In Vivo Visualization of Cerebro-microvasculature using 3D ΔR2-Based Microscopic MR Angiography (3D mMRA)

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Synopsis

3D ΔR2-Based Microscopic MR Angiography (3D mMRA) method is proposed and validated in order to evaluate the cerebro-microvasculature. The results demonstrate that 3D mMRA is a promising technique in monitoring and quantitatively evaluating microvascular remodeling in cerebro-microvascular disease.

Introduction

The function and structure of cerebro-microvessels are considered as important for the surviving of neural cell, since the actual nutrient trafficking takes place through their walls. It has been reported that the structural and functional cerebro-microvascular abnormalities are implicated in the pathogenesis of brain (1). Therefore, understanding the evolution of cerebro-microvasculature may indicate an early sign of neurological disorders. It is thus important to develop imaging method for 3D noninvasive visualization of the cerebro-microvasculature. Conventional magnetic resonance angiography (MRA) including time-of-flight MRA (TOF-MRA) and contrast-enhanced MRA (CE-MRA) can only image larger arteries and veins (2). However, these methods have the limitations in visualizing microvessels such as arterioles, venules and capillaries. Recently, ΔR2 map, based on the measurement of the spin echo transverse relaxation rate before and after the injection of a contrast agent, has been proposed to be correlated well with the morphology of capillaries and other small vessels (3). The purpose of this study is thus to propose a new method, a steady-stateΔR2-based microscopic MRA method using 3D high-resolution volumetric ΔR2 images in combination with volume rendering technique, to directly visualize cerebro-microvasculature.

Material and Methods

All images were performed on a 7T Pharmascan 70/16 MR scanner with an active shielding gradient. All experiments were carried out on male Long-Evan rats (300-350 g). Stroke animal model was created by the transient middle cerebral artery occlusion (MCAO) for 60 minutes. The rats were initially anesthetized with 5% isoflurane at 1L/min air flow. When fully anesthetized, the animal was placed in a prone position and fitted with a custom-designed head holder inside the magnet. Isoflurane was then maintained with 1~1.2% at 1L/min air flow throughout the experiments. Images were acquired using a 38-mm volume coil as both the transmitter and receiver coil. To determine ΔR_2, T2-weighted images were performed before and after an injection of iron oxide (IOP, Industry Technology Research Institute, Taiwan) at a dose of 30 mg Fe/kg. The post-contrast image acquisition was delayed by 1-2 minutes for ensuring a steady state distribution of contrast agent in the vascular network. T2-weighted MRI were acquired using 3D RARE sequence with a TR of 1700 ms, TEeff of 70 ms, ETL of 32, 4 averages, FOV = 2.8 cm × 2.8 cm × 1.4 cm, acquisition matrix = 192 × 192 × 96 (zero-padding to 384 × 384 × 192). The image resolution can be reached to 73 × 73 × 73 μm. ΔR_2 map was calculated pixel-by-pixel using an in-house software written by Matlab (MathWorks, Natick, MA, USA). 3D view of microvasculature was constructed with 3D ΔR2 map using a volume-rendering utility (TGS, Amira, San Diego, CA).

Results and Discussion

Three orthogonal views of 3D ΔR2-based microscopic MRA were shown in Fig. 1. Small vessels appear bright owing to the signal difference around the vessels prior to and after the injection of contrast agent. These images illustrate the rich and complicated small vessel structure in the deep brain, as well as in the more superficial intracortical microvasculature. Figure 2a demonstrated the distribution of small vessels in coronal view of normal rat using the proposed method. The micro-vascular structure on the surface of the cerebrum and cerebellum can be seen clearly and are correlated very well with the photo of dorsal bird view (Fig. 2b). These findings suggest that 3D mMRA method provide good contrast of cerebro-microvascular delineation. Ischemic brain was induced by the MCAO and was used to examine the capability of this visualization method in evaluating microvascular remodeling caused by the brain pathology. Figure 3a shows the T2-weighted image of ischemia lesion in the ipsilateral cortex at day 7 after reperfusion. 3D mMRA exhibits higher vessel density in ipsilateral side (Fig. 3b), compared to contralateral side, which is consistent with our previously study (4).

Conclusion

The proposed 3D mMRA method demonstrates its ability in visualizing small vessels that can be used to quantitatively evaluating and monitoring cerebro-microvasculature in intact and pathological brains. Moreover, this method can be considered to be a useful tool in detailed microvascular analysis of whole-brain such as characterizing brain phenotypes of mutants.

Reference

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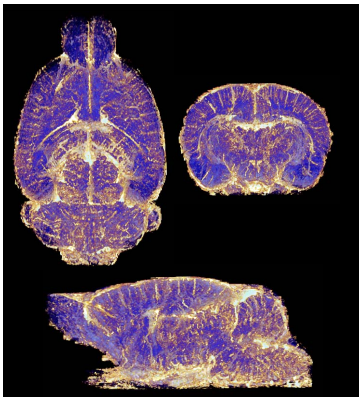

Fig. 1. 3DΔR2-based microscopic MR angiography in coronal, axial and sagittal views.

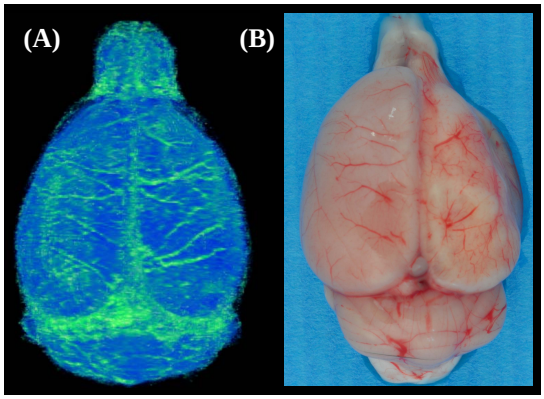

Fig. 2. 3D mMRA in coronal view (A) and its corresponding vascular photo (B) on the brain surface.

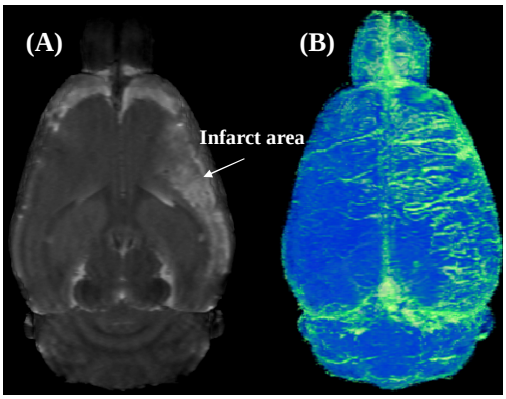

Fig.3. (A) T2-weighted imaging showing the infarct area in ipsilateral side at day 7 after reperfusion. (B) 3D mMRA showing the vessel distribution on the brain surface after reperfusion.