Computing spinal cord atrophy using the Boundary Shift Integral a new feasible outcome for clinical trials

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Background: Atrophy measurements obtained from structural MRI are useful biomarkers of neurodegeneration. Spinal cord atrophy in multiple sclerosis (MS) has been shown to correlate with clinical disability but its measurements using MRI has been limited by poor reproducibility and responsiveness making difficult its application as outcome in clinical trials.

Aims: to demonstrate the feasibility of using Boundary Shift Integral (BSI) for computing atrophy in the spinal cord and introduce it as a potential outcome in MS clinical trials.

Methods: we included 10 healthy subjects (age: 45.5±8.9 years, gender 6F:4M) and 17 MS patients (age: 54.01±12.8 years, gender 9F:8M, including 6 RRMS, 4 PPMS and 7 SPMS). T1-weighted MPRAGE volume (1x1x1mm) at baseline and at 18 months was acquired using a 3T Philips scanner with a 16-channel neurovascular coil (which permitted coverage of the entire cervical spinal cord). One experienced observer manually outlined the SC between C2 and C5 at both time points. Then images were denoised, bias field corrected, straightened, rigid registered to the half-way space, symmetrical bias field corrected and finally we calculated the atrophy at intensity changes in the vicinity of the tissue boundaries using BSI. Moreover, in order to enable a fair comparison between methods, atrophy values based on cross-sectional area (CSA) were computed using the same manual masks.

Results: BSI and CSA atrophy results are annualised. Atrophy mean, standard deviation and confidence interval (CI) values for controls BSI=-0.01±0.13 CI(-0.09 to 0.07) and CSA=0.07±1.83 CI(-1.06 to 1.21), and patients BSI=-0.05±0.07 CI(-0.09 to -0.02) and CSA=-0.06±1.28 CI(-0.67 to 0.55). There is no evidence of differences in performance between the two techniques (p=0.87). Sample size with and without controlling for normal ageing were computed, for a hypothetical trial with 80% power at the 5% significance level and looking for 25% reduction in disease progression. Sample size without controlling for normal ageing BSI=465 vs CSA=108527, and with controlling for normal ageing BSI=675 vs CSA=22461.

Conclusion: we have demonstrated the feasibility of BSI for computing atrophy in the spinal cord, as a sensitive, quantitative and objective measure of longitudinal tissue volume change. Furthermore, BSI produces a significant reduction in sample sizes needed in clinical trials in comparison with CSA.

Disclosure

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