Aggregation of MRI biomarkers in Multiple Sclerosis clinical trials using geometric PCA

S. Rebbah[1,2], I. Berry[1,3], S. Puechmorel[2], F. Nicol[2], D. Delahaye[2], P. Maréchal[4]

[1]INSERM ToNIC (Toulouse Neuroimaging Center) ; [2] ENAC (Ecole Nationale de l'Aviation Civile) ; [3] CHU Rangueil ; [4] IMT (Institut de Mathématiques de Toulouse)

Magnetic resonance imaging (MRI) of the brain plays an important role in the diagnosis and the treatment of Multiple sclerosis (MS), an inflammatory, demyelinating disease that is characterized by the presence of multiple lesions in the central nervous system and clinically by relapses and accumulation of neurological disability.
Disability progression, unlike relapses, are poorly associated to macroscopic lesion progression and we still lack a simple and robust marker to implement in clinical practice. Since progression mechanisms are complex and diffuse, the identification of effective markers requires multimodal approaches to generate combined measures reflecting the respective weight of mechanisms leading to permanent disability.
Thanks to scientific advances, we have access to many MRI biomarkers such as Apparent Diffusion Coefficient ADC and the Fractional Anisotropy FA from the diffusion tensor Imaging, the Magnetization Transfer Ratio MTR from the Magnetization Transfer Imaging and Cortical Thickness CTH from T1-weighted images. But unfortunately, none of them individually have the power to reflect all the MS mechanisms.
The aim of this study is to propose a combined biomarker approach, with the goal to conclude more effectively on the effect of a treatment in a clinical trial.

The study is based on a clinical trial population composed of progressive MS patients receiving a high dose biotin (n=29) and progressive MS patients receiving a placebo (n=11).
In our study, the biomarkers ADC, FA, MTR and CTH are measured in the whole brain and are represented with histograms. We propose to work on the quantiles of the biomarkers. Each Biomarker histogram is represented by a set of 11 quantiles. To combine the biomarkers a Multiple Factor Analysis (MFA) is performed on the quantiles of the biomarkers histograms followed by a Hierarchical Clustering on Principal Components (i.e. linear combinations of the biomarkers) to classify the treated patients and the placebo patients. Rand Index (RI) is used to evaluate the clustering.
This poster will present some of the results of this approach.