Anomalous diffusion γ-imaging model provides new information on spinal cord microstructure

A. Caporale[1,2], M. Palombo[2,3], S. Capuani[2,4]

[1]Physics Department Sapienza University of Rome, Rome, 00185, Italy
[2]CNR-ISC Roma Physics Department Sapienza University of Rome, Rome, 00185, Italy
[3]CEA/DSV/12BM/MIRCen, Fontenay-aux-Roses, France
[4]Center for Life NanoScience@LaSapienza, Istituto Italiano di Tecnologia, Rome, Italy

e-mail: alessandra.stella.caporale@gmail.com

Keywords: anomalous diffusion, magnetic resonance imaging, spinal cord, mouse

Currently, Diffusion Magnetic Resonance Imaging (D-MRI) is the only means able to measure the diffusion coefficient in vivo, with a completely non-invasive modality and without requiring exogenous contrast agents. Diffusion measurement of water molecules in human tissues, as a consequence of the interactions between molecules and obstacles that hinder and or restrict their motion, gives information about size, orientation and shape of cellular structures. Conventional diffusion techniques, such as diffusion tensor imaging (DTI) [1] are based on Gaussian diffusion.

However, diffusion in biological tissues is clearly non-Gaussian, due to macromolecular crowding, restricted and hindered diffusion in tissues. Recently, we have introduced an NMR method to experimentally quantify parameters coming from anomalous diffusion (AD) theory based on the framework of the Continuous Time Random Walk model [2,3]. Specifically, the γ parameter, which quantifies pseudo-superdiffusion provides important physiological and structural properties of tissues to increase the potential of D-MRI investigations [4].

In this work we used AD MRI to obtain structural information from a 4%glutaraldehyde-fixed mouse spinal cord (C57-BL6). In particular we would like to confirm previous results obtained in ad hoc phantoms [2,5] which underline that γ depends on both diffusion multi-compartimentalization and magnetic susceptibility differences ($\Delta\chi$) at the interface between different tissues. The experimental protocol performed at 9.4T, allows to extract, from a series of diffusion weighted images at different weights, the stretched exponent γ of the stretched exponential signal decay. The new metrics characterized by the mean value of γ (Mγ) and its anisotropy (Aγ) γ_{par} and γ_{ortho} (defined as the stretched exponents computed respectively in the direction parallel and orthogonal to the main white matter fibers direction), were evaluated and compared to the one obtained using conventional DTI parameters (MD and FA) and relaxometry (T2*), and to histological information [6-7].

Signal in each voxel was fitted to the expression [5] $S(q) = S(0)e^{-A(4\pi^2)^{\gamma}q^{2\gamma}\Delta}$, where $q = \sqrt{\frac{b}{4\pi^2(\Delta-\delta/3)}}$, $M\gamma = (\sum_{i=1,2,3}\gamma_i)/3$, $A\gamma = \sqrt{3\sum_{i=1,2,3}(\gamma_i - M_\gamma)^2 / 2\sum_{i=1,2,3}\gamma_i^2}$. Homogeneity of variances was tested by using Levene's test. Pairwise comparisons were made using a Welch ANOVA. Games-Howell corrections were performed to correct for multiple testing. Relationship between pairs of parameters were assessed with linear correlation analysis (Pearson's r coefficient). P-values <0.05 were considered statistically significant.

Differently from T2*, MD and FA maps, Aγ and γ_{ortho} significantly discriminates between different sub-regions of white matter. Differently from FA and according to T2*, Aγ shows a positive correlation with the myelin fraction and, unlike FA and T_2^*, a negative correlation was found between Aγ and the axon diameters axon density. Finally, Mγ shows a significant positive correlation with T2* in the gray matter.

The correlation between Aγ and myelin fraction is in agreement with recent results [8] that underline the existence of high anisotropy and $\Delta\chi$ variation along White-Matter fibers due to the presence of specific anisotropic rearrangement of fatty-acids constituting myelin sheaths. This characteristic of myelin fibers can be experimentally detected by AD γ-parameters, due to their dependence on both water multi-compartmentalization and $\Delta\chi$ at the interface between different compartments. In this contest, γ-imaging allows to go beyond the resolution of conventional DTI.

[1] P.J. Basser. NMR Biomed. 8 (1995). 333-344.
[2] M. Palombo et al., J Chem Phys. 135, 034504 (2011).
[3] S. Capuani et al., Magn Reson Imaging. 31 (2013) 359-365.
[4] S. De Santis et al., Magn Reson Med. 65 (2011) 1043-1052.
[5] M. Palombo et al. Journal Magn Reson 216 (2012).
[6] H.H. Ong et al., Neuroimage. 40 (2008) 1619-1632.
[7] H.H. Ong H et al., NeuroImage 51(2010) 1360-66.
[8] D.A. Yablonskiy and A.L. Sukstanskii, Magn Reson Med. 71 (2014)1956-1958.

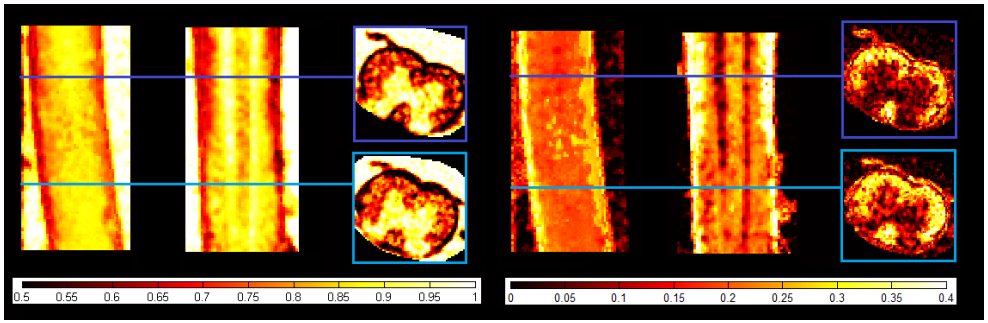

Figure 1. Parametric maps of γ-metrics in the sagittal, coronal and axial views of the mouse spinal cord. The mean value of γ (Mγ) and its anisotropy (Aγ) are shown, respectively, on the left and on the right. Please note the enhancement at the interface between the spinal cord and the PBS medium surrounding it, due to magnetic susceptibility differences. The spinal roots are visible in the axial AD-parameters maps.

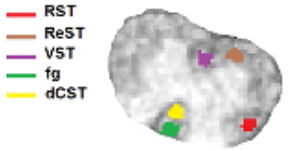

Figure 2. Selected sub-regions of white matter tracts.
RST RubroSpinal Tract
ReST ReticuloSpinal Tract
VST VestibuloSpinal Tract
fg funiculus gracilis
dCST dorsal CorticoSpinal Tract.

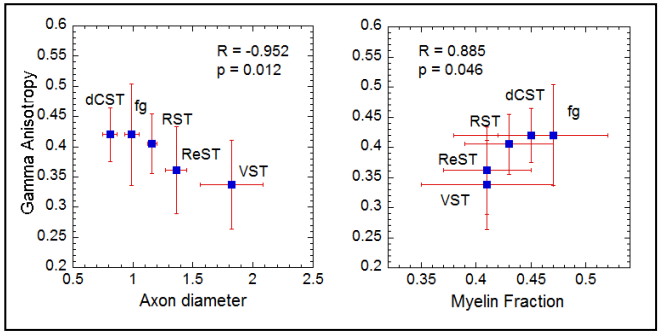

Figure 3. Anisotropy of the γ-parameter plotted against the mean axon diameter and the myelin fraction of each sub-region, with the values of the Pearson correlation coefficient and the significance level.