In-vivo monitoring of magnetically labeled mesenchymal stem cells in kidneys after selective intrarenal injection in a glomerulonephritis model in rats at 3T

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Introduction
Early-stage kidney disease and end-stage renal failure is a major clinical and socio-economic problem. The current therapeutic opportunities to slow the progression of the disease are limited. Pluripotent stem cells, and especially mesenchymal stem cells (MSC), seem to have therapeutic potential in repair, revascularisation and regeneration of tissues in numerous genetic, degenerative or malignant diseases [1]. In renal diseases, MSC may have therapeutic potential to repair damaged renal structures or to improve kidney function [2,3]. In-vivo monitoring of cells with MRI after magnetically cellular labeling procedures was shown by several groups [4-6].

The purpose of this study was to detect Superparamagnetic Particles of Iron Oxide (SPIO)-labeled mesenchymal stem cells of the rat after selective injection in the renal artery and to monitor their in-vivo distribution with MRI at 3T using an experimental rat model of glomerulonephritis.

Material and Methods
For in-vitro cell labeling rMSC of Sprague Dawley (SD) rats were incubated with Resovist® (Schering AG, Berlin, Germany) for 24 h and cellular uptake was proven cytologically by Prussian blue staining. In 5 male SD rats (250.8 ± 5.5g body weight) a Thy-1 glomerulonephritis was induced by intravenous (i.v.) injection of anti-Thy 1 monoclonal antibodies. 4 days after induction of glomerulonephritis two groups with catheter-guided, selective intraarterial injection of 1×10^6 rMSCs (MSC group, n=3) and pure saline injection (control group, n=2) were built. MRI scans were performed 6 days before (baseline), 1-2 hours, 4, 7, 11 and 22 days after stem cell or saline injection. MRI Imaging and Relaxometry was performed on a clinical 3T MR Scanner (Philips Intera) using a custom-made small animal solenoid coil. MRI data were acquired using a T2*-weighted 2D gradient echo sequence before (baseline), 1-2 hours, 4, 7, 11 and 22 days after stem cell or saline injection. MR Imaging and Relaxometry was performed on a clinical 3T MR Scanner (Philips Intera) using a custom-made small animal solenoid coil. MRI data were acquired using a T2*-weighted 2D gradient echo sequence (TR/TE 224/4.6ms, flip angle 80°, Field of View (FoV) 100 × 75 mm, Matrix 512×228, NSA 6, slices 12, slice thickness 1.5mm, effective voxel volume 20×33×1500µm).

Discussion and Conclusions
In this study we demonstrate the ability of serial in-vivo imaging of magnetically labeled stem cells (rMSC) in an animal model of glomerular disease in a clinical whole body 3T MRI scanner. We have shown the persistence of rMSC in glomeruli after intrarenal perfusion in MRI for at least 3 weeks after cell administration in correlation to histology and have indicators for a delayed migration to liver and spleen. Using MR Relaxometry, an initial approach for the quantification of labeled cells in tissue was given. Our preliminary study demonstrates the potential of MRI for a non-invasive in-vivo monitoring of magnetically labeled cells and offers the possibility of monitoring cell-based therapies in therapeutic treatment models in the future.

References