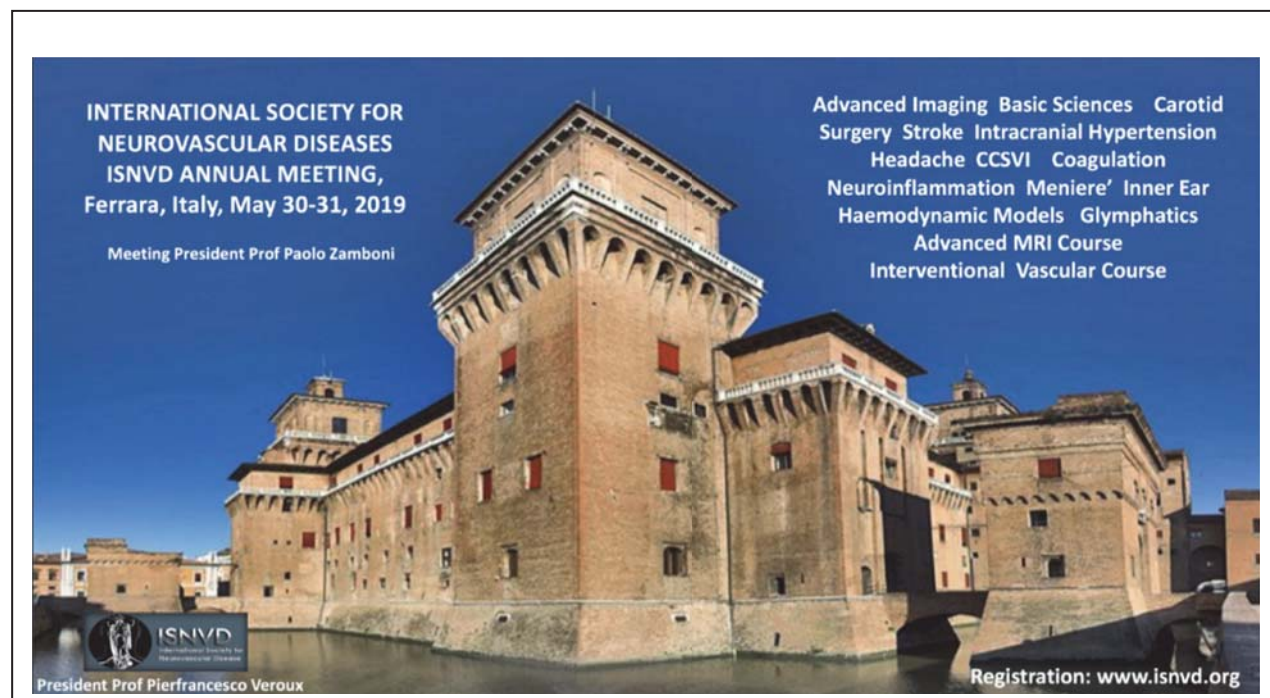


## Neurovascular Prospects



### Newsletter of the 9<sup>th</sup> International Society for Neurovascular Disease (ISNVD)

The 9th annual meeting of the ISNVD was hosted by Prof. Zamboni at University of Ferrara from May 30 to May 31.

During the two days' meeting, more than 60 invited speakers presented the state of the art of neurovascular imaging, vascular or interventional surgery, vascular risk factors, cerebrospinal fluid dynamics, during 11 thematic sessions with Italian simultaneous translation. In parallel to the main conference, there were five satellite courses, lectures and workshops over the meeting period. Selected abstracts were presented during a short presentation session. Finally, six abstracts from young investigators were presented during the "Young Investigator Award" session.

More than 150 attendees from around the world participated in the conference, and 40 PhD students-residents from Ferrara and other Italian Universities.

A day before the official start of the 9<sup>th</sup> annual meeting, the ISNVD Executive board met at the breathtaking Salone D'Onore in Palazzo Roverella. This building is an example of work from Biagio Rossetti in his project of enlarging the city of Ferrara during the 16<sup>th</sup> century. The board members present at the meeting included Dr. Veroux, Dr. Zamboni, Dr. Sclafani, Dr. Lagana, Dr. Haacke, Dr. Ge, Dr. Menegatti, Dr. Toro, Dr. Bruno, Dr. Jakimovski, Dr. Agrawal, Dr. Hu, Dr. Wang, Sean Sethi, and Carol Schumacher. During the meeting, Dr. Zamboni was the host of the annual meeting and Dr. Veroux as President welcomed the rest of the board members. Dr.

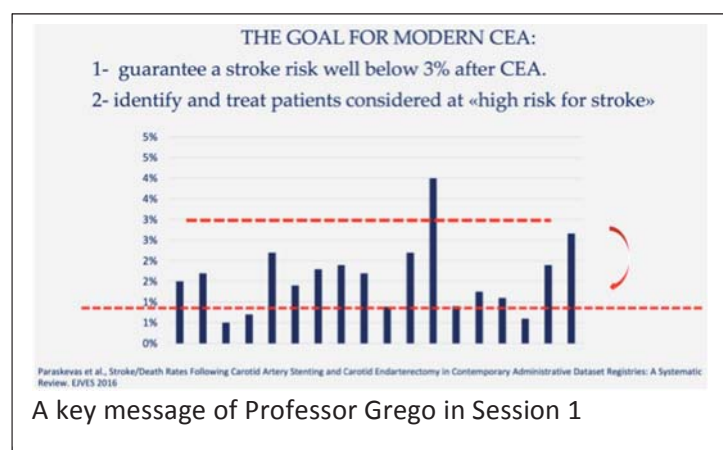


Salone D'Onore in Palazzo Roverella, Ferrara, Italy

Zamboni presented the details regarding the upcoming scientific sessions, opening ceremonies, and the overall schedule of the meeting. Dr. Yulin Ge (New York University School of Medicine) as the incoming ISNVD President and future host of the 10<sup>th</sup> ISNVD meeting in New York City, 2020 opened the discussion regarding the future main scientific program, particularly about ideas for invited speakers, scientific meeting location and current and planned society finances. Lastly, discussions regarding application for R13 National Institute for Health (NIH), endorsement from International Society for Magnetic Resonance in Medicine (ISMRM), and list of private company sponsorships were held. After the meeting, the executive board was joined by the guest speakers and University officials for a welcome reception.

## Day 1

One of the main themes of the 9<sup>th</sup> ISNVD annual meeting is on vascular surgery in neurovascular and neurodegeneration diseases. Therefore, the annual meeting started with the **first session** termed “Debates in Carotid Surgery” chaired by Dr. Veroux, Dr. Reid and Dr. Zamboni. The session was based on five specific debates regarding “*Asymptomatic patients: surgery, antiplatelets, or angioplasty and stenting?*” by Drs. Grego from Padua and Reid from Edinburgh, “*Are vulnerable plaques age-related?*” by Drs. Ippoliti from Rome and Faggioli from Bologna, “*Carotid endarterectomy versus carotid stenting-a never-ending story*” by Drs. R. Chiesa from Milan and Petrov from Sofia, “*CAS can be performed soon after neurologic symptoms?*” by Dr. Speziale from Rome and again Dr. Reid, and “*Carotid stenosis treatment: variations in institutional and international practice*” by Drs. Gossetti from Rome and Castelli from Varese. After the presentations, all speakers were invited for a joined discussion started by Dr Traina.

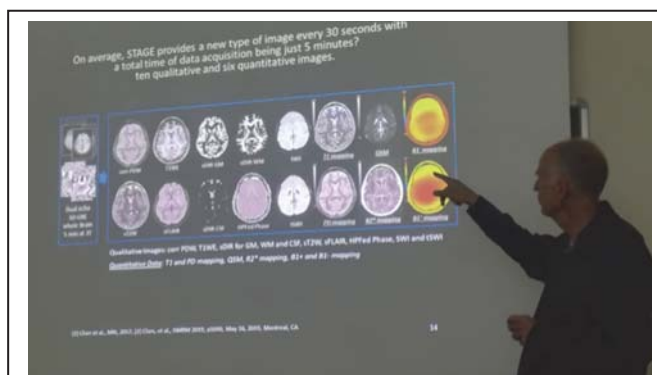


After a short break, **Session 2** expanded on the need for cerebral protection and monitoring in vascular and endovascular surgery. The session moderators Dr. Chiesa and Dr. Ronchey invited 6 further Debaters. The debates in this session included “*Monitoring the intracerebral flow during CEA under general anesthesia*”, by Dr. Scuderi from Catania and Dr. Manfredini from Ferrara, “*Better embolic protection may reinvigorate CAS?*” by Drs. Setacci from Siena and Pulli from Bari, and “*Is local anesthesia the best method to avoid complications during carotid cross clamping?*” by Dr. Mascoli from Ferrara and Dr Spinelli from Rome. The subsequent young investigator corner further expanded on the prevalence of brain injury during carotid artery stenting and on potential measures to prevent cerebral embolization.

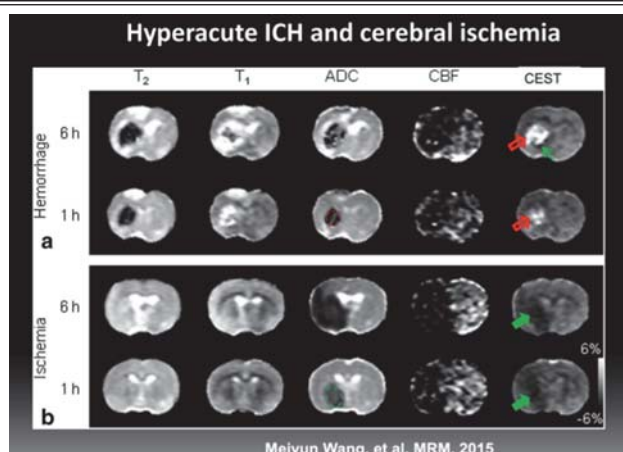
On Day 1, an additional **parallel workshop** on the topic of “*Strategically Acquired Gradient Echo (STAGE) imaging for brain tissue quantitative mapping and vessel enhancement*” was chaired by Dr. Lagana and Dr. Haacke. The workshop had the aim to discuss quantitative mapping in MRI, its possible clinical applications and how to run a practical rapid multi-contrast imaging protocol for obtaining different brain tissue maps. The beauty of STAGE sequence is that

within 5-7 min scan, multi-contrast proton spin density, T1, R2\* and QSM quantitative maps, as well as T1-weighted, PD-weighted, MR Angiography and SWI images can be reconstructed at clinical 3T or 1.5T MR scanners.

The highlight of the scientific part of Day 1 included the keynote lecture by Dr. Wang from Zheng-Zhou, China. Dr. Wang discussed the role and applicability of non-contrast enhanced MRI in Stroke detection. Appropriately, the keynote lecture was followed by the **3<sup>rd</sup> scientific session** which discussed the emerging challenges in stroke, moderated by Dr. Setacci, and Dr. Giaquinta. Uniquely, the session included a panel of 12 international experts which included neurologists, neurointerventional radiologists, vascular surgeons and neuroradiologists from the USA, Italy, Bulgaria and China who discussed the timing of carotid and intracranial thrombosis recanalization after stroke. The debate was further supplemented by discussion with the audience started by Dr. Le Than Po from Vietnam and Dr Saletti from Ferrara.



Dr. Haacke talked about STAGE imaging



A slide of Dr Wang Key Note Lecture

Similarly to the morning workshop, the Torquato Tasso hall hosted another **workshop** by another keynote speaker Dr. Raymond Damadian. Dr. Damadian is the pioneer of MR body scan and his lectures are a rare possibility to learn MRI from one of the field inventors. The lecture, outlined the journey starting from his initial quest to image the sodium/potassium pumps within cells, to research led him to the world of nuclear magnetic resonance, going into great detail of the history of the NMR. His research was generally focused on the CSF flow MRI quantification using upright MRI scanners. The pathophysiology of cerebral fluids and circulation and the paramount role of CSF dynamics in Chiari, syringomyelia as well as in several neurodegenerative disorders with particular respect to multiple sclerosis were also presented in detail.



Dr. Damadian & Dr. Ge

The **4<sup>th</sup> scientific session** was focused on indications for CCSVI treatment and was moderated by Dr. Reid, Dr. Petrov and Dr. Salvi. The session included speakers from Italy, China and the USA. More specifically, the session consisted of talks regarding “Symptoms of patients with jugular venous outflow disturbances” by Dr. Yang from Beijing, “Effects on the MRI biomarker of the draining flow in multiple sclerosis” by Dr. Zamboni from Ferrara, “Effects of balloon angioplasty on symptoms in CCSVI-MS patients” by Dr. Bavera from Milan, “CCSVI Prevalence

and Jugular PTA in Menière's disease” by Dr. Bruno from Benevento and “Reasons for and solutions to failures of endovascular treatment of CCSVI” from Dr. Sclafani from New York.

Lastly, the official scientific part of the first day of the 9<sup>th</sup> ISVND annual meeting ended with a session (**Session 5**) on associations between abnormalities in the cerebral venous system and its relationship with headache. The session was chaired by Dr. Veroux and Dr. De Bonis and featured speakers from Italy and China. The last talk also included discussion regarding potentially novel form of high-pressure hydrocephalus termed JEDI (jugular entrapment, dilated ventricles, intracranial hypertension) syndrome and its treatment with jugular vein decompression.



Prof Zamboni with Dr Reid and Dr Petrov in Session 4th

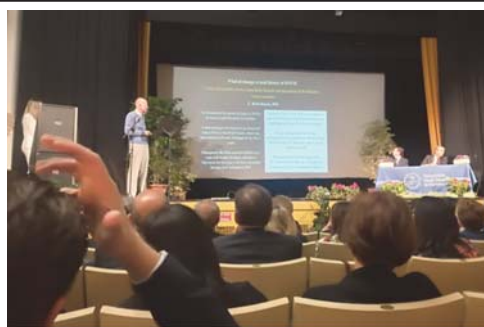
During the late afternoon, a **parallel session** of short 3-minutes abstract presentations was chaired by Dr. Bergsland and Dr. Malagoni. Eleven (11) speakers presented on variety of topics including cerebrospinal fluid flow measurement and mathematical modeling in multiple sclerosis, internal jugular vein valve mechanics, cerebrovascular hemodynamic mathematical modeling and assessments using 3D digital subtraction angiography, vein pathology in Ménière's disease and chronic migraine, and treatment options and side effects during carotid artery stenting. The speakers of these presentations were: Dr. Laganà (Milan, Italy); Dr. Mohammed (Baghdad, Iraq and Ferrara, Italy); Dr. Muller (Trento, Italy); Dr. El Hadji (Milan, Italy); Prof. Baselli (Milan, Italy); Dr. Di Girolamo (Rome, Italy); Prof. Bavera (Milan, Italy); Dr. Frau (Rovereto, Italy); Dr. Toma (Rome, Italy); Dr. Lamberti (Ferrara, Italy); Dr. Catanese (Sassari, Italy); Dr. Tucker (T. Tucker Inc.).

### Opening ceremony at the evening of the Day 1.

The official opening ceremony was hosted in Sala Estense in Piazza Del Municipio. Sala Estense, currently a theatre venue was originally build as a court chapel named “Chiesa Nuova” during the city expansion in the 15<sup>th</sup> century. Dr. Zamboni, Dr. Veroux, and Dr Zauli, Chancellor of the University of Ferrara, welcomed all participants and wished them a successful meeting. The opening ceremony continued with a comprehensive history of the ISNVD presented by previous gold medal winner Dr. Haacke. The beginnings of the society and short description of all previous meetings are already published in *Veins and Lymphatics* journal and can be readily accessed at <https://www.pagepressjournals.org/index.php/vl/article/view/7839/7859>. The meeting organizers also presented a breath-taking video performance of previously recorded official soundtrack for the 9<sup>th</sup> ISVND meeting termed “*Wind of Change*” by Viola & Viola (Roberto Molinelli and Anna Serova)



Sala Estense in Piazza Del Municipio.



Dr. Haacke talked about the history of ISNVD society

and accompanied by the dancers Ivana Caffaratti and Melania Larturo. The 6 minutes video, broadcasted by Arturo Pellegrini and Federico Pacciani on the concept and direction of Michele Zamboni, can be found at [https://youtu.be/EDo0IO\\_mSk4](https://youtu.be/EDo0IO_mSk4). Furthermore, the can be downloaded through Amazon Music and the funds will directly support the research activities of the ISNVD. (Amazon link: <https://amzn.to/2LyAnGV>)



President, Past-Presidents and President Elect

After the official part of the opening ceremony, the meeting participants headed towards Palazzo Pendaglia, a building from the 16<sup>th</sup> century which currently hosts the headquarters of “Orio Vergani” School of Hotel Management and Catering. The palace court served as an excellent environment for meeting other participants, exchanging ideas, and discussing the aforementioned meeting presentations. Participants also had a chance to enjoy traditional appetizers (assortment of local salami and typical fried dumplings) served with local Italian wine. The dinner continued in the foyer of the palace where a

selected teams of chefs competed at creating award winning 4 course meal.



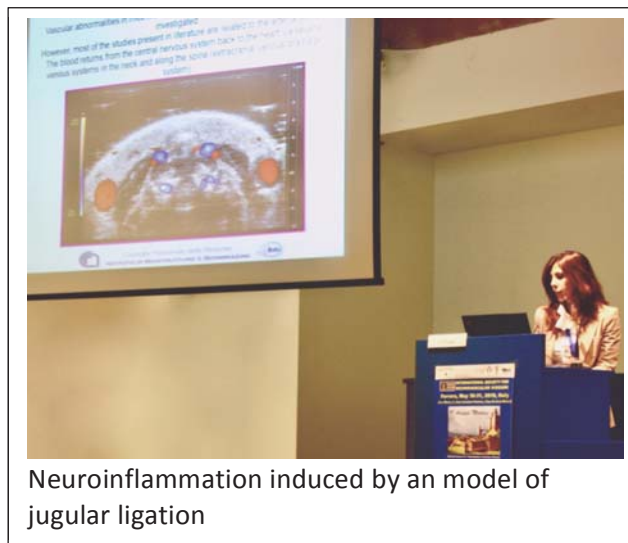
The staff of the Gala Dinner

## Day 2

*Session 1:* Day 2 of the 9<sup>th</sup> Annual ISVND conference started with a session chaired by Dr. Zivadinov and Dr. Granieri which was focused on the vascular risk factors and their role in neuroinflammatory and neurodegenerative processes. Appropriately, Dr. Jakimovski from Buffalo (USA) opened the session with recent MS findings regarding associations between presence of modifiable lifestyle risk factors including lack exercise, increased body weight, smoking, alcohol consumption and poorer diet preferences with the corresponding mid-term disease worsening as measured by MRI-derived neuroinflammatory and neurodegenerative outcomes. Furthermore, the talk also included additional MS work, which demonstrated deleterious effects of decreased total cerebral arterial blood flow measured at the level of the major extracranial vessels and congruently poorer cognitive performance, in particular, poorer cognitive processing speed. The talk was followed by presentation from Dr Adelaide Greco, which first described an animal model for study

of cerebral venous insufficiency, and secondly, new findings that may further imply greater inflammatory activation. Moving intracranially, Dr. Bergsland from Buffalo (USA) presented comprehensive review of the limited but expanding findings of perfusion deficits and their association with both cardiovascular comorbidities and their effect on the clinical and cognitive MS outcomes. Switching onto Parkinson's disease, Dr. Lagana from Milan (Italy) showed that functional alterations measured using functional MRI at rest, for example in the occipital brain regions, might be associated with hypoperfusion.

This presentation was followed by Dr. Bernardi from Ferrara (Italy) which provided comprehensive summary of recently implicated coagulation circulating proteins including associations between Factor XII, plasminogen activator inhibitor 1 (PAI-1), and disintegrin-like and metalloprotease with thrombospondin type 1 motif 13 (ADAMTS13) with greater occurrence of cerebral microbleeds in MS patients. Lastly, the session was concluded by a talk from Dr. Haacke from Detroit (USA) and the ability of QSM/SWI technique in detecting the aforementioned cerebral microbleeds within the settings of multiple neurodegenerative states.



Both the designated discussion started and the greater participation from the audience continued with an interesting discussion regarding the potential role of autonomic nervous system as an effector and mediator between the central cardiac and cerebral vascular homeostasis.

*Keynote lecture.* Dr. Scott Chiesa from the UCL Institute of Cardiovascular Science gave the keynote lecture, "Arterial Pulsatility, Cognitive Decline and Dementia." The subjects involved are part of the Whitehall II study started in 1985 involving roughly 10,000 subjects to examine social determinants of health, specifically the cardiovascular disease prevalence and mortality rates among British civil servants. This particular study investigates the role of arterial pulsatility with the risk of cognitive decline. Atherosclerosis causes a subsequent increase in pulse pressure. This has the potential to cause end-organ damage in low-resistance areas like the kidney and the brain. The study aimed to quantify the pulsatile energy using carotid wave intensity analysis. Duplex Doppler ultrasound was used to calculate peak forward-travelling compression wave intensity (FCWI) within the common carotid artery in 3191 individuals. After stratification of FCWI into quartiles, subjects with the highest FCWI were associated with changes in cognitive function. This bolsters other evidence that the disease process underlying the development of dementia may begin decades before the first signs of overt cognitive impairment. Carotid pulse pressure has great potential as a biomarker in predicting cognitive decline early and taking steps to treat or prevent it.



*Session 2:* The 2nd scientific session was focused on Age Related Vascular Changes and was moderated by Dr. Ge, and Dr. Wang. Dr. Volpato from Ferrara (Italy) showed several risk

factors for dementia and Alzheimer’s Disease, among which dyslipidemia, sedentary lifestyle and unhealthy diet. Dr. Zivadinov presented a review about the “*Epidemiology of cardiovascular comorbidities in aging of multiple sclerosis*”, discussing that advancing age, the disease transitions towards a less inflammatory and more neurodegenerative course. Dr. Menegatti from Ferrara presented “*Is jugular venous pulse involved in aging?*”, showing that using ultrasound measures, jugular venous pulse variations were observed in people with mild cognitive impairment compared to healthy controls. Dr. Alperin from Miami presented “*The effect of sleep quality on a MCI susceptible brain regions in cognitively intact elderly subjects*”. The main result of his study is that the normal sleepers compared to the poor sleepers had a better removal of brain toxins during sleep, because they had a greater cerebrospinal fluid flow stroke volume. Dr. Ge from NYU spoke about “*New perspectives on age-related white matter hyperintensities in VCID research*”, using MRI. Sean Sethi from Detroit presented MRI studies about “*Aging and vascular dementia*”.

Session 3: After the initial three scientific sessions, Dr. Veroux, Dr. Ge, Dr. Zivadinov and Dr. Zamboni chaired a lunch session which highlighted previously selected 5 best abstracts of young investigators that were submitted to the ISNVD. These five abstract presentations were accompanied by an assigned experienced discussant within the field of the presentation topic which was responsible facilitate discussion after the talk. Short synopsis of all 5 abstracts are shown hereafter:

- **Jakimovski D (Buffalo, USA)** *Decrease in secondary neck vessels and cerebral aqueduct enlargement in multiple sclerosis: a 5-year longitudinal MRI study.* Both at baseline and follow-up, 83 PwMS and 25 HCs underwent Magnetic Resonance Angiography (MRA) imaging whereas, a subset of 40 PwMS and 20 HCs underwent also longitudinal phase contrast cine imaging. Both the number and the size (cross-sectional area;CSA) of secondary neck vessels and measures of CSF aqueduct of sylvius (AoS) were acquired, respectively. Within this study, the MS patients demonstrated significant mid-term decrease in the number and the size of the secondary neck vessels. Furthermore, a significant AoS CSA enlargement may reflect local atrophy of the surrounding brain structures.
- **Pelizzari L (Milan, Italy)** *Cerebral blood flow and cerebrovascular reactivity in Parkinson’s disease: relationship with severity of motor symptoms.* Cerebral blood flow (CBF) and cerebrovascular reactivity (CVR) were investigated with arterial spin labelling (ASL) MRI in a group of Parkinson's disease (PD) patients in the early disease stage, focusing on cortical and subcortical regions of the motor circuit. The correlation between CBF, CVR and the severity of motor symptoms (quantified with UPDRS-part III score) was assessed. Positive significant (pFDR<0.05) CBF-



Dr Beggs presented a model for predicting jugular pressure from the ultrasound technique of iugular



Dr. Pelizzari presented her work at YIA session

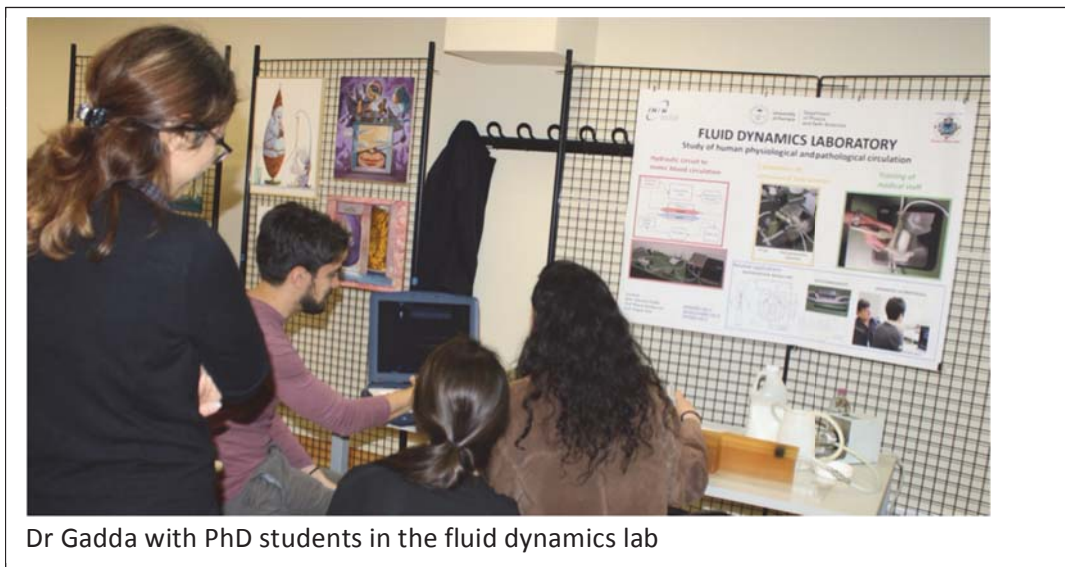
UPDRS III correlation was observed in the regions of interest. Conversely, significant negative CVR-UPDRS III correlation was found in the striatum ( $\rho=-0.720$ ,  $pFDR=0.048$ ). These results support the hypothesis of a neurovascular involvement at the mild to moderate stages of PD.

- **Zillioto N (Ferrara, Italy)** *Expression profile of haemostasis genes in vascular wall: is internal jugular vein protected from thrombosis in impaired outflow condition?* A microarray-based transcriptome analysis of the wall of internal jugular veins, characterized by disturbed outflow, and the wall of saphenous veins revealed differences in the expression of haemostasis genes. The increased expression of anticoagulant and profibrinolytic components suggest thromboprotective internal jugular vein wall features in response to flow disturbance.
- **Scerrati A (Ferrara, Italy)** *The eagle jugular syndrome.* Eagle syndrome is a rare condition characterised with elongation of the styloid process that results with both pain and dysphagia (classical presentation) or with pressure on the carotid artery resulting in cerebral ischemia. The study presented case series of patients with potentially new venous variant of Eagle syndrome where the styloid process causes significant compression on the internal jugular vein. Patients with such presentation commonly complained of headache and head greater comorbidity of peri-mesencephalic haemorrhage. Based on these findings, the authors suggest that the management of Eagle syndrome would benefit from expanding the role of CT angiography with inclusion of the venous phase.
- **Pisastru A (Milan, Italy)** *Brain perfusion patterns: consistency and similarity with fMRI resting state networks and arterial vascular territories.* The aim of the work was to apply the well-known ICA algorithm ASL data in order to: 1) assess the consistency of the extracted components; 2) quantify the degree of the overlap between ASL-IC and RSfMRI derived components; 3) assess the degree of the overlap between ASL-IC and vascular territories. As a result the study concluded that: 1) The ASL derived components are consistent independently from the subgroups from which they were extracted; 2) ASL and RSfMRI data provide complementary information since they are both hemodynamically-driven techniques; 3) The ASL-derived components mirror the hemispherical segregation of the anatomical supply.
- **Bonilauri A (Milan, Italy)** *Effects of channel displacements vs. cortical anatomy on fNIRS sensitivity: a simulation study.* Within the context of functional Near-Infrared Spectroscopy (fNIRS), this study presents the post-analysis of an atlas-based Monte Carlo simulation in order to statistically assess the effect of measurement channel displacements and brain depth over NIR-light sensitivity profile according to a real-case scenario. Results show that there is a noticeable effect with respect to longitudinal and transverse direction. Future studies will consider subject-specific anatomies in order to account for individual variability due to conformation of gyri and sulci and support the interpretation of fNIRS findings.

*Session 5:* was titled “*Cerebral fluids, blood, and barriers: are the extracranial veins an overlooked actor?*” and chaired by Dr. Anile, Dr Taibi and Dr Damadian. Dr. Gadda from Ferrara explained “*A multiscale mathematical model for the simulation of cerebral and extracerebral blood flows and pressures in humans*”, a new mathematical of cerebral and extracerebral blood flows and pressures. The model considered time variation of flow and pressure, besides the effects of posture change, carbon dioxide variation, and stenosis. The talk of Dr. Hu (Detroit) showed the “*Interaction between the CSF and the venous system*”, by tracking MRI injected tracers. Dr. Alperin (Miami) discussed his studies about “*Investigating the separate effects of venous outflow and breathing on the CSF flow dynamics using two types of phase contrast sequences*”, involving advanced non-conventional MRI methods for quantifying CSF flow. Dr. Agarwal (Utah-Trento) spoke about “*MR imaging of perivascular spaces in veno-obstructive diseases*”. Dr. Agarwal

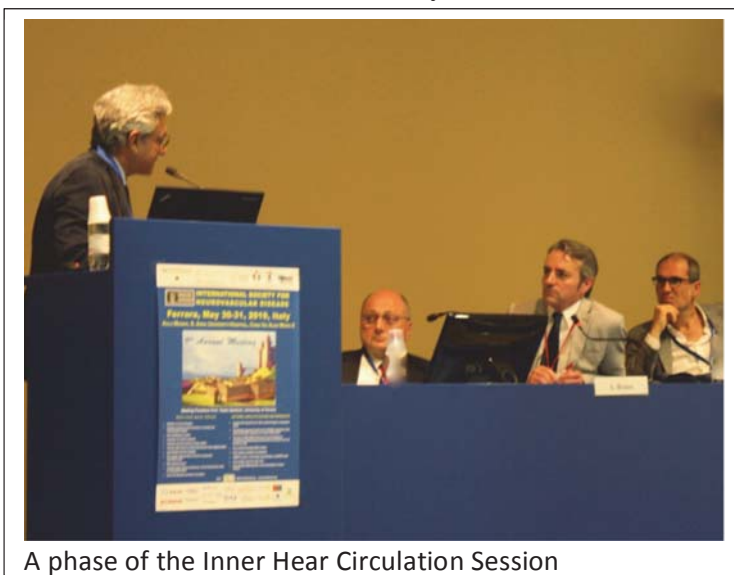


hypothesized the possible impact on size and shape of perivascular spaces in veno-obstructive disease by presenting clinical examples of patients harboring intracranial dural venous sinus thrombosis or extracranial internal jugular vein compression .



*Session 6:* was titled “Inner Ear Disease and Brain Circulation” and was composed of eight presentations moderated by Drs. Bruno and Ciorba. Dr. Guerkov discussed the imaging and classification of hydroptic ear disease with respect to some of the recent published diagnostic criteria by the Bárány Society. Dr. Lopez-Escamez’s research is to identify major genes involved in autoimmune Ménière's Disease (MD) as well as the biochemical pathways associated with sporadic MD to decode the driving and modifiers genes of MD. Novel mutations have been discovered in DTNA, FAM136A, PRCKB, DPT and SEMA3D genes. These may be related to signalling pathways that determine the cochlear and vestibular phenotype of MD. Dr. Toro is using computational mathematics to model intracranial blood and CSF flow in MD. His team found that extracranial venous strictures alter inner ear circulation. The findings are consistent with some recent literature which links extracranial flow to MD. Dr. Ciorba from Ferrara talked about cerebral inflow and outflow discrepancies in severe sudden sensorineural hearing loss (SSNHL). The presence of CCSVI/jugular flow reduction was noted in SSNHL vs. healthy controls with a consequent activation of venous collaterals. The session continued with

“*What is Known and what is Unknown in Inner Ear Diseases: the role of neuroinflammation*” by Dr. Casani, Pisa (Italy), followed by Dr. Neri (Chieti, Italy) who talked about “Sigmoid and transverse sinus disorders related to vertigo, dizziness and headache”. The session ended with two talks about Ménière's Disease and CCSVI: “*MRI Imaging of Brain and Neck Veins in Patients with Ménière's Disease and CCSVI*” (Dr. Giugliano, Benevento, Italy) and “*Results of jugular PTA on symptoms of Ménière's Disease with concomitant CCSVI*” (Dr. Califano, Benevento, Italy).



A phase of the Inner Hear Circulation Session

## Closing ceremony and announcement of awards

At the end of the ISNVD conference, three young investigators were awarded: Dr. Dejan Jakimovski, Dr. Alba Scerrati, Dr. Laura Pelizzari. Moreover, the student in Medicine Francesca Cozza was awarded for the competition at the “Cerebral fluid dynamics lab.” This was a fluid dynamics lab at the exhibition area, where the cerebral circulation was mimicked and showed with researchers available for discussion with the team of Medical Physics of Prof. Gambaccini. It was also possible to measure cross sectional area and velocity of the flow by the means of Doppler ultrasound, and Francesca measured the flow rate with the best approximation among the participants.

Finally, Dr. Veroux passed the gavel to the President Elect Dr. Ge, who officially announced that the 10<sup>th</sup> ISNVD Meeting will be held in NYC on May 21 & 22 2020.



Dr Jakimovski won the YIA Award

## Patients Day

The more interesting and educational messages of the congress were presented to a group of more than 120 patients, in a session chaired by Carol Schumaker, Nicoletta Mantovani, and Paolo Zamboni. Drs Zivadinov, Chiesa, Salvi, Bruno, Ge and Veroux answered all the questions from the patients floor, giving a further solid educational support to a highly successful congress.