Segmentation of subtraction images yields improvement in reproducibility and sensitivity of lesion change measurements in MS.

Y. Duan[1,2], D. F. Tate[1,3], P. G. Hildenbrand[1,4], I. Csapo[1], D. S. Meier[1], and C. R. Guttmann[1]

[1]Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States, [2]Radiology, The Second Clinical College & The Second Affiliated Hospital, China Medical University, Shenyang, Liaoning, China, People's Republic of, [3]Pscyhiatry and Behavioral Medicine, Brown Medical School, Providence, RI, United States, [4]Radiology, Lahey Clinic, Burlington, Massachusetts, United States

Introduction:

Image segmentation has been widely used to measure lesion burden in MS, monitoring of plaque progression and assessing therapeutic response[1,2,3].Direct segmentation of lesion change based on subtraction of co-registered serial MR images has not yet been extensively studied, but promises to be a more robust and sensitive alternative to measuring disease progression on MRI. In this study, we assess the reproducibility of these two image analysis strategies by comparing their bias from a same-day scan/rescan data set: conventional **numeric difference** (ND) between total lesion volumes (using manually edited automated segmentation) from unregistered (native) MRI exams versus **segmentation of subtraction images** (SSI)). Furthermore, we calculated and compared average yearly change in MS lesion burden using each of these two methods. We hypothesize that subtraction imaging, which cancels stable anatomy, provides enhanced sensitivity to lesion burden change by identifying and quantifying new, enlarging and resolving MS lesions separately.

Methods:

Twenty-one MS patients (4 M, 17 F, 20 Relapsing/Remitting MS, 1 Secondary Progressive MS, mean age 43.6 years) were examined in this study. Each participant underwent MRI imaging on a 1.5 T GE Signa Scanner. Dual echo PD/T2 weighted MR images (TE=30/80 ms, TR=3000 ms, 192 phase-encoding steps, $0.93\times0.93\times3$ mm^3 nominal voxel size) were acquired and analyzed. Each patient was imaged twice with an inter-scan interval of between 1.5 and 4.7 years (Average ± SD=3.1 ± 0.86 years). Utilizing the same MRI protocol, we also obtained pairs of scan / rescan MRI exams (within 30 minutes) in 10 other MS patients. Template-driven segmentation (TDS+) [2,3] was performed and edited by an expert on each of the 62 native scans to obtain lesion volumes for each time-point. The ND of resulting lesion volumes was calculated. Following procedure was applied to obtain outlines of lesion changes (new lesions, enlarging lesions, and resolving lesions): each of the 31 patients' paired PD/T2W images were co-registered and intensity normalized [1]. Computer-assisted SSI was performed by an expert on images resulting from the subtraction of the registered and intensity-normalized PD pairs. SSI yielded separate label maps for new, enlarging, and resolving lesions. Net change in lesion load was determined from SSI results by subtracting the resolving lesion volume from the sum of new and enlarging lesions. Scan-rescan reproducibility was estimated by calculating the absolute lesion volume bias (average of lesion volume differences) for each method. Yearly rate of change in the 21 patient cohorts was expressed as percentage of baseline volume. One-tail pair-wise Student's t-test was performed to assess differences between ND and SSI results.

Results: The lesion volume bias from scan-rescan (N=10) was significantly lower for SSI (Average±SD= 0.15 ±0.27 cm^3) compared to ND (Average±SD=0.77 ±1.08cm^3) (p=0.025). The average yearly percent lesion volume change (N=21) was 10.82±16.82% (Average±SD) per year using ND, versus 28.00±44% (Average±SD) per year using SSI (p=0.022).

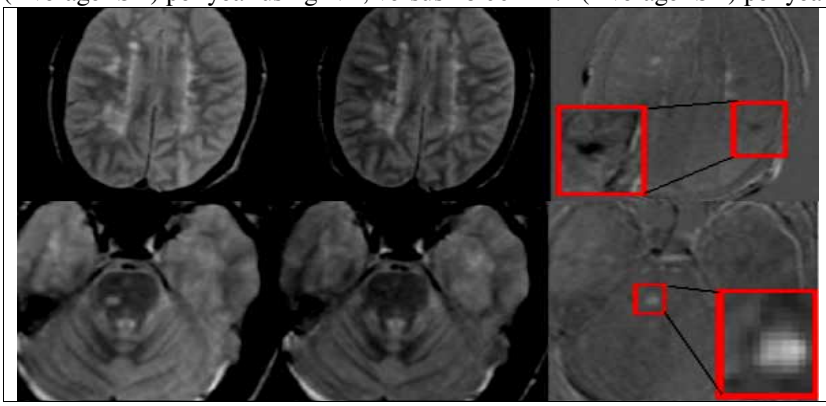

Figure:

Subtraction of PD images from a patient scanned at an interval of 4.7 years. Left column: second time-point images; Middle column: co-registered baseline images; Right column: subtraction images (time-point two minus baseline) highlighting both resolving and new plaques. Red boxes zoom-in on typical examples of resolving (upper) and new plaques (lower) detected by subtraction imaging.

Discussion:

SSI compares favorably to ND both in its reproducibility and sensitivity to change. Both methods were supervised and edited by the same expert radiologist (YD). The nearly three-fold increased detection of net change rate using SSI vs. ND is likely due to the added information presented by the subtracted images, as well as by sampling errors on images scanned at slightly different angles at different time-points. The latter sampling errors are likely to result in inconsistent lesion outlines by image segmentation, with the consequence that real net changes may be drowned by the relatively small real changes in lesion burden.

Acknowledgement:

This study was supported in part by the National Multiple Sclerosis Society (RG3574-A-1)

Reference:

1. Meier DS, Guttmann CR. Time-series analysis of MRI intensity patterns in multiple sclerosis. *Neuroimage* 2003; 20(2): 1193-1209.
2. Wei X, Warfield SK, Zou KH, Wu Y, Li X, Guimond A, et al. Quantitative analysis of MRI signal abnormalities of brain white matter with high reproducibility and accuracy. *J Magn Reson Imaging* 2002; 15(2): 203-209.
3. Warfield SK, Kaus M, Jolesz FA, Kikinis R. Adaptive, template moderated, spatially varying statistical classification. *Med Image Anal* 2000; 4(1):43-55.