Chapter 2.1. Can other image types be used for reliable whole-brain atrophy measurements in MS besides the gold-standard T1-weighted pre-contrast?

Chapter 2.2. What is the performance of FSL-BET in MS patients' images by comparison to a manual gold standard, and how does this performance vary with the value of the main BET parameter, “f”, the fractional intensity threshold? What is the effect of adding the main FSL-BET options (“B” – bias field correction and neck cleanup, “R” – robust brain center estimation or “S” eye and optic nerve cleanup) and of additional preprocessing strategies, namely of removing the neck slices, and of performing intensity inhomogeneity correction using N3 software?

Chapter 2.3. Can lesion-filling be performed in with co-registered WM lesion masks from 2DT2-weighted images instead of gold-standard 3D lesion masks? Does the resulting segmentation differ inside lesion areas, in other regions, or both?

Chapter 3. What is the pathological substrate of cortical volume loss as measured with MRI in MS?

Chapter 4.1. What is the prognostic value for 10-year disability in MS, of whole-brain atrophy, central brain atrophy and T2 lesion volumes, in a large MS patient group, taking into account disease type, disease modifying treatment (DMT) and initial clinical status?

Chapter 4.2. Do the three software packages (FSL, FreeSurfer and SPM) most frequently in MS GM atrophy literature, give consistent results of regional GM measurements in a large cohort of MS patients with similar disease duration?

Conclusions

Chapter 2.1. Brain atrophy in MS can be reliably be measured with SIENA(X) using other input image types, T1-weighted images with contrast enhancement, if consistently available, should be the method of choice. Otherwise, pseudo-T1 images or T2-weighted images can also be used.

Chapter 2.2. In MS, the removal of the neck slices, has a marked positive effect on the brain extraction quality. FSL-BET option “B” with f=0.1 after removal of the neck slices seems to work best.
for all acquisition protocols.

Chapter 2.3. In MS lesion-filling with lesion masks outlined on PDT2 images yields accurate GM atrophy quantification in MS. Without lesion-filling segmentation errors occur both within and outside the lesion area.

Chapter 3. In chronic MS neuronal and axonal pathology are the predominant pathological substrates of MRI-measured cortical volume.

Chapter 4.1. In MS early brain atrophy rates are related to subsequent long-term disability, and atrophy and lesion volumes have a complementary predictive value.

Chapter 4.2. Regional GM volumes in MS vary substantially with the software used, especially for cortical regions and to a lesser degree for DGM. Correlations with cognitive and clinical measures in MS should be interpreted with great caution.