Visualization of Lupus Nephritis using SPIO

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Target Audience: Researchers interested in kidney disease and contrast agents

Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease with a variety of clinical manifestations such as arthritis, CNS lupus, and lupus nephritis. Previous research had revealed that anti-Smith (anti-Sm) antibody is a specific marker for SLE [1]. However, the sensitivity and specificity of anti-Sm antibody for lupus nephritis is not so high, and furthermore the noninvasive assessment of lupus nephritis is not easy. Our previous MRI studies with mice showed that the brush-afforded super paramagnetic iron oxide particles (ba-SPIO) have a unique distribution pattern in the kidney [2,3]. The distribution pattern might reflect the specific tissue functions, inflammations and diseases [4]. We speculated that ba-SPIO containing anti-Sm antibody (ba-SPIO-ab) could be used for the assessment of the lupus nephritis in in-vivo. In this study, we used ba-SPIO-ab to SLE model mice whether the particles show the specific distribution and retention properties in the kidneys.

Methods: We made pristane-induced SLE model animals using Aryl Hydrocarbon Receptor (AhR) knock out (KO) mice and wild type (WT) ones. The KO mice show an over expression of type I IFN-dependent autoantibody and have severe proteinuria. Wild type mice without pristane (WT (control)) were also used as a control to compare to experimental groups. The ba-SPIO is a ferric oxide particle with concentrated polymer brush generated by living radical techniques [2]. The diameter of the core magnetic particle and the overall diameter are 15 nm and 100 nm, respectively. The blood half-life is about 20 hours. Anti-Sm antibodies were conjugated with ba-SPIO (ba-SPIO-ab). After baseline MR imaging, the suspension of ba-SPIO-ab was inject into tail vein at a dose of 200 μmol Fe/kg body weight. MRI of mouse kidneys were obtained under 1.2% isoflurane anesthesia by 2D-FLASH using Bruker AVANCE II 500WB (11.7T). After the in-vivo MRI study, kidneys of each mouse were isolated after perfusion fixation, and precise MRI of fixed kidneys were obtained by 2D-FLASH.

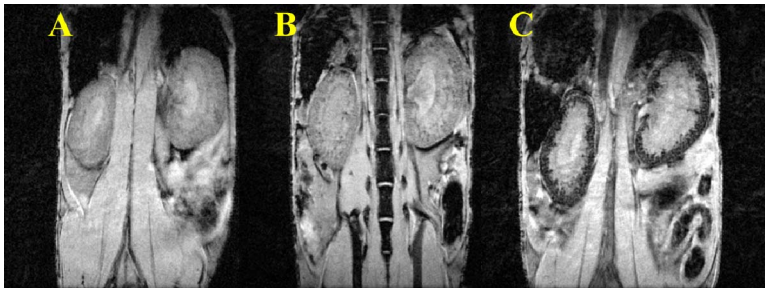

Figure 1. Mice abdomen images 1day post ba-SPIO-ab injection. A: WT (control). B: WT (pristane). C: KO (pristane).

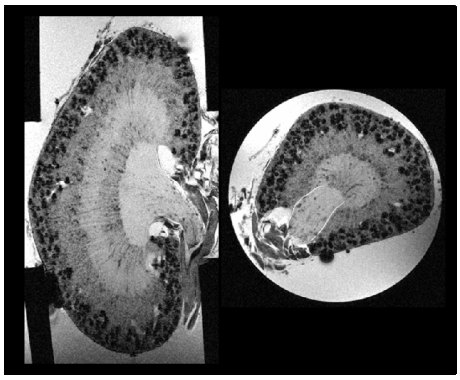

Figure 2. Ex vivo micro imaging of mouse kidney 1day after ba- SPIO-ab injection (KO). Left: coronal section. Right: axial section.

Results and Discussion: The signal intensity was markedly decreased in the liver and the spleen of WT (pristane) mice at one day after ba-SPIO-ab injection, and the cortex of kidney showed a slight decrease of signal intensity (Fig. 1 B). We found no particle distribution in the lymph nodes of each three group. The control group showed a similar imaging result to that of WT (pristane) mice in this study (Fig. 1 A & B). On the other hand, the KO-mice kidneys showed the marked signal reduction in the cortex (Fig. 1 C). The reduction in the kidney cortex was proven to be due to the marked accumulation of ba- SPIO-ab in the renal corpuscles (Fig. 2). The particle distribution in the renal corpuscle was higher in KO mice than in the other two groups, this is in line with our previous research. The ba- SPIO-ab showed a specific distribution and retention in the SLE model mice kidneys. The distribution pattern of it in the renal corpuscle may reflect the symptoms of kidney disease in SLE model mice, and it also showed us the possibility of diagnosing the SLE by this new particle.

References: 1) wikipedia (http://en.wikipedia.org/wiki/Anti-nuclear_antibody) 2) K. Ohno, et al. Biomacromolecules 2012; 13: 927-936. 3) T. Chen, et al. ISMRM: 2013; # 2210. 4) T. Chen, et al. JSMRM: 2014; P-3-219.