Title: Investigating neurological complication in patients with TTP and the implementation of quantitative myelin water imaging

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Structured Abstract:

Introduction: Thrombotic thrombocytopenic purpura (TTP) is a rare, life-threatening blood disorder. It is characterized by insufficient activity in ADAMTS13 (a protein to prevent blood clotting) which results in spontaneous blood clotting throughout the microvasculature. Other symptoms include kidney failure, low platelet count, and neurological changes (such as confusion and a higher likelihood of having a stroke or a seizure). Despite treatments which restore hemostasis, these neurological changes persist. The objective of this study is to observe brain changes over time in patients with TTP by using a comprehensive magnetic resonance imaging (MRI) protocol. A specific aim is to implement quantitative myelin water imaging, which was first validated in volunteers.

Methods: Individuals with diagnosis of TTP are included if they are ≥18 years and in remission, meaning no signs or symptoms of microvascular injury for at least 30 days. The 65-minute 3T MRI (Siemens mMR Biograph) includes 20 minutes for high-resolution qualitative acquisitions (including T1-weighted, T2-weighted, and diffusion-weighted images) and 45 minutes for quantitative acquisitions, featuring mcDESPOT (multi-component driven equilibrium single pulse observation of T1 and T2) for white matter imaging. 3 patients were scanned after the protocol was validated in 3 volunteers at two time-points. Interpretation of the qualitative MRI images was done by a neuroradiologist and mcDESPOT analysis to generate quantitative maps (T1, T2, and myelin water) was done by QUIT (Quantitative Imaging Tools).

Results: Upon neuroradiologist evaluation, two patients exhibit multiple non-specific spots in white matter regions of T2-weighted images, however no other qualitative images indicate a difference from a healthy brain. In validating the myelin water imaging, quantitative T1 and T2 maps were reproducible and provided accurate relaxation times by tissue, such as a T2 in myelin water of 10-40 ms. Myelin water maps are generated but require further processing steps including co-registration of T2-weighted volumes.

Discussion: These outlined white matter regions will be further analyzed by mcDESPOT to quantify the white matter by measurement of myelin. We will test the hypothesis that white matter decreases over time in comparison to age-matched healthy controls using Student’s t-test. Patients will continue to be recruited (to a sample size of 10) and follow-up scans will be at 6 and 12 months. To our knowledge, this is the first study of its kind and we hope to better understand these neurological changes in order to improve the quality of life of individuals who experience TTP.