

TIME RESOLVED MR ANGIOGRAPHY IN PATIENTS WITH MS, THEIR HEALTHY SIBLINGS AND UNRELATED CONTROLS.

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Target audience: Neurologists, (interventional) radiologist, MR researchers, basic scientists.

Introduction: It was suggested that multiple sclerosis (MS) may be associated with changes in the brain's draining veins¹. It was proposed that hemodynamic flow abnormalities are present only in patients with MS and not in healthy people and that venous reflux (detected by Doppler ultrasound) is a common finding in MS, but never seen in controls². Cerebral circulation time (CCT) using ultrasound was reported to be substantially prolonged in people with MS compared with healthy controls³. However, ultrasound is very operator dependent and objective measures for the assessment of hemodynamics are needed. 4D-TRAK is a novel time resolved MR technique for high contrast enhanced angiography with high temporal resolution⁴, making it a potential tool for the evaluation of cerebrospinal venous behavior. In this study we analyze the cerebral circulation times in MS patients, their healthy siblings and unrelated healthy controls.

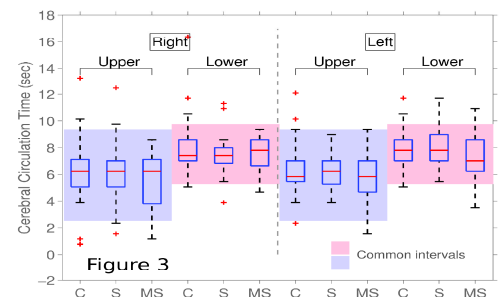
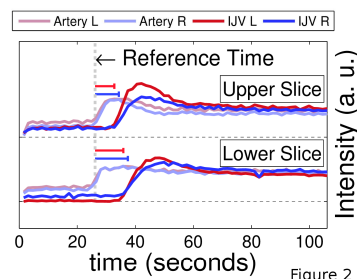
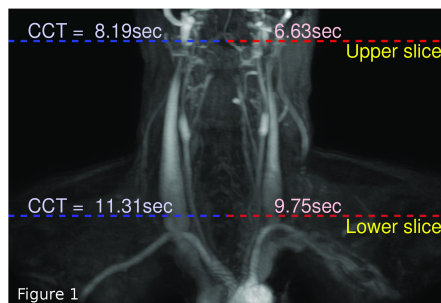
Upper	N<2.54 (right/left)	N>9.36 (right/left)
Controls	3 (2/1)	5 (2/3)
Siblings	2 (2/0)	2 (2/0)
MS	10 (6/4)	0 (0/0)
Lower	N<5.27 (right/left)	N>9.75 (right/left)
Controls	2 (1/1)	9 (5/4)
Siblings	1 (1/0)	5 (2/3)
MS	4 (1/3)	3 (0/3)

compared with healthy controls³. However, ultrasound is very operator dependent and objective measures for the assessment of hemodynamics are needed. 4D-TRAK is a novel time resolved MR technique for high contrast enhanced angiography with high temporal resolution⁴, making it a potential tool for the evaluation of cerebrospinal venous behavior. In this study we analyze the cerebral circulation times in MS patients, their healthy siblings and unrelated healthy controls.

Methods: Patients with clinically definite MS, their healthy siblings and non-related healthy controls were recruited. In total, 101 subjects were scanned. Data were acquired from January to December 2011 on a 3T Philips Achieva scanner. 4D-TRAK acquisitions were obtained with CENTRA keyhole (keyhole diameter 20%)⁵. 68 dynamic scans with a temporal resolution of 1.56s. (TR/TE=4.8/2.3ms); voxel size 1.00x1.40x2.40mm³ acquired and 0.83x0.83x1.20mm³ reconstructed; field of view=360x360x72mm³. The analysis of the images was performed by a blinded reader using inhouse matlab-based software. The reader selected the transversal section of the arteries and internal jugular veins (IJV) in the slice located 2cm above the subclavian vein and 2cm below the sigmoid sinus (Fig. 1). The reader identified arteries and veins, scrolling along all the 68 time points in the individual axial slices. The enhancement of the different tissues at different timepoints allowed for identification of these structures. Regions of interest (ROIs) were placed inside the arteries and veins at these levels. The average of the intensities within these ROIs defined for the arteries and veins was calculated for every timepoint. The arrival time was defined according to the first enhancement of the signal for arteries and veins. A reference time was calculated averaging all the arrival times in the arteries (Fig. 2). Cerebral

circulation times (CCT⁶) were defined as the difference in arrival times at each of the two landmarks in IJV and the reference time for both left and right IJVs. Statistical analysis was done using Kruskal-Wallis and ANCOVA analysis, taking the age as a covariant.

Results: CCTs of 94/101 subjects were obtained for upper and lower levels of the IJV. 7 subjects showed not enough signal enhancement in the IJVs to reliably define the ROIs. We found no significant (p>0.2) differences in the CCTs for the different groups. We observed the shortest CCT in the right upper landmark in one of the members of the unrelated control group (CCT=0.78sec) and the longest CCT in the lower landmark of one element of the same group (CCT=16.38sec). CCT values common to all three groups were defined as common intervals and were [2.54-9.36] seconds (pink shading Fig. 3) for the upper landmark and [5.27-9.75] seconds (blue shading Fig. 3) for the lower landmark. Table 1 shows the number of CCTs that are outside these intervals for the three groups.



Discussion: The lack of significant differences in venous flow between patients with MS, their siblings and unrelated controls and the high variability within groups suggests that flow abnormalities are not characteristic for MS. This is in agreement with findings using Doppler ultrasound and venography in the same cohorts⁷.

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References: [1] Zamboni P et al. J Neurol Neurosurg Psychiatry 2009; 80. [2] Zamboni P et al. J Neurol Sci 2009; 282. [3] Mancini M et al. Radiology 2012; 262(3) [4] Hadizadeh D et al. Proc. ISMRM. 14 (2006). [5] Willinek WA et al. JMIR 2008; 27. [6] Oldendorf et al. J Nuc Med 1962; 3 [7] Traboulsee T et al. The Lancet 2013.