Detection of Atherosclerotic Lesions in Apolipoprotein E Knockout Mice

Using USPIO-Enhanced Magnetic Resonance Imaging

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Atherosclerosis is a cardiovascular disease with an accompanying inflammatory response, in which macrophages play an important role. Magnetic resonance imaging (MRI) using ultrasmall superparamagnetic iron oxide (USPIO) particles as a contrast agent has been used in several inflammatory diseases. The USPIO taken up by macrophages reduces the signal intensity on MRI images. Using USPIO-enhanced MRI at 7 T, we could detect atherosclerotic lesions in the brachiocephalic artery of apolipoprotein E (ApoE) knockout (KO) mouse fed a high-fat diet as a model of atherosclerosis.

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Fig. 1  Two-dimensional cardiac-triggered time-of-flight MR angiography of the aortic arch in (a) C57BL/6J mouse injected with USPIO (USPIO+), (b) C57BL/6J mouse as control (USPIO−). (c) ApoE KO injected with USPIO, (d) ApoE KO as control. USPIO (15 mg Fe/mL) was injected through the tail vein on 2 consecutive days (0.1 mL/day). Two days after the second injection, MRI scans were performed. The arrows in (c) indicate the atherosclerotic lesions.

Fig. 2  Enlargement (e) of Fig. 1(c) and corresponding macroanatomy (f) of the heart and aorta harvested from the same mouse after the MRI scan. The locations of the signal voids (green arrows) in (e) are consistent with lipid deposition (yellow arrows) in (f). Histopathologic examination showed lipid accumulation in the arterial intima (g), and Prussian blue stain indicated the presence of iron particles in the lesions (h) (i).