The International Society for Neurovascular Disease (ISNVD) is a recently formed non-profit professional association devoted to furthering the development of research for neurovascular related diseases, with a strong focus on the venous vascular component. Mounting evidence suggests that a number of inflammatory and neurodegenerative central nervous system diseases may be related to altered venous vascular mechanisms. Because of this novel concept, the Society has decided to target various medical groups for membership. These include, but are not limited to, Basic Scientists, Neurologists, Interventional Radiologists, Vascular Surgeons, Neurosurgeons, Physicists and Vascular Technologists. We welcome individuals in these categories to become members of the Society by visiting our official website (www.isnvd.org).

In the role of ISNVD President over the next year, I intend to help the Society advance its message and foster growth in several ways: by promoting communication, research, and development; by leading the discussion on establishing guidelines; and by increasing the availability of information on neurovascular and related neurodegenerative diseases internationally. The Society’s goal will be to develop and provide channels and facilities for continuing education and communication in the field, publishing selected contributions in its official journal and abstracts on the CCSVI hypothesis.

The Society will hold annual scientific meetings and sponsor educational and scientific workshops for both patient and medical audiences. In this context, I would like to take the opportunity to congratulate Dr. Paolo Zamboni, the first President of ISNVD for the outstanding organization of the Society’s First Annual Scientific Meeting that took place in Bologna, Italy on March 13-15, 2011. The meeting primarily focused on advancing better understanding of the recently described condition called chronic cerebrospinal venous insufficiency (CCSVI) and its relationship to multiple sclerosis. A great amount of fresh and original information was presented on this condition. Included were discussions on the role of imaging techniques, diagnostic guidelines and standard consensuses to be used for diagnosing CCSVI. Basic scientific and hemodynamic contributions, lectures and abstracts on the CCSVI hypothesis generated a significant level of interest among the 350+ participants. Also discussed was the role of iron and other potential biomarkers for vascular involvement in neurological diseases. And finally, the event included a thorough and enlightening discourse on the role of the venous vascular component in the treatment of neurodegenerative disorders, with an emphasis on Alzheimer’s disease and multiple sclerosis. Consequently, it is to be noted that one of the primary Society goals is to encourage safe and ethical approaches in designing new clinical trials that will investigate this important part of the puzzle.

I hope that, based on the remarkably high level of scientific fundamentals that grounded the first Annual Scientific Meeting, the Society will continue on this path at the Second Annual Scientific Meeting that will take place in Orlando, FL between February 18-22, 2012. I look forward to welcoming you in Orlando next year!

Sincerely,
Dr. Robert Zivadinov
President ISNVD
The first annual meeting was met with great enthusiasm by participants and organizers alike. The venue was in the beautiful old city of Bologna which has perhaps the largest walking city center in Europe. This three-day event was a culmination of efforts by the executive committee, the board, the Idea Laboratory, and administrative support from various groups in the United States. Its success was predicated on the involvement of a broad range of participants covering many aspects of neurovascular disease. Although there was much discussion about the vascular nature of multiple sclerosis there were guest lecturers on aging and the biochemistry of vascular breakdown and understanding the endothelium. A variety of treatments related to different diseases were also presented. The spirit of the meeting was evident in the constant participation of the audience in questions during the various sessions but was perhaps most evident during the breaks and lunch where the din was caused by the numerous ongoing conversations about what people had just heard. This was one of those meetings where you did not want to miss a single talk and people were taking notes constantly throughout the meeting. There were more than 350 attendees from around the world, several companies presenting their material and there were a variety of key contributors to the financial success of the meeting.

There were several very nice features of this meeting. First, there were offered three plenary/abstract sessions during each half day. This broke the meeting up to allow more discussion between talks. The presentations themselves were short, being 15 minutes in length for plenary talks and 10 minutes for accepted papers. The moderators did a great job both asking questions and taking questions from the floor. The speakers were equally responsive in their answers. The audio/visual coordinators did an excellent job. This simple feature and the skill and organization of this group made things run very smoothly. Although there were no posters this year, the top abstracts were chosen as presentations in their own special session. Having no parallel sessions was conducive to a much closer interaction of participants in discussions and made it possible not to miss a single interesting talk. Look for some very exciting results to be presented in Orlando, Florida in 2012. Preceding the meeting there was a consensus group meeting to discuss standards in ultrasound imaging for CCSVI.

Contributions to the Society were received from: Fondazione Cassa Di Risparmio in Bologna, Fondazione Hilarecere, Bard, Boston Scientific, Carife, Ducati, Esaota, Flebyscan, and Volcano Corporation. The executive and board members met twice during the meeting, first at the Royal Carlton Hotel in the later afternoon of March 12th and again at the end of the meeting at the conference center itself on March 15th. Finally, a special thanks to Camilla Consorti, Rachel Martis-Laze and Jahzel Misner for their constant efforts both before and during the meeting. Also, my thanks to Sandra Morovic and Arlene Hubbard for their notes related to this meeting.

Left to Right: Dr. Fabrizio Salvi, Dr. Paolo Zamboni, Dr. Robert Zivadinov, and Dr. E. Mark Haacke
Sunday, March 13, 2011: Doppler ultrasound consensus meeting summary

This critical meeting was chaired by Dr. Andrew Nicolaides and co-chaired by Dr. Paolo Zamboni. Doppler ultrasound has been used as the main means to screen for CCSVI to date. A five point scale was originally developed by Dr. Paolo Zamboni in 2009 and has been used since that time as a rapid and inexpensive means to determine if a patient or individual has indications of CCSVI. The basic concepts behind the comprehensive doppler protocol were presented by Dr. Erica Menegatti and Karen Marr. It was noted that it takes extensive training to become proficient at this protocol. The ultrasound exam itself can take well over an hour and focuses on both venous anatomy and valvular abnormalities. Also, Dr. Sandra Morovic spoke about normal haemodynamics of cerebral venous return and Dr. Gisel Viselner spoke about Doppler evidence for CCSVI. An open discussion followed the presentations. One of the five CCSVI ultrasound criteria requires the use of transcranial Doppler ultrasound. There was much discussion on the use of this particular criterion since transcranial Doppler is not available to everyone. Nevertheless, it was still felt to be important and to maintain as one of the five criteria. To date, many sites are just focusing on the remaining four criteria. A document summarizing the discussion and approach is in preparation. Overall, Dr. Andrew Nicolaides did an excellent job directing questions and keeping the discussion focused.

Monday, March 14, 2011: The session was opened by Paolo Zamboni with a welcome to all participants to the meeting and to Bologna.

Plenary Session 1: CCSVI Imaging

This session contained a number of current approaches in imaging CCSVI using ultrasound (US), magnetic resonance venography (MRV), catheter venography and intraluminal ultrasound. The session was introduced by Dr. Stefano Bastianello, Editor of the Journal “Functional Neurology”, who reviewed the current status of CCSVI. The role of contrast ultrasound in evaluation of cerebral hemodynamics was discussed by Dr. Marcello Mancini. A significantly prolonged cerebral arterio/venous transit time was found in MS patients in comparison with control subjects. This could be secondary to venous outflow obstruction or reflux, affecting the hydrostatic pressure gradient. Contrast Ultrasound could be a non invasive method to assess the effects of venous outflow obstructions on cerebral circulation in MS patients. The role of intravascular ultrasound was discussed by Dr. Salvatore Scalfani who demonstrated a number of key advantages with this technology such as visualizing the true lumen and its surrounding tissue in order to best choose how to balloon that region. Dr. Vittorio Iaccarino reviewed the role of CTA as an alternate means to MRA, especially when it came to imaging the azygos vein. Dr. Paolo Zamboni, in his usual insightful way, raised the critical question of being able to fuse different imaging modalities. This would allow merging of information from each method to paint a more complete picture of the status of the anatomy and function of the vascular system. Catheter venography was reviewed by Dr. Roberto Galeotti. He noted that when using ultrasound to test for flow abnormalities that one must pay attention to both posture and respiration. Finally Dr. Robert Zivadinov discussed the advantages and disadvantages of MRV in diagnosing CCSVI.

Keynote Lecture by Berislav Zlokovic

Dr. Berislav Zlokovic discussed the concepts of vascular pathology including the role of reduced perfusion, hypoxia, tissue damage and endothelial damage. His main point was neurodegeneration occurs secondary to vascular damage and there may be hypoxia mediated vascular damage. He discussed the role of pericytes and how certain animal models show that pericytes play a key role in recovery and went so far as to discuss potential treatment with low dose APC. He suggested that novel pharmaceuticals might be designed to target inflammation and endothelial pathology.

Plenary Session 2: Iron in neurodegenerative disorders

The potential role of iron as a culprit in neurodegenerative disease was felt important enough to dedicate an entire session to it. Dr. Costantino Iadecola discussed the role of iron as a potential inflammatory agent, the role of oxidative stress and endothelial damage. He further suggested there might be a relationship with poor vascular conditions and that these could lead to the production of beta amyloid plaque. Dr. Robert Zivadinov followed with examples from imaging demonstrating increases in iron content in MS patients and also suggesting that these increases may correlate with the severity of the disease. Dr. Paolo Pinton discussed the immune-mediated loss of myelin and the mitochondrial dysfunction roles in the pathogenesis of MS. In particular, he explained the mitochondrial regulation of cellular Ca^{2+} and the consequences of mitochondrial alterations due to a pathological Ca^{2+} overload, i.e., demyelination. He evaluated TNFalpha effects on Ca^{2+} homeostasis and on mitochondrial physiology and the role of iron on these mechanisms. Dr. Donato Gemmati studied the main iron homeostasis genes, their variants in the different MS groups, and their correlation with EDSS and MS progression index. Finally, Bonara reviewed the biochemistry of iron free radicals on tumor necrotic factor (TNF) and brain cell damage.
Plenary Session 3: Update on Carotid Surgery and Stroke
New developments in understanding vulnerable plaque and which patients are at risk for stroke were presented. These findings have significant impact on the decision to perform stenting for a narrowed carotid artery. Dr. Giorgio Biasi discussed the importance of plaque morphology in carotid atherosclerosis and which types of plaque were indicative of high risk for stroke or problems during stenting. The goal was to review the indications for choosing between endarterectomy versus stenting. Dr. Andrea Stella's talk was about serological and morphological markers of carotid plaque. He gave discussed in great detail how the risk of stroke in asymptomatic plaques could be dramatically improved by detection of vulnerable plaque. Continuing along these lines, Dr. Francesco Mascoli discussed the role of surgery in treating carotid artery disease and preventing stroke. He concludes that early carotid endarterectomy can prevent future damage. Dr. Adnan Siddiqui closed the session discussing the CREST trial and carotid revascularization strategies. In the end he shows that the risk of stroke and adverse events has continued to drop over 60 years and that carotid endarterectomy and carotid stenting have similar risks but both have important places in treating carotid artery disease.

Plenary Session 4: Best abstract presentations, Part 1
A variety of topics were covered here. The opening presentation by Dr. David Hubbard was extremely interesting where he showed that functional MRI could be used to detect indirectly changes in blood oxygen saturation levels pre and post treatment. Dr. Manish Mehta followed with a review of an open-label trial for endovascular treatment of CCSVI. The goal is to evaluate the safety, feasibility and clinical efficacy of percutaneous transluminal angioplasty (PTA) in treating extracranial venous abnormalities. In 150 patients, 267 lesions with greater than 50% stenosis were found. One vein was affected in 24% of cases and more than one in 76% of cases. PTA was viable in 97% and successful in improving vessel lumen in 77%. Restenosis of the internal jugular vein occurred in 9% of cases after four months. On average, physical, mental and fatigue scores all improved after four months. Dr. Nikolaos Liasis showed convincing data suggesting that 3D MRV is an important means to visualize the brain and neck vasculature to allow for a comparison with color Doppler. Dr. E. Mark Haacke presented for Dr. Kriti Agarwal. Their data showed that less than 8% of 250 non-MS patients with a variety of diseases such as atherosclerosis, stroke, tumors, etc., showed great than 65% stenosis. This provides a key baseline that suggests stenoses in normals is not high. Dr. Ma'moon Al-Omari followed with a comparison between angiography and Doppler ultrasound. He evaluated 287 patients and found that 93% showed some form of CCSVI. He concluded that most angiographic findings could be correlated with echo Doppler criteria.

Workshop on ECD for diagnosis of CCSVI
The workshop was coordinated by Dr. Paolo Zamboni and Dr. Stefano Bastianello from Italy, as well as Dr. Robert Zivadinov form the USA. Around 70 people participated in the session and the ensuing case discussions. The following topics were presented: anatomy and normal haemodynamics of cerebral venous return by Dr. Sandra Morovic; assessment of the US equipment and practical guidelines by Karen Marr; and Doppler criteria for CCSVI diagnosis Dr. Erica Menegatti. Following these lectures, there was a one hour video demonstrating case studies including pitfalls and open discussions. Workshop participants were led through video cases by experienced clinical instructors: Karen Marr (USA); Erica Menegatti, PhD (Italy); Marcello Mancini, MD (Italy); and Gisel Viselner, MD (Italy). The video demonstrations generated the most discussion among participants. The workshop was an ideal place to share knowledge and opinions with colleagues from different parts of the world. The feedback at the workshop was encouraging and the e-mails received after the meeting were supportive of continued hands on and educational sessions at the next meeting in Orlando.

Tuesday, March 15, 2011
Plenary Session 5: Basic sciences and pathology of CCSVI and MS
Dr. Robert Zivadinov began this session with an exciting presentation about the role of perfusion as a biomarker for affected cerebral blood flow in MS patients. His data clearly showed that MS patients have reduced perfusion to the brain confirming a number of previous studies. Dr. Bruce D. Trapp then spoke about the role of hypoxia in brain parenchyma in patients with MS. He suggested that cortical neurons are unable to compensate for oxidative stress and the needs of demyelinated axons. The next speaker, Dr. Porama Thanaporn, won the “Young investigator abstract award” for his discussion of the effects of venous ligation in a mouse model. Further discussion of the role of vessel wall damage was presented by Dr. Giulio Gabbiani. He showed abnormalities in the vein wall in MS which could not be explained by traditional atherosclerotic disease. Finally, a most enthusiastic presentation on the role of fluid mechanics in mimicking the human brain/neck system was presented by Dr. Clive Beggs. This is a very promising direction where basic science can feed into clinical practice as an ideal example of “clinical translational research".
Plenary Session 6: Vascular mechanisms in neurological disorders
Dr. Giovanni Zuliani reviewed the vascular risk factors (e.g., hypertension, diabetes mellitus, alcohol abuse, cigarette smoking, obesity and metabolic syndrome) negative effects on vascular dementia and cognitive decline. Dr. Costantino Iadecola discussed the common risk factors underlying cerebrovascular diseases and Alzheimer’s Disease (AD). He showed a review of epidemiological, pathological and experimental observations, suggesting a cerebrovascular dysfunction role to the structural and functional alterations of AD. Dr. Fabrizio Salvi presented some interesting data suggesting that it might be possible to develop MS induced Parkinson’s like symptoms. He also discussed the role of normotensive hydrocephalus in MS. Dr. Roberto Manfredini reviewed the seasonality in vascular disorders (i.e., myocardial infarction, stroke, transient ischemic attack, dissection of aortic aneurysms) and presented preliminary results suggesting the existence of a biphasic pattern (peaks in spring and autumn) in severe MS relapses.

Plenary Session 7: Modeling CCSVI haemodynamics
CCSVI opens the door to inquire more into the basic fluid dynamics and hemodynamics of the cerebral vascular system. Much is to be learned about the effects of collateral blood flow, posture, breathing, cardiac cycle, vaslava manoeuvres, pressure changes, oxygen saturation changes and hematocrit changes. Dr. Sergio Gianesini discussed the role of CSF flow in CCSVI. Dr. E. Mark Haacke presented for Dr. Wei Feng, showing for the first time that there are at least two sub-populations of MS patients. They broke the MS population into those with structural abnormalities as seen with MRV and those without. Those without followed a normal flow distribution in terms of how much blood was carried by the internal jugular veins compared to total arterial flow while those with structural abnormalities showed a shift in the number of people with high IJV flow to much lower flows. This could prove valuable in understanding why some people who are treated respond better than others. Dr. Paolo Zamboni introduced an alternate approach to try and evaluate abnormal flow patterns in MS patients using cervical plethysmography. The session was completed with a second talk on this subject by Dr. Simon Shepherd showing that the plethysmographic data can be fit with a second order system. Both gave preliminary data that it may be possible to separate CCSVI patients from normals with this approach.

Plenary Session 8: Endovascular aspects and treatment of CCSVI
During the last year it is estimated that more than 10,000 procedures have been performed to improve venous return in MS patients. Several presenters discussed the approach they take in terms of ballooning, pressures applied, testing for wall abnormalities, and stenting. Dr. Grazia Filippini discussed a large proposed double blinded trial involving many sites in Italy to assess the safety and efficacy of endovascular treatment of CCSVI. This study is to involve remitting and secondary progressive MS patients (BRAVE DREAMS, BRAin VEnous DRAINage Exploited Against Multiple Sclerosis) as well as a sham controls with primary endpoints being at one year. Dr. Adnan Siddiqui discussed the beginning of the PREMISE (propsective randomized endovascular therapy in MS) trial. They plan to use MRI, CTA, IVUS and PTA to evaluate efficacy of treatment. Material presented included inclusion/exclusion criteria, study population, randomization, treatment outcomes, processing methods, statistical approaches and preliminary results. Dr. M. Zarebinski presented the effects of CCSVI treatment of 420 MS patients at 6-months, discussing the number and the kinds of treatment complications, and observing an improvement in the Fatigue Severity Scale and yet no significant change in EDSS. Dr. E. Mark Haacke reviewed the potential role of MRI as a treatment planning tool with a focus on using 3D MRV and flow quantification to deal with complicated venous pathways. He also gave an overview of other potential aspects of MRI that would be useful in the study of MS including: iron, perfusion and oxygen saturation measurements. He outlined why it was critical for patients to have a baseline scan prior to having venous angioplasty including the key observation that the baseline scan serves a key role for the neurologist, radiologist and interventional radiologist as well as being a key control for the patient themselves.

Plenary Session 9: Best abstract presentations, Part 2
Dr. Marian Simka discussed optical coherence tomography which is sensitive to optic nerve fibers and ganglion cells. Both of these appear to be damaged in patients with MS. Those with a previous history of neuritis showed more severe symptoms. OCT measures also correlated with EDSS scores. Finally, he noted that even patients that showed no evidence of CCSVI still showed worsening retinal conditions. Dr. Marjeta Denislic showed in a cohort of 65 MS patients that after treatment fatigue scores improved but EDSS did not. He also noted that PP MS patients tended to have more procedures than RR MS or SP MS. Dr. Robert Zivadinov discussed the differences between intraluminal, extralaminal and functional abnormalities. The former included the presences of flap, septum, web or malformed valve. The next referring to primarily stenosis, and the final category to flow abnormalities not covered by the first two categories. He also compared results from these three categories using 3D contrast enhanced MRA, 2D time-of-flight (TOF) and ultrasound and found the latter to be the preferred method for extracranial evaluation of the data. Dr. Andrzej Cieszanowski presented a comparison of 3D CE MRV in 50 MS cases and 50 normals. They evaluated narrowings in the upper C1 region and the middle range of the IJVs. They found no difference in the presentation of stenoses or narrowings between the two groups. Dr. Michael Dake presented for Dr. C.J. Elkins on the role of 3D flow quantification in studying abnormal flow characteristics. This technique offers much larger coverage than the 2D methods and opens the door to a global study of the fluid dynamics of the head/neck system. He also noted a particular bimodal cardiac flow characteristic in the flow pattern of MS patients. 
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.

JOIN US AT THE SECOND ANNUAL ISNVD MEETING FOR THE FOLLOWING EXCITING VENUES:

A SPECIAL MR CONSENSUS DISCUSSION ON SATURDAY, FEBRUARY 18, 2012 AND SUNDAY, FEBRUARY 19, 2012

SPECIAL LECTURES ON 3D/1D FLOW QUANTIFICATION OF THE HEAD AND NECK

FLOW DYNAMICS IN CCSVI

MR ANGIOGRAPHIC TECHNIQUES IN MONITORING ABNORMAL VASCULATURE IN MS PATIENTS

www.isnvd.org

Tentative Schedule of Events

MS patient parallel session from 10:00am - 3:00pm

Saturday - February 18, 2012
1:00pm – 1:15pm  Welcome by Paolo Zamboni
1:15pm – 3:00pm  Ultrasound
3:30pm – 5:30pm  Magnetic Resonance Imaging
7:00pm – 9:00pm  Evening Reception

Sunday - February 19, 2012
8:30am – 10:00am  Experience in Venous Balloon Angioplasty
10:00am – 10:30am  Coffee Break
10:30am – 12:00pm  Establishing a Consensus on Treatment, Safety and Outcomes

Beginning of the Second Annual ISNVD Scientific Meeting

Sunday - February 19, 2012
1:00pm – 1:15pm  Welcome by Robert Zivadinov
1:15pm – 1:30pm  Awards by Paolo Zamboni - Gold Metal
1:30pm – 2:30pm  Keynote Speaker
2:30pm – 3:00pm  Coffee Break
3:00pm – 5:00pm  Abnormal Venous Flow and Neurodegenerative Disease: Part 1
-Neurological Evaluation of Patients
7:00pm – 9:00pm  Opening Reception

Monday - February 20, 2012
8:30am – 10:00am  Perfusion, Hypoxia, Ischemia, Reperfusion
10:00am – 10:30am  Coffee Break
10:30am – 12:00pm  Summary of US consensus
12:00pm – 1:00pm  Lunch
1:00pm – 2:30pm  Animal Studies-Putnam Review + Animal Models
2:30pm – 3:00pm  Coffee Break
3:00pm – 5:00pm  MS Society Funded Studies

Tuesday - February 21, 2012
8:00am – 9:30am  Abnormal Venous Flow and Neurodegenerative Disease: Part 2
9:30am – 10:30am  Summary of MRI consensus
10:30am – 11:00am  Coffee Break
11:00am – 12:30pm  CCSVI Review
12:30pm – 1:30pm  Lunch
1:30pm – 3:00pm  Endovascular Technology – Consensus
3:00pm – 3:30pm  Panel Discussion
3:30pm – 4:00pm  Coffee Break
4:00pm – 5:30pm  Iron in Neurodegenerative Disease

Wednesday - February 22, 2012
8:30am – 10:00am  Abnormal Venous Flow and Neurodegenerative Disease: Part 3
10:00am – 10:30am  Abstracts
10:30am – 11:00am  Coffee Break
11:00am – 12:30pm  Hypertension
12:30pm – 1:30pm  Lunch
1:30pm – 2:30pm  Measuring Flow and Computational Fluid Dynamics
2:30pm – 3:30pm  Multi-Modal Imaging
3:30pm – 4:00pm  Coffee Break
4:00pm – 5:30pm  Panel Discussion: Abnormal Vasculature in Neurological Disease
5:30pm  Meeting Adjourned
# ISNVD BOARD COMMITTEE MEMBERS

## Executive Committee:

<table>
<thead>
<tr>
<th>Role</th>
<th>Name</th>
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</thead>
<tbody>
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<tr>
<th>Committee</th>
<th>Chair</th>
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<td>Finance Committee</td>
<td>David Hubbard, MD</td>
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<tr>
<td>Nominating Committee</td>
<td>Salvatore Sclafani, MD</td>
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<tr>
<td>Awards Committee</td>
<td>Paolo Zamboni, MD</td>
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<tr>
<td>Publications Committee</td>
<td>Adnan Siddiqui, MD, PhD</td>
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<td>Stefano Bastianello, MD</td>
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<td>Public Relations Committee</td>
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<th>Chair</th>
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<tr>
<td>Annual Meeting Program Committee</td>
<td>E. Mark Haacke, PhD and Michael Dake, MD</td>
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<tr>
<td>Sub-Committee on Ultrasound Workshop</td>
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<tr>
<td>Sub-Committee on MRI Workshop</td>
<td>E. Mark Haacke, PhD and Robert Zivadinov, MD, PhD</td>
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<td>Sub-Committee on Venous Angioplasty Workshop</td>
<td>Michael Dake, MD, Adnan Siddiqui, MD, PhD, and Others (TBD)</td>
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<td>Sub-Committee on MS Workshop</td>
<td>William Code, MD and Sharon Richardson</td>
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