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Impact of spatial distribution of T2 and T1 Lesion Load on Disability and Brain Atrophy

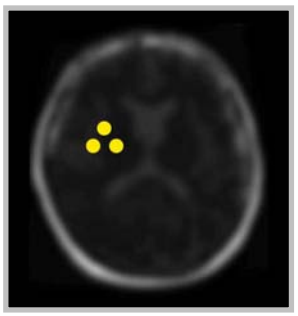
Objective: To examine the relationship between clinical disability, atrophy, and a variety of 3-dimensional quantitative lesion load measures incorporating both volume and spatial distribution information.

Background: Quantitative volumetric lesion load (LL) measurement in multiple sclerosis (MS) has consistently demonstrated limited utility in predicting clinical disability and brain atrophy. This may be due in part to the fact that volume measures alone do not adequately reflect the distribution in space of acute disease processes, yielding similar results for both tightly clustered lesions and widely dispersed lesions. Metrics taking spatial distribution (geometric size) into account may therefore be of great use in quantitative characterization of lesion burden, and may provide more clinically relevant results.

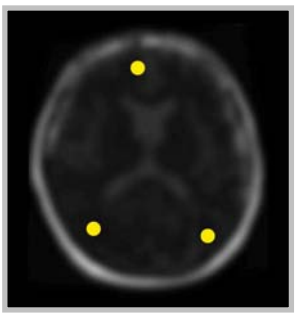
Design/Methods: We studied 301 patients with MS (mean age 46.8 +/- 10.1 years) using 1.5T MRI. Disease course was RR=192, SP=106, and RR/SP=3, with a mean disease duration of 14.3 +/- 9.2 years. Mean EDSS was 3.7 +/- 2.1. Lesion identification was performed using a highly reproducible previously published semi-automated edge-contouring technique. Volumes of both T2-LL and T1-LL were obtained, as well as voxel-wise lesion masks. Atrophy measures were performed with the Sienax software package, and brain parenchymal fraction (BPF) values were obtained. From these masks, the following distribution-based measures were obtained: spatial standard deviation (SSD, calculated as the mean Euclidian distance to the centroid), moment of inertia (MOI, calculated with each lesion voxel having a unit mass), Frobenius norm (FN, calculated as the Euclidian 3-norm), and centroid size (CS). With the exception of SSD, each of these measures incorporates both lesion volume and spatial distribution. Parametric and non-parametric correlations were used as appropriate to evaluate the relationship between these measures, EDSS, and BPF.

Results: With the exception of spatial standard deviation, all measures (including volume alone) showed significant correlations with EDSS. For T2-LL, CS showed a slightly stronger correlation with EDSS than LL alone (r=0.272 for CS vs. r=0.266 for LL), and all distribution measures with the exception of SSD showed a stronger correlation with BPF than LL alone (max r=0.458 for CS vs. r=0.448 for LL). For T1-LL measures, LL was the best predictor of EDSS, but as with T2-LL all distribution measures, with the exception of SSD, were more strongly correlated with BPF than LL alone (max r=-0.498 for CS vs. r=-0.487 for LL).

Conclusions: While EDSS does not appear significantly more dependent on distribution than on LL alone, higher levels of spatial distribution are associated with more pronounced brain volume loss. Furthermore, CS appeared to be the most sensitive of the various distribution measures.



Lesions closely grouped



Lesions distributed in