Early diagnosis and treatment of neurodegenerative diseases is crucial to sustaining the quality of life of patients. Treatments that can slow down or arrest disease progression, generate the prospect for preventive interventions. Surrogate markers of disease progression are required for measuring treatment effects of the putative disease-modifying therapies that are under development.

Alzheimer’s disease (AD) is the most common cause of neurodegenerative dementia and is an ideal model for development of imaging biomarkers for neurodegenerative pathologies. In vivo quantitative analysis of different aspects of AD pathology is possible with the current MRI technology. Quantitative MR techniques are being evaluated to qualify as surrogate markers in AD. The features of an ideal imaging marker are: 1) detecting a fundamental feature of the neurodegenerative pathology, 2) being diagnostically sensitive and specific through validation in neuropathologically confirmed cases, 3) being precise with good test re-test reproducibility for monitoring the therapeutic effects on the pathology, 4) being available and accessible for multi-center studies.

Current standards for assessing the progression of Alzheimer's disease (AD) are clinical and neuropsychologic measures. The search for potential disease-modifying treatments however, has created a need for non-invasive markers that can measure the therapeutic effectiveness on biological disease progression. MR based volumetry techniques in AD may have enough power to measure the rate of structural change in the brain in a clinical trial setting ¹⁻⁴. The feasibility of MR based volumetry as a treatment outcome measure in AD was tested in multisite therapeutic trials ⁵, ⁶. Using a centrally coordinated quality control program for MRI, the hippocampal volume measurements were found to be consistent across sites, validating the feasibility of multisite acquisition MR based volumetry in AD. These studies however did not prove that MR based volumetry is a valid biomarker of therapeutic efficacy, because therapeutic efficacy was not demonstrated. The validity of MR based volumetry as a surrogate marker for therapeutic efficacy in AD needs to be tested in a disease-modifying drug trial with a positive outcome.

Other potential surrogate MR markers for various aspects of the neurodegenerative pathology include proton MR spectroscopy (¹H MRS) for biochemical changes, diffusion tensor imaging (DTI) and FLAIR imaging for white matter degeneration, arterial spin labeling (ASL) for perfusion and f-MRI for brain function. It is expected that, depending on the stage of disease progression, a combination of imaging markers will likely contribute to the best prediction model for the neurodegenerative pathology. Recent data suggest that this approach is already bearing fruit ⁷, ⁸.
References