New Magnetic Nanoparticle for Kidney Function

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Introduction: Contrast reagents such as magnetic particles are easily taken by macrophages in general and retain for a long time in liver and lymph nodes.[1] The biodistribution and pharmacokinetics of particles differ by the size and the coating or chelating materials. The cationic ferritin was shown to be applicable to label the basement membrane of rat kidney glomeruli by the physicochemical interaction between the probes and the glomerular basement membrane.[2,3] The new SPIO particle showing a marked increase of circulation time in the blood was developed.[4] The particle is taken little by liver Kupffer cells and peripheral macrophages.[4,5] The aim of this study is to investigate the biodistribution and retention property of the new particle in the mouse and to compare it with Resovist.

Methods: The new probe is a magnetic nano particle with concentrated polymer brush generated by living radical techniques.[4,5] The diameter of the core magnetic particle and the overall diameter are 15nm and 100nm, respectively. The half-life in a mouse blood circulation is about 20h. The new SPIO particle containing a little FITC was also synthesized and used for histology. After baseline imaging, the suspension of the particle was inject into tail vein of 8-week-old C57BL/6L male mice at a dose of 200μmol Fe/kg body weight. Resovist was also used for the comparison. The three main axes images were obtained in vivo under 1.2% isoflurane anesthesia by 2D-FLASH using Bruker AVANCE II 500WB (11.7T) [TR/TE=400ms/3ms, FA=30 degree, FOV=25.6mm, matrix=256x256, thickness=0.5mm, NS=8]. After the MRI at 4 weeks post injection, mice were sacrificed, and their organs were excised after body perfusion with 0.9% NaCl and 4% paraformaldehyde. High resolution images of fixed organs were obtained ex vivo by 2D-FLASH [TR/TE=500ms/6ms, FA=30 degree, FOV=10mm, matrix=512x512, thickness=0.12mm, NS=128]. After the ex vivo MRI, organs were sectioned to evaluate them histologically.

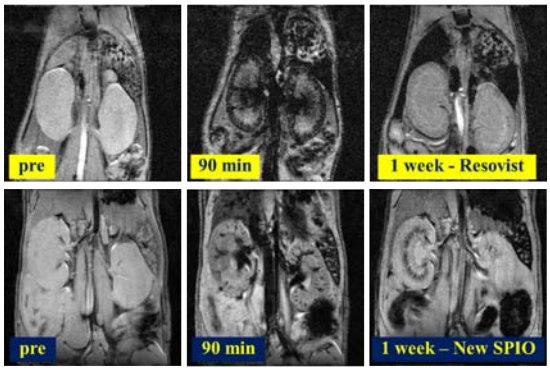

Figure 1. In vivo mouse abdomen images pre and post SPIO injections. Upper: Resovist. Lower: new SPIO.

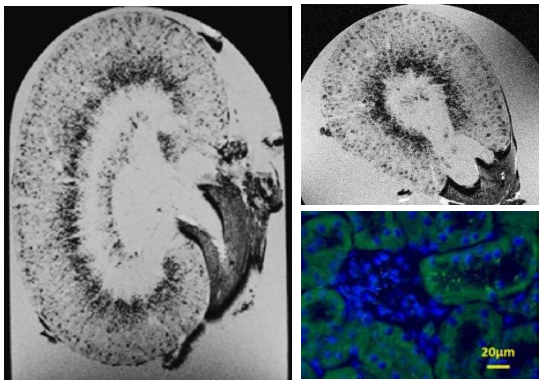

Figure 2. Left & right upper: ex vivo micro imaging of mouse kidney 4 weeks after new SPIO injection.
Right lower: Histology of mouse kidney after new SPIO-FITC injection.

Results and Discussion: The liver and lymph nodes in mice injected new SPIO showed the transient decrease of signal intensity. The intensity recovered almost at one week after injection (Fig. 1 lower). On the other hand, the intensities in spleen and bone marrows were still low even at one week. This shows that there is the different distribution mechanism from macrophages in spleen and bone marrows. Resovist retained for a long time in liver, lymph nodes, spleen, sub maxillary glands, and also bone marrows as expected (Fig. 1 upper). The new SPIO showed the marked distribution pattern in live mouse kidneys (Fig. 1 lower). The SPIO retained much in the boundaries between cortex and medulla and between outer medulla and inner medulla. The particle distribution was higher in cortex than in medulla. The ex vivo high resolution images of kidney (Fig. 2) showed the many round dark spots in the cortex. These round spots are glomerular corpuscles. The existence of new SPIO in renal corpuscles and tubules was confirmed histologically (green spots in Fig. 2). The filtration of the blood is performed by the renal corpuscles. The corpuscle number is, therefore, a very important indicator of kidney function.[2,3] The round dark spots could be used as a measure of the number of renal corpuscles. The distribution pattern of new SPIO in mouse body is unique. The particle in the kidney may show the normal functions of kidney cells since the mice used were all normal. These distribution patterns show the possibility to assess tissue functions, inflammations, and diseases by the new SPIO.

References: 1) P. Storey, et al. Invest Radiol. 2012; 47: 717-724. 2) K.M. Bennett, et al. MRM 2008; 60: 564–574. 3) K. M. Bennett KM, et al. Am J Physiol Renal Physiol. 2013; 304: F1252-F1257. 4) K. Ohno, et al. Biomacromolecules 2012; 13: 927-936. 5) Y. Tago, et al. JSMRM 2012; P-2-130.