

Neurovascular Perspectives

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

EDITORS

Salvatore Sclafani &
Robert Zivadinov

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

I've been reading a great book, **The fantastic Laboratory of Dr Weigl**, written by Arthur Allen. It is a historical account of attempts to create a vaccine against typhus in the first half of the Twentieth Century. I particularly enjoyed learning about Ludwik Fleck, a country doctor of Polish and Jewish heritage, who also developed an interesting philosophy of medical thinking. He asked, "How do we find a law for lawless phenomena?" The lawless phenomena for doctors being the varied clinical presentations of patients with the same disease and similar presentations of patients with different diseases. "Only statistical observations allow us to create a type out of many individual cases." In the modern era, this seems quite obvious to us but in 1927, we relied upon "authorities" and "heroes". Fleck proposed that medical science advances are not made through individuals, heroes or authorities, but rather through societal collaborations because the lone scientist cannot do it all in the modern medical arena. It is just too complicated. Moreover, he argued that society determines the need, the focus, and the relevance of science. For example, society determines that some diseases deserve our attention and funding for the research and demands to be informed about the progress in discovery. On another level, a society of physicians can accept or reject the science and therefore can have an impact on how the scientific discovery is translated into care. Clearly societies can have a positive or negative influence on science.

In 2010, a group of physicians chose to establish a Society (ISNVD) as a response to concepts proposed by Dr. Paolo Zamboni because none of us had all of the knowledge or expertise to understand CCSVI and its

relevance to and relationship with Multiple Sclerosis.

The truths we sought could only be achieved by collaboration. In the past five years, we have expanded our membership, widened our search and discovered things we did not imagine. Our meeting in Naples was an astounding success! The levels of expertise, the nuances of knowledge as well as the scope of the topics had grown so much from 2010.

On **April 29-30, 2016** our Society will reunite in the hallowed halls of the New York Academy of Science, one of the oldest American scientific societies, at the resurrected World Trade Center at the foot of Manhattan. I look forward to seeing you there as we, a society of colleagues, seek further understanding and truth.

Enjoy our Spring 2015 newsletter focusing on the Naples, Italy conference held March 27-29th of this year. Pictured below is Dr. Paolo Zamboni's Gold Medal Award in Naples for you to view as well.

Best,
Dr. Salvatore Sclafani,
President, ISNVD



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Annual Meeting Overview

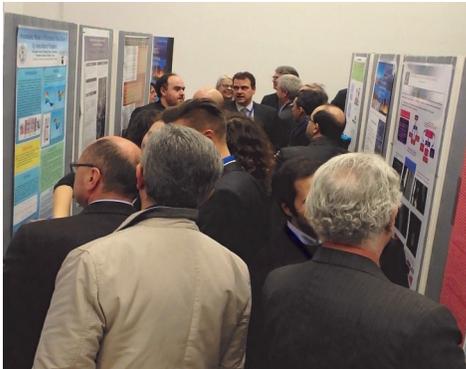
The 5th meeting of the ISNVD, held in Naples, Italy on March 27-29th, 2015 continued with the tradition of bringing together researchers with different expertise coming from all over the world, focusing on the functional and structural alterations of arterial and venous vessels in neurological disorders.

Day one began with a most interesting ultrasound course that was provided by Dr. Marcello Mancini. Invited speakers such as Dr. Erica Menegatti and Dr. Sandro Sanguigni spoke on topics such as extracranial veins and cerebral parenchymal ultrasonography. This ultrasound class made for a most educational opportunity for conference attendees.



(Above: Drs. Zivadinov, Mancini and Zamboni discuss new ultrasound techniques used in diagnosing neurovascular disease).

After Dr. Mancini's ultrasound course, the much-anticipated poster abstract session was held at the conference venue. There were many very original poster abstracts this year that were of a very high quality. The poster session was chaired by Dr. Enrico Tedeschi and Dr. Hector Ferral.



(Above: Attendees of the 2015 annual meeting analyze and discuss the many brilliant abstract posters that were accepted for presentation.)

A special mention is well-deserved by the winners of the poster competition. Best poster presentation as well as runner up and runner up number two were given to Qinghui Zhang, Marcello Moccia and Antonio Carotenuto respectively. The award for best oral presentation was given to Serena Monti from Naples, Italy. This year, the Young Investigator Award was presented to Federica Caforio from Trento, Italy.



Above: Abstract winners celebrate with Drs. Sclafani, Ferral and Toro. Students pictures from left are Antonio Carotenuto, Qinghui Zhang and Federica Caforio.

After the poster presentation on Friday evening, we were fortunate enough to host our key-note speaker from The Netherlands, Dr. Mat Daemen. Dr. Daemen's talk was titled, "*The Heart-Brain Axis; An overlooked Cause of Brain Aging*" which was very well-received. This session was chaired by our new President, Dr. Salvatore Sclafani.

(Below, Keynote Speaker, Dr. Mat Daemen delivers his talk as members of the audience look on.)



The multicenter project depicted in Dr. Daemen's lecture linked together the hemodynamic status of the heart and brain with cognitive impairment and will likely have a major impact on the diagnosis and possibly, treatment of some cognitive disturbances in the elderly. A correlation between cardiovascular risk factors and neurodegenerative disorders was also reported on by Dr. Robert Zivadinov using MRI measurements in patients with Multiple Sclerosis. Dr. Zivadinov touched on this subject and his talk was titled, "*Cardiovascular risk factors and neurodegenerative disorders.*"

Following the deliverance of the keynote speaker address, Dr. Mancini hosted a lovely welcome reception at the conference venue which was the "Congress Center Federico II" located on the waterfront in Naples.

Annual Meeting Outline (con'td)



Above: Guests talk and enjoy dinner at the opening night reception.)

There were four sessions scheduled throughout the whole conference. Session number one was titled, "Hemodynamics of the brain." During this session, the group led by Drs. Marcello Mancini and Marco Salvatore from Naples, Italy talked about how they had studied the characteristics of arterial and venous flow both in the neck and intracranial vessels in Multiple Sclerosis and in an animal model of the disease which showed the feasibility of an automated segmentation of brain veins with a novel MRI approach.

Also during session one, the intriguing possibilities offered by susceptibility-weighted MR imaging in the morphological and functional study of the cerebral microvascular were best summarized by Dr. Mark Haacke from Wayne State University in Detroit, Michigan USA. The title of his talk was, "Imaging of the Microvasculature."

Session two was titled, "Quantitative flow and computational fluid modeling." During this session, Dr. Bart Romeny from Amsterdam, The Netherlands gave an impressive 3D and 4D blood flow visualization of the vascular vectors. This presentation was most impressive and very informative.

Dr. Clive Beggs (below) from The UK, Dr. Mauro Ursino from Bologna, Italy and Dr. Eleuterio Toro from Trento, Italy, described the computational fluid modeling aimed to more fully understand the factors influencing the CSF motion and the intracranial hemodynamics, respectively.



Also during session two, Dr. Zamboni discussed a novel ultrasonographic method to reproducibly evaluate the internal jugular vein (IJV) pulse which was the focus of this discussion that showed differences in IJV functionality between normal subjects and the chronic cerebrospinal venous insufficiency (CCSVI).

During sessions three and four, several speakers focused on the role of the endothelium in neurodegenerative diseases; in particular, the interesting results of basic research on the endothelial response to shear stress and the expression of amyloid precursor protein were presented by Dr. Steve Alexander from LSU, Dr. Chih-Ping Chung from Veteran's Hospital, Taipei, Taiwan, while Dr. Pedro D'Orleans-Juste from Canada described the role of the mast-cells products in a murine model of MS with possible application in genetic therapy trials.



(Above: Drs. Pedro D'Orleans-Juste and Lucia Monti address the crowd with their presentations.)



(Above: Dr. Ivo Petrov from Sofia, Bulgaria asks a question during the lecture session as both Drs. Steve Alexander and Mark Haacke listen in.)

The hope for new therapeutic approaches for human neurodegenerative disorders is fostered by the important studies of Dr. Jacques De Keyser and his group from Brussels, Belgium who demonstrated the reversibility of the reduction in cerebral blood flow observed in MS patients by using antagonists of endothelin-1 (ET-1), a vasoactive peptide which is also over-expressed in Alzheimer's Disease and other disorders associated with chronic brain hypoperfusion. The effects of ET-1 and other markers of endothelial dysfunction of the autoregulation of cerebral vessels and cerebral circulation time in MS patients were also quantitatively demonstrated by Serena Monti, M.S. from Siena, Italy using digital subtraction angiography.

Annual Meeting (Cont'd)

Finally, as far as presentations are concerned, timely reviews on the advances in treatment strategies for extra cranial venous diseases and on the recent literature on the CCSVI-debate were provided by Drs. Hector Ferral from Chicago, Northshore University Healthcare System, USA and Michael Dake from Stanford University, U.S.



(Above: Dr. Marcello Mancini hosted a well-attended luncheon on day 2.)

This year, The ISNVD annual meeting included more than 100 attendees and 25 invited speakers. In addition to the poster presentation, we also heard abstracts that were selected for oral presentation which all demonstrated outstanding research.

(Below: Dr. Mancini speaks to the media about advances in medical research pertaining to neurovascular disease.)



We also participated in our usual traditions such as the passing of the President's gavel. This year, our current President, Dr. Ziv Haskal, passed the gavel to our new incoming President, Dr. Salvatore Sclafani from Brooklyn, New York. Below-pictures is Dr. Haskal passing the gavel to Dr. Sclafani.



In order to thank Dr. Ziv Haskal for all of his hard work in guiding the ISNVD during the past year, The Board presented him with a special award to honor his service.



Additionally, The ISNVD Executive Committee presented Dr. Marcello Mancini with an award to show their appreciation for the excellent job he did in Chairing the annual meeting in his home city, Naples, Italy.



Dr. Marcello Mancini, Annual Chair 2015

Furthermore, a special award was given this year to Dr. Paolo Zamboni for all of his hard work, diligence and research in the field of neurovascular disease. The Executive Committee reserves the right to present this award at an annual meeting if they feel that it is appropriate. This year, it was determined that Dr. Zamboni was deserving of a "Gold Medal Award." Below-pictured is Dr. Paolo Zamboni with his Gold Medal Award. Congratulations to Dr. Zamboni and his staff!



Annual Meeting (Cont'd)

This year, our Gala dinner was at the Complesso Monumentale San Lorenzo Maggiore Sala Sisto V which is a 1,000 year old monastery that is also currently used as a banquet hall. The facility was exquisite in design and architecture. It is located in one of the oldest sections of the city of Naples. Additionally, there are catacombs housed underneath the structure that showcase what life was like in ancient Naples. A guided tour was provided to all attendees of the dinner. Also featured was our annual fundraiser at the Gala dinner which was a silent auction that was organized and sponsored by Mrs. Carol Schumacher and her husband, Scott. Carol is on the ISNVD Public Relations Committee and also serves in the role of a patient advocate Chairperson. Shown below are Dr. Ziv Haskal, Carol Schumacher and Dr. Hector Ferral enjoying the event. Dr. Ferral was kind enough to craft a beautiful glass piece that was successfully auctioned off at the event.



The next morning, Carol and Scott Schumacher were also gracious enough to host a beautiful breakfast at their mountain top condo in Naples which overlooked the bay and Mount Vesuvius. Here, scientists gathered for a more intimate conversation regarding neurovascular research and enjoyed a wonderful brunch prepared by Carol and Scott.



(Above at the brunch are from left: Mrs. Carol Schumacher, Dr. Steve Alexander, Margreet Sienstra and Dr. Alireza Minagar who is Chair of the Department of Neurology at Louisiana State University,)



(Above: Margreet Sienstra, Dr. Evangelia Tsati, Dr. Clive Beggs and ISNVD President Salvatore Sclafani further discuss medical research at the send-off brunch.)



(Above: A beautiful view of Mount Vesuvius from The Schumacher's condo as well as an example of the beautiful hand-crafted glass gifts that The Schumacher's made as awards).

Board Meetings

During the two and one-half day conference, there were two separate board meetings that were held. The two Board meetings included the business meeting.

The first board meeting was held Friday afternoon at the conference venue at 4:30 p.m. The following items on the agenda were discussed:

- Publications
- Direction the Society is moving in
- Membership drive
- Various committee chair openings
- Suggestions for new committees
- Site of next year's meeting
- Financial status of the Society which is good

The second meeting was the annual board/business meeting which was held on Saturday morning at the conference center hotel. The following items were discussed:

- Financial status of the Society which is good
- Site of next year's annual meeting
- Publications
- Committee Chair positions open
- Changes/additions to by-laws

AFRND Awards

The Annette Funicello Research Fund for Neurological Disease (AFRFND) joined with the International Society of Neurovascular Diseases (ISNVD.org) in the Fall of 2014 to request proposals in clinical and basic science research into neurovascular disease emphasizing the relationship to multiple sclerosis (MS) and neurodegeneration.

Numerous international submissions were judged by a scientific review panel and four grantees were announced by Society President, Professor Ziv J Haskal M.D. at the annual meeting. Winners included:

Melbourne's Dr. Helen Kavnoudias, PhD: A randomised, double-blinded, controlled (with sham) study of percutaneous transluminal angioplasty for extracranial vein stenoses in patients with multiple sclerosis. (Clinical angioplasty treatment trial CCSVI in MS)

Buffalo's Dr. Robert Zivadinov: A case-control, 5-year follow-up study of cardiovascular, environmental and genetic risk factors for disease progression in patients with multiple sclerosis (CEG-MS study).

Milan's Dr. Maria Lagana PhD: Combined study of neurodegeneration, cerebrovascular reactivity and venous drainage impairments in Parkinson's Disease (PD) and Multiple Sclerosis (CCSVI in PD & MS)

Shreveport's (LSU) Dr. J. Stephen Alexander: 'Diagnostic and prognostic use of neurolymphatic biomarkers in Multiple Sclerosis'. (MS-CCSVI biomarker)

"With these grants, the AFRFND takes a substantial step forward in directly supporting sophisticated research into palliating, treating and curing neurovascular diseases, such as MS. Our grant winners represent a remarkably broad range of study, from controlled trials to basic receptor science and I expect great things," said Dr. Ziv Haskal, Professor of Interventional Radiology at the University of Virginia and Editor of the Journal of Vascular and Interventional Radiology. "The submissions were very diverse—I'm looking forward to the reports from these interesting and potentially pivotal studies," said Professor Michael Dake, M.D., Cardiothoracic Surgery at Stanford University.

The Annette Funicello Research Fund for Neurological Diseases is a 501(c)3 non-profit and has a specific interest in supporting clinical studies that seek to expose the underlying cause of neurodegenerative diseases like Multiple Sclerosis and therapies that show the promise of reversing disease progression. For more information, go to their website at: www.annetteconnection.com.

Thank You

Many thank yous go out to everyone who worked very hard on putting together this conference as well as to those of you who attended. We take great pride in the fact that our 2015 annual meeting was a huge success! Special thank yous go out to Carol and Scott Schumacher for all of their hard work in supporting the conference, MP Congressi for supporting the on-site logistics of the conference, Ms. Florence D'Eon, RN for providing spectacular photos and Drs. Enrico Tedeschi and Giuseppe Palma for providing the editorial for this publication.

We also owe a large debt of gratitude to our loyal sponsors that included:

- The Canadian Coalition for the Study of Venous Insufficiency
- The CCSVI Alliance - United States
- The Annette Funicello Research Fund for Neurological Dis.
- National Research Council of Italy
- Bayer HealthCare
- Sereco Medical
- SIUMB
- BRACCO
- Regione Campania
- RISM
- Esaote
- SDN

We are eternally grateful. We hope to see everyone again next year!

Becoming a Member

On a separate note, we have heard many positive things that came out of our conference and had a lot of positive feedback—especially from non-members. In fact, as a result of our Naples meeting, we have had seven new members join.

If you are interested in becoming an ISNVD member or know of someone who may be interested, please go to our website at www.isnvd.org for more information or contact our Buffalo, New York office at (716) 859-3579.



Blood and Fluid Circulation of the Brain: The Neurovascular Component of Neurodegeneration

In recent years, there has been considerable interest in the link between the cerebral vascular system and neurodegeneration, precipitated by the realization that the heart-brain axis plays an influential role in the pathophysiology of the brain. However, research in this field is still in its infancy and much remains unknown, particularly concerning the role of vascular haemodynamics. The lack of experimental and clinical data on brain haemodynamics and intracranial fluid dynamics linked to the neurodegenerative process, prompted (in 2010) the formation of the International Society for Neurovascular Diseases, an interdisciplinary society dedicated to advancing understanding of neurovascular haemodynamics and promoting collaborative exchanges between biophysical scientists and clinical researchers, the former including biologists, physicists, bioengineers, and mathematicians and the latter including neurologists, vascular/neuroradiologists, and vascular surgeons. This multidisciplinary approach has yielded new insights into the role of circulation and intracranial fluid dynamics in neurodegeneration and aging. Consequently, the knowledge base has rapidly advanced in recent years, something that is well illustrated by the recent description of lymphatic conduits in the central nervous system, closely connected with cervical lymph nodes, veins, and cerebrospinal fluid. In response to this, we invite investigators from all disciplines to contribute original papers and review articles for a special issue dedicated to this exciting field of research.

Paper submission topics include, but are not limited to:

- Blood Brain Barrier: biophysics and experimental data
- Models of brain circulation in relationship to parameters clinically assessed by imaging
- Perfusion and neurodegeneration/aging
- CSF flow and neurodegeneration/aging
- Animal models of brain haemodynamic impairment
- Flow abnormalities and transduction of biological signal
- Vasoactive agents and changes in endothelial cell morphology in neurodegeneration/aging
- Neurosensorial and cognitive function related to haemodynamic abnormalities
- Assessment of cerebral venous return
- Brain Lymphatics and metabolite drainage
- Intracranial biomechanics related to neurodegeneration /aging
- Jugular valves and jugular pulsatility
- Heart-brain haemodynamic axis

Authors can submit their manuscripts via the Manuscript Tracking System at <http://mts.hindawi.com/submit/journals/bn/bfcb/>.

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