# Nanoparticle-distribution after Magnetic Drug Targeting

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## Introduction

In medicine magnetic nanoparticles can be used in vivo as MR-imaging contrast agents [1]. A new approach in regional cancer therapy is Magnetic Drug Targeting (MDT). Functionalised magnetic nanoparticles, bound to mitoxantrone, were given intraarterially and attracted in the tumor region with an external magnetic field (1.7 Tesla). Figure 1 shows a electromicroscopic picture of nanoparticles, which were used in our experiments. Using this delivery system we could achieve total tumor remissions without negative side effects in tumor bearing rabbits by the use of only 20% and 50% of the regular systemic chemotherapeutic dosage [2, 3, 4]. Measurements of radioactive $^{59}$Fe-nanoparticles showed 114 times more activity in the tumor region after Magnetic Drug Targeting compared to the control without magnetic field [5]. HPLC-analysis of the chemotherapeutic agent after MDT revealed a 75 times higher concentration of the administered dose in the tumor region compared to the regular systemic administration [6, 7].
In the present study the distribution of the particles after MDT was investigated by non invasive common imaging techniques and by spatially resolved magnetorelaxometry [8].

## Material and Methods

In correspondence to histological examination the investigations on the biodistribution of magnetic nanoparticles after MDT were performed with a high resolution 3-dimensional x-ray-tomography (CCD-Camera).


Figure 1: Electromicroscopic picture of nanoparticles used in MDT embedded in agar.

Furthermore enrichment and distribution of the nanoparticles were displayed qualitatively by the use of a 4.7 Tesla MRI. In addition, the nanoparticle enrichment in the tumor region was quantified by SQUIDs, which measured their relaxation signal after magnetization in a homogeneous field.

## Results

In correspondence to the 2-dimensional histological examination of the tumor tissue after MDT, X-ray-tomography verifies, that the vascular system of the tumor can be reached by Magnetic Drug Targeting (fig. 2).

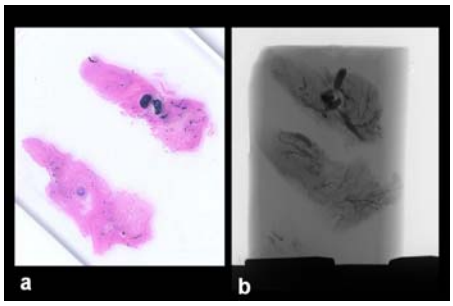


Figure 2: VX2-tumor tissue embedded in paraffin and stained with Prussian blue after MDT (fig. 2a). figures 2b show a X-ray tomography picture of the respective tissue. The nanoparticles are visible in the tumor supplying vessels.

With Magnet Resonance Imaging (MRI) the enrichment of the nanoparticles can be shown qualitatively after MDT.
SQUID-measurements of the tumor region revealed a high concentration of the magnetic nanoparticles in the tumor tissue (fig. 3).

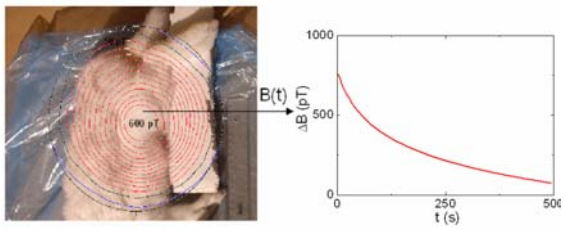


Figure 3: Magneotrelaxometry measurements of the tumor region after MDT. Left: Magnetic field distribution generated by the magnetic nanoparticles after magnetization. The location of the magnetization corresponds to the tumor position. Right: Single channel relaxation signal of the magnetic nanoparticles.

## Conclusions

Common imaging techniques (x-ray, MRI) offer non invasively information about the biodistribution of magnetic nanoparticles.
Quantitative information on particle accumulation is provided by magnetrelaxometry. A combination of these techniques may become a promising tool to visualize and quantify the specific enrichment of magnetic nanoparticles in certain body compartments.

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