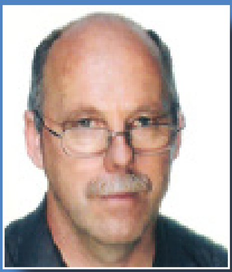

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MagnetoTheranostics

FROM SUPERPARAMAGNETIC NANO-PARTICLES UNTIL TOOLS FOR DETECTION AND TREATMENT OF CANCER





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What it's about…

Developing a platform based on superparamagnetic nanoparticles for diagnosis and treatment of cancer.

Context and project goals

The use of superparamagnetic iron oxide nanoparticles as contrast agents is well known, additionally, such particles are used in as source for local heating of cancer (Hyperthermia, clinical tests). In these two applications, dextran coated nanoparticles are used; for example in imaging of the liver a passive accumulation of the particles occurs, whereas for hyperthermia the particles are injected directly into the tumor. Our work with such particles as well as that presented in the literature shows that the potential of superparamagnetic nanoparticles for medical application is much larger. Specific adsorption of the particles at tumor cells, organs or even as shown by EPFL at organelles inside cells, opens a very large field of diagnostic applications, especially as contrast agent for molecular imaging by MRI. Interestingly, particles used as contrast agent are also useful for hyperthermia applications because superparamagnetic nanoparticles have relaxation times which allow heating by applying alternating magnetic fields with field strengths and frequencies applicable to human bodies.

Unfortunately the magnetic properties of the nanoparticles used today - maghemite (gamma-Fe_2O_3) - has too low a specific absorption rate, so that heating with the typical amount of particles, which can be transported after systemic injection to the cell of interest, is too low. This means that as of today a combination of diagnosis (specific adsorption of nanoparticles) and concurrent therapy is not possible. However, we are convinced that with improved superparamagnetic nanoparticles and an alternating magnetic field with a frequency and magnetic field strengths well adapted to the magnetic properties of the particles we will be able to develop a platform enabling diagnosis and therapy of some type of cancer (theranosis) to be specified.

It is obvious that the long term aim of our project is extremely challenging. Therefore, we like to start this project with two approaches:

a) molecular imaging with specific adsorbed nanoparticles
b) hyperthermia with nanocomposites that later will be combined

For both applications we start with superparamagnetic iron oxide nanoparticles because each of the partners has experiences and were successful with this type of nanoparticles and additionally in one or more of the following research areas:

- Synthesis, surface modification and characterisation (including primary toxicity studies) of superparamagnetic particles for medical applications
- Engineering of ac-magnetic field generators and modelling of interaction of ac magnetic fields in human bodies
- Use of nanoparticles in diagnosis and therapeutic applications
- Working in complex multidisciplinary projects

Focusing on one type of cancer (prostate for example) the diagnostic tool will be developed for the detection of metastasis in lymph nodes, whereas the therapeutic development (hyperthermia with nanocomposites using a, magnetic field generator and software for temperature distribution prediction) is focused on the corresponding primary tumor. In parallel new nanoparticles will be developed which fulfill the materials as well as biological properties simultaneously and in an improved manner, so that at the end of the 4 years at least 2 applications of nanoparticles are ready for clinical research and furthermore the combined theranostic approach would be ready for a focused development together with clinics and equipment/software manufacturer.

How it differentiates from similar projects in the field

Today, most of the research work is done in the field of contrast agent or magnetic hyperthermia. Only very few research groups try to combine both applications. The reason is that the magnetic properties of the particles have to be well adapted to the application. The approach of MagnetoTheranostics is the controlled synthesis and coating of the particles which will allow multifunctional use of the injected particles.

Quick summary of the project status and key results

In the first year, the researchers were able to develop a synthesis method which allows them the manufacturing of superparamagnetic iron oxide nanoparticles with mean sizes between 7 and 25 nm in a very reproducible way.

Important is that the synthesis is carried out in water and therefore easy to scale up. The particles which show also a narrow size distribution were characterized in detail regarding their structure and magnetic properties and were further functionalized with 11 different molecules. The same particles were successfully used for the preparation of injectable formulation foreseen for the treatment of primary tumors.

On the biological and medical side of the project, the animal model was determined and the most promising antibodies/epitopes for a high specificity of particle adsorption tested in vitro. To accelerate the development process, a model system was developed which allows a fast selection of functionalization methods and to investigate the behavior of nanoparticles in biological systems. The results showed that the functionalization of the nanoparticles with the selected antibodies is successful.

On the engineering side, the construction of the magnetic field generator is well advanced, a second prototype is under construction.

Success stories

The most important success in the project is to have reached after a short period a common scientific language which bridges the gaps between physics, medicine and engineering. Especially to be underlined is the very close cooperation of young researchers from all partners covering all scientific fields of the project.

Regarding the scientific progress, it is important to mention the fast development of a very flexible particle synthesis process which allows the reproducible manufacturing of particles for all partners of the project at an early stage.

New developments of our contrast agent in MRI was rated among the top 165 abstracts (out of 6038) at the annual meeting of the International Society for Magnetic Resonance in Medicine in Toronto, May 2015.

Main publications

JAM Bastiaansen, H Feliciano, AJ Coristine, JB Ledoux, D Bonvin, M Mionic H Hoffman, M Stuber, Non-invasive off-resonance gradient-free positive contrast flow-imaging using extraneous paramagnetic biomarker-induced spin-labeling, Proc Intl Soc Mag Reson Med 23, 102 (2015).

Sebastiano Barbieri, Olivio F. Donati, Johannes M. Froehlich, Harriet C. Thoeny, Impact of the Calculation Algorithm on Biexponential Fitting of Diffusion-Weighted MRI in Upper Abdominal Organs, Magnetic Resonance in Medicine, 2015.

“Theranostic platform combining nano-technology, biology, medical research & engineering for diagnosis and treatment of tumors with minimal side effects”