



Consensus Statement on Neurofilament Proteins in Multiple Sclerosis Under Development by Consortium of Multiple Sclerosis Centers (CMSC) Expert Panel

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Neurofilaments are intracellular cytoskeletal proteins that leak into cerebrospinal fluid (CSF) and blood as a result of neuronal damage.¹ Blood and CSF neurofilament levels are elevated in a number of neurologic diseases such as multiple sclerosis (MS), amyotrophic lateral sclerosis, and Parkinson disease, as well as in traumatic brain injury.^{2,3} In MS, change in serum or CSF neurofilament levels is emerging as an important biomarker to detect disease progression and response to treatment.⁴ Such blood and CSF biomarkers are significantly lacking and much needed in MS care and research.

Many studies have used neurofilament levels—especially neurofilament light chain (NfL)—as outcome measures to determine MS disease severity and detect changes in disease activity or response to treatment.^{5,6} Serum and CSF assays for NfL are expected to be commercially available soon. To inform the MS community about how to apply and interpret these promising biomarkers in MS research and clinical practice, the program chairs Mark Freedman and Sharmilee Gnanapavan developed the curriculum and partnered with the Consortium of Multiple Sclerosis Centers (CMSC) to convene an international panel of experts at the forefront of neurofilament research and clinical applications in MS. Twenty-five international faculty members met in two virtual consensus conferences held on September 3, 2020, and October 16, 2020, to present a comprehensive

overview of available data, determine practical applications of these data in MS, and debate confounding information and unanswered questions. A full list of the conference participants and a summary of the consensus panel's goals and objectives can be found in Tables S1 and S2 (published as online supplementary material at ijmsc.org). The end product will be a series of consensus papers covering these subject areas, to be published as a supplement to the *International Journal of MS Care*, in the spring of 2021.

Neurofilament research will surely continue to advance in the coming years. There is still much we don't know, but further work and clinical experience will continue to refine the role of these biomarkers in MS and other forms of neurodegeneration. Speakers from the CMSC's consensus panel have predicted that, over time, NfL and other serum or CSF biomarkers have the potential to become as significant in MS as magnetic resonance imaging is now. It is important to keep the CMSC membership and broader MS care community informed about these advances. We look forward to presenting this guidance to the MS community. □

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References

1. Leppert D, Kuhle J. Blood neurofilament light chain at the doorstep of clinical application. *Neurol Neuroimmunol Neuroinflamm*. 2019;6:e599.
2. Olsson B, Portelius E, Cullen NC, et al. Association of cerebrospinal fluid neurofilament light protein levels with cognition in patients with dementia, motor neuron disease, and movement disorders. *JAMA Neurol*. 2019;76:318-325.
3. Varhaug KN, Torkildsen Ø, Myhr KM, et al. Neurofilament light chain as a biomarker in multiple sclerosis. *Front Neurol*. 2019;10:338.
4. Kuhle J, Kropshofer H, Haering DA, et al. Blood neurofilament light chain as a biomarker of MS disease activity and treatment response. *Neurology*. 2019;92:e1007-e1015.
5. Sormani MP, Haering DA, Kropshofer H, et al. Blood neurofilament light as a potential endpoint in phase 2 studies in MS. *Ann Clin Transl Neurol*. 2019;6:1081-1089.
6. Kuhle J, Plavina T, Barro C, et al. Neurofilament light levels are associated with long-term outcomes in multiple sclerosis. *Mult Scler*. 2019;1352458519885613.

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