Quantification of magnetic nanoparticles in tissue demonstrated by magnetorelaxometry tomography

F. Wiekhorst[1], D. Eberbeck[1], U. Steinhoff [1], R. Jurgons[2], C. Seliger[2]
C. Alexiou[2], L. Trahms[1]

[1] *Physikalisch-Technische Bundesanstalt, Berlin, Germany*
[2] *Head and Neck Surgery University Erlangen-Nürnberg, Germany*

Introduction

Magnetic nanoparticles find wide application in medical diagnostics and therapy, examples are magnetic drug targeting, hyperthermia, magnetofection, and contrast agents in magnetic resonance imaging. For these applications it is of great importance to monitor and to control the accumulation of magnetic nanoparticles in the body regions of interest. Additionally, any quantitative information further improves the results.
Magnetorelaxometry (MRX) [1] is a technique to investigate with high sensitivity the properties of magnetic nanoparticle ensembles [2]. In the present work we describe a method to quantify the relative mass of magnetic nanoparticles in biological tissue using magnetorelaxometry data. As an example the method is applied to determine the relative mass of magnetic nanoparticles in a squamous VX-2 carcinoma of a rabbit treated by locoregional chemotherapy after magnetic drug targeting [3].

Magnetorelaxometry

In a typical magnetorelaxometry measurement the sample containing magnetic nanoparticles is magnetized in a magnetic field of defined duration. After the field is switched off, the decay of the sample magnetization is measured by a SQUID magnetic field sensor. Undesirable remanent background signals are suppressed.
Two different relaxation mechanisms can be distinguished. One is the Brownian relaxation with the magnetization decaying by rotation of the whole particles. The other is the Néel relaxation, where the decay of magnetization is caused by changing the direction of the magnetic moments inside the nanoparticles.
Usually, both relaxation mechanisms are present and the process with the shortest relaxation time will dominate. In samples of immobilized nanoparticles the Brownian relaxation is suppressed, so that bound particles can be identified by their relaxation behavior [4].

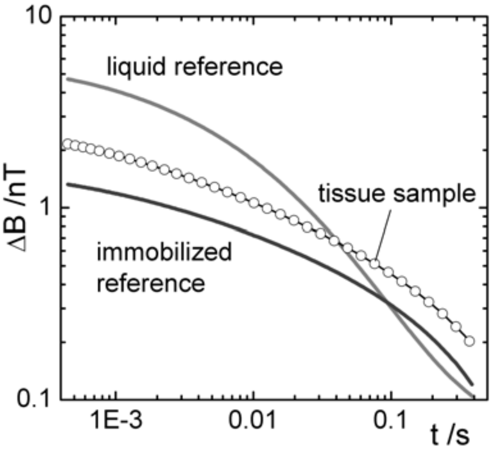

Figure 1: MRX relaxation curves of liquid, immobilized reference, and tissue sample, respectively.

Quantification method

The basic procedure to quantify the relative mass of magnetic nanoparticles in tissue starts with the preparation of a suitable set of reference samples and the characterization of their relaxation behavior. Then, the relaxation curve of the tissue sample is measured. By comparing the shape of the tissue sample curve with the reference curves the general relaxation behavior of the tissue sample is identified. Finally, the quantification of the relative mass of mag-

netic nanoparticles in the tissue sample is carried out by amplitude comparison with the identified reference curve.
In detail, we consider for the characterization of the reference samples the ratio of signal amplitude to iron concentration of the nanoparticles and the shape differences between Brownian and Néel relaxation curves as shown in Fig.1. Furthermore, to assess the aggregation behavior of the particles, a scaling investigation of different particle concentrations is essential. Thereby, different suspending biological media have to be taken into account [5].
As an example of the method, we quantified the relative mass of magnetic nanoparticles in a squamous VX-2 carcinoma induced in a rabbit after magnetic drug targeting [6]. One ml of magnetic nanoparticles (targetMAG, chemicell, Berlin) in suspension were intraarterially administered and then attracted and concentrated by a high magnetic field gradient focused at the tumor region. After sacrificing the animal, the tumor was extracted and magnetorelaxometry was performed.

Results

Figure 1 shows the different relaxation signals of the liquid and the immobilized reference sample, and of the tissue sample. From the shape of the tissue sample curve we conclude that the magnetic nanoparticles in the tissue are immobilized. The quantification directly follows from normalizing the signal amplitude of the tissue signals to the chosen reference signal.
As a first application of the method, we quantified the relative mass distribution of magnetic nanoparticles within a small slice of the extracted tumor. The slice was divided into a number of small pieces, the pieces were measured by magnetorelaxometry and the relative mass of the particles was quantified.
The results are shown in Fig. 2. The relative mass of magnetic nanoparticles could be resolved down to 10 ng per mg tissue by this method. These data provide important information to optimize the drug targeting process.

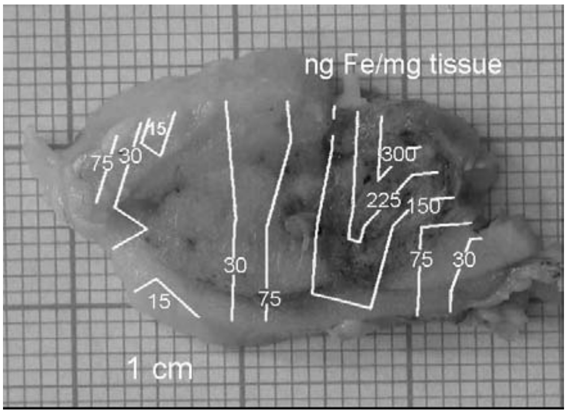

Figure 2: Relative mass of magnetic nanoparticles throughout a slice of VX-2 squamous carcinoma.

Discussion and summary

Magnetorelaxometry is a fast and integral technique for quantification of the relative mass of magnetic nanoparticles in tissue. Quantification is reached by relating the tissue relaxation curves to reference curves with identical relaxation behavior.
This method is not limited to in-vitro samples, but suited for in-vivo applications as well. For this purpose, we presently construct a dedicated magnetorelaxometry device for in-vivo measurements in small animals [7].

Acknowledgments

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