Effects of an X-ray Contrast Medium Administration on Renal T_2* and T_2

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Introduction. X-ray contrast media (CM) are widely used in diagnostic and therapeutic procedures. Although usually well tolerated, CM can cause acute kidney injury (AKI). Medullary hypoxia is pivotal in the pathophysiology of CM-induced AKI (CI-AKI), as indicated by animal studies that invasively measured renal tissue oxygenation [1]. These invasive probes cover small renal areas only. Since renal oxygenation displays a marked spatial heterogeneity, methods that enable spatially resolved measurements are urgently warranted. BOLD MRI is increasingly used to monitor kidney oxygenation in basic science. Recent studies reported on the effects of intravenous CM administration on renal T_2* (or R_2* = 1/T_2*) [2,3], but did not benchmark these effects against effects induced by other interventions to provide a stringent interpretation of BOLD data. We studied the effects of injecting a high viscous CM into the thoracic aorta on renal T_2* and T_2 by use of a 9.4 T animal scanner in rats. The CM effects were benchmarked against pathophysiological relevant reversible interventions, i.e., brief periods of hypoxia and aortic occlusion.

Methods. Seven male Wistar rats were anesthetized (Urethane 20%; 6ml/kg BM i.p.) and equipped with a remotely controlled supra-renal aortic occluder and a carotid artery catheter with its tip towards the aorta. The catheter is used for CM administration to emulate percutaneous cardiac interventions that carry a higher risk for CI-AKI than intravenous injections. ***Experimental procedures:*** Following transfer into the MRI scanner and baseline T_2*/T_2 mapping, hypoxia was induced (inspiratory oxygen fraction 10%) for 9 min. Thereafter, the aorta was occluded for 3 min. Subsequently, CM (1.5 ml Iodixanol) was injected and T_2*/T_2 mapping repeated until up to 2 hours post CM-injection. ***MR imaging:*** Images were acquired on a 9.4T Bruker Biospec (Ettlingen, Germany) using a four-element RX surface coil array and a TX volume coil with a diameter of 72mm. T_2 mapping: MSME, TR = 550ms, TE = 10-70ms (7 values), TA = 1:40min. T_2* mapping: MGE, TR = 50ms, TE = 1.43-20.69ms (10 values), FA = 16°, TA = 1.20min. Renal T_2/T_2* were monitored for a coronal oblique slice (FOV (38.2x50.3)mm^2, matrix 169x215, in plane resolution (230x230)µm^2, slice thickness 1.4-1.5mm). Time-of-Flight (TOF) MR angiography was performed to verify the completeness of aortic occlusion. TOF angiography consisted of an untriggered spoiled gradient echo sequence (2D FLASH, TR = 11ms, TE = 3ms, FA = 80°, in plane resolution of (200x268)µm^2) with 15 slices of 1.0 mm thickness placed perpendicular to the major renal blood vessels, acquired in 24 seconds. Regions of interest were determined according to morphological features in the cortex (COR), outer medulla (OM), inner medulla (IM), and papilla (PAP).

Results. Hypoxia decreased T_2* in all layers (Fig. 1). The decrease was smaller in COR (~40%) than in the other layers (~55-60%). The T_2 decreases were smaller than those in T_2*. The short aortic occlusion decreased T_2* in all layers (Fig.2). The decrease was smaller in COR (~18%) than in the other layers (~30-40%). The T_2 decreases were smaller than those in T_2* in OM and PAP. Upon injection of CM, T_2* increased by about 20% within the first 10 min in COR and OM, then decreased again, finally reaching values slightly below (~10-20%) baseline (Fig. 3). In IM and PAP, the initial increases were smaller and the later decreases were more pronounced (~30-40%). In neither layer did T_2* regain control level within the observation period. T_2 did not drop significantly below baseline in COR, OM, and PAP, in OM it even remained above baseline values.

Discussion. T_2*/T_2 mappings during hypoxia and aortic occlusion correspond qualitatively with previous data obtained by invasive tissue pO_2 measurements. T_2* mapping upon CM injection corroborates invasively obtained data and demonstrates that CM affects medullary oxygenation. The CM-induced T_2* decrease in OM was small versus hypoxia and aortic occlusion. T_2* decreases more during hypoxia than during aortic occlusion. This indicates that T_2* may not accurately reflect blood oxygenation under certain conditions.

References. [1] Seeliger et al. *J Am Soc Nephrol* 2007; [2] Zhang et al. *Contrast Media Mol Imaging* 2012; [3] Haneder et al. *Invest Radiol* 2012.

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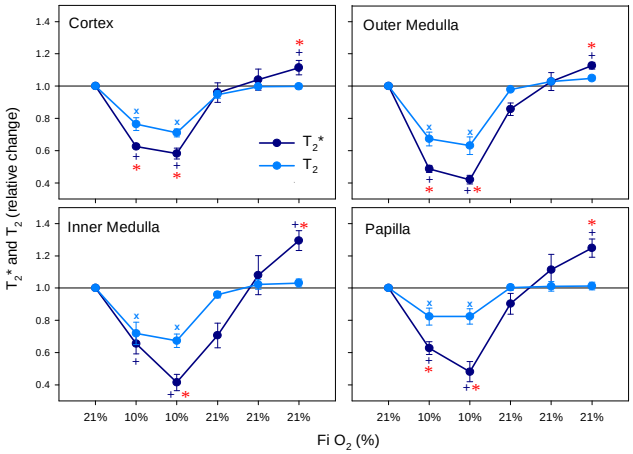

Fig.1. Relative changes of T_2* and T_2 induced by changing the inspiratory oxygen fraction (FiO_2) from normoxia (21%) to hypoxia (10%) and than to normoxia again. Values are mean ± SEM; n = 7 rats; (+) $p < 0.05$ *versus* baseline T_2*, (x) $p < 0.05$ *versus* baseline T_2, (*) $p < 0.05$ T_2* *versus* T_2.

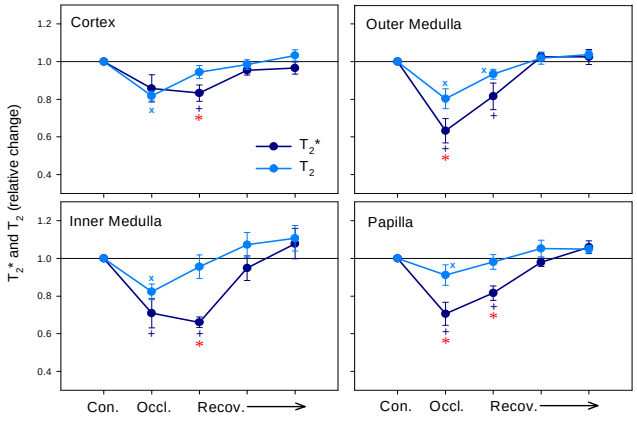

Fig.2. Relative changes of T_2*/T_2 from baseline (Con.) during 3 min of aortic occlusion (Occl.) and after releasing the occlusion (recovery; Recov.) Values are mean ± SEM; n = 7; significance is denoted as in Fig. 1.

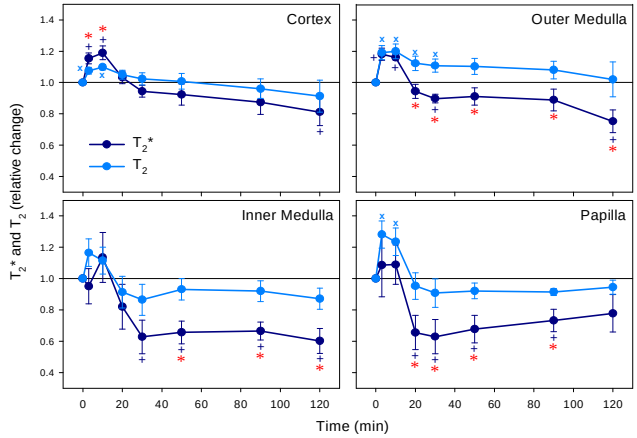

Fig. 3. Relative changes of T_2*/T_2 induced by intra-arterial bolus injection of the x-ray contrast medium at time zero. Values are mean ± SEM; n = 7; significance is denoted as in Fig. 1.