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## American Academy of Neurology (AAN) Annual Meeting, Toronto, 10–17 Apr 2010.

Last modified: 23.03.2010 - 22:45 CET Created: 23.03.2010 - [simplex](#)There is soon the big neurology meeting: American Academy of Neurology (AAN) Annual Meeting 2010. Toronto, 10–17 Apr 2010. [[aan10a](#)]

## Presentations covering CCSVI

## 1 Platform Session:

Poloni GU, Zamboni P, Haacke EM, Bastianello S, Dwyer MG, Bergsland N, Schirda C, Wack D, Magnano C, Weinstock-Guttman B, Salvi F, Hojnacki D, Zivadinov R: **Quantitative Venous Vasculature Assessment on Susceptibility-Weighted Imaging Reflects Presence of Severe Chronic Venous Insufficiency in the Brain Parenchyma of Multiple Sclerosis Patients. A Case-Control Study.** [[pres\\_poloni10a](#)]

## 5 Poster Sessions:

Magnano C, Schirda C, Weinstock-Guttman B, Hojnacki D, Bergsland N, Kennedy C, Reuther J, Brooks C, Dwyer MG, Zivadinov R: **Cine Cerebrospinal Fluid Imaging in Multiple Sclerosis. A Case-Control Study.** [[pos\\_magnano10a](#)]

Zivadinov R, Marr K, Ramanathan M, Zamboni P, Benedict RRHB, Cutter G, Kennedy C, Elfadil M, Hojnacki D, Munschauer F, Reuther J, Brooks C, Hunt K, Andrews M, Weinstock-Guttman B: **Combined Transcranial and Extracranial Venous Doppler Evaluation (CTEVD Study). Description of the Design and Interim Results of an Epidemiological Study of the Prevalence of Chronic Cerebrospinal Venous Insufficiency in MS and Related Diseases.** [[pos\\_zivadinov10a](#)]

Zamboni P, Menegatti E, Weinstock-Guttman B, Dwyer MG, Schirda C, Malagoni AM, Hojnacki D, Kennedy C, Carl E, Bergsland N, Magnano C, Bartolomei I, Salvi F, Zivadinov R: **Hypoperfusion of Brain Parenchyma Is Strongly Associated with the Severity of Chronic Cerebrospinal Venous Insufficiency in Patients with Multiple Sclerosis.** [[pos\\_zamboni10a](#)]

Dwyer MG, Zamboni P, Haacke EM, Menegatti E, Weinstock-Guttman B, Schirda C, Malagoni AM, Hojnacki D, Kennedy C, Carl E, Bergsland N, Hussein S, Heininen-Brown M, Bartolomei I, Salvi F, Zivadinov R: **Chronic Cerebrospinal Venous Insufficiency and Iron Deposition on Susceptibility-Weighted Imaging in Patients with Multiple Sclerosis.** [[pos\\_dwyer10a](#)]

Schirda C, Zamboni P, Magnano C, Lindzen E, Wack D, Weinstock-Guttman B, Ramasamy D, Carl E, Hojnacki D, Kennedy C, Dwyer MG, Bergsland N, Cox JL, Salvi F, Zivadinov R: **Objective Quantification of Cerebrospinal Fluid (CSF) Flow Rate in Cerebral Aqueduct in Patients with Multiple Sclerosis.** [[pos\\_schirda10a](#)]

## Abstracts

[\[pres\\_poloni10a\]](#)

## Abstract

**OBJECTIVE:** To develop an objective method for quantifying venous vasculature in brain parenchyma on susceptibility-weighted imaging (SWI). To apply this technique in multiple sclerosis (MS) patients and in healthy controls (HC). **BACKGROUND:** SWI is a MRI application that can directly image cerebral veins by exploiting venous blood oxygenation. **DESIGN/METHODS:** Sixty-two (62) MS patients (44 relapsing-remitting and 18 secondary-progressive) and 33 age- and sex-matched HC were imaged on a 3T GE scanner using pre-contrast SWI. A subset of MS patients (50) and HC (7) obtained SWI-post gadolinium contrast sequence (0.1 mMol/Kg Gd-DTPA with 10 min delay). In-house developed segmentation algorithm, based on a 3D multi-scale line filter, was applied for vein segmentation. Absolute volumetric measurement for total vein vasculature was performed in milliliters (ml) and the relative venous intracranial fraction (VIF) was obtained to correct for head size and amount of brain atrophy. The size of individual veins was measured in mm and 4 groups were created according to their mean diameter: <0.3mm, 0.3-0.6mm, 0.6-0.9mm and >0.9 mm. Voxel brain average distance-from-vein maps was also calculated with higher distance indicating fewer veins. **RESULTS:** A significantly lower absolute venous volume was detected in MS patients compared to HC, both in pre-contrast (67.5 vs. 82.7ml, -18.3%, p<0.001) and post-contrast (70.4 vs. 87.1ml, -19.1%, p<0.011) images. The VIF was significantly lower in MS patients (p<0.001). The highest mean diameter difference was found for the smallest veins (<0.3 mm), both on pre- (p<0.001) and post-contrast (p<0.018) images. The distance-from-veins was also significantly higher in MS patients (p<0.001). **CONCLUSIONS/RELEVANCE:** We developed and validated a quantitative vein segmentation method that showed altered visibility of venous vasculature on SWI pre- and post-contrast images in MS patients. These findings suggest severely compromised brain venous system in MS patients.

Category - MS and Related Diseases - Clinical Science

Wednesday, April 14, 2010 2:30 PM

Platform Session: Integrated Neuroscience: Multiple Sclerosis Imaging (2:00 PM-3:30 PM)

[\[pos\\_magnano10a\]](#)

## Abstract

**OBJECTIVE:** To investigate the cerebrospinal fluid (CSF) dynamics in Sylvius aqueduct in multiple sclerosis (MS) patients versus healthy controls (HC) and to define correlates with other specific disease metrics. **BACKGROUND:** CSF velocity and flow dynamics, as measured by MRI in MS patients, may be impaired and associated with higher disease activity. **DESIGN/METHODS:** Fifty eight (58) consecutive MS patients (41 RR and 17 SP) with mean age 45.3 yrs, mean disease duration 13 yrs and median EDSS 4.0 and 22 age- and sex-matched HC were scanned on a GE 3T scanner. A two-dimensional, phase-contrast gradient-echo MR acquisition using peripheral cardiac gating, with in-plane resolution 0.39x.039mm<sup>2</sup> and 32 phases, corresponding to a full cardiac cycle, was collected on one 4mm thick slice positioned perpendicular to the Sylvius aqueduct. In addition to CSF measures, we calculated T2, T1- and contrast enhancing (CE) lesion volume (LV), global, tissue-specific and central brain atrophy measures. **RESULTS:** All CSF flow and velocity measures were significantly altered in the patients with MS, compared to HC. Net CSF flow in the aqueduct, which

physiologically is towards 4<sup>th</sup> ventricle, was significantly lower in MS patients than in HC (3.8 vs. 8.4,  $p=0.011$ ). There were no CSF dynamics differences between RR and SP MS patients. In MS patients, lower net CSF flow was significantly related to a higher number of relapses in the previous year ( $r=-0.28$ ,  $p=0.029$ ) and longer disease duration ( $r=-0.25$ ,  $p=0.048$ ). The lower CSF flow was related to central atrophy, as measured by the enlargement of the lateral ventricle volume and third ventricle width ( $r=0.3$ ,  $p<0.02$ ). **CONCLUSIONS/RELEVANCE:** This study shows that CSF flow is significantly altered in MS patients, compared to HC. Altered CSF dynamics may play an important role in the pathophysiology of MS disease process and warrants further investigation.

Category - MS and Related Diseases - Clinical Science

Wednesday, April 14, 2010 7:30 AM

Poster Session III: Multiple Sclerosis and Related Diseases: MRI/Technique (7:30 AM-12:00 PM)

[pos\_zivadnov10a]

#### Abstract

**OBJECTIVE:** To ascertain the prevalence of chronic cerebrospinal venous insufficiency (CCSVI) in a large cohort of patients with multiple sclerosis (MS), patients with other neurological diseases (OND) and in normal controls (NC), by using specific proposed Doppler criteria (Zamboni et al, JNNP, 2009). **BACKGROUND:** CCSVI is a complex vascular condition characterized by anomalies of the main extracranial cerebrospinal (CS) venous routes that interfere with the normal CS venous outflow. This condition was previously associated with clinically definite MS. **DESIGN/METHODS:** Cross-sectional study that will enroll consecutive 1700 subjects at one MS center including: 1000 adult patients with possible and definite MS (50 clinically isolated syndrome, 50 radiologically isolated syndrome, 500 relapsing-remitting, 300 secondary-progressive, 50 primary-progressive MS and 50 neuromyelitis optica). A comparative group will include 300 OND patients and 300 adult age- and sex-matched NC. Fifty pediatric patients (<18 yrs) with acquired demyelinating diseases (MS and acute disseminated encephalomyelitis) and 50 pediatric NC will be assessed. All participants will undergo clinical examination and a Doppler scan of the head and neck. All MS patients and a subcohort of NC and OND will undergo an MRI of the brain. A consecutive subgroup (MS, NC and OND) will have also an MRI of the veins of the neck to corroborate the Doppler diagnosis of CCSVI. The Doppler, and MRI evaluators are blinded to the subject status. The prevalence and severity of venous hemodynamic abnormalities identified in the different groups will be analyzed. Data will be unblinded at three predetermined time-points based on the number of subjects enrolled: at 500, 1000 and 1700 subjects respectively. **RESULTS:** As of 1 Nov 2009, 473 subjects signed informed consent. The initial interim analysis following the first 500 subjects is scheduled for December 2009. **CONCLUSIONS/RELEVANCE:** The interim results of the first 500 enrolled subjects will be presented.

Category - MS and Related Diseases - Clinical Science

Thursday, April 15, 2010 3:00 PM

Poster Session VI: Multiple Sclerosis and Related Diseases: Clinical Trials (3:00 PM-7:30 PM)

[pos\_zamboni10a]

#### Abstract

**OBJECTIVE:** To investigate the relationship between chronic cerebrospinal venous insufficiency (CCSVI) and cerebral perfusion in patients with multiple sclerosis (MS). **BACKGROUND:** CCSVI is a vascular condition described in MS patients, characterized by stenoses of the main extracranial veins with hampered cerebral venous outflow. We hypothesized that the impaired venous outflow contributes to hypoperfusion of brain parenchyma. **DESIGN/METHODS:** Sixteen consecutive relapsing-remitting MS patients (mean age 36.1yrs, mean disease duration 7.5yrs and median EDSS 2.5) and 8 age- and sex-matched normal controls (NC), were scanned on a GE 3T scanner using dynamic susceptibility contrast enhanced perfusion-weighted imaging (PWI). Cerebral blood flow (CBF), blood volume (CBV) and mean transit time (MTT) were measured in the gray matter (GM), white matter (WM), normal appearing (NA) GM, NAWM, thalamus, caudate, putamen, globus pallidus, hippocampus, amygdala, nucleus accumbens, red nucleus and substantia nigra. Diagnosis of CCSVI was established based on the venous hemodynamic (VH) Doppler criteria (Zamboni, JNNP, 2009) and the severity was based on fulfilled VH criteria (score 0-5) and VH insufficiency severity score (VHISS) (score 0-16). **RESULTS:** All 16 MS patients fulfilled the diagnosis of CCSVI (median VH=4, median VHISS=9) and none of the NC. There was a significant association between VH criteria and VHISS, and CBF, CBV and MTT in all examined regions of the brain parenchyma in MS patients. The most robust correlations were observed for lower CBF and higher VHISS in the GM, WM, NAWM and NAWM ( $r= -0.70$  to  $-0.72$ ,  $p<0.002$ ), and in the thalamus, caudate, putamen, hippocampus, nucleus accumbens ( $r= -0.6$  to  $-0.72$ ,  $p<0.008$ ). The correlation coefficients for CBV and MTT were in a range between  $r= -0.5$  to  $-0.65$ . No relationship was observed for NC. **CONCLUSIONS/RELEVANCE:** This study demonstrates that severity of CCSVI is directly associated with hypoperfusion of the brain parenchyma in MS. Supported by: Hillarscere Foundation and Buffalo Neuroimaging Analysis Center.

Category - MS and Related Diseases - Clinical Science

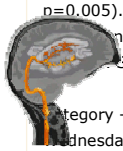
Wednesday, April 14, 2010 7:30 AM

Poster Session III: Multiple Sclerosis and Related Diseases: MRI/Technique (7:30 AM-12:00 PM)

[pos\_dwyer10a]

#### Abstract

**OBJECTIVE:** To investigate the relationship between chronic cerebrospinal venous insufficiency (CCSVI) and iron deposition in the brain of multiple sclerosis (MS) patients by correlating venous hemodynamic (VH) parameters and iron concentration in deep-gray matter (DGM) structures and lesions, as measured by susceptibility-weighted imaging (SWI). To preliminarily define the relationship between iron measures and disability outcomes. **BACKGROUND:** CCSVI is a vascular picture recently described in MS patients that is characterized by stenoses affecting the main extracranial venous outflow pathways and by a high rate of cerebral venous reflux that may lead to increased iron deposition in the brain. **DESIGN/METHODS:** Sixteen (16) consecutive relapsing-remitting MS patients (mean age  $36.1\pm 7.3$  yrs, mean disease duration  $7.5\pm 1.9$  yrs and median EDSS 2.5) and 8 age- and sex-matched normal controls (NC) were scanned on a GE 3T scanner, by using SWI. Iron concentration was measured in the following DGM structures: thalamus, caudate, putamen, globus pallidus, hippocampus, amygdala, nucleus accumbens, red nucleus and substantia nigra. Iron concentration was also measured in T2, T1, SWI phase and SWI magnitude lesions. Diagnosis of the CCSVI was established based on the previously published VH Doppler criteria (Zamboni, JNNP, 2009). **RESULTS:** All 16 MS patients fulfilled the diagnosis of CCSVI (median VH=4, median VHISS=9) and none of the NC. There was a significant association between higher number of VH criteria and higher iron concentration in T2 ( $r=0.64$ ,  $p=0.007$ ) and T1 ( $r=0.56$ ,  $p=0.023$ ) lesion volumes. The only DGM structure that correlated significantly with VH criteria was globus pallidus ( $r=0.58$ ,  $p=0.019$ ). No relationship was observed for NC. Higher iron concentration in DGM structures was predictive of higher disability status (EDSS) in almost all examined regions. The highest correlations were detected for thalamus ( $r=0.79$ ,  $p<0.0001$ ) and red nucleus ( $r=0.7$ ,



$p=0.005$ ). **CONCLUSIONS/RELEVANCE:** The findings from this pilot study suggest that CCSVI may be an important mechanism leading to iron deposition in brain parenchyma of MS patients. In turn, iron deposition, as measured by SWI, is a strong predictor of disability progression in patients. Supported by: Hillarsberg Foundation and Buffalo Neuroimaging Analysis Center.

## Venous Multiple Sclerosis | CCSVI

Category - MS and Related Diseases - Clinical Science

Wednesday, April 14, 2010 7:30 AM

Poster Session III: Multiple Sclerosis and Related Diseases: MRI/Technique (7:30 AM-12:00 PM)

[pos\_schirda10a]

### Abstract

**OBJECTIVE:** To develop an objective MRI technique for quantifying the cerebrospinal fluid (CSF) flow in Sylvius aqueduct. To apply this technique in a pilot study in multiple sclerosis (MS) patients versus normal controls (NC) and provide further correlates with other MRI specific disease metrics.

**BACKGROUND:** Non-invasive MRI investigation of the CSF dynamics in MS has not been previously reported. **DESIGN/METHODS:** For consistency and objective quantification of the antegrade (towards 4<sup>th</sup> ventricle), retrograde (towards 3<sup>rd</sup> ventricle) and net CSF flow rates, a semi-automated program was developed. The CSF flow quantification technique was validated on a tube phantom, using a power injector which provided a controlled flow rate. 2 NC and 2 MS patients were scanned and rescanned within a week, to test reproducibility. Sixteen (16) consecutive relapsing-remitting MS patients and 8 age- and sex-matched NC were scanned on a GE 3T scanner using a two-dimensional phase-contrast gradient-echo MR technique with high spatial-temporal resolution (in-plane resolution 0.39x.039mm<sup>2</sup> and 32 phases, corresponding to a full cardiac cycle) on one 4mm thick slice positioned perpendicular to the Sylvius aqueduct. In addition to CSF flow measures, lesion volume (LV) and atrophy MRI outcomes were calculated.

**RESULTS:** Net CSF flow scan-rescan reproducibility was 10.9%. Net CSF flow rate (stroke volume) was significantly lower in MS patients than in NC ( $p=0.038$ ). In MS patients, T1-LV was strongly correlated with CSF retrograde ( $r=0.71$ ,  $p=0.002$ ) and antegrade flow rates ( $r=-0.64$ ,  $p=0.008$ ). T2-LV was also related to CSF flow rate ( $0.58$ ,  $p=0.019$ ). Lower net CSF flow rate was related to gray matter ( $r=-0.63$ ,  $p=0.009$ ), whole brain and cortical atrophy ( $p<0.037$ ). **CONCLUSIONS/RELEVANCE:** CSF flow rate in the Sylvius aqueduct is significantly lower in MS patients than in NC. In MS patients, robust correlations between higher LVs, and advanced atrophy, and altered flow rate measures were found.

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Wednesday, April 14, 2010 3:30 PM

Poster Session: Integrated Neuroscience: Multiple Sclerosis Imaging (3:30 PM-4:30 PM)

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