

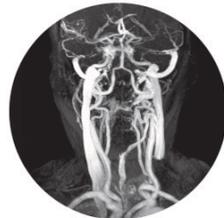
## Neurovascular Perspectives

Neurovascular Perspectives is the newsletter of the International Society for Neurovascular Disease (ISNVD)

### EDITOR

E. Mark Haacke, PhD

The International Society for NeuroVascular Disease (ISNVD) is a non-profit professional association devoted to furthering the development of research for neurovascular related diseases – including CCSVI. The society will hold annual scientific meetings and sponsor educational and scientific workshops. Target medical groups include, but are not limited to, Vascular Surgeons, Interventional Radiologists, Neurologists, Neurosurgeons, Physicists, and Technologists.



## ISNVD

International Society for Neurovascular Disease

## President's Column

**T**he International Society for Neurovascular Disease (ISNVD) has been founded to promote and scientifically coordinate research on a new and intriguing topic: vascular—particularly venous—background of a number of neurological disorders. For this purpose *the Society* encourages the exchange of information and ideas, and provides continuous education in this newly emerged area.

Over the last century venous circulation in the central nervous system has been largely ignored by the mainstream research. However, it seems that abnormal venous outflows from the brain and spinal cord may contribute to injury of the nervous system in a number of diseases. It is now more than 5 years after the 7th annual meeting of the *European Venous Forum* (London, UK, 2006), when Professor *Paolo Zamboni* for the first time suggested that a link may exist between multiple sclerosis and cerebral venous insufficiency. An unequivocal causative relationship between pathological venous outflow and multiple sclerosis has not yet been proven. Nonetheless, an accumulating body of evidence suggests that—in addition to multiple sclerosis—the signs of impaired cerebral and spinal venous outflow can also be demonstrated in the patients with other neurological pathologies, as well as in some healthy individuals, still, with unknown meaning of these phenomena.

The research on venous aspects of neurological pathology is still at its infancy and—at present—most of the questions and uncertainties related to this topic remain unanswered. To answer these questions, there is no other way than discussion, involving specialists in different fields. Such an interdisciplinary endeavor—with methodological awareness and up-to-date knowledge—is necessary, if we are to better understand vascular component of neurological disorders. Thus, *ISNVD* provides a forum for the wide range of medical specialists: basic scientists, vascular surgeons and angiologists, neurologists and neurosurgeons, interventional radiologists, neuroradiologists, physicists, vascular technologists and others.

I would like to congratulate the Past President of *ISNVD*, Dr. *Robert Zivadinov*, for the successful 2<sup>nd</sup> annual meeting of the Society, which took place in Orlando, USA. In this issue of *Neurovascular Perspectives* a summary of this outstanding conference is presented.

Next year's meeting of *ISNVD* will be held from February 23 through February 25, 2013 in the beautiful former capital of Poland, Cracow (*Kraków*). The conference will be held under the honorary patronage of *the Mayor of the Royal Capital City of Kraków*, Professor *Jacek Majchrowski*. Third annual meeting of *ISNVD* will build on the successes of this year, and further expand the program's offerings. The scientific program of the conference will cover a large array of topics: ultrasonographic and magnetic resonance diagnostics of venous insufficiency of the brain and spinal cord, reports on clinical trials on the treatment for chronic cerebrospinal venous insufficiency (CCSVI), and evidence of venous disorders in the settings of non-MS neurological disorders. Next year's conference will be special in that we plan to include in the program also the management of acute stroke. Stroke represents a major health burden and nowadays—thanks to the progress in neuroimaging and interventional radiology—in substantial percentage of its victims is potentially treatable. Yet, similarly to the case of CCSVI, a successful management of stroke requires close and coordinated collaboration between different medical professionals. It is hoped that our meeting will provide a common platform for doctors to overcome the barriers that make management of stroke less effective than it could theoretically be.

I look forward to welcoming you to the 2013's annual meeting of *ISNVD* next February.

Sincerely,

*Marian Simka, MD PhD*  
President of the *ISNVD*

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# ANNUAL MEETING SUMMARY

*“Research is to see what everybody else has seen and to think what nobody else has thought”*  
Albert Szent-Gyorgyi

Scientists from diverse fields and locations were welcomed to Orlando to share their research and discuss current consensus and future directions for studies into chronic cerebrospinal venous insufficiency (CCSVI) as well as neurovascular disease. The five day meeting was full of discussions, questions and talk of future collaborations in the coming year. The interest of the attendees was clear by the many questions posed during the various sessions of the meeting.

The five day conference had more than 50 international speakers, a venue fit for any major meeting in the field. Apart from the patient day and the workshop, there were 17 sessions filled with state-of-the-art presentations. A unique feature of this meeting, one continued from the meeting at Bologna, was that the top posters were also chosen as oral presentations interspersed with the plenary speakers. This gave young people, particularly students and post-doctoral fellows an opportunity to gain first hand conference speaking experience and exposure.

The weekend began with the patient day forum, with around 19 speakers. This was webcast live. There were 125 attendees at the meeting. The panel discussions were lively and as many questions entertained from the audience as possible. More questions from the web audience would have been nice had time permitted. Some of these questions could be addressed after the fact at the ISNVD website if possible. The consensus workshop started Saturday afternoon with presentations, and continued Sunday morning with breakout sessions and concluded with a final set of summary statements. It was decided that there would be a white paper produced from this meeting stating where we are today with value of ultrasound, magnetic resonance imaging, catheter venography and intraluminal ultrasound for diagnosis of CCSVI. Sunday at 1pm, the formal ISNVD scientific sessions began. Each day was organized into a breakfast, followed by a session, then coffee for discussions and visiting the exhibitor's area. Also during the coffee breaks the poster presentations were given, four at each break. Another session preceded lunch and another following lunch. Attendees met in the exhibitor's area to discuss about the conference in two special rooms set up for lunch. The second coffee break had four more poster presentations. The final sessions were then presented usually finishing by 5pm.

The Young Investigators oral presentations lasted five minutes each and included two awards for best presentations. Stefania Marcotti was awarded first on the topic of “A lumped-parameter model for the study of cerebrospinal venous flow” and Dr. Marcella Lagana was awarded second on the topic of “Evaluation of cerebrospinal fluid flow in multiple sclerosis with phase contrast MRI”.



*Left to Right:* Drs. Marian Simka, E. Mark Haacke, Gabriela Trifan, Robert Zivadinov, Michael D. Dake, Paolo Zamboni

# ANNUAL MEETING SUMMARY

**Saturday, February 18, 2012**

## ***Workshop on Vascular Imaging in CCSVI: Ultrasound and MR Imaging Sessions***

The workshop participants were welcomed by Dr. Robert Zivadinov with an introductory note on vascular imaging.

### ***Ultrasound***

The opening session focused on ultrasound. Dr. Sandra Morovic discussed the five original and four revised CCSVI ultrasound screening criteria during her talk. The B-mode anomalies and IJV stenosis advancement were discussed by Karen Marr. The protocol of Dr. Paolo Zamboni was reviewed along with the “positive threshold” by Angela Lagace. She discussed the reflux in the internal jugular veins (IJV), vertebral veins (VV) and deep cerebral veins (DCV); B-mode abnormalities; no flow in the jugular veins; and cross sectional area measurements. These criteria can be difficult to assess due to respiration, positioning, and level of disability. Erica Menegatti talked on assessment of the thoracic pump and showed that the thoracic pump modulates flow and velocity but it is limited to the extra-cranial veins. She also provided a useful dataset of the main haemodynamic parameters assessed in normal volunteers and just published on the Journal of Applied Physiology. Dr. Marian Simka compared sonography and angiography and mentioned diagnostic accuracy of both modalities.

### ***MR Imaging***

Dr. Joseph Hewett began by discussing the CCSVI MRI protocol from his site which has collected MRV data on over 800 patients. He discussed the potential for data collected using time resolved 3D MRV, subtracted MRV, 2D time of flight, jugular and azygos imaging. He commented that the flow data is an important complement to the structural data and is important if the patient is going to have follow-up studies. In addition to the anatomic information available to MR, Dr. Hewett noted other important information includes: the empiric evaluation of CSF flow, lesion characterization with iron, diffusion tensor imaging and perfusion imaging to study the progression of the disease. He discussed his experience imaging the azygos vein using MR and the current difficulties. His emphasis was to provide comprehensive follow up imaging and patient friendly report summaries.

Dr. Robert Zivadinov talked on morphological MRV multimodal studies in CCSVI. Different modalities are used for diagnosis of CCSVI: Invasive and non-invasive. Various studies were performed beginning with first negative study for Magnetic Resonance Venography (MRV) and the following multimodal MRV techniques studies in favor. Intraluminal abnormalities are inside the veins and extra-luminal is outside the veins. No knowledge about the origin of the abnormalities exists. MRV flow studies have no normative data yet available. However, no differences were observed between MS patients and controls in some preliminary controlled studies. Morphological stenosis and non-stenosis approach showed significant differences between MS disease courses. MRV has various advantages and disadvantages in CCSVI diagnosis.

Dr. Michael Dake spoke on flow quantification. Various studies on diffuse hypo-perfusion precede development of MS plaques, initial hyper-perfusion related to ischemia and not hypo-metabolism/ tissue degeneration. Flow quantification is necessary to track physiological changes in addition to anatomical structures. For flow, pulsatility, phasicity, amplitude, and low flow need to be measured. Dr. E. Mark Haacke brought up the need for an MS and healthy control database among many institutions. FLAIR/T2, T1, SWI, MRAV and flow quantification could prove useful across sites and manufacturers. If all researchers using MR are using the same protocol, the data could be pooled and shared amongst researchers around the world. The centennial and millennium projects were also discussed, the idea being to image 100 and then 1000 normal controls to provide a much needed background of what is normal.

# ANNUAL MEETING SUMMARY

**Saturday, February 18, 2012**  
*(con't from Page 3)*

Dr. Paolo Zamboni discussed CCSVI diagnosis, multimodality techniques and the jugular entrapment syndrome. The three forms of venous obstruction are intraluminal defects (septum, malformed valve), stenosis (twisting, agenesis), and external compressions (bone or muscular compression). Compressions of the IJVs can be caused by the turning of the head that is normal. A stenotic jugular vein at rest and bite shows no stenosis during yawn. In the limit between inferior and superior omohyoid belly there is no connective tissue and tendon but only muscle therefore during bite and rest there is compression and obstruction by external compression of the vein. Strain gauge Plethysmography was presented as possible good method for screening. Dr. Sandra Morovic discussed about ISNVD consensus on ultrasound chronic cerebrospinal venous insufficiency screening criteria. Five new, revised and accepted criteria were discussed as follow: bidirectional flow in one or both of the IJVs and vertebral veins; bidirectional flow in the intracranial veins and sinuses, reduced IJV cross sectional area in supine position and/or intraluminal defects such as flaps; septa or malformed valves along with hemodynamic changes; absence of detectable flow in IJV and /or VV; CSA of IJV greater in sitting position compared to supine or remain unchanged with the posture.

Karen Marr talked on B-Mode anomalies and IJV stenosis CCSVI Criterion 3 - 2008 to 2012. The B-mode anomalies and IJV stenosis of 19 published articles was presented. The studies discussed in the talk were performed with varying results, 0% to 89%, due to varying definitions of stenosis, location of measurement of stenosis and B-mode anomaly definition used by each author. Karen presented the recent publication of Extra-luminal and Intra-luminal Structural and Functional Venous Abnormalities in MS along with two reported pathology reports and how the pathology reports correlate with the venous abnormalities in MS patients. The CSA for stenosis is now considered as less than or equal to  $3\text{mm}^2$ . Various questions were put forward on quantitative data to define stenosis, length to be considered for stenosis, stenotic area as flow measurement or lumen measurement and what defines an abnormal or malformed valve. Angela Lagace discussed Diagnostic Value of CCSVI criteria. The protocol of Dr. Zamboni was reviewed along with the "positive threshold". The reflux in IJV, VV and DCV; B-mode abnormalities; no flow in the jugular veins; CSA measurements. Ultrasound is good because of the complications in post angioplasty.

**Sunday, February 19, 2012**

## ***Continuation of the Workshop Consensus on Imaging & Treatment Protocols***

Each group from ultrasound, MR imaging and balloon angioplasty met separately from 8:30am to 10:00am to discuss the state-of-the-art in each area with an eye toward creating a white paper. The ultrasound discussion centered about the consistency of this technique and the loss of one of Dr. Paolo Zamboni's original five points. Dr. E. Mark Haacke also suggested that there might be two other points that could be addressed: that is total jugular flow normalized to total internal carotid artery and vertebral artery flow and the ratio of dominant to sub-dominant jugular flow.

The MR discussion focused on several tiers of a possible CCSVI MRI protocol that would make it more accessible to clinical sites. Dr. Robert Zivadinov pointed out that the MS societies have already established core MRI brain and spinal cord protocols so we need consider only a few additional sequences. For this reason, several tiers were proposed. Tier II would be simply adding a contrast enhanced 3D MRV scan post contrast injection and prior to the post-contrast T1 weighted scan. This adds no extra time to the usual Tier I level neurological scans. On top of this, flow data would be acquired at both C2/C3 and C6/C7 possibly with a Venc value of 50cm/sec. Collecting C2/C3 flow with a Venc value of 10cm/sec for CSF flow would be optional. Tier III would include SWI as part of the pre-scan data acquisition for iron studies and small vein information. Tier IV would include other scans such as PWI, DTI, MTI and/or MRSI.

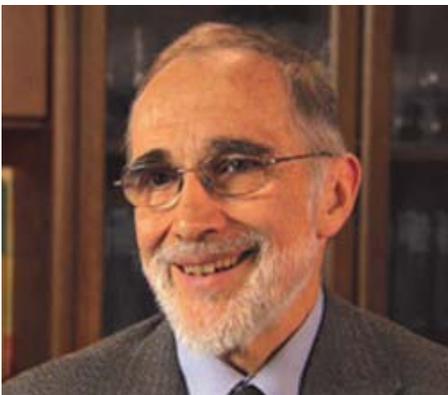
# ANNUAL MEETING SUMMARY

**Sunday, February 19, 2012**  
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The catheter venography and IVUS imaging discussion opened with a review presenting results of a survey done by Dr. Salvatore Sclafani prior to the ISNVD about interventional radiologists' practices. The discussion attempted to come up with a standardized approach to vascular assessment and the venoplasty procedure itself. Questions of safety brought up the issue that there are many variants of treating patients but what was being done was safe as evidenced by three major papers recently published on this topic.

The basic elements of these were then presented with a lot of questions following in the session from 10:30am to noon. Dr. Raj Attariwala talked on establishing an MRI CCSVI protocol; and the summary of the consensus on an MRI CCSVI protocol. Dr. Salvatore Sclafani talked on establishing catheter venography and IVUS imaging standards; and summary of consensus on catheter venography and IVUS. Dr. Nikolaos Liasis talked on establishing US imaging standards; and summary of the consensus on US imaging standards. His talk mentioned that noninvasive assessment of venous hemodynamic parameters indicating CCSVI can be done by transcranial and extracranial Doppler ultrasound. CCSVI evaluation requires ultrasound equipment and standard methodology. The board later determined that a single position statement should be put together by those involved for publication on behalf of the Society.

## **Official Opening of the ISNVD Scientific Sessions**



*Dr. Franz Schelling*

The session opened with a welcome from the President, Dr. Robert Zivadinov who introduced the Annual Meeting Chairmen Drs. E. Mark Haacke and Michael D. Dake. The keynote speaker was invited to talk about the role of the vasculature in neurodegenerative disease. This task was accomplished admirably by Dr. Michael Chopp from Henry Ford Hospital, Detroit, MI. He discussed vascular responses to neural injury and neurorestorative therapies. His work focused on using drugs such as Niaspin (niacin or vitamin B3) and sildenafil (Viagra) to help generate the formation of new micro-vessels to regenerate brain tissue. After this, Dr. Paolo Zamboni announced the winner of this year's Gold Medal Award to Dr. Franz Schelling for his pioneering contributions to understanding the role of the venous vasculature in multiple sclerosis. Dr. Schelling then gave an overview of some of the history and where he thought we still needed to forge ahead to clearly address the role of abnormal venous vasculature in MS.

## **Abnormal Venous Flow and Neurodegenerative Disease: Part I**

The keynote speaker in this session was Dr. Han-Hwa Hu from Taiwan, Taipei. His vast experience in jugular venous reflux was brought to bear from a neurologist's perspective. He talked on venous outflow abnormalities in neurological diseases. He mentioned that lot of neurological disorders are linked to the venous outflow impairment. Pathology of venous outflow and clinical treatment for venous abnormalities require more research. Venous involvement in neurological disorders was discussed by Dr. Robert Zivadinov. He discussed on treatment issues about short and long term studies. At the end of his talk he mentioned critical points such as what CCSVI represents, is it unique to MS, what is most accurate diagnostic test for detecting it, its significance to MS and treatment needed when it is detected. These main points can provide the direction to future study. Dr. John Cooke talked about the effects of hemodynamics on endothelium adhesion and permeability. Disturbed flow because of stenosis can cause increased strain acting on the venular wall and reverse stress acting on the endothelial cells. This can lead to an extravasation of the immune cells into the surrounding tissue, which can be one of the causes of inflammatory pathophysiology of MS. In general, the changes in venous hemodynamics could cause alterations in histological properties of endothelium which might be one of the reasons leading to local tissue inflammation.

# ANNUAL MEETING SUMMARY

**Sunday, February 19, 2012**  
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Dr. Michael Chopp, Dr. John Cooke, Dr. Han-Hwa Hu, Dr. Paolo Zamboni and Dr. Robert Zivadinov were the members of the abnormal vasculature in neurological disease panel discussion. At the end of the day Sunday, there was the annual reception of the ISNVD. This event provided an opportunity for the participants to sit and enjoy a quiet evening in style with a guitarist and excellent hors d'oeuvres, for some it was enough for dinner itself. The tables were nicely spaced throughout a well decorated room, and there was time to relax and discuss the days events with colleagues. The event ran from 5pm to 7pm immediately after the ending of the last session. Although coffee and treats throughout the event was very good, this was the highlight of the meeting from a culinary perspective.

**Monday, February 20, 2012**

## ***Perfusion, Hypoxia, Ischemia and Reperfusion***

Review lecture was discussed on stroke and brain perfusion by Dr. Vida Demarin. Dr. Yulin Ge focused on the hemodynamic perfusion changes and vascular abnormalities in MS, evaluated with advanced MRI techniques such as SWI, DSC-MRI, and ASL. Particularly, the oxygen saturation and oxygen metabolic changes of superior sagittal venous sinus in MS were measured with T2 Relaxation Under Spin Tagging (TRUST). Increased oxygen saturation and decreased CMRO<sub>2</sub> were found in MS patients. The under-utilization of oxygen in MS could be caused by over-production or storage of nitric oxide (NO) due to vascular inflammation, which can cause inhibition in mitochondria function. Dr. Robert Zivadinov talked about the perfusion changes in MS patients. He presented some preliminary results from a pilot study which demonstrated the relationship between CCSVI severity and perfusion changes in the brain parenchyma. He also pointed out the importance of understanding the role of CSF in the perfusion patterns in MS. He further talked about studies with perfusion changes in CCSVI, and neurodegeneration at early onset. There is hyper-perfusion in CCSVI, and oxygen saturation is higher in these people. SWI phase images showed a 20% reduction in venous volume in the CCSVI sample in good agreement with what Dr. Ge had discussed earlier. Dr. David Hubbard talked about fMRI BOLD and ASL perfusion before and after venoplasty.

## ***Abnormal Venous Flow and Neurodegenerative Disease: Part II***

Dr. Csaba Juhasz talked on changes in venous anatomy associated with sustained venous insufficiency in Sturge-Weber disease. Dr. Robert Zivadinov talked on venous and CSF flow in brain parenchyma of MS patients. Dr. John Cooke discussed endothelium in CCSVI. He outlined the role of endothelium but it was mostly centered on the arteries. Endothelial cells, which make up the capillary system, and line the lumen of blood vessels engage in signal transduction and respond to blood flow patterns with chemical signaling and vessel changes. ECs can sense pressure and respond to shear rate forces, and cyclic forces. If shear forces are low, the vessel will develop larger intima to regulate the blood pressure in the vessel. This occurs in arteries but it is not certain whether veins were implied as well. Perivenular cuff made of fibrin sometimes occur in the venules. Endothelium can respond to damage with adhesion molecules, chemokines, changes in permeability, vascular smooth muscle cell proliferation, and extracellular matrix elaboration. An egress of red blood cell iron in the form of hemosiderin was suggested in CCSVI. Dr. Fabrizio Salvi discussed normal pressure hydrocephalus and CCSVI. Cranial instability and CCSVI was discussed by Dr. David Williams.

## ***CCSVI Introduction: Part I***

Dr. Paolo Zamboni discussed historical overview of CCSVI. Dr. Robert Fox talked on post-mortem assessment of the venous system in MS and controls. 7 MS patients and 6 control patients were assessed. Valvular and intraluminal abnormalities with flow consequences were found in 5/7 MS. Dr. J. Steven Alexander talked on MS and cerebral endothelial dysfunction. SVC syndrome knowledge on the CCSVI was discussed by Dr. Ziv J. Haskal and Dr. Andrew Nicolaidis talked on asymptomatic carotid stenosis and risk stratification.

# ANNUAL MEETING SUMMARY

**Monday, February 20, 2012**  
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## ***CCSVI Consensus Guidelines: Part II***

Angela Lagace discussed ultrasound consensus. Dr. E. Mark Haacke discussed MRV consensus. Dr. Marian Simka discussed catheter venography. IVUS consensus was discussed by Dr. Adnan H. Siddiqui. Dr. Sandra Morovic talked on the abstract "consensus on ultrasound chronic cerebrospinal venous insufficiency screening criteria". The discussions were based on Saturday presentations.

**Tuesday, February 21, 2012**

## ***Abnormal Venous Flow and Neurodegenerative Disease: Part III***

Keynote speaker Dr. Chih-Ping Chung discussed the effects of jugular venous reflux in aging. Dr. Richard Hoge discussed vascular and metabolic neuroimaging applications in healthy aging. Task induced changes in cerebral oxygen consumption can be determined by fMRI calibration methods, information on resting metabolism can also be determined using these methods. Differences in physiologic baseline impact the fMRI responses in the aged population. Dr. E. Mark Haacke talked on high resolution imaging of the brains vasculature. It's possible to investigate the vascular system without artifact to 250 microns. The advent of high fields and parallel imaging it is possible to do on clinical basis. High resolution can provide veins draining to the activated region can be seen. Dr. Kamil Ugurbil talked on neurovascular coupling and cerebral venous organization.

## ***Iron and its Role in Neurovascular Disease***

Dr. James R. Connor discussed the role of brain iron in neurovascular disease. He explained the importance of the HFE gene (Hemochromatosis) which detects and helps in regulating the amount of iron in the body, and effects due to its mutation. The HFE gene is expressed in the endothelial cells of the microvasculature, choroid plexus epithelial cells, and ependymal cells lining the ventricles in the brain. It can influence the iron uptake into the brain. HFE gene mutations are associated with excess iron accumulation in different organs. Practically, the presence of this gene can cause iron overload. Gender, age, genes and diet affects the iron transport into the brain. Dr. Donato Gemmati talked on hepcidin and ferroportin genetic variants in MS susceptibility and progress. Iron imbalance is critical in MS and the clinical variation is genetically determined. Dr. Stefan Ropele discussed iron in MS. He mentioned that iron in basal ganglia is marker for neurodegeneration and is associated to feratin. Diamagnetism of myelin and a low concentration of iron in MS lesions hinders iron assessment in MS lesions. Mr. Charbel Habib discussed assessing abnormal iron content on deep gray matter of patients with MS versus healthy controls. Mr. Habib showed that more than 50% of MS patients, especially a large cohort of young patients, have high iron content in the basal ganglia or thalamus. He also showed that iron in the pulvinar thalamus may serve as a biomarker for MS.

## ***CCSVI Computational Fluid Dynamics and Measuring Flow: Part III***

Dr. Michael Markl discussed the future of 4D imaging of flow. Translation of the technology into a clinical environment is missing but can do the systemic impact of pathology of disease. Dr. E. Mark Haacke talked on flow characteristics in a study of 300 MS patients. Quantitative analysis provides the potential sub-characterize the MS population into low flow and high flow and those dominated by one jugular. Future work requires more controls to validate these biomarkers. Dr. Paolo Zamboni talked on postural control of cerebral venous return. Cervical plethysmography is a novel device for non-invasive, cost effective, reproducible assessment of cerebral venous return. Dr. Trevor Tucker discussed physics linked between cerebral venous reflux and venule hypertension, hypoxia and scleroses. Ms. Vesela Melisa Vera talked on metals as possible contributing factors in CCSVI and MS.

# ANNUAL MEETING SUMMARY

**Tuesday, February 21, 2012**  
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## ***Abnormal Venous Flow and Neurodegenerative Disease: Part IV***

Dr. Timothy Q. Duong talked on investigating the vasculature of the eye. MRI offers depth resolved, layer-specific anatomical layers, quantitative retinal and choroid blood flow, BOLD fMRI responses in the human retina. Dr. Simka talked about retinal abnormalities in multiple sclerosis patients with associated chronic cerebrospinal venous insufficiency. The asymmetric outflow from the brain to the asymmetric stenosis of the IJV was associated with higher risk of retinal neurodegeneration. High prevalence of ocular pathology was also observed in MS patients without CCSVI. Dr. Diana Driscoll discussed the CCSVI and eyes. She gave an introduction of vagus nerve suppression when IJV and/or ICA (internal carotid artery) expand due to insufficient venous blood flow or stenosis in the jugular veins. On the basis of her interpretation of the symptoms presented, it might be important to study vagus nerve compression as a likely cause (secondary to CCSVI) of the symptoms for MS. She explained vagus nerve compression and CCSVI angioplasty (after controlling the mast cells/ inflammatory cytokines) helps with some of the symptoms immediately.

**Wednesday, February 22, 2012**

## ***CCSVI clinical trials methodological considerations: Part IV***

Dr. Patricia Coyle discussed disability related outcomes in CCSVI. Disability is a strictly clinical measure, but most important. There are measures of disability, such as the EDSS, MSFC score, MS score, cognitive status, the transition to progressive MS, and more. Some of these measures have reliability and accuracy issues. The most important may be the transition to progressive MS, but this is long term. Modified MSFC may eventually replace EDSS. Dr. Robert Zivadinov discussed MRI outcomes in MS. The current clinically used MRI techniques are not suitable for finding cortical lesions, and these lesions represent about 60% of the total lesion volume in MS patients. Gd-enhanced and T2 enhances lesions do help show active lesions. New contrast agents can be used to show microglia and macrophage activity. Sensitivity and specificity of T2 lesion detection can be improved through sequence parameter adjustment. Most of the available drugs have been shown to reduce lesions. Brain atrophy can be measured with different MRI scans. Dr. Benedict provided an excellent talk about cognitive outcomes in MS. Dr. Bianca Weinstock-Guttman discussed CCSVI interdisciplinary approach. She also reviewed the usage of different modalities, like catheter venography, IVUS, CT venography, to confirm and study the abnormalities of neurodegenerative disorders. People without MS can have CCSVI and some people with MS do not have CCSVI. However, a higher percentage of MS patients do have CCSVI than normals. There are risk factors for CCSVI, like smoking and heart disease. A multi-modal study would be helpful for diagnosing CCSVI. The PREMise Study can be used as a multi-disciplinary approach to test the safety and effects of angioplasty on MS patients.

## ***Treatment of other venous diseases, abnormal vasculature: Part V***

Dr. Seshadri Raju discussed lessons from endovascular management of lower extremity venous obstruction. Stents placed in the lower limbs show great patency over long periods of time. Symptom relief has shown to be excellent, including ulcer healing. He mentioned that venography is not perfect in identifying venous abnormalities and IVUS is much better. Specifically, he noted that vessel wall imaging using IVUS can distinguish normal and abnormal vessel wall efficiently. This technique is essential in studying vascular abnormalities, and can play an integral part in supporting the venographic MRI data, especially for the azygous vein. Stenting in venous system is different than in arterial because of different pressures and flows. Stents are better than balloons because balloons recoil of lesions. Iliac vein stenting is very good for treating CVI. Collaterals will go away when larger pathway opens.

# ANNUAL MEETING SUMMARY

**Wednesday, February 22, 2012**  
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Dr. Salvatore Sclafani gave a talk on consequences of venous obstruction involving other vascular beds. CCSVI can be compounded by obstruction of CS veins, collaterals, or involvement of peripheral nerves. The different syndromes can change the common vascular pathways and introduce collaterals that may affect other vascular systems. Nutcracker syndrome is a compression caused stenosis of the renal vein. This diversion of flow can be significant. MRI and CT are good noninvasive ways to test for these syndromes. Stenting is the method of choice for treatment, though doing this for “inflow” veins may be the cause of treatment failure. Treatment of just IJV and AZV may not be sufficient.

Dr. Bulent Arslan discussed open procedures are now reserved for stent failures only occlusion, recanalization and thrombolysis. Treatment of venous circulation is handled clinically in different areas of the body, usually in the lower extremities. The cause is usually congenital, compression, or lesions. Deep venous thrombosis is common and very serious. A treatment ranges from systematic anticoagulation to the placement of a stent. Bringing back proper venous blood flow this way provides relief in patients who were feeling discomfort prior.

Dr. Randall Benson, a neurologist, discussed idiopathic intracranial hypertension (IIH): similarities & differences with CCSVI. Hypertension has no known cause. Usually affects overweight females. One of the best treatments is weight loss. It involves elevated intracranial pressure, increased CSF pressure. Tinnitus, Eye pain, and TVO are unique symptoms. No known cause, but maybe sleep apnea, kidney disease, systemic lupus are involved. Diagnosis involves swollen optic nerve head, can also do imaging or spinal tap. Similarities with CCSVI include stenosis in the transverse and sigmoid sinuses. Recent study showed 18/18 IIH patients had venous outflow compromise. Stenting has helped patients. Papilledema resolved in 15/16 patients and has not recurred. Not sure if it is cause or effect of IIH.

## ***Abstract Presentations and Abstract Awards***

Dr. James McGuckin discussed recanalization of the jugular veins and CCSVI. Diagnosing before treatment is very important. Dr. Matteo Coen discussed CCSVI in MS is characterized by altered collagen expression in the neck brain draining veins. The morphological and biological features of the IJV in MS patients were studied. Dr. Kenneth Mandato reviewed data from a study done using the Zamboni protocol after angioplasty, and concluded that CCSVI is not a true entity, however, correlation with ultrasound is strong. Dr. Mamoon Al-Omari discussed IJV morphology in patients using schematic demonstrations for intraluminal valvular abnormalities. These include: fused, accessory, long, ectopic and transverse leaflets, and inverted valves, double valve, sigmoid valve among others. The most common abnormalities are the septum and annulus. Mr. David Utriainen presented for Mr. Yi Zhong on a study showing cerebral blood flow collected at the C2 and C6 levels for the IJV. Flow measurements were also performed and it was concluded that the IJV flow may be considered a biomarker for stenosis. Dr. Wei Feng presented blood flow and reflux through the IJV and posed the question of how to better delineate between stenotic groups. Results showed that the left IJV showed reduced pulsatility as well as varying levels of stenosis and intraluminal defects in patients. Mr. Paul Kokeny presented for Ms. Aisha Tai and discussed results for azygous flow. Although there were little differences in the histograms between normal controls and MS patients, the MS patients had more narrowed azygous veins than the normals. Dr. Andrew Dueck discussed the prevalence of CCSVI in several studies that were performed as a literature review. There was a large variation when performing sensitivity analysis, with none of the studies being performed blindly.

# ANNUAL MEETING SUMMARY

**Wednesday, February 22, 2012**  
*(con't from Page 9)*

## **CCSVI Clinical Trials Outcomes: Part V**

Dr. Robert Zivadinov discussed the topic of whether or not CCSVI is a disease in itself. Phenotyping for clinical symptoms of CCSVI still needs to be determined. Doppler sonography is commonly used for the terminology of vascular abnormalities in CCSVI. There are intra-luminal (web, flap, septum, membrane, valve), extra-luminal (stenosis, annulus), and functional (reflux, flow, no flow) abnormalities in the veins. Sensitivity and specificity must be established between groups, and gold standards, etc. We need standardized guidelines to diagnostic techniques. MS is difficult to assess because of the different types. Lesions can happen with no symptoms. Dr. Adnan H. Siddiqui talked on design of randomized, placebo-controlled endovascular trails in MS. A national approach to gather prospective data for MS outcomes was discussed by Dr. David Hubbard. Dr. Jack Burks talked on neurologists perspective is to put data first, then commercialization. At present there is not enough concrete data on all the cases of CCSVI that have been treated. Neurologists do need to be open to the idea of CCSVI and not just dismiss it. A data registry and better designed trials is needed with a collaborative approach. Dr. Paolo Zamboni discussed "BRAVE Dreams" about multi-center, randomized, blinded, sham-controlled, parallel group study with 1 year follow ups. Perform functional tests on MS patients with CCSVI and randomize. Perform venous angioplasty and venography on some and only venography on others. Do follow ups. Observe if this treatment helps people with MS and CCSVI. Check walking, balance, dexterity, sphincter control, and visual activity. MRI will check T2 lesions.



*Left:* Dr. Wei Feng, Dr. Timothy Q. Duong, Zahid Latif, Saifeng Liu, Sagar Buch, Karen Mok, and Jin Tang.

## PASSING OF THE GAVEL



The session was closed by passing the Gavel from Dr. Robert Zivadinov (right), President 2011-2012 to Dr. Marian Simka (left), President 2012-2013.



Left to right: After a passing of the gavels at the end of the second annual ISNVD in Orlando, Florida.

Dr. Marian Simka  
(3rd President)

Dr. E. Mark Haacke  
(Founding President)

Dr. Robert Zivadinov  
(2nd President)

Dr. Michael D. Dake  
(Annual Meeting Chairman)

Dr. Paolo Zamboni  
(1st President)



Dr. Robert Zivadinov (left), 2nd President 2011-2012  
Dr. Paolo Zamboni (right), 1st President 2010-2011

# ISNVD ANNUAL MEETING COMMITTEE AND STAFF

## Conference Chair

Robert Zivadinov, MD, PhD  
President of ISNVD  
Professor of Neurology, University of Buffalo

## Annual Meeting and Workshop Committee Chairmen

E. Mark Haacke, PhD and Michael D. Dake, MD

## Staff

The ISNVD had staff support for this meeting during the last year courtesy of The MRI Institute for Biomedical Research and the Buffalo Neuroimaging Analysis Center who helped especially in preparation for CME Accreditation. The press support came from Tara A. Ellis and videographer Frank A. Pacella.

*Executive Director:* Rachel Martis-Laze (who subsequently received the Silver Medal Award of the Society for significant contributions to the success of the meeting and the running of the Society during 2011/2012).

*Supporting staff:* Rana El Hachem-Habib and Judith Farah

*Technical staff:* Emil Pacurar

*Supporting student:* Charbel Habib



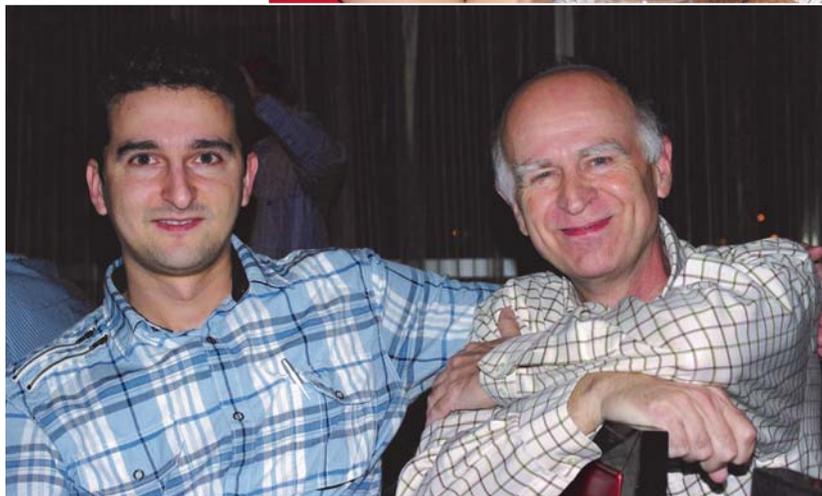
*Left:* Dr. Wei Feng, Dr. Marian Simka, David Utriainen, Dr. Marcella Lagana, Rachel Martis-Laze, Dr. Donato Gemmati, Stefania Marcotti, Ana Chaudhary, and Dr. Gabriela Trifan.



*Above:* Judith Farah and Rachel Martis-Laze



*Right:* Rana El Hachem and Charbel Habib



*Right:* Emil Pacurar and Dr. E. Mark Haacke

# INVITED SPEAKERS (\*) – MS Patient Day Speaker

J. Steven Alexander, PhD – USA  
Michael Arata, MD – USA\*  
Bulent Arslan, MD – USA\*  
Raj Attariwala, MD, PhD – CANADA\*  
Ralph H. B. Benedict, PhD – USA  
Randall Benson, MD – USA  
Jack S. Burks, MD – USA\*  
Michael Chopp, PhD – USA  
Chih-Ping Chung, MD, PhD – TAIWAN  
William Code, MD – CANADA\*  
Matteo Coen, MD – SWITZERLAND  
James R. Connor, PhD – USA  
John P. Cooke, MD, PhD – USA  
Patricia K. Coyle, MD – USA  
Michael D. Dake, MD – USA\*  
Vida Demarin, MD, PhD – CROATIA  
Diana Driscoll, OD – USA  
Kirsty Duncan, PhD – CANADA\*  
Timothy Q. Duong, PhD – USA  
Eric Feigenbutz, RVT – USA\*  
Robert Fox, MD – USA  
Yulin Ge, MD – USA  
Donato Gemmati, PhD – ITALY  
E. Mark Haacke, PhD – USA\*  
Ziv J. Haskal, MD – USA  
J. Joseph Hewett, MD – USA\*  
Richard Hoge, PhD – CANADA

Han-Hwa Hu, MD – TAIWAN  
David Hubbard, MD – USA\*  
Csaba Juhasz, MD, PhD – USA  
Angela Lagace, RVT – CANADA\*  
Nikolaos Liasis, MD, PhD – GREECE  
Michael Markl, PhD – USA  
Karen Marr, RVT – USA  
James F. McGuckin, MD – USA  
Erica Menegatti, PhD – ITALY  
Sandra Morovic, MD, PhD – ITALY-CROATIA  
Andrew Nicolaidis, PhD – UK  
Gerald A. Niedzwiecki, MD – USA\*  
Seshadri Raju, MD – USA  
Stefan Ropele, PhD – AUSTRIA  
Fabrizio Salvi, MD – ITALY  
Franz Schelling, MD – AUSTRIA  
Salvatore Sclafani, MD – USA\*  
Adnan H. Siddiqui, MD, PhD – USA  
Marian Simka, MD, PhD – POLAND  
Daniel Simon, MD – USA\*  
Trevor W. Tucker, PhD – CANADA  
Kamil Ugurbil, PhD – USA  
Bianca Weinstock-Guttman, MD – USA  
David Williams, DDS – CANADA\*  
H. Charles Woodfield, RPh, DC – USA\*  
Paolo Zamboni, MD – ITALY\*  
Robert Zivadinov, MD, PhD – USA\*

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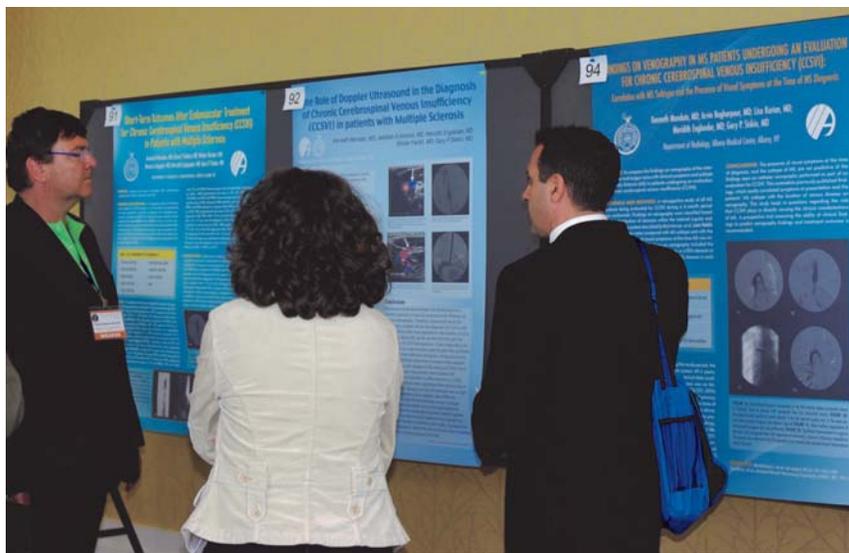
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CCSVI Coalition

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Above: Dr. Paolo Zamboni and Dr. Kenneth Mandato

# ISNVD BOARD COMMITTEE MEMBERS 2012-2013



Dr. Robert Zivadinov, President 2011-2012 with other committee members during a discussion.

## Executive Committee:

<b>President</b>	Marian Simka, MD, PhD
<b>President Elect</b>	Michael D. Dake, MD
<b>Vice President</b>	To be elected
<b>Secretary</b>	To be elected
<b>Treasurer</b>	David Hubbard, MD
<b>Chairperson</b>	To be decided
<b>Chairperson</b>	To be decided
<b>Past President</b>	Robert Zivadinov, MD, PhD

## Committee Chairmen:

<b>Finance Committee</b>	David Hubbard, MD
<b>Nominating Committee</b>	Salvatore Sclafani, MD
<b>Awards Committee</b>	Robert Zivadinov, MD, PhD
<b>Publications Committee</b>	To be decided
<b>Education Committee</b>	Franz Schelling, MD
<b>Governance Committee</b>	Robert Zivadinov, MD, PhD
	J. Joseph Hewett, MD
<b>Section and Affiliations Committee</b>	Zahid Latif, RT
<b>Public Relations Committee</b>	Sandy McDonald, MD
	Thomas Gilhooly, MD

# REPORT OF BOARD MEETING MINUTES

The International Society for Neurovascular Disease (ISNVD) board members held five meetings at the Hilton Hotel in Orlando during the Second Annual Scientific Meeting on February 18th, 19th, 20th, 21st and 22nd, 2012. Present at the meetings, were not only the executive committee members, but also many of the board members of the society. Many interesting topics were brought up at those meetings, mainly focusing on how to get new members to sign up for the society, starting the journal of the ISNVD, the 2013 ISNVD Meeting in Poland and as well as electing new board members for the 2012-2013 fiscal year.

Dr. Robert Zivadinov, ISNVD President, encouraged all board members to invite scientists and clinical people to run for the available board positions. He also shared with the present board members that “for next year’s meeting, the society needs to have a third party on the Annual Meeting Program Committee to assist with the organization of the meeting and help branch out to different people who might be interested in speaking at the 2013 ISNVD meeting in Poland”.

Regarding the new journal, many ideas were suggested to get some momentum in beginning a journal. The main focus of the discussion was to get the publications from this journal to be on pubmed.gov. Dr. E. Mark Haacke mentioned that “the first most important aspect in a society is the annual meeting and the second most important is the journal”. Dr. Haacke continued saying “now is the right time to initiate the Society’s journal”. Dr. Zivadinov spent some time discussing the difference between an electronic journal and a more conventional approach. Dr. Zivadinov also proposed that he and Dr. Marian Simka would research further how to proceed with the journal and come up with two alternate proposals.

There was also discussion about the potential of a statement or white paper on the consensus issues discussed at the meeting. Dr. Zivadinov suggested assigning two people to write a draft on each component of roughly 600 words which everyone would then review as a whole. The timeline for the first draft was suggested to be June 1st, 2012. The sessions and assigned people were as follows: Introduction: Dr. Michael D. Dake and Dr. Robert Zivadinov; MRI: Dr. E. Mark Haacke and Dr. Stefano Bastianello; Ultrasound: Dr. Sandy McDonald and Dr. Paolo Zamboni; and Angiography: Dr. Ziv J. Haskal and Dr. Kenneth Mandato.

Dr. Simka, ISNVD President-elect at the time, talked about the 2013 ISNVD Annual Scientific meeting taking place in Krakow, Poland. He mentioned that the society will be grouping different specialists to solve clinical and scientific problems related to neurological pathologies with vascular background, some of which are neurologists, vascular surgeons, neuroradiologists, interventional radiologists and others. In addition, the main topics of next year’s conference were proposed to be: management of acute stroke, chronic cerebrospinal venous insufficiency and venous disorders in the settings of neurological disease.

Finally, suggestions for the 2012-2013 board members were given, and the executive committee, along with the many board members agreed on nominating a broad group of Scientists and Clinicians from Europe, the United States and Canada.

## **Upcoming Elections for New Board Members**

The ISNVD will be holding elections for ten (10) new positions in April 2012 for Vice President, Secretary, and eight (8) Board Members.

Be on the lookout for the ballots and please remember to vote!

# 3rd Annual ISNVD Scientific Meeting (*Poland 2013*)

## Tentative Schedule of Events

### **Saturday - February 23, 2013**

8:00am – 9:00am	Registration of Workshop participants
9:00am – 11:00am	Workshop on trans cranial Doppler
9:00am – 11:00am	Workshop on Doppler examination of neck veins
9:00am – 11:00am	Workshop on trans esophageal Doppler examination of azygous vein
9:00am – 11:00am	Workshop on evaluation of MRV in CCSVI Patients
11:00am – 11:30am	Coffee Break
11:30am – 1:00pm	How do I do it: IVUS in CCSVI Patients
11:30am – 1:00pm	How do I do it: PTA and cutting balloons in CCSVI Patients
11:30am – 1:00pm	Workshop: How to set up an acute stroke service
11:30am – 1:00pm	Workshop on MR and CT assessment in stroke patients
1:00pm – 2:30pm	Lunch
2:30pm – 4:30pm	Workshop on trans cranial Doppler
2:30pm – 4:30pm	Workshop on Doppler examination of neck veins
2:30pm – 4:30pm	Workshop on trans esophageal Doppler examination of azygous vein
2:30pm – 4:30pm	Workshop on evaluation of MRV in CCSVI Patients
4:30pm – 5:00pm	Coffee Break
5:00pm – 6:30pm	How do I do it: IVUS in CCSVI Patients
5:00pm – 6:30pm	How do I do it: PTA and cutting balloons in CCSVI Patients
5:00pm – 6:30pm	Workshop: How to set up an acute stroke service
5:00pm – 6:30pm	Workshop on MR and CT assessment in stroke patients
8:00pm – 11:00pm	Meet-together for workshop participants

### **Sunday - February 24, 2013**

8:00am – 9:00am	Registration for ISNVD Annual Meeting
9:00am – 9:30am	Official opening of the ISNVD Annual Meeting
<b>9:30am – 11:00am</b>	<b>Acute stroke management: session 1 – basic science and prevention</b>
9:30am – 9:50am	Stroke in animal models
9:50am – 10:10am	Asymptomatic carotid stenosis: who should be treated?
10:10am – 10:30am	TBD
10:30am – 10:50am	TBD
10:50am – 11:00am	Panel Discussion
11:00am – 11:30am	Coffee Break with Poster session 1
<b>11:30am – 1:00pm</b>	<b>Acute stroke management: session 2 – Diagnosis and treatment</b>
11:30am – 11:50am	How to set up an acute stroke service
11:50am – 12:05pm	Emergence CT and MR imaging in stroke patients
12:05pm – 12:25pm	Mechanical thrombectomy in acute stroke
12:25pm – 12:40pm	Systemic vs. local fibrinolysis in acute stroke
12:40pm – 12:45pm	Percutaneous left atrial appendage closure for stroke prophylaxis
12:45pm – 1:00pm	Panel discussion and closing remarks
1:00pm – 2:30pm	Lunch
<b>2:30pm – 4:30pm</b>	<b>CCSVI session 1 – Ultrasonography</b>
2:30pm – 2:45pm	Cerebral circulation time in MS patients
2:45pm – 3:00pm	Quantitative color Doppler evaluation of cerebral venous outflow in MS patients and healthy controls
3:00pm – 3:15pm	How reliable are current sonographic CCSVI criteria
3:15pm – 3:30pm	Comparison between ultrasound and venography in MS patients
3:30pm – 3:45pm	Transesophageal sonographic assessment of the azygous vein
3:45pm – 4:00pm	Prevalence of CCSVI in MS patients and healthy controls
4:00pm – 4:30pm	TBD
4:30pm – 5:00pm	Coffee Break with Poster session 2

# 3rd Annual ISNVD Scientific Meeting (*Poland 2013*)

## Tentative Schedule of Events

### **Sunday - February 24, 2013 (con't from page 16)**

#### **5:00pm – 6:30pm**

5:00pm – 5:15pm

5:15pm – 5:25pm

5:25pm – 5:35pm

5:35pm – 5:45pm

5:45pm – 5:55pm

5:55pm – 6:15pm

6:30pm – 8:00pm

#### **CCSVI session 2 – Clinical trials on CCSIV**

Meta-analysis of open-label interventional studies on CCSVI

Current status of RCT on CCSVI: Italy

Current status of RCT on CCSVI: USA

Current status of RCT on CCSVI: USA

Current status of RCT on CCSVI: Australia

Panel Discussion

Welcome reception (free of charge)

### **Monday - February 25, 2013**

8:00am – 9:00am

Registration for ISNVD Annual Meeting

#### **9:00am – 10:00am**

#### **Venous disorders in non-MS neurologic pathologies**

9:00am – 9:15am

Abnormal MRI drainage pattern in Parkinson disease

9:15am – 9:30am

Venous drainage in MS and migraine

9:30am – 9:45am

Abnormal arterial vasculature in Parkinson disease

9:45am – 10:00am

Cerebral venous hemodynamics in chronic disorders of cerebral circulation

10:00am – 10:15am

TBD

10:15am – 10:30am

TBD

10:30am – 11:00am

Coffee Break with Poster session 3

11:00am – 11:30am

Key note Lecture: TBD

#### **11:30am – 1:00pm**

#### **CCSVI session 3 – endovascular and surgical interventions for CCSVI**

11:30am – 11:45am

Endovascular interventions in other venous territories

11:45am – 12:00pm

Venous angioplasty using cutting balloons

12:00pm – 12:15pm

The role for IVUS in decision making

12:15pm – 12:30pm

Redo angioplasty in CCSVI patients

12:30pm – 12:45pm

TBD

12:45pm – 1:00pm

Panel Discussion

1:00pm – 2:30pm

Lunch

2:30pm – 4:30pm

TBD

4:30pm – 5:00pm

Coffee Break with Poster session 4

#### **5:00pm – 6:00pm**

#### **CCSVI session 5 – MRI**

5:00pm – 5:15pm

Quantitative MRV in MS patients

5:15pm – 5:30pm

MR hemodynamic changes in MS and CIS

5:30pm – 5:45pm

Positional venous MR angiography

5:45pm – 6:00pm

TBD

6:00pm – 6:30pm

Closing Session

8:00pm – 11:00pm

Gala Dinner



**ISNVD**  
International Society for  
Neurovascular Disease

# 3<sup>rd</sup> ANNUAL ISNVD MEETING

## 23-25 FEBRUARY 2013

### CRACOW, POLAND

#### MAIN TOPICS OF THE CONFERENCE:

- Management of acute stroke
- Chronic cerebral venous insufficiency
- Venous disorders in the settings of the neurological disease



#### **The International Society for Neurovascular Disease (ISNVD)**

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