

The EPSMS Study: A Multiple Sclerosis Clinical Trial in Progress*

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Background

The EPSMS Study investigates use of state-of-the-art entire-body PET scans (EPS) with molecular imaging of the nervous system to evaluate both peripheral and central demyelination and remyelination in multiple sclerosis (MS). This study hypothesizes that the improved sensitivity and resolution of advanced PET scanners can detect demyelination not only in the brain and spinal cord but also in peripheral nerves, an approach that has not been fully explored in past conventional imaging for MS with MRI. The study employs FDA-approved PET amyloid imaging radiopharmaceuticals (F18-florbetapir, F18-florbetaben, and F18-flutemetamol) which also bind to myelin, enabling the assessment of demyelination and remyelination dynamics. Related radiotracers have shown promise in prior studies demonstrating quantifiable changes in myelin content and remyelination potential (Stankoff 2011; Glodzik et al. 2014; Veronese et al. 2015; Matías-Guiu et al. 2015; Bodini, Veronese, et al. 2016; Pietroboni et al. 2018; Bodini, Tonietto, et al. 2021). Future phases of the EPSMS Study will involve novel radiotracers to evaluate neuroinflammation and microglial activity. The EPSMS Study NCT04390009 was initially registered at ClinicalTrials.gov in 2020 with the protocol published in 2020 and amended in 2023 (Taswell 2020; Taswell 2023) but was then delayed with a hold on the start due to the COVID19 pandemic. The trial protocol emphasizes standardization of PET molecular imaging at multiple imaging sites to ensure consistent data acquisition across different scanners. If successful, the findings could support better patient care decisions, improve clinical trial outcome measures, and advance therapeutic evaluations for MS. This study represents a pioneering effort to apply entire-body PET molecular imaging for comprehensive monitoring of MS pathology for the entire nervous system.

Methods

The experimental paradigm involves an approach similar to that demonstrated for amyloid imaging tracers used for Alzheimer's disease and related disorders with safety of imaging results disclosure monitored with pre- and post-scan psychometrics (Taswell, Villemagne, et al. 2015; Taswell, Donohue, et al. 2018). The current phase of the EPSMS Study uses advanced PET-CT imaging to analyze the activity of myelin-binding radiopharmaceuticals in the nervous systems of patients with MS. This study aims (1) to assess the differences in uptake of the radiotracer F18-florbetapir in demyelinated and remyelinated white matter between MS patients and healthy controls, and (2) to explore the psychological effects on participants when informed about their imaging results. Participants will undergo PET-CT scans with the most

recent state-of-the-art high-resolution PET scanners at international imaging sites. The trial has started and several scans have been completed. A total of 20 participants (15 MS patients + 5 healthy controls) will participate in the initial phase of this study. Specific assessments include MS-related disability, psychological health (pre- and post-scan), and myelin-related changes in the brain, spinal cord, and peripheral nerve roots as visualized in the PET scans. Eligibility includes adults age 25–55 as control subjects with normal health or as MS patients diagnosed by credentialed neurologists with MS experience, and excludes individuals with complicating illnesses, recent medical procedures, or contraindications to medical imaging. PET scan images will be analysed to measure relative tracer activity levels in key regions, correlating these results with clinical symptoms, psychometrics, and with MS-related lesions observed in other imaging modalities (especially MRI) when available from the patients' medical records. Findings expected include (1) differences in radiotracer activity between MS patients and healthy controls, (2) identification of topographic variations in activity across regions of the central and peripheral nervous systems, and (3) an initial data repository with web-enabled workflow infrastructure to support future studies on the role of PET imaging for MS diagnostics, monitoring of disease modifying therapies, and future theranostics. All participants must consent to the study and can opt in/out of imaging results disclosure for neither, either, or both of gray and white matter results. Radiation exposure levels are minimal and within safety standards for the FDA-approved radiopharmaceuticals used. Potential risks include adverse reactions to the tracer, discomfort during imaging, and the possibility of unrelated incidental findings. The website EPSMS.brain-healthalliance.net serves as the publicly accessible management site for the EPSMS Study.

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