**Pathological and MRI markers of deterioration**

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The reasons we keep inspecting samples of MS tissue, mainly in *post mortem* and sometimes in biopsy tissue, are manifold. Despite the availability of numerous disease models, the pathology of MS remains unique. Novel pathological insights (sometimes important rediscoveries of observations made many decades ago) include the significant degree of axonal damage and loss in acute inflammatory demyelinating lesions, the involvement of the grey matter, meningeal inflammation, and the non-lesional (diffuse) pathology of the MS brain. The pathology of disease deterioration in MS is a game of numbers: inflammation, the accumulation and severity of lesions, the loss of neurons and axons, gliosis – all these features can (some more straightforward than others) be quantified. However, 'deterioration' refers to a clinical scenario, and in order to use pathological observations for the benefit of people with MS (pwMS) translation into clinically applicable indices is required. The main tool for this purpose remains MRI. The interplay between pathological observation, and hard- and software development in MRI has resulted in (i) contrast mechanisms that can now be exploited for pwMS, such as susceptibility weighted imaging, (ii) the fine tuning of previously used indices for better assessment and monitoring of specific pathological features of MS, including quantitative techniques, such as magnetisation transfer, relaxation time measurements, diffusion and spectroscopy, and (iii) the current key measure of overall tissue loss and prediction of disability – atrophy.