Perfusion MRI for Monitoring Therapy Effects in Experimental Chronic Limb Ischemia

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Introduction: Until today, imaging of lower extremity blood supply and perfusion is limited to the display of the macroscopic vasculature by angiographic methods like DSA, CTA or MRA [1, 2]. However, all these methods are limited to high spatial resolution imaging of the arterial or venous vessels but do not display changes at the microvascular level in regard to tissue perfusion. MR perfusion imaging may overcome this limitation in experimental and clinical settings and may allow non-invasive monitoring of modern therapeutic options including angiogenisis.

Purpose: To implement and evaluate the use of perfusion MR in monitoring angiogenetic therapies and their effects based on a rabbit model of iatrogenic induced chronic lower limb ischemia.

Material & Methods: MR perfusion imaging was performed in 8 rabbits with chronic lower limb ischemia after unilateral SFA excision at 3 Tesla (Magnetom Verio, Siemens Healthcare) using a 32-element coil. In 4 animals MRI was performed at day 7 and in 4 animals at day 7 and 35 (after angiogenesis therapy). Multi-slice coverage was provided using a 2D-TurboFLASH technique at 1.5s temporal resolution with repeated measurements over 10min after injection of 0.1mmol/kg gadobutrol (Gadovist, Bayer Schering Pharma). One slice was placed through the aorta for measuring the Arterial Input Function (AIF) and 7 sliced covered the gluteal, thigh and knee musculature. Precontrast T1-mapping was performed using a variable TI GRE technique at identical slice locations (27 steps from 110 ms - 5s). Data were post-processed off-line using in-house written software PMI 0.3 including calculation of plasma flow (PF), plasma volume (PV) and extraction flow (EF) based on a 2-compartmental model. T1 mapping data were used to convert signal-time courses to tracer concentration [3].

Results: T1-maps produced robust results on with precontrast T1-values close to typical reference values at 3T. PF was significantly different between the non-ischemic and ischemic limb (14.3±11.5 vs. 8.4±3.9ml/100ml/min) on day 7 (**figure 1**) whereas there was no significant difference on day 35 after therapy (9.3±2.3 vs. 10.5±3.2 ml/100ml/min). EF showed similar findings with 2.17±1.71 vs. 1.71±1.6 ml/100ml/min on day 7 and 2.3±1.98 vs. 2.15±1.68 ml/100ml/min on day 35. PV did not show significant differences either before or after therapy.

Conclusion: Chronic experimental limb ischemia results in significant changes of MR derived perfusion parameters, with reconstitution after experimental therapy. Initial data indicate that perfusion MRI provides a useful tool for the evaluation of muscle ischemia and of therapy effects.

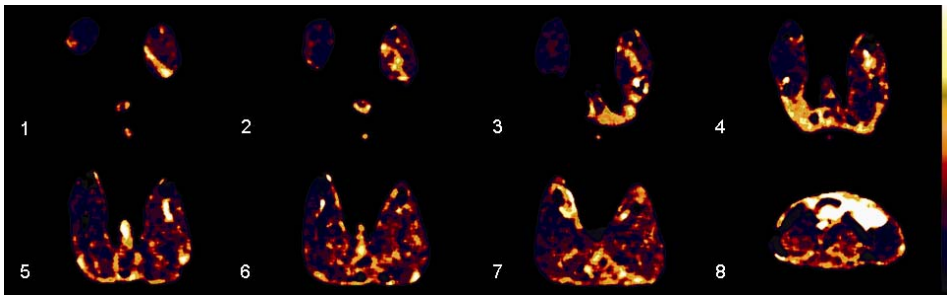

Figure1: Colour coded plasma flow images over 8 slices (1=distal, 8=central) at day 7 after left side SFA excision. Images show significantly higher plasma flow on the ischemic side before angiogenetic therapy.

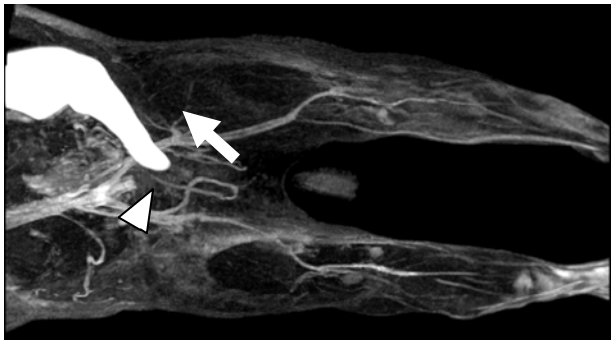

Figure 2: Peripheral angiography of the lower extremities of a rabbit after SFA excision (arrowhead). Contralateral side shows SFA and SFV (arrow).

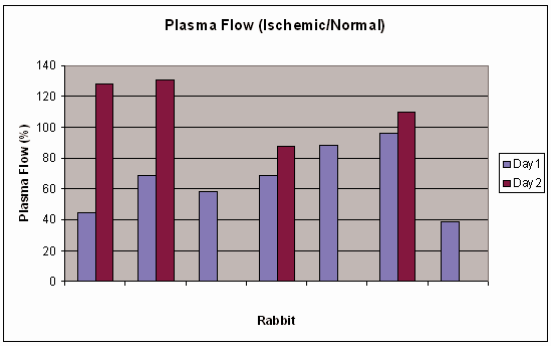

Figure 3: Plasma Flow Ratios between ischemic and non-ischemicextremity on day 7 and day 35 of therapy. PF is significantly reduced in the ischemic leg before therapy and increases again after therapy.

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3. Sourbron, S., et al., Choice of the regularization parameter for perfusion quantification with MRI. Phys Med Biol, 2004. 49(14): p. 3307-24.