

## Non-Gaussian diffusion MR maps of human brain

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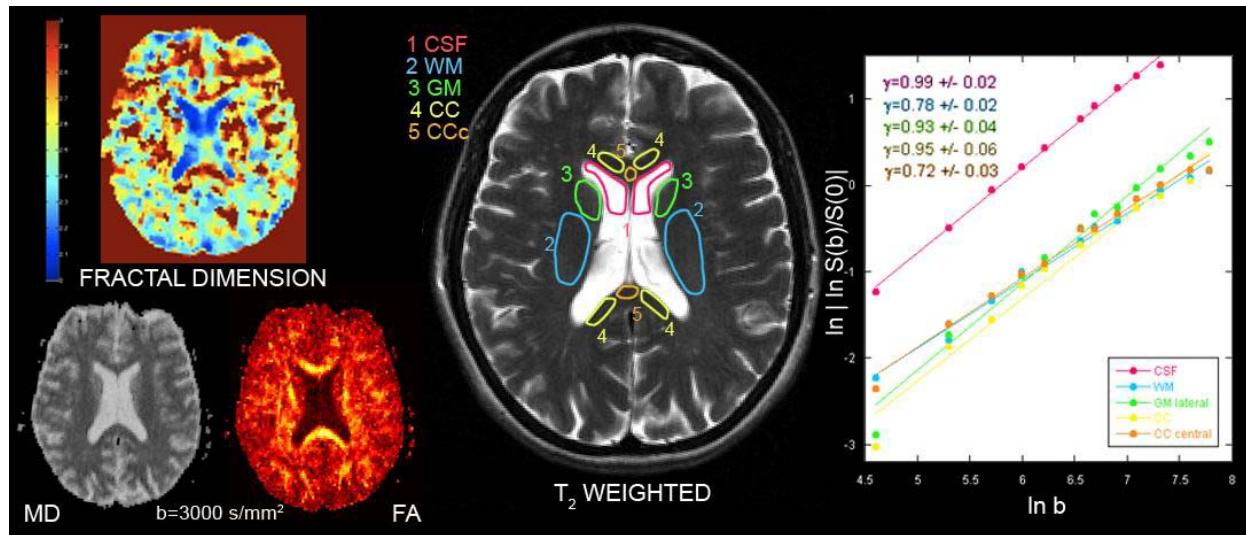
### Introduction

DWI and DTI methods are currently based on Einstein's classical equation for which the mean squared displacement of diffusing spins scales linearly with the diffusion time:  $\langle r^2(t) \rangle \propto t$ . This relation (known as "regular diffusion") assumes that the environment experienced by diffusing spins is locally homogeneous. However, the diffusion signal measured in biological tissues is extremely heterogeneous due to water compartmentalization, restriction and hindrance in the intra- and extracellular space. As a consequence, the diffusion environment experienced by diffusing spins in biological tissues is not locally homogeneous, and the mean squared displacement of diffusing spins scales as  $\langle r^2(t) \rangle \propto t^\gamma$  with the diffusion time, where  $\gamma$  values lower than 1 reflect the constrained diffusion regime described by a non-gaussian displacement probability density.

Conventional DTI methods are based on the Stejskal-Tanner analysis which predicts that diffusion weighted signal attenuation is dependent on  $b$  values through a mono-exponential decay function. Bennett et al.[1] proposed a new method to characterize the multiplicity of water pools in heterogeneous tissues, which is based on stretched-exponential behavior of the signal decay in the Stejskal-Tanner equation. The stretching parameter used to assess (to quantify) sample heterogeneity showed a high sensitivity in detecting early pathological changes in tumor tissues [2]. Moreover, Hall and Barrick [3] reported a simple method to obtain the stretching parameter  $\gamma$ , parametric maps representative of the mean  $\gamma$  value, and maps of the anisotropy displacement of  $\gamma$  values. These authors indicate also the possibility to estimate the fractal dimension  $dw$  from the relation:  $\gamma=2/dw$ , which is related to the complexity of the environment, or to the micro-structural complexity of the examined tissue. The goal of the present work, was to investigate the potential role of non-gaussian diffusion parametric maps in discriminating among the different cerebral tissues (i.e. white matter, WM; grey matter, GM; and cerebral spinal fluid, CSF) and in detecting differences into a selected tissue characterized by a known MR parameter such as mean diffusivity (MD) or fractional anisotropy (FA).

**Methods:** Two healthy subjects underwent a MRI examination on a 3T scanner (Siemens Allegra) including: dual-echo turbo spin echo (TSE, TR = 6190ms, TE = 12/109 ms); DTI protocol using diffusion weighted SE EPI (TR= 6s, TE=107 ms, bandwidth 1860 Hz/px, slice thickness 4mm, in plane resolution 1.8mm<sup>2</sup>) acquired in 6 non collinear directions at 16 different  $b$ -values: (0, 100, 200, 300, 400, 500, 700, 800, 1000, 1200, 2000, 2400, 3000, 4000, 5000) s/mm<sup>2</sup>. Twenty-four contiguous axial slices were collected with NS=2. A region of interest analysis (Fig.1, in the centre) was performed to assess regional values of  $\gamma$ . High spatial resolution T2-w images, co-registered to the diffusion weighted scans, were used to define, in each studied subject, ROIs in the head and splenium of the corpus callosum, in the corona radiata, and in the head of the caudate bilaterally. Two additional ROI were placed into the lateral ventricles. All ROIs were then transferred to the diffusion maps, and the relative quantities were derived.

**Results:** In Figure 1 (right side) there are reported the mean (SD)  $\gamma$  values obtained from the two studied subjects in the different ROIs. These values were higher in the CSF compared to the brain tissue, and in grey as compared to white matter. Moreover, corpus callosum, which is a white matter regions characterized by a more structured and oriented displacement of fibre tracts had the lowest  $\gamma$  values only in its central zone (orange ROIs\_5 in the figure). Conversely, the corpus callosum extremities (yellow ROIs\_4) had higher  $\gamma$  values compared to the central zone and the WM zone in blue ROIs\_2. Finally, the curve describing  $\gamma$  value changes as a function of  $b$  value increasing was different for gray and white matter. MD and FA maps were also reported in the left side of the figure, together with an example of fractal dimension (dw) map (blue colour:dw=2, red colour:dw=2.8).



**Discussion and Conclusion** This preliminary study shows a different pattern of  $\gamma$  values when considering WM and GM tissues. These quantities change differently in the two brain tissues as a function of  $b$  value increasing. As expected, this does not happen to the control measures obtained in the CSF in which  $\gamma=0.99$  reflects a Gaussian diffusion. Moreover, a different pattern of change is detectable for WM regions with a higher (i.e., corpus callosum) as compared to those with a lower level of fiber tracts coherency (i.e., corona radiata). These quantities have already shown the ability to detect changes in macroscopic pathological substrates, such as brain tumors [2]. More interestingly, they might be suitable for detecting subtle changes in neurological and psychiatric disorders which are not associated with a macroscopic tissue damage.

**References:** [1] Bennett KM et al. MRM 2003;50:727-734. [2] Bennett KM et al. MRM 2004;52:994-1004. [3] Hall MG, Barrick TR., MRM 2008; 59: 447-455