Venous and glymphatic drainage of the brain: Brief history of the International Society for Neurovascular Disease

Ewart Mark Haacke,[1-4] Meiyun Wang,[5] Xiaoyue Ma,[5] David Utriainen[2,3]

[1]Wayne State University, Detroit, MI, USA; [2]The Magnetic Resonance Imaging Institute for Biomedical Research, Detroit, MI, USA; [3]Magnetic Resonance Innovations, Inc., Detroit, MI, USA; [4]Spintech, Inc., Detroit, MI, USA; [5]Henan Provincial Peoples' Hospital, Zhenzhou, Henan Province, China

Abstract

The International Society of Neurovascular Diseases is an International, Interdisciplinary Scientific Organization (ISNVD: www.isnvd.org) devoted to the study of intracranial and extracranial vasculature. Different from other scientific societies, ISNVD is interested also in the investigation of the cerebral drainage, including the venous and glymphatic systems. Moreover, ISNVD promotes studies on: stroke, carotid surgery, neurovascular aspects of neurodegeneration, models of circulation, vasoactive peptides, and basic science. This review summarizes the contribution of the society to the fields above, as well as the history of the annual meetings and the major impact papers promoted by ISNVD.

Introduction

The foundation of the ISNVD had its history in the first meeting held on chronic venous hypertension by Dr. Paolo Zamboni in Bologna, Italy in 2009. His pioneering work on iron and vascular effects in multiple sclerosis (MS) opened the door to a more intensive international effort to study the vascular sources of neurodegenerative disease.[1,2] The story really began with his seminal paper on iron: *The big idea: iron-dependent inflammation in venous disease and proposed parallels in multiple sclerosis*.[3] After the Bologna meeting, it became clear that there was not a major focus on venous effects in neurodegenerative disease and even the role of the arterial system was under-represented.[4,5] This spurred a group of leading scientists to meet in 2010 at the house of Sal Sclafani, M.D. (one of the past Presidents of the Society). At that meeting it was decided to go ahead and form a 501(c)3 Non-Profit Society which was then centered in Detroit, Michigan for the first 3 years. Subsequently the office moved to Buffalo for the next 3 years with Robert Zivadinov, M.D., Ph.D. (also one of the past Presidents of the Society) and then to Shreveport for two years with Steve Alexander (also one of the past Presidents of the Society) and then back to Detroit in 2017 with Mark Haacke Ph.D. (the current past president).

Highlights of the past eight meetings

Bologna, Italy 2011; President and Annual Meeting Chair Paolo Zamboni

The ability to understand the vascular system has the potential to lead to new treatments. Dr. Berislav Zlokovic had the insight to focus on the fundamental aspects of vascular pathology including: the role of: reduced perfusion, hypoxia, tissue damage and endothelial damage.[6-8] He suggested that neurodegeneration occurs secondary to vascular damage and that novel pharmaceuticals might be designed to target inflammation and endothelial pathology. Today trials are underway using activated protein C, which is a blood protease with its anti-coagulant functions turned off so that it is a multiple cell signaling neuroprotective agent, 3K3A-APC, reducing the risk of hemorrhage.[9] This is being studied in stroke today and Zlokovic is an active participant in this work.

This was followed by Dr. Costantino Iadecola who discussed the role of iron as a potential inflammatory agent, the role of oxidative stress and endothelial damage.[10-12] He further suggested there might be a relationship with poor vascular conditions and that these could lead to the production of beta amyloid plaque.[13,14] Today, along with the glymphatic system to be discussed later, this is now a very promising direction of research.

Dr. Robert Zivadinov followed with examples from imaging demonstrating reversible cerebrospinal fluid stagnation and increased iron content in MS patients, and also suggesting that these increases may correlate with the severity of the disease (Figure 1).[15-19]

Orlando, Florida, USA 2012; President Robert Zivadinov, Annual Meeting Chair Mark Haacke

The keynote speech was given by Michael Chopp, Ph.D., from Henry Ford Hospital. 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.[20-22]

A highlight of this workshop was the focus on providing a *Consensus on Imaging & Treatment Protocols.* Ultrasound, Magnetic Resonance Imaing (MRI) and balloon angioplasty groups met separately to discuss the state-of-the-art technology in each area with an eye toward creating a white paper. The outcome of this effort was a paper published in 2014 in JVIR, 2014, 25, 1785.[23]

The Gold Medal was given to Franz Schelling for his pioneering contributions to understanding the role of the venous vasculature in MS. Dr. Schelling then gave an overview of some of the history and where he thought we still needed to forge ahead to clearly addresses the role of abnormal venous vasculature in MS.

Krakow, Poland, 2013; President and Annual Meeting Chair Marian Simka

At this meeting the venue of presentations continued to expand and covered a number of new concepts including the work of Jaap Valk from Amsterdam.[24] He presented the results of a prospective study on patients with chronic intractable headache and other concurrent symptoms such as vertigo, dizziness, tinnitus and visual disturbances. The patients were examined by the use of magnetic resonance venography.

Correspondence: Ewart Mark Haacke, Wayne State University, School of Medicine, Department of Radiology, 4201 St. Antoine, Detroit 48201, MI, USA.
Tel.: +1.313.745.1395 - Fax: +1.313.745.9182.
E-mail: nmrimaging@aol.com

Key words: Chronic cerebrospinal venous insufficiency; glymphatic system; neurovascular disease; cerebrospinal fluid; cerebral drainage.

Contributions:e author contributed to writing the paper.

Received for publication: 19 September 2018.
Accepted for publication: 24 September 2018

Veins and Lymphatics 2019; 8:7839
doi:10.4081/vl.2019.7839

Often the patients were found to have intracranial abnormalities such as persistent occipital sinus with loop formation or thrombosis of the intracranial sinuses. He concluded that venous intracranial pathology is prevalent in patients presenting with neurological symptoms and that MRI would play a key role in diagnosing these patients.

San Francisco, California, USA 2014; President and Annual Meeting Chair Mike Dake

Reflecting the expanding interest and collaborations within the society, a special focus on traumatic brain injury (TBI) was the theme of the 2014 meeting. Dr. Diaz-Arrastia discussed treatment of patients with TBI.[25-28] He presented several different treatment options including: sildenafil, erythropoietin, statins, G-CSF, VEGF, pioglitazone, exercise, enriched endothelia progenitor cells, from cord blood or bone marrow, and low level laser light therapy. His findings in humans were similar to the keynote lecture in 2012 by Dr. Michael Chopp.

Naples, Italy, 2015; President Ziv Haskal, Annual Meeting Chair Marcello Mancini

Research into new therapeutic approaches for human neuro-degenerative disorders is part of the effort by Dr. Jacques De Keyser and his group from Brussels, Belgium.[29-31] They 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 (AD) and other disorders associated with chronic brain hypoperfusion.[32]

The role of vessel wall began taking on importance at this meeting. 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 quantitatively demonstrated by Serena Monti, M.S. from Siena, Italy using digital subtraction angiography.[33]

The Gold Medal was given to Paolo Zamboni for his pioneering contributions to understanding the role of the venous vasculature in chronic cerebral spinal venous insufficiency (CCSVI).[34] Paolo continues to be a leader in this field not only constantly probing the effects of venous hypertension but also developing new means by which to monitor these vascular abnormalities.[35]

New York City, New York, USA 2016; President and Annual Meeting Chair Sal Sclafani

A new area of interest sprang up this year that continues to be an important topic today. The session on *Vascular Function, Glymphatic System and New Drug Development* was led by the the next President, Dr. Steve Alexander.[36-38] He spoke on *Alterations in Hemodynamic Flow Patterns and Endothelial Dysfunction in Neurodegeneration*.

The Gold Medal was given to Mark Haacke for his pioneering efforts in developing MR vascular imaging methodologies such as magnetic resonance angiography, susceptibility weighted imaging, and MICRO imaging. He continues to push the use of MRI to study the vascular system in all neuro-degenerative diseases with a special focus on MS, Parkinson's disease (PD), stroke, TBI and vascular dementia.[39]

Taormina, Sicily, Italy, 2017; President Steve Alexander, Annual Meeting Chair Pierfrancesco Veroux

Harking back to the foundations of the society, Byung-Boong Lee presented the keynote lecture: *Defective Development of Vena Cava: Embryological interpretation of Hemodynamic Consequences*.[40,41] He also presented *Obstructive truncular venous malformations*, which was an excellent overview of how venous malformations could contribute to blood flow disturbances in general with a focus on CNS participation. These truncular venous malformations are known to occur in MS patients and recent evidence suggests they occur in Parkinson's patients as well.[42]

Zhengzhou, Henan Province, China, 2018; President Mark Haacke, Annual Meeting Chair Meiyun Wang

Bringing together efforts that recognize the link between the arterial, venous and cerebrospinal fluid systems as a whole, Prof. Jiani Hu spoke on *The interaction between the vascular and glymphatic systems*.[43] Prof. Eleuterio F. Toro delivered a talk titled *Modeling flow in the head and neck*.[44] He had reviewed the work of Warnert *et al*. and assessed Warnert's hypothesis by using a state-of-the-art global mathematical model for human circulation.[45,46] He found that congenital anatomical variants (VHA and iCoW) do not exhibit alterations in cerebral blood flow. Dr. Jie Li, representing the team of Satish Krishnamurthy, presented a talk on *Delayed macromolecular transport at the neurovascular unit in hydrocephalus*. His studies have shown that excess macromolecules in the ventricles are sufficient to cause hydrocephalus. He said these macromolecules are transported in both normal and hydrocephalic states from the ventricles *via* the perivascular pathways (glymphatic pathways) and eliminated into the vascular system (serum). Imaging has shown that the iron dextran used in their experiments finds its way into the venous system and is then drained out of the brain.[47]

The Gold Medal was given to Robert Zivadinov for his pioneering efforts in applying MRI methods to study MS. He continues to evaluate MS using a variety of new methods in an attempt to understand the underlying etiology (Figure 2).[48,49]

The Zhengzhou meeting was the first time the ISNVD went to Asia. This year we were fortunate enough to have Dr. Meiyun Wang of Henan Provincial People's Hospital agree to host the 8th Annual Meeting of the ISNVD in Zhengzhou, China from May 31th-June 2th, 2018.[50] During the three days of the meeting, more than 40 well-known radiologists and neurologists gave presentations with more than 300 attendees from around the world active-

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

Figure 1. Five Presidents of the ISNVD, at that time Robert Zivadinov was the current President, Paolo Zamboni the past President and Mike Dake the President Elect.

ly participating. The speakers were able to give their presentations in both Chinese and English as simultaneous interpretation was provided through special headsets. This ensured easy understanding of the speeches and a fluent exchange of information throughout the meeting. The meeting was formally hosted by Henan Provincial People's Hospital in Zhengzhou, Henan, China, which is one of the largest hospitals in China with a history of more than 114. Please visit our website at www.isnvd.org for more information about the ISNVD or e-mail info@isnvd.org

The opening ceremony welcomed everyone with a video of the history and culture of Henan Province, the Henan Provincial People's Hospital and the ISNVD. Dr. Meiyun Wang gave a welcome speech and introduced the other invited guests including: Dr. Longde Wang, an academician of the Chinese Academy of Engineering, Honorary President of the ISNVD 2018 Annual Meeting and President of the Chinese Preventive Medicine Association from Stroke Prevention and Control Project Committee, National Health Commission; Dr. Jianping Dai, a foreign academician of the American Academy of Medical Sciences, Past Vice-President of the Chinese Medical Association; Prof. Lawrence L. Wald, President-Elect of ISMRM; Prof. Bernd Hamm, the chairperson of the European Society of Radiology (ESR) Board of Directors, President of the ESR and European Congress of Radiology (ECR) 2018. Prof. Xiaoliang Zhang, President of the Overseas Chinese Society for Magnetic Resonance in Medicine (OCSMRM); Dr. Wei Huang, Vice-President and Inspector of the Health and Family Planning Commission of Henan Province; Dr. Jianqin Gu, President of Henan Provincial People's Hospital who spoke about the hospital's development and endeavor in improving the diagnostic level of neurovascular diseases; Dr. Fengmin Shao, Secretary of the Party Committee of Henan Provincial People's Hospital; Dr. Peichun Sun, the Vice President of Henan Provincial People's Hospital and Prof. E. Mark Haacke, 2017/2018 President of the ISNVD (Figure 3).

Highlights of the 2018 meeting

Dr. Longde Wang gave a lecture entitled *Exploration on the prevention and control of stroke in China*. He elaborated the major challenges, preliminary achievements and future plans in stroke prevention in China.[51] This was followed by a speech on *Imaging techniques of cerebral ischemia* by Dr. Jianping Dai.[52] He said new therapies of recanalization of cerebral ischemia may improve patient outcome and that early diagnosis by imaging is significant for choosing a suitable treatment. He noted that precision medicine requires the combination of P4 medicine, integrated imaging, artificial intelligence (AI) and molecular medicine but that despite advances in this era of precision medicine, challenges remain.

Prof. Lawrence L. Wald gave the second keynote speech titled *MRI unchained; removing hardware constraints to make faster, portable and motion tolerant images*. From the insight of biomedical imaging and bioengineering, Prof. Wald gave an excellent talk on several advanced technologies, mainly about MR image reconstruction (based on modeling the structure of interest rather than using Fourier Transform), the portable brain MRI, accelerated imaging and removing motion artifacts.[53] He said, *"If you can measure a systematic error, you can fix the systematic error"*. Many in the audience were excited about this new technology and its implications in the field of medical imaging.

Prof. E. Mark Haacke spoke about a rapid multi-contrast MRI method using strategically acquired gradient echo (STAGE) imaging.[54,55] He noted that STAGE provides a rapid standardized imaging approach of the entire brain in less than 5 (7) minutes that can be used for all 3T (1.5T) manufacturer' systems.[57-61]

Dr. Meiyun Wang talked about chemical exchange saturation transfer (CEST) imaging in stroke. She introduced two CEST concepts: 1) amide proton transfer (APT) and length and 2) offset varied saturation (LOVARS). She and her team have pioneered the application of these methods to demonstrate that they can be used to detect stroke and distinctly differentiate hyperacute intracranial hemorrhage from cerebral ischemia thus opening the door for a rapid single scan evaluation of stroke.[62,63]

Prof. Paolo Zamboni talked about *Eagle jugular syndrome*. He said that the jugular variant of the Eagle syndrome is a distinct

Figure 2. Gold medal winners Franz Schelling (2012), Mark Haacke (2016), Robert Zivadinov (2018) and Paolo Zamboni (2015).

Figure 3. Presidium and invited speakers. All the invited speakers and honorary guests were present for this picture.

clinical entity with respect to both classic and carotid variants, and it seems to be a factor which potentially increases the susceptibility to subarachnoid hemorrhage (SAH).[56] Prof. Bruno's talk was called *Venous lesions in patients with Meniere's Disease (MD): Results of a multicentric Italian study and guidelines for an international project*. His research found that the prevalence of CCSVI in Meniere's disease is high and PTA has a significant curative effect on MD.[57] He believed that the venous stasis of the head and neck veins may be considered a further etiopathogenetic mechanism which adds to many other already known mechanisms that still define MD as a multifactorial disease.

Prof. Paolo Zamboni also discussed the Brave Dreams trial.[58,59] He believed CCSVI contributed to a better understanding of the function and role of the extracranial venous system. He then suggested, *"Rather than rejecting this accumulated new knowledge, we should use it more appropriately for future endeavors"*. Prof. Robert Zivadinov discussed the role of cardiovascular (CV) comorbidities in the pathogenesis of neurological disorders.[60] He pointed out that CV comorbidities are associated with higher susceptibility to neurodegenerative disorders and disease progression, there is a stronger link between CSA of neck vessels and CV risk factors, and that the heart-brain axis should be better investigated in diseases such as MS, AD and PD. Prof. Salvatore Sclafani discussed *Carotid arterial trauma and minimally invasive treatments*. He believed that treating carotid injury surgically is challenging and endovascular options are essential for survival.[61] The 2019 meeting will be held in Ferrara, Italy, bringing us back to our roots. The ISNVD is a non-profit organization registered in the United State of America. To become a member, please go to www.isnvd.org.

References

1. Zamboni P, Galeotti R, Menegatti E, et al. Chronic cerebrospinal venous insufficiency in patients with multiple sclerosis. J Neurol Neurosurg Psychiatry 2009;80:392-9.
2. Zamboni P, Sisini F, Menegatti E, et al. An ultrasound model to calculate the brain blood outflow through collateral vessels: a pilot study. BMC Neurology 2013;13:81.
3. Zamboni P. The big idea: iron-dependent inflammation in venous disease and proposed parallels in multiple sclerosis. J R Soc Med 2006;99:589-93.
4. Dake MD, Zivadinov R, Haacke EM. Chronic cerebrospinal venous insufficiency in multiple sclerosis: a historical perspective. Funct Neurol 2011;26:181-95.
5. Siskin GP, Haskal ZJ, Mclennan G, et al. Development of a research agenda for evaluation of interventional therapies for chronic cerebrospinal venous insufficiency: proceedings from a multidisciplinary research consensus panel. J Vasc Interv Radiol 2011;22:587-93.
6. Zlokovic BV. The blood-brain barrier in health and chronic neurodegenerative disorders. Neuron 2008;57:178-201.
7. Sweeney MD, Sagare AP, Zlokovic BV. Blood-brain barrier breakdown in Alzheimer disease and other neurodegenerative disorders. Nat Rev Neurol 2018;14:133-50.
8. Brown R, Benveniste H, Black SE, et al. Understanding the role of the perivascular space in cerebral small vessel disease. Cardiovasc Res 2018;114:1462-73.
9. Griffin JH, Zlokovic BV, Mosnier LO. Activated protein C, protease activated receptor 1, and neuroprotection. Blood 2018;132:159-69.
10. Kunz A, Park L, Abe T, et al. Neurovascular protection by ischemic tolerance: role of nitric oxide and reactive oxygen species. J Neurosci 2007;27:7083-93.
11. Faraco G, Park L, Anrather J, Iadecola C. Brain perivascular macrophages: characterization and functional roles in health and disease. J Mol Med (Berl) 2017;95:1143-52.
12. Iadecola C. The neurovascular unit coming of age: a journey through neurovascular coupling in health and disease. Neuron 2017;96:17-42.
13. Iadecola C. Vascular and metabolic factors in Alzheimer's disease and related dementias: introduction. Cell Mol Neurobiol 2016;36:151-4.
14. Kahl A, Blanco I, Jackman K, et al. Cerebral ischemia induces the aggregation of proteins linked to neurodegenerative diseases. Sci Rep 2018;8:2701.
15. Zivadinov R, Magnano C, Galeotti R, et al. Changes of cine cerebrospinal fluid dynamics in patients with multiple sclerosis treated with percutaneous transluminal angioplasty: a case-control study. J Vasc Interv Radiol 2013;24:829-38.
16. Zivadinov R, Heininen-Brown M, Schirda CV, et al. Abnormal subcortical deep-gray matter susceptibility-weighted imaging filtered phase measurements in patients with multiple sclerosis: a case-control study. Neuroimage 2012;59:331-9.
17. Hagemeier J, Weinstock-Guttman B, Heininen-Brown M, et al. Gray matter SWI-filtered phase and atrophy are linked to disability in MS. Front Biosci (Elite Ed) 2013;5:525-32.
18. Hagemeier J, Zivadinov R, Dwyer MG, et al. Changes of deep gray matter magnetic susceptibility over 2 years in multiple sclerosis and healthy control brain. Neuroimage Clin 2018;18:1007-16.
19. Zivadinov R, Tavazzi E, Bergsland N, et al. Brain iron at quantitative MRI is associated with disability in multiple sclerosis. Radiology 2018;180136.
20. Zhang R, Wang Y, Zhang L, et al. Sildenafil (Viagra) induces neurogenesis and promotes functional recovery after stroke in rats. Stroke 2002;33:2675-80.
21. Li L, Jiang Q, Zhang L, et al. Angiogenesis and improved cerebral blood flow in the ischemic boundary area detected by MRI after administration of sildenafil to rats with embolic stroke. Brain Res 2007;1132:185-92.
22. Zhang RL, Chopp M, Roberts C, et al. Sildenafil enhances neurogenesis and oligodendrogenesis in ischemic brain of middle-aged mouse. PLoS One 2012;7:e48141.
23. Zivadinov R, Bastianello S, Dake MD, et al. Recommendations for multimodal noninvasive and invasive screening for detection of extracranial venous abnormalities indicative of chronic cerebrospinal venous insufficiency: a position statement of the International Society for Neurovascular Disease. J Vasc Interv Radiol 2014;25:1785-94.
24. Valk J, Van Vucht N, Pevenage P. MR Venographic patterns in chronic intractable headache. Neuroradiol J 2011;24:13-9.
25. Hudak AM, Peng L, Marquez De La Plata C, et al. Cytotoxic and vasogenic cerebral oedema in traumatic brain injury: assessment with FLAIR and DWI imaging. Brain Inj 2014;28:1602-9.
26. Kenney K, Amyot F, Haber M, et al. Cerebral vascular injury in traumatic brain injury. Exp Neurol 2016;275:353-66.
27. Okonkwo DO, Shutter LA, Moore C, et al. Brain oxygen optimization in severe traumatic brain injury phase-II: a phase II randomized trial. Crit Care Med 2017;45:1907-14.
28. Haber M, Amyot F, Kenney K, et al. Vascular abnormalities within normal appearing tissue in chronic traumatic brain injury. J Neurotrauma 2018 [Epub ahead of print].

29. Cambron M, Mostert J, Haentjens P, et al. Fluoxetine in progressive multiple sclerosis (FLUOX-PMS): study protocol for a randomized controlled trial. Trials 2014;15:37.
30. D'haeseleer M, Hostenbach S, Peeters I, et al. Cerebral hypoperfusion: a new pathophysiologic concept in multiple sclerosis? J Cereb Blood Flow Metab 2015;35:1406-10.
31. Vande Vyver M, Beelen R, De Keyser J, et al. Plasma citrulline levels are increased in patients with multiple sclerosis. J Neurol Sci 2018;387:174-8.
32. D'haeseleer M, Beelen R, Fierens Y, et al. Cerebral hypoperfusion in multiple sclerosis is reversible and mediated by endothelin-1. Proc Natl Acad Sci U S A 2013;110:5654-8.
33. Monti L, Donati D, Menci E, et al. Cerebral circulation time is prolonged and not correlated with EDSS in multiple sclerosis patients: a study using digital subtracted angiography. PLoS One 2015;10:e0116681.
34. Zamboni P, Zivadinov R. Extracranial veins in multiple sclerosis: is there a role for vascular surgery? Eur J Vasc Endovasc Surg 2018;pii:S1078-5884(18)30387-3.
35. Zamboni P, Sisini F, Menegatti E, et al. Ultrasound monitoring of jugular venous pulse during space missions: proof of concept. Ultrasound Med Biol 2018;44:726-33.
36. Alexander JS, Zivadinov R, Maghzi AH, et al. Multiple sclerosis and cerebral endothelial dysfunction: mechanisms. Pathophysiology 2011;18:3-12.
37. Yun JW, Xiao A, Tsunoda I, et al. From trash to treasure: the untapped potential of endothelial microparticles in neurovascular diseases. Pathophysiology 2016;23:265-74.
38. Shrestha B, Prasai PK, Kaskas AM, et al. Differential arterial and venous endothelial redox responses to oxidative stress. Microcirculation 2018;e12486.
39. Liu S, Buch S, Chen Y, et al. Susceptibility-weighted imaging: current status and future directions. NMR Biomed 2017;30.
40. Lee BB. Venous malformation and haemangioma: differential diagnosis, diagnosis, natural history and consequences. Phlebology 2013;28:176-87.
41. Lee BB, Baumgartner I, Berlien P, et al. Diagnosis and treatment of venous malformations. Consensus Document of the International Union of Phlebology (IUP): updated 2013. Int Angiol 2015;34:97-49.
42. Liu M, Xu H, Wang Y, et al. Patterns of chronic venous insufficiency in the dural sinuses and extracranial draining veins and their relationship with white matter hyperintensities for patients with Parkinson's disease. J Vasc Surg 2015;61:1511-20.
43. Bacyinski A, Xu M, Wang W, Hu J. The paravascular pathway for brain waste clearance: current understanding, significance and controversy. Front Neuroanat 2017;11:101.
44. Contarino C, Toro EF. A one-dimensional mathematical model of collecting lymphatics coupled with an electro-fluid-mechanical contraction model and valve dynamics. Biomech Model Mechanobiol 2018 [Epub ahead of print].
45. Warnert EA, Murphy K, Hall JE, Wise RG. Noninvasive assessment of arterial compliance of human cerebral arteries with short inversion time arterial spin labeling. J Cereb Blood Flow Metab 2015;35:461-8.
46. Warnert EA, Hart EC, Hall JE, et al. The major cerebral arteries proximal to the Circle of Willis contribute to cerebrovascular resistance in humans. J Cereb Blood Flow Metab 2016;36:1384-95.
47. Krishnamurthy S, Li J, Shen Y, et al. Normal macromolecular clearance out of the ventricles is delayed in hydrocephalus. Brain Res 2018;1678:337-55.
48. Dwyer MG, Bergsland N, Ramasamy DP, et al. Atrophied brain lesion volume: a new imaging biomarker in multiple sclerosis. J Neuroimaging 2018; 28:490-5.
49. Lin F, Zivadinov R, Hagemeier J, et al. Altered nuclei-specific thalamic functional connectivity patterns in multiple sclerosis and their associations with fatigue and cognition. Mult Scler 2018 [Epub ahead of print].
50. Van Beek EJR, Kuhl C, Anzai Y, et al. Value of MRI in medicine: more than just another test? J Magn Reson Imaging 2018 [Epub ahead of print].
51. Fu W, Cao S, Liu B, et al. Association of general and central adiposity with blood pressure among Chinese adults: results from the China National Stroke Prevention Project. J Hypertens 2018 [Epub ahead of print].
52. Zhang P, Wang J, Xu Q, et al. Altered functional connectivity in post-ischemic stroke depression: a resting-state functional magnetic resonance imaging study. Eur J Radiol 2018;100:156-65.
53. Polimeni JR, Wald LL. Magnetic resonance imaging technology-bridging the gap between noninvasive human imaging and optical microscopy. Curr Opin Neurobiol 2018;50:250-60.
54. Chen Y, Liu S, Wang Y, et al. STrategically Acquired Gradient Echo (STAGE) imaging, part I: Creating enhanced T1 contrast and standardized susceptibility weighted imaging and quantitative susceptibility mapping. Magn Reson Imaging 2018;46:130-9.
55. Wang Y, Chen Y, Wu D, et al. STrategically Acquired Gradient Echo (STAGE) imaging, part II: Correcting for RF inhomogeneities in estimating T1 and proton density. Magn Reson Imaging 2018;46:140-50.
56. Aydin E, Quliyev H, Cinar C, et al. Eagle syndrome presenting with neurological symptoms. Turk Neurosurg 2018;28:219-25.
57. Bruno A, Quarto G, Califano L, et al. Chronic cerebrospinal venous insufficiency in Ménière's disease: diagnosis and treatment. Veins and Lymphatics 2014;3:3854.
58. Zamboni P, Tesio L, Galimberti S, et al. Efficacy and safety of extracranial vein angioplasty in multiple sclerosis: a randomized clinical trial. JAMA Neurol 2018;75:35-43.
59. Juurlink BHJ, Bavera PM, Sclafani S, et al. Brave Dreams: an overestimated study, crippled by recruitment failure ad misleading conclusions. Veins and Lymphatics 2018;7:7340.
60. Zivadinov R, Ramasamy DP, Benedict RR, et al. Cerebral microbleeds in multiple sclerosis evaluated on susceptibility-weighted images and quantitative susceptibility maps: a case-control study. Radiology 2016;281:884-95.
61. Ghanaat M, Goldenberg C, Walsh J, Sclafani SJ. Endovascular management of an intracardiac bullet. Injury 2015;46:166-8.
62. Ma X, Bai Y, Lin Y, et al. Amide proton transfer magnetic resonance imaging in detecting intracranial hemorrhage at different stages: a comparative study with susceptibility weighted imaging. Sci Rep 2017;7:45696.
63. Wang M, Hong X, Chang CF, et al. Simultaneous detection and separation of hyperacute intracerebral hemorrhage and cerebral ischemia using amide proton transfer MRI. Magn Reson Med 2015;74:42-50.