

# Medical Update Memo

January 31, 2011

## Research Teams Report Progress from First Six Months of 2-Year Projects Focusing on CCSVI and MS

### Summary

Six-month progress reports from seven multi-disciplinary teams investigating [CCSVI \(chronic cerebrospinal venous insufficiency\) in MS](#) indicate that they have established rigorous protocols, are successfully recruiting participants, and are on-track to evaluate and deliver important data when the two-year projects are completed. All seven studies are two years in length but will be closely monitored while in progress in order to expedite clinical trials should the data show it is warranted. The studies were launched on July 1, 2010 with a more than \$ 2.4 million commitment from the MS Society of Canada and the National MS Society (USA).

### Details

Most of the teams have received approval to begin their studies from the required Institutional Review Boards in the U.S. or the Research Ethics Board in Canada, a required first step established by regulatory authorities to protect human subjects involved in research projects. (Read more about [steps involved in conducting clinical research](#).)

Already more than 200 people have undergone scanning with various imaging technologies being used by the studies, including the Doppler ultrasound technology originally used by Dr. Paolo Zamboni and his collaborators, as well as magnetic resonance studies of the veins (MR venography), catheter venography, MRI scans of the brain, and clinical measures.

Owing to the significant interest in the MS community about CCSVI, we are providing 6-month updates rather than the more standard 12-month reporting cycle. Because the studies employ rigorous blinding and controls designed to attain objective and comprehensive data, the full results of the ongoing research will be available only after significantly more scans have been completed and evaluated. They will collectively involve more than 1300 people representing a spectrum of MS types, severities and durations, as well as individuals with other disease types and healthy controls.

“We are pleased with the progress reported by the research teams we have funded,” advised Dr. Tim Coetzee, chief research officer at the National MS Society, “and look forward to providing as quickly as possible the understanding and answers these projects reveal on the relationship between CCSVI and the MS disease process.”

Jon Temme, senior vice-president of research and programs for the MS Society of Canada concurs, “The grants were selected for having the greatest potential to quickly and comprehensively determine the significance of CCSVI in the MS disease process. It is very encouraging to see how effectively the work has advanced among all groups.”

The funded investigators, which include an integration of both MS and vascular experts, report progress in establishing their teams, putting their protocols in place, recruiting participants and beginning their studies, as summarized below.

- **Dr. Brenda Banwell, The Hospital for Sick Children, Toronto, Ontario:** Her team received Research Ethics Board approval in the fall and has begun enrolling participants and studying vein abnormalities in children and teenagers who have MS, and healthy controls of the same age, using non-invasive MRI measures of vein anatomy and novel measures of venous flow, as well as ultrasound. The team’s ultrasound experts have received training in Dr. Zamboni’s original techniques. Read details of Dr. Banwell’s plans:

[http://www.mssociety.ca/ccsvi/resources/funding/Paediatric\\_Banwell\\_CSVI.pdf](http://www.mssociety.ca/ccsvi/resources/funding/Paediatric_Banwell_CSVI.pdf)

- **Dr. Fiona Costello, Hotchkiss Brain Institute, University of Calgary, Calgary, Alberta:** Her team received Research Ethics Board approval in the fall to begin recruiting a cross-section of people with MS compared to other neurological

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diseases and healthy volunteers. They also recruited two ultrasonography experts who have begun ultrasound scanning as originally used by Dr. Zamboni. Dr. Costello's team slowed recruitment briefly to upgrade to a new 3T MRI machine (twice as strong as standard clinical MRI) that will be used to perform MR venography scans to compare against the ultrasound tests. Read details of this team's plans:

[http://www.mssociety.ca/ccsvi/resources/funding/Calgary\\_Costello\\_CCS\\_VI.pdf](http://www.mssociety.ca/ccsvi/resources/funding/Calgary_Costello_CCS_VI.pdf)

- **Dr. Aaron Field, University of Wisconsin School of Medicine and Public Health, Madison:** His team will be using MR venography and ultrasound techniques originally used by Dr. Zamboni to investigate CCSVI in people with early and later MS, controls with other conditions and healthy volunteers. An ultrasound expert has been hired and is slated to receive training in the Zamboni techniques. Dr. Field has been negotiating with the Institutional Review Board on issues related to study details and informed consent, and hopes to have these issues resolved to obtain IRB approval in the coming weeks so that scanning can begin. Read details of this team's plans:

<http://www.nationalmssociety.org/research/intriguing-leads-on-the-horizon/ccsvi/ccsvi-study-by-field-team/index.aspx>

- **Dr. Robert Fox, Cleveland Clinic, Cleveland:** His team has received Institutional Review Board approval for using MR venography, ultrasound, MRI and clinical measures in people with MS or who are at risk for MS (CIS) and comparison groups, and recruitment is ongoing. Two ultrasound researchers underwent training in the technique originally used by Dr. Zamboni, and the team has obtained a new ultrasound machine previously used in other CCSVI studies. The ultrasound team found several aspects of the published methodology ambiguous, and they have standardized the protocol and analysis to achieve consistent results. To share ideas and solutions to these methodological challenges, Dr. Fox's team has submitted an abstract for consideration for presentation at the American Academy of Neurology's annual meeting in April. Read details of this team's plans: <http://www.nationalmssociety.org/research/intriguing-leads-on-the-horizon/ccsvi/ccsvi-study-by-fox-team/index.aspx>

- **Dr. Carlos Torres, The Ottawa Hospital, University of Ottawa, Ontario:** His team obtained Research Ethics Board approval in the winter and at once began the first phase of scanning using MR venography in people without MS, which will

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be used to compare with various scans in people with MS. Dr. Torres's team has overcome several obstacles including negotiating with the Research Ethics Board over elements of the informed consent form used to explain the study's procedures and potential outcomes to participants. Team members are slated to be trained using the ultrasound techniques originally used by Dr. Zamboni, and they are on track recruiting more participants for the study. Read details of this team's plans: [http://www.mssociety.ca/ccsvi/resources/funding/Ottawa Torres CCSVI .pdf](http://www.mssociety.ca/ccsvi/resources/funding/Ottawa_Torres_CCSVI.pdf)

- **Dr. Anthony Traboulee, UBC Hospital MS Clinic, UBC Faculty of Medicine and Dr. Katherine Knox, Saskatoon MS Clinic, University of Saskatchewan:** The teams at both sites have received Research Ethics Board approval and have begun to recruit and scan participants. Their ultrasound technologists were trained by Dr. Zamboni, and they are also using catheter venography and MR venography to investigate the prevalence of CCSVI in people with MS and controls without MS. The radiologists on the teams of Drs. Traboulee and Knox are meeting in February 2011 to ensure the consistency of their protocols across sites. The teams are on target for accrual of recruits and completion of the study. Read details of their plans: [http://www.mssociety.ca/ccsvi/resources/funding/BC Traboulee Knox CCSVI.pdf](http://www.mssociety.ca/ccsvi/resources/funding/BC_Traboulee_Knox_CCSVI.pdf)

- **Dr. Jerry Wolinsky, University of Texas Health Science Center at Houston:** His team applied in advance and obtained Institutional Review Board approval in the spring, and the team's neurosonographer has received intensive training for intracranial and extracranial ultrasound scanning techniques. The team has already scanned a significant number of participants, which includes people with different types of MS, people with other conditions, and people with no known health problems. One obstacle Dr. Wolinsky's team is addressing is the difficulty of recruiting non-MS control subjects who don't have a personal interest in the purpose of the trial. The team is testing whether other imaging methods can confirm the ultrasound findings, while identifying the most reliable technique to screen for CCSVI. Read details of this team's plans: <http://www.nationalmssociety.org/research/intriguing-leads-on-the-horizon/ccsvi/ccsvi-study-by-wolinsky-team/index.aspx>

**Going Forward:** These seven teams were chosen by an international panel of experts that included specialists drawn from all key relevant disciplines including

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radiology, vascular surgery and neurology. The [grants were selected](#) for having the greatest potential to quickly and comprehensively determine the significance of CCSVI in the MS disease process. The teams are now established and scanning procedures are underway at all but one of the study sites. Researchers have demonstrated a clear willingness to share technical advice and information so that projects can move forward as smoothly as possible. At this six-month milestone they are making significant progress on plans for these two-year studies.

The next update on the work of the seven grantees will be reported in six months.

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