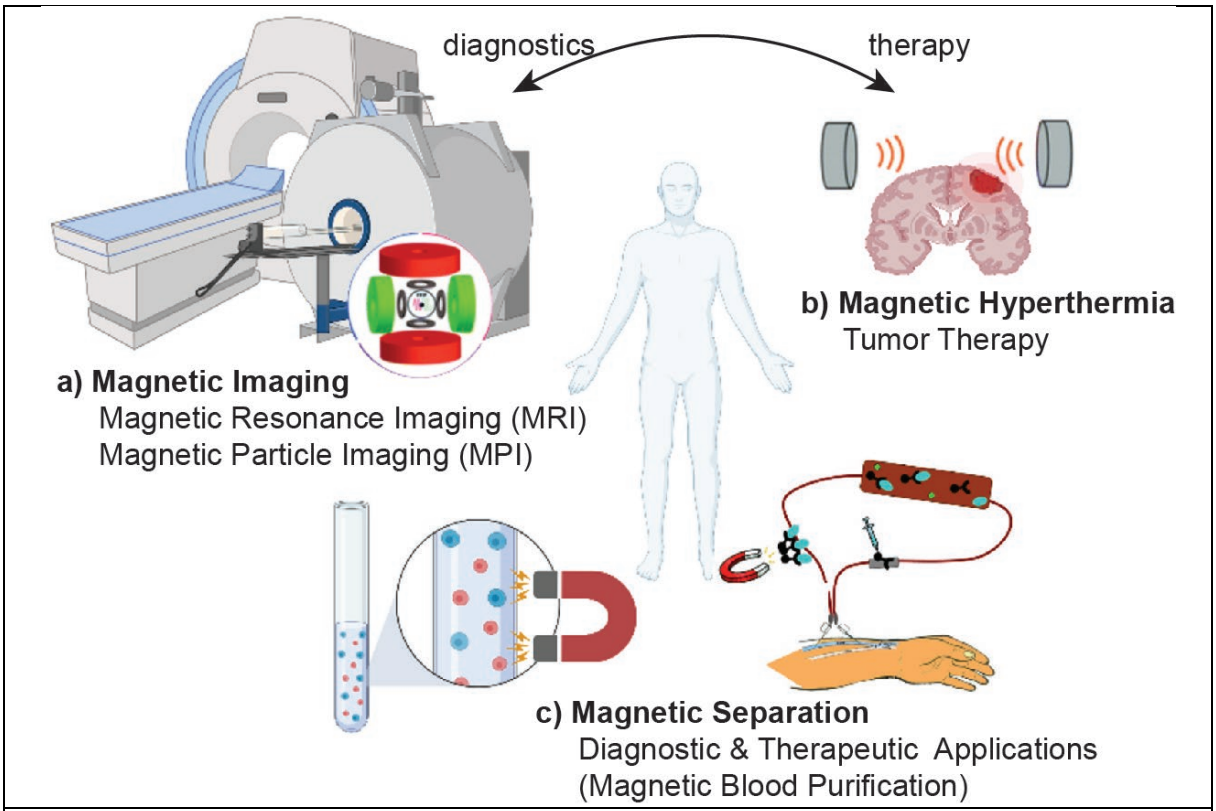

Figure 1: Biomedical applications of magnetic nanoparticles.
a) Medical Imaging: Apart from the established Magnetic Resonance Imaging (MRI) techniques, Magnetic Particle Imaging (MPI) is a promising new approach.
b) Magnetic Hyperthermia for tumor therapy
c) Magnetic Separation for diagnostics and therapeutic applications (e.g. magnetic blood purification). Figure prepared with bioRENDER.

Suspensions of MNPs have been widely applied in promising diagnostic and therapeutic approaches, including magnetic particle imaging (MPI) and (localized) hyperthermia treatment of tumors (see for example Fig. 1 in Tay et al. ACS Nano **12** (2018) 3699. However, with the current, chemically synthesized MNPs, a human sized MPI scanner would require magnetic field gradients that cannot be reached because of inherent limits given by physics. Consequently, MNPs with properties enhanced more than 10x would be a game changer.

Sputter-deposition of magnetic thin film systems is used for wide-spread applications such as cloud-based data storage, sensors e.g. for automotive applications. First steps have been undertaken to harness this technology for MNPs with enhanced properties for biomedical applications. However, to date, the current system designs have not yet optimally addressed the biomedical needs.

We have developed two candidate systems [superparamagnetic (SP-MDPs) and synthetic antiferromagnetic (SAF-MDPs) particles, 1 patent appl. EP20211045 by Profs. Hug/Suess / 1 in preparation] overcoming the current limits. With our competencies spanning from thin film magnetism, micromagnetic simulations, microfabrication, to pre-clinical MNP developments, two partners with established expertise in upscaling, fabrication and clinical opinion leaders, we can overcome current limits and demonstrate the advantageous properties arising from thin film-based MNPs for the envisioned biomedical applications (Fig. 2).

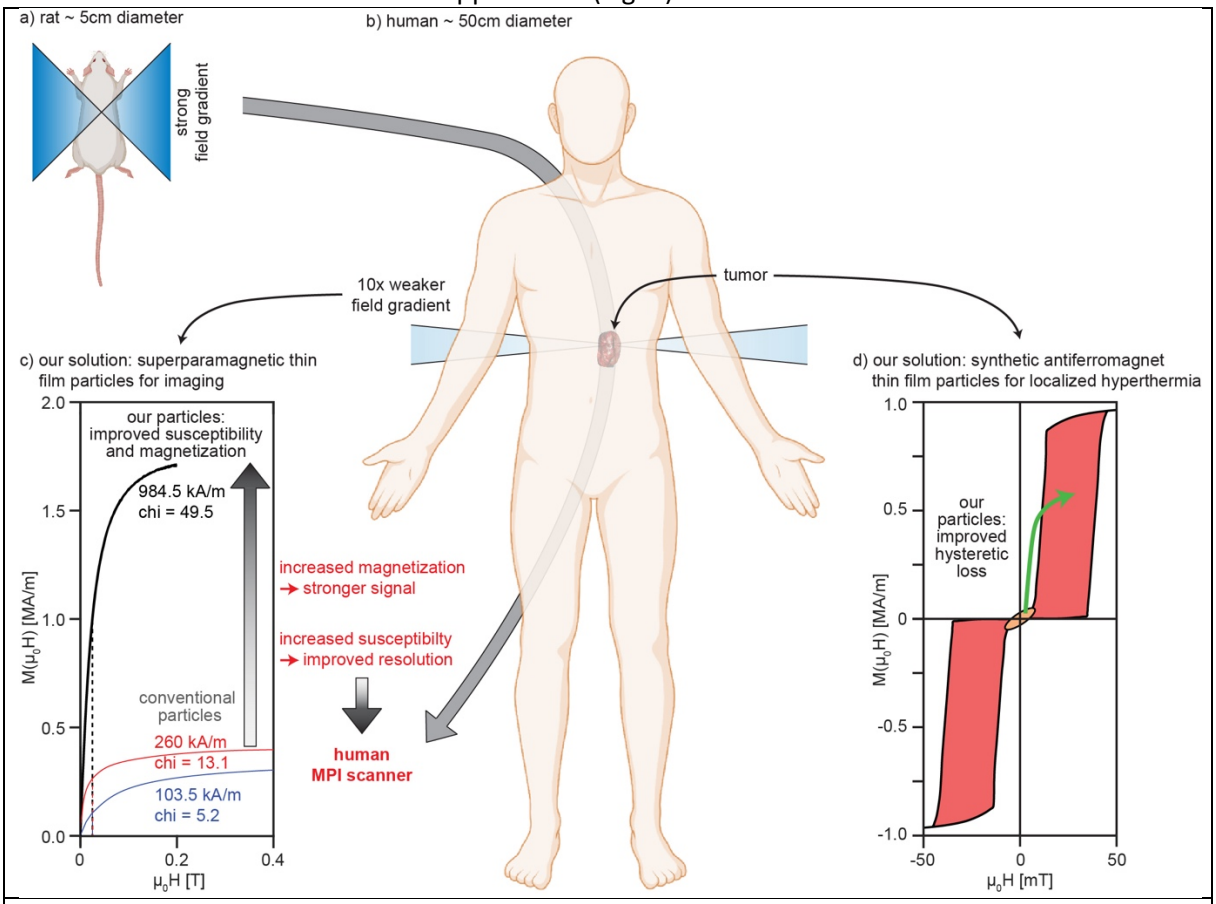

Figure 2: Human magnetic particle imaging (MPI) scanner and localized hyperthermia treatments become possible with our improved magnetic thin film nanoparticles.

a) MPI scanners for rat-sized objects are available, because the small-sized objects permit high magnetic field gradients.

b) the much larger size of the human body reduces the maximum possible field gradient by about a factor of 10 and with it the sensitivity and spatial resolution of the MPI signal.

c) our thin film superparamagnetic nanoparticles with increased susceptibility and magnetization improve the detection sensitivity and spatial resolution and will ultimately permit the construction of a human MPI scanner, in-spite of the reduced magnetic field gradient.

d) our synthetic antiferromagnet magnetic nanoparticles with an increased hysteretic heat loss compared to classical superparamagnetic iron-oxide particles (green area) will permit an efficient localized hyperthermia treatment of a tumor.

Fabrication Approach

We seek to investigate the biomedical potential of magnetic particles with performance-optimized physical properties (only limited by physics and no longer by synthesis constraints). We will create sufficient performance-optimized magnetic disk-shaped particles (MDPs) by thin-film deposition followed by microfabrication to assess their biomedical potential (Fig. 3). While this process may be considerably more expensive than chemical synthesis routes, it gives access to magnetic particles with unseen properties, which may open entirely new frontiers in diagnostics and therapy with disruptive potential. For this unique project, we have gathered expert academic and industrial partners to test this hypothesis. Our innovative magnetic thin film approaches as well as established industry collaborations for upscaling differentiates our approach from the state-of-the-art activities in the field.

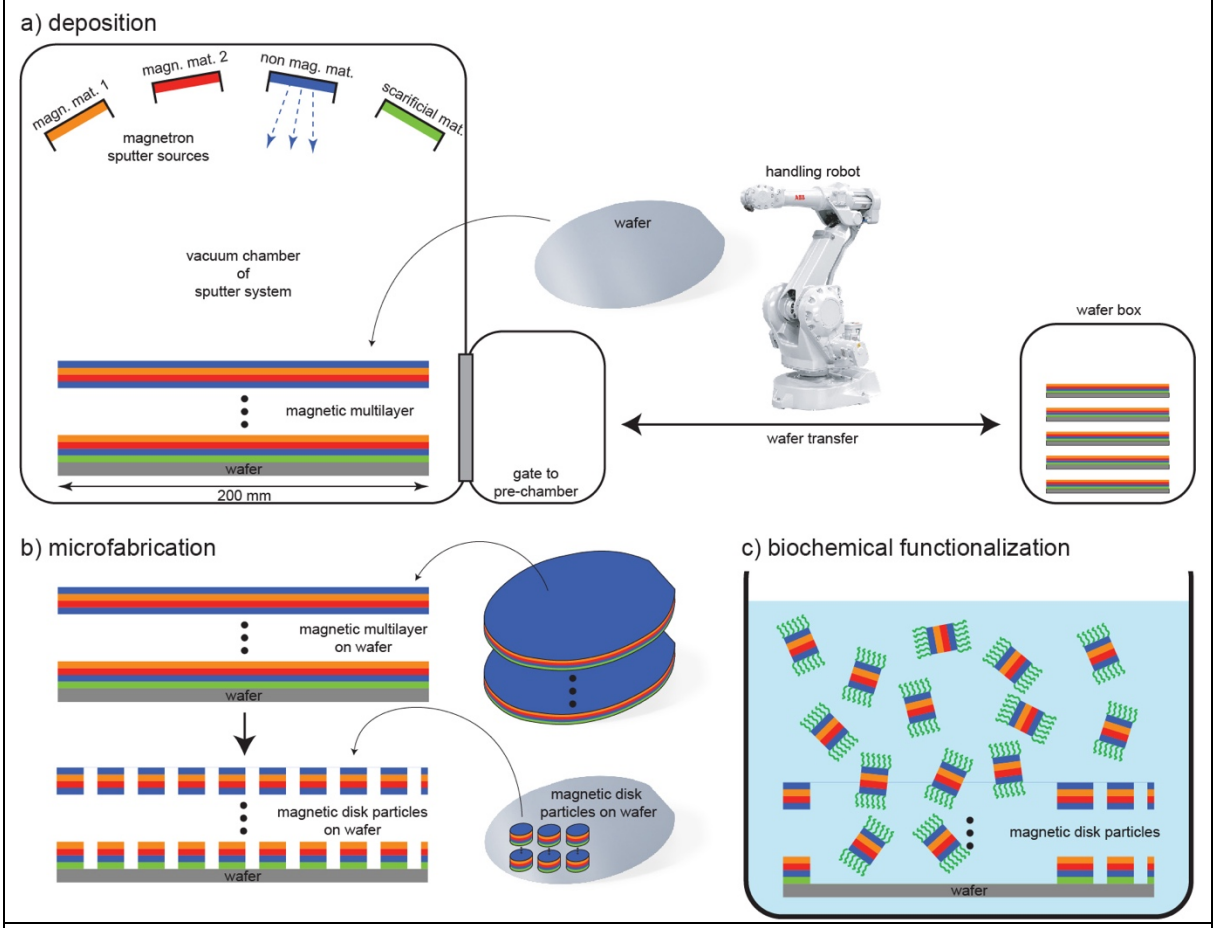

Figure 3: Schematics of our approach.
a) high-throughput sputter-deposition equipment available at an industrial partner is used to deposit two magnetic multilayer candidate systems with superior magnetic properties for MPI and hyperthermia applications onto 200mm wafers.
b) high-throughput microfabrication of stacked multilayer systems available at an industrial partner will be employed to pattern 500nm-diameter islands on the 200mm wafers.
c) the particles will then be detached from the wafers and biochemically functionalized to obtain stable particle suspensions.

Analytical Services

The combination of our profound expertise in magnetism and magnetic materials and the availability of various state-of-the art and lab-built equipment for magnetic property analysis is advantageously used to consult our partners [Dr. Peter Wick (Empa) and Prof. Dr. Inge K. Herrmann (Empa & ETHZ)] and characterize magnetic properties of their magnetic nanoparticles for biomedical applications (Fig. 4).

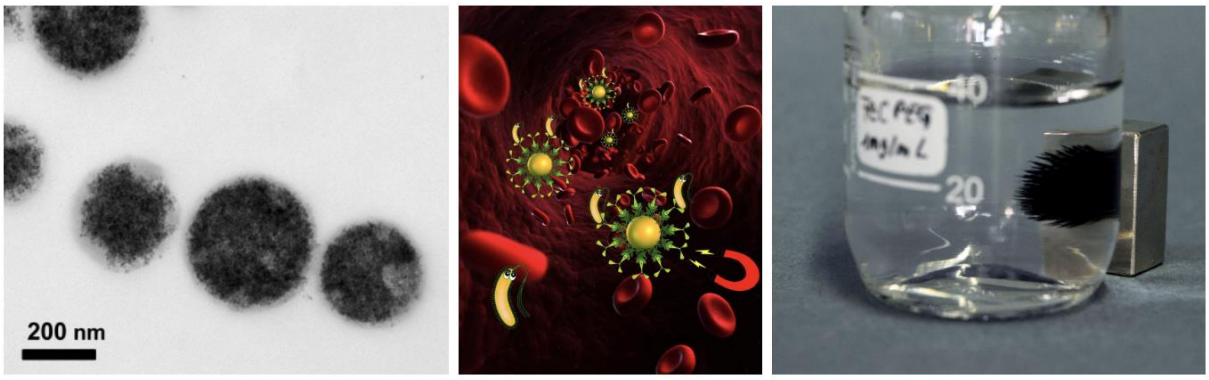

Figure 5. Surface functionalized magnetic nanoparticle clusters to capture and remove pathogens from blood.

Financing

The project is presently supported through Empa-internal resources. Further research applications have been submitted. Additional financial support from private foundations is presently searched.

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