Quantitative MRI of Brain Perivascular Space

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Target Audience: Scientists and clinicians interested in vascular dementia, amyloid-ß (Aß) clearance, and Alzheimer's disease (AD).

Introduction/Purpose: Perivascular spaces, also called the Virchow-Robin spaces (VRS), surround small arteries and arterioles as they perforate the surface of the brain and extend into the brain tissue. Perivascular spaces have been detectable from healthy subjects and patients at all ages on clinical MR scanners[1]. Although dilated perivascular spaces are found to be associated with many conditions, including aging, dementia, cerebral amyloid angiopathy (CAA), neuroinflammation, and neoplasm, it is necessary to determine whether dilated VRS is a normal variant or related to a disease process. Conventionally, such determination is mainly based on the subjective observations of the number, size and shape of the observable VRS in MR images[1]. Quantitative methods are in need to objectively assess VRS density and its spatial distributions in the brain. In this study, we aim to develop an image analyzing method to quantify the brain VRS in AD patients and age-matched healthy controls.

Methods: AD patients (n=5, 78.2 ± 7.6 years old) and age- and education-matched healthy controls (n=3, 69.3±18.0 years old) were scanned under an approved protocol by the institutional review board (IRB) on a 7T whole-body MR scanner with a commercial 32 channel head coil. 3D T_2-weighted turbo spin echo (TSE) sequence based on SPACE (Sampling Perfection with Application optimized Contrasts by using different flip angle Evolutions) was used for the acquisition of 224 contiguous coronal slices (1mm) covering the entire brain with TR/TE = 3000/388 ms, voxel size = 0.42 x 0.42 x 1 mm^3, and acquisition time = ~7.5 min.

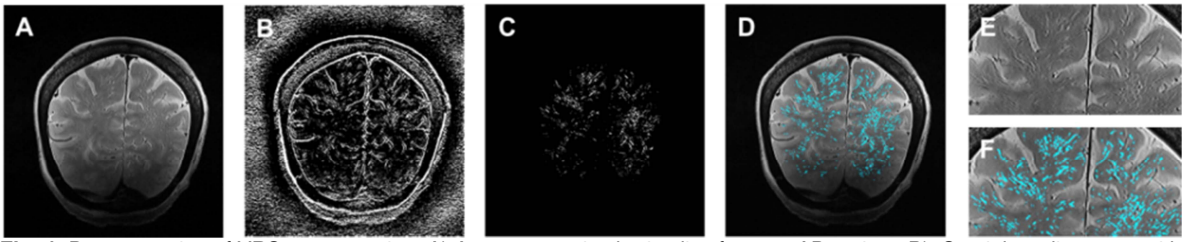

Fig. 1. Demonstration of VRS segmentation. A) A representative brain slice from an AD patient. B). Spatial gradient map with high spatial gradient; C). Segmented VRS in white matter; D). Segmented VRS color-coded and overlaid over the brain image; E-F) Magnified brain images demonstrating the performance of the VRS segmentation algorithm.

Our quantitative algorithm for brain VRS segmentation is illustrated in Fig. 1. White matter regions were segmented automatically after heuristic B_1-field correction and a k-means clustering algorithm. Spatial gradient map was generated pixel-by-pixel using MATLAB routine "imgradient" (Fig. 1B). Pixels with high gradient magnitude (empirically set at >100 per pixel) in white matter were then segmented as brain VRS (Figure 1C). MATLAB routine hole-filling and edge-detection algorithms were applied to retain VRS pixels while removing edge pixels. The segmented VRS were color-coded and overlaid onto the gray-scale brain images (Fig. 1D). Figs. 1E-F illustrate the performance of the brain VRS segmentation algorithm. VRS density in volume percentage (v/v%) was calculated as the percentage of volume occupied by VRS in white matter. Two-tailed unpaired Student's t tests were performed to compare healthy control and AD groups.

Results: Maximum intensity projection (MIP) of the segmented brain VRS showed an obvious increase in VRS density for AD patients when compared to age-matched healthy controls (Figs. 2A-B). The quantified VRS volume percentage in AD and controls were 8.0 ± 2.1% and 4.9 ± 1.3%, respectively ($p<0.05$, Fig. 2C). By comparing the VRS MIP image of an AD patient with a typical brain fiber tractogram generated by diffusion tensor MRI (Figs. 2B,D), we observed that brain VRS appeared to be in parallel with white matter axonal tracts.

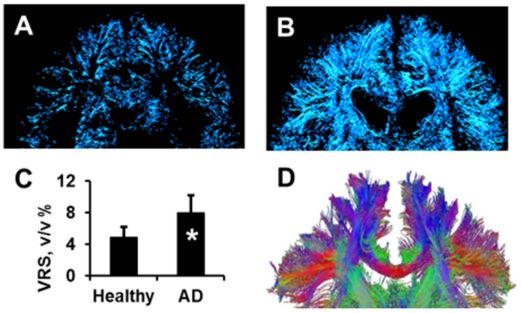

Fig. 2. Representative MIP images of brain VRS generated from 25 contiguous slices in the midbrain of a representative healthy control (A) and an AD patient (B) (displayed on the same quantitative scale). C). Summarized results on whole brain VRS density (*$p<0.05$) from all subjects; D) A representative axonal tractogram with DTI (www.biomed.ee.ethz.ch/research /bioimaging/brain/diffusion_fiber_tracking).

Discussion: VRS contains immunocompetent cells[2] and apolipoprotein E (apoE)[3], the transporter of Aß proteins. Recent studies support that VRS serves as the perivascular drainage pathway for the clearance of interstitial fluid and solutes, including Aß, from the brain[4]. We hypothesize that the formation of insoluble Aß plaques in VRS may partially block this drainage pathway and lead to VRS dilation. Based on MR signal intensity and pattern, perivascular spaces can be separated from brain micro-vessels, lacunar infarcts and white matter hyperintensities. To use the proposed technique, it is important to have a consistent image acquisition protocol and analysis as factors such as signal to noise ratio can affect the VRS quantification. Despite this and other limitations, the ability to quantify VRS, as illustrated in this study, is expected to find applications in characterizing a number of diseases that involve VRS changes. .

References: 1. Groeschel S, et al., Neuroradiology 2006;48(10):745-754. 2. Bechmann I, et al., The European journal of neuroscience 2001;14(10):1651-1658. 3. Rolyan H, et al., Journal of neural transmission 2011;118(5):699-712. 4. Rolyan H, Journal of neural transmission 2011;118(5):699-712.