Iron oxide enhanced MRI for monitoring of anti-angiogenic tumor treatment

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PURPOSE:

The aim of this study was the evaluation of iron oxide enhanced MRI for non-invasive, early detection of the efficacy of anti-angiogenic tumor treatment.

MATERIALS AND METHODS:

Human fibrosarcoma bearing nude mice (HT 1080, tumor size 5- 15 mm) were i.v. injected with a vascular targeting agent (VTA) inducing selective thrombosis in tumor neovasculature (treatment group, n = 11) or saline (controls, n = 13) respectively. MRI was performed before and after i.v. injection of an ultrasmall superparamagnetic iron oxide (USPIO, SHU 555 C, Schering® AG Berlin) 4-8 hours after initiation of treatment. Iron oxide induced changes in R2* (ΔR2*) were measured using a T2 weighted dual Echo-EPI sequence. The vascular volume fraction (VVF) was determined by calibration of ΔR2* values of tumor tissue with ΔR2* of muscle. Parametric ΔR2*-maps were calculated for visualization of tumor perfusion patterns. MRI results were correlated with the immunhistochemistry of tumor sections.

RESULTS:

After injection of the VTA a significant reduction of the VVF (2.25 ± 1.08 % versus 0.48 ± 0.3 %; $p < 0.01$) and an approximate 80% decrease of ΔR2* in treated animals compared to controls was measured (Fig. 1). ΔR2*-maps revealed a clear reduction of tumor perfusion after anti-angiogenic tumor therapy (Fig. 2a,b). The immunhistochemistry with extensive tumor thrombosis after treatment confirmed the MRI results (Fig. 2 c,d).

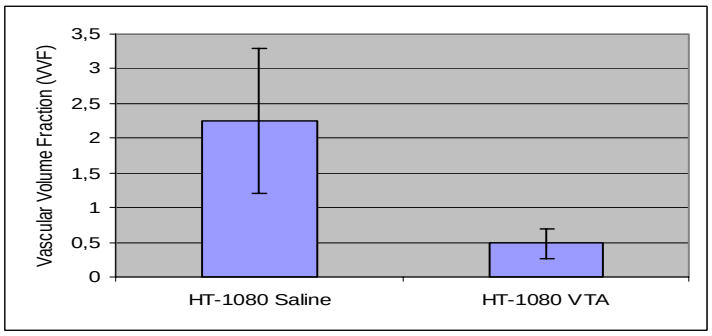

Figure 1: Vascular Volume Fraction (VVF) in fibrosarcoma (HT-1080) bearing mice after i.v. injection of saline (control) and a vascular targeting agent (VTA).

CONCLUSION:

Iron oxide enhanced MRI is a useful method for early non-invasive monitoring of tumor response of anti-angiogenic treatment. With the availability of bolus-injectable, long circulating iron oxides, which are currently in phase III clinical trials, this technique can readily be adapted for patient use.

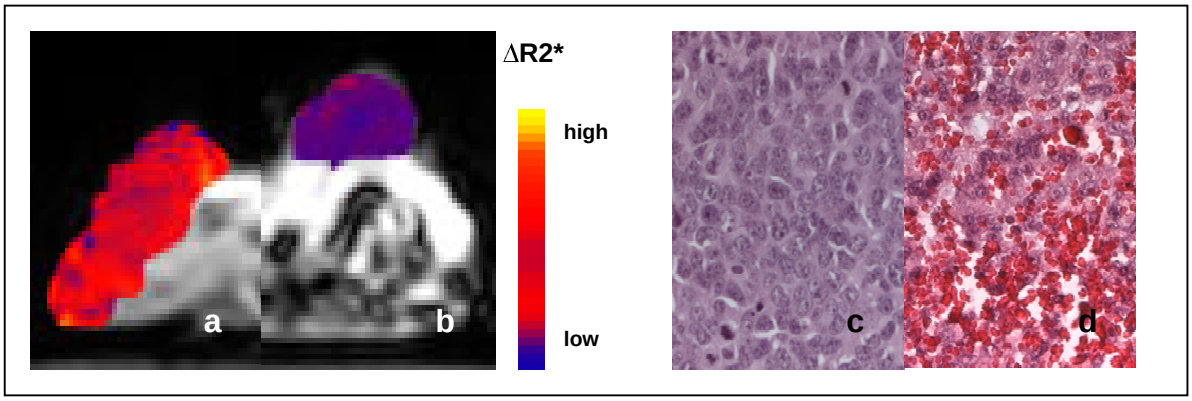

Figure 2: Human fibrosarcoma (HT-1080) bearing mice after i.v. injection of saline (a,c) and a vascular targeting agent (b,d) with a clear reduction of tumor perfusion in MRI parametric ΔR2*-maps (a,b) and an extensive tumor thrombosis at the immunhistochemistry (c,d) after anti-angiogenic tumor therapy.