Changes in Intrarenal Oxygenation as Evaluated by BOLD MRI in a Rat Biliary Obstruction Model

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INTRODUCTION: Blood oxygenation level-dependent (BOLD) MRI was shown to allow non-invasive observation of renal oxygenation in human diseases and animal models [1-3]. BOLD MRI signal intensity (SI) is measured by using a gradient-echo sequence at several different echo times. The apparent spin-spin relaxation rate, R2* (=1/T2*) is calculated by using the slope of LN(SI) versus echo time [1]. R2* is directly proportional to the tissue content of deoxyhemoglobin and in turn to tissue PO2. By contrast, the blood flow to the medulla is low, and generally, the medulla is poorly oxygenated, resulting in a medullary PO2 consistently lower than that in the cortex. Thus, there is a high R2* in medulla than that in cortex [1, 4]. It was reported that there was alteration of cortical R2* (CR2*) and medullary R2* (MR2*) in human with chronic kidney disease, transplanted kidneys, and diabetic nephropathy [5-7]. The association between renal dysfunction and obstructive jaundice is well established, however, the exact incidence and extent of the problem has not been determined accurately [8]. Experimental bile duct ligation has been widely used as an animal model to evaluate the renal molecular changes after acute biliary obstruction [9-10]. This study aims to investigate the alteration of R2* in the kidney of rats, and MR2* in renal medulla of rat model induced by bile duct ligation.

MATERIALS AND METHODS: Animal Preparation: There were 9 normal male Sprague-Dawley rats (200 ± 20 g) were used in this study. Four rats were enrolled in the model group on the 9th day after bile duct ligation. Five rats were enrolled in the control group without any treatment. MRI experiments were repeated once on 5 days intervals in control group, and repeated once at 2 days intervals in model group. All rats were anesthetized with 10% chloral hydrate during MR scan.

MRS Protocol: All MRI measurements were acquired utilizing the Siemens Avanto 1.5 T clinic scanner with a phased array coil for rat (Shanghai Chenguang Medical Technologies Co., Ltd). Axial and coronal T2W were acquired using turbo spin echo, repetition time (TR) / echo time (TE) = 2500/134 ms, flip angle = 150°, field of view (FOV) = 200 x 150mm2, acquisition matrix = 256 x 192, slice thickness = 2.5mm. T2*WI MRI was performed in coronal slices covering the kidneys using a gradient-echo sequence with 10 TE s (3.85, 9.95, 16.04, 22.13, 28.22, 34.31, 40.4, 46.49, 52.58 and 58.67ms), TR = 65 ms, flip angle = 30°, FOV = 200 x 150mm2, acquisition matrix = 256 x 192, slice thickness = 2.5mm and number of averages (NEX) = 14. Data Analysis: All MR images were analyzed using the Siemens MR Workstation. A region of interest (ROI) was defined to measure signal intensity (SI) at all TEs in the right kidney. The ROIs (ROI, large than 0.27cm2, 45 pixels) in the cortex and medulla were carefully defined over the coronal T2WI and T2*WI at TE = 3.85ms. All MR images were carefully observed to avoid the susceptibility artifacts on the kidneys caused by bowel gas. Mean signal intensity (SI) within each region of interest is measured and used to generate LN (SI/SL1=3.85) versus TE curve, which is then fit to a straight line to determine the slope (R2*) [1]. All data were expressed as mean ± SEM. CR2* and MR2* in control and model groups were compared with One-way ANOVA test. P < 0.05 was considered as statistical significant.

Histology Preparation: After the MRI experiments, 3 rats were selected for histological HE staining to observe renal injury induced by bile duct ligation. Five rats were enrolled in the control group without any treatment. MRI experiments were repeated once on 5 days intervals in control group, and repeated once at 2 days intervals in model group. All rats were anesthetized with 10% chloral hydrate during MR scan.

RESULTS: Fig.1 showed a typical T2WI, T2*WI at TE = 3.85 and R2* map in a rat. Fig.2 showed two typical LN curves of the cortex and medulla in a normal rat, which were fit to two straight lines, and cortical R2* (CR2*) and medullary R2* (MR2*) were generated by using the slopes of two lines. There was no difference in cortical R2* and medullary R2* values in an individual rat in twice BOLD MRI experiments. Fig.3 showed mean CR2* and MR2* values in control and model groups. The MR2* was significantly higher than CR2* in both control group (42.49 ± 2.15 v.s. 34.62 ± 2.19) and model group (50.31 ± 1.80 v.s. 38.25 ± 1.60), respectively. And MR2* in model group is higher than that in control group (Fig.3), but the difference in CR2* was not significant between two groups. Fig.4 showed the HE staining in the kidneys. The medullary tubular in the animal model was damaged compared to the normal tubular.

DISCUSSIONS: The results of this study suggested that, there was an increase in R2* values in the renal medulla of rat model induced by bile duct ligation. Bile duct ligation induces an acute obstructive jaundice, and liver fibrosis is subsequently achieved between seven days to four weeks [11]. Renal function is altered by acute biliary obstruction [8-9]. Our results implicated that acute biliary obstruction induced an alteration of renal medullar oxygenation. It was reported that bilirubin transport in renal tubular was enhanced in biliary obstruction model, so as to facilitate the bilirubin clearance [10]. This enhanced tubular function might cause much oxygen consumption and lead to R2* increasing in the medulla. We also observed medullary tubular necrosis induced by obstructive jaundice, as Fogarty BJ has found [12]. Acute tubular necrosis might be a possible contributor to a high R2* in the medulla. A previous study has reported that there was a high R2* in the kidney transplantation when an acute tubular necrosis occurred [13].

CONCLUSION: The increase of R2* in renal medulla of rat with biliary obstruction implicated an alteration of renal medullar oxygenation. And there was no significant change in cortical R2* in this biliary obstruction model.

REFERENCES: