# DW-MRI evaluation of the serial changes of diffusion and microperfusion in adriamycin induced renal injury rat

Haoran Sun[1], Huanhuan Wu[2], and Ziheng Zhang[3]

*[1]Radiology, Tianjin Medical University Hospital, Tianjin, Tianjin, China, [2]Tianjin Medical University Hospital, China, [3]MR Research China,GE Healthcare, Shanghai, China*

**Introduction:** Adriamycin is a potent anticancer agent. Its clinical use is limited for its marked cardiotoxicity and nephrotoxicity. Adriamycin-elicited proteinuric renal injury in rodents is an established model, which mirrors chronic kidney disease due to primary focal segmental glomerulosclerosis seen in humans[1]. Diffusion weighted (DW) MRI techniques, based on the Brownian motions of water molecules between tissues and cells, provide a non-invasive assessment of molecular diffusion and microcirculation in vivo. Intra-voxel incoherent motion (IVIM)[2] DWI has recently shown a potential to assess kidney function, through the parameters that reflect changes in overall diffusion (apparent diffusion coefficient, ADC), perfusion fraction f, pseudo diffusion D* and true diffusion D[3]. The aim of this study is to evaluate the feasibility of the mono- and bi-exponential models through multi-b DW-MRI measurements in reflection of the serial variation of diffusion and microperfusion noninvasively on adriamycin induced rodent renal injury models. Histopathological examinations were performed for reference.

**Materials and Methods:** This study was approved by Animal Care and Use Committee, XXX. Adriamycin was administered into the tail vein (9mg/kg) to induce renal injury in 15 rats. MR scanning was performed for each rat before and 1w, 2w, 3w, 4w, 5w, 6w, 7w and 8w after the injection on a 3.0T scanner (MR750, GE, USA) using an animal coil (Magtron, China). Besides $T_1$WI and $T_2$WI, axial single shot echo planar imaging (SS-EPI) DW images with 13 b values from 0 to 1500s/mm$^2$ was acquired. The results were analyzed using both mono- and bi-exponential model at Advantage Workstation (GE, USA) with the mappings of ADC, f, D* and D obtained, as illustrated in Fig 1. The regions of interest (ROIs) on cortex (CO), outer stripe of the outer medulla (OM) and inner stripe of the outer medulla (IM) at the hilum level were selected. Two model rats were scarified at each time point after MR acquisition for histopathological examination, with exception at the 2nd week which had only one sample as well as the normal rats which waivered histological examination.

**Results and Discussion:** As shown on DW images, one could readily delineate the strips of CO, OM and IM in normal kidneys. The ROIs in each strip were sketched on b=0 DW images (Fig. 1). From Fig. 2a, one could disclose ADC values and f fractions of all three stripes decreased in overall trend, while the changed relatively unstably, which decreased at first before increased transiently then decreased following. ADC value behaves as a weight of the true diffusion and pseudo-diffusion. The f fraction reflects tissue dynamic fluid content[4]. The decreasing of f fraction was associated with the progressive loss of vascular structures[5], which was confirmed by the histological results: Glomerulosclerosis, inflammatory cell infiltration and interstitial fibrosis had been replacing the vascular structure along with the progression of renal injury (Fig. 3). D* values showed a tendency of steadily increasing on all three stripes. D* value is sensitive to flow velocity within both renal vessels and tubules[4]. The excess of vasoconstrictor substances, such as angiotensin-II and endothelin-1[6] during renal injury might cause the dynamic fluid content decreasing and the velocity increasing as a compensating and repairing mechanism, resulting in the decreasing of f fraction and increasing of D* values. D value, which reflects water molecules pure diffusion in vivo, is sensitive to microstructural barriers that may limit free diffusion[4]. Surprisingly, no significant variation of D value was observed in CO and OM stripes, while the change in IM was unstable.

**Conclusion:** The ADC, f, and D* values are sensitive to the progression of the chronic kidney disease induced by adriamycin and according to the histological findings, which suggests one can noninvasively assess renal injury using DW-MRI method.

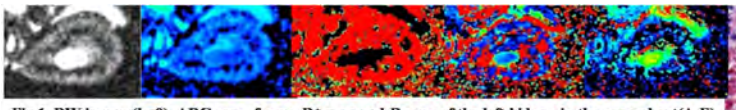

Fig 1. DW images(b=0), ADC map, f map, D* map and D map of the left kidney in the normal rat(A-E).

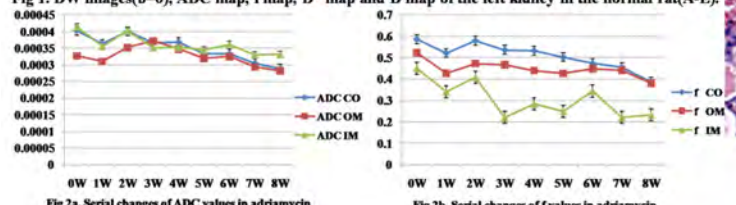


Fig 2a. Serial changes of ADC values in adriamycin induced renal injury




Fig 2b. Serial changes of f values in adriamycin induced renal injury

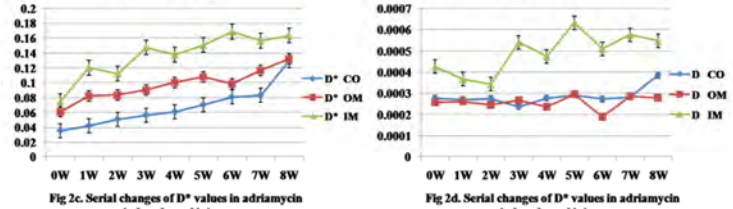


Fig 2c. Serial changes of D* values in adriamycin induced renal injury




Fig 2d. Serial changes of D* values in adriamycin induced renal injury

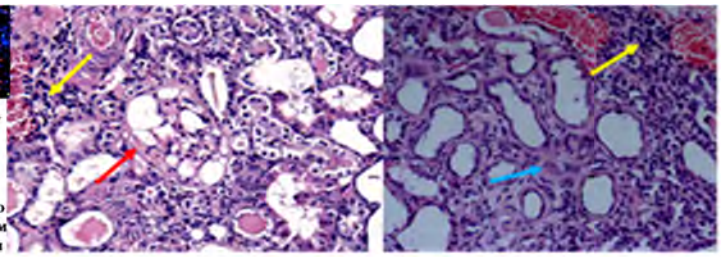

**Fig 3. Histology of glomerular and renal tubules. Glomerulosclerosis (red arrow), inflammatory cell infiltration (yellow arrow) and interstitial fibrosis (blue arrow) could be seen at the 8th week after adriamycin administration .**

**References:** 1. Lee VW, Harris DC. Nephrology (Carlton) 2011;16: 30– 38.2. Le Bihan D, et al., Radiology1986; 161(2): 401-407. 3. Chandarana, H. et al. Invest Radiol, 2011. 46(5): 285-291. 4. Zhang JL, et al. Radiology. 2010; 254: 783Y792. 5. Kairaitis LK, et al. Am J Physiol Renal Physiol 2005; 288: F198–206. 6. Ong AC, et al. Am J Kidney Dis 1994; 23:205–209