# Renal Blood Oxygen Level Dependent (BOLD) Magnetic Resonance Imaging in a Rodent Model of Hypertension Mediated End Organ Damage

**S. C. Lenhard[1], A. Grill[1], K. Aravindhan[1], R. Bentley[1], K. Maniscalco[1], C. P. Doe[1], R. N. Willette[1], and B. M. Jucker[1]**

[1]GlaxoSmithKline, King of Prussia, PA, United States

**Introduction:** The BOLD MRI technique exploits the magnetic properties of both oxy-and deoxyhemoglobin. Changes in the renal BOLD MRI signal can be interpreted as changes in tissue $pO_2$ in hypoxic environments such as the renal medulla and possibly cortex (1). In this study, we have implemented BOLD MRI in the renin dTg (double transgenic overexpressing both human angiotensinogen and human renin) rat model of hypertension to characterize changes in renal tissue oxygenation during the progression of renal dysfunction.

**Methods:** Age matched Sprague Dawley and renin dTg rats, 7-10 weeks of age were used in the study. Imaging was performed on a 4.7T Bruker Biospin scanner (Billerica, MA) using a multiple gradient-recalled echo (mGRE) sequence (TR/TE/flip angle/bandwidth = 400 msec/3.15-50.89 msec/30°/54 kHz) to acquire 12 $T_2$*-weighted images. The field of view (FOV) was 6 cm, with a matrix size of 256 × 256 and slice thickness of 2.0 mm. Bruker ParaVision software was used to manually trace ROIs for cortex and outer medulla. The image ROI data were fitted to calculate $R_2$*. Urine was collected weekly in order to measure the microalbumin concentration.

**Results:** Serial $T_2$* weighted images in same animal were acquired in age matched Sprague Dawley and renin dTg rats at 7, 9 and 10 (approximate moribund age in renin dTg rats) weeks of age to illustrate changes in the renal cortical and medullary BOLD signal in healthy and in renin dTg rats as they progress to renal failure (Figure 1,2). While cortical and medullary $R_2$* remained stable in the SD rats (Figure 2), it continued to increase in the renin dTg rats with large increases in cortical $R_2$* which is reflected by the temporal cortical signal loss observed in the $T_2$* weighted image in Figure 1. These pilot results in a small cohort of animals led to the design of a study in which we characterized changes in urine microalbuminuria and found it to significantly correlate with the cortical and medullary $R_2$* signal (r=0.69 and r=0.71 respectively, P<0.0001) (Figure 3).

**Summary:** Kidney BOLD MRI can be utilized non-invasively to detect spatially distinct changes to renal tissue oxygenation in the renin dTg rodent model of aggressive hypertension mediated renal dysfunction.

**References:**

1) Prasad et al., *Circulation* 94:3271, 1996

**Figure 1** $T_2$* weighted images in a renin dTg rat

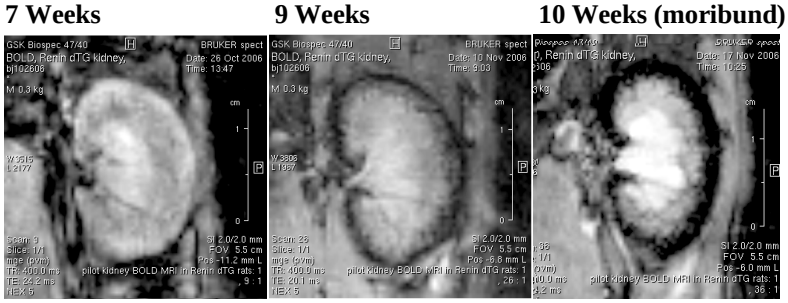


**Figure 2** Temporal renal $R_2$* in Sprague Dawley and renin dTg rats

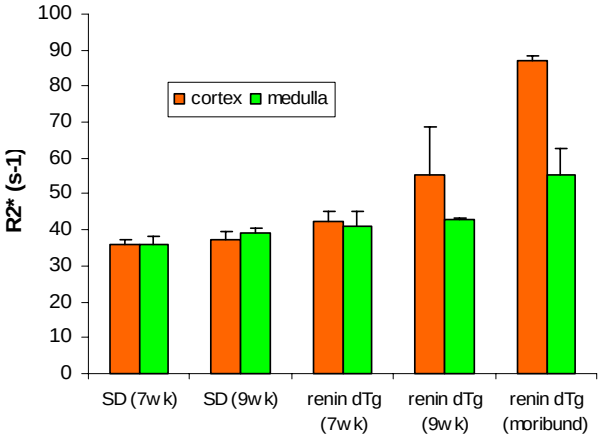


**Figure 3**