# MR MEASUREMENTS OF ANOMALOUS DIFFUSION INDICES &[ALPHA] AND &[GAMMA] BY MEANS OF PGSTE TECHNIQUES AT VARYING OF TIME AND OF GRADIENT STRENGTH IN PHANTOMS

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**Introduction:** In the last years, several experiments have demonstrated that water diffusion in biological systems is anomalous [1-3]. Translational self-diffusion in liquid systems can be measured by using MR acquisitions such as PGSTE [4]. The signal attenuation, which depends on both diffusion gradient strength g and diffusion time Δ, is the Fourier transform (FT) of the motion propagator (MP). When MP is Gaussian, the PGSTE signal attenuation follows a mono-exponential Stejskal-Tanner decay [4]. Conversely, when the motion is described by a non-Gaussian MP, the signal attenuation deviates from the mono-exponential decay [1-3].

This work introduces a novel method to better characterize and give more insides on anomalous diffusion processes of water in heterogeneous systems, by means of MR techniques. The approach is based on the theory of Continuous Time Random Walk (CTRW) [5], where the MP is defined as the solution of fractional diffusion equations. These equations introduce two parameters, the fractional exponent in time α and the fractional exponent in space γ, which are the time and space derivatives fractional orders. Briefly, to study sub-diffusive processes for which the mean-square displacement (MSD) of diffusing particles grows sub-linearly in time, it is possible to assume the following asymptotic behavior for the FT and MP:

$$W(k,t) \propto \exp(-K_\alpha k^2 t^\alpha) \qquad \text{when } k^2 << 1/(K_\alpha t^\alpha) \tag{1}$$

where k= 1/(2π)gδϒ and 0<α<1. Conversely, to study super-diffusive processes characterized by a divergence of the jump length variance, it is possible to use the following function:

$$W(k,t) \propto \exp(-K^{2\gamma} |k|^{2\gamma} t) \tag{2}$$

Where 0<γ<1. When a competition between subdiffusive and superdiffusive processes occurs, it is possible to introduce a pseudo-MSD as follows:

$MSD \propto t^{\alpha/\gamma}$ for which α/γ grater or smaller than 1 defines superdiffusion and subdiffusion processes respectively.

As a consequence, the specific anomalous diffusion behavior of water in each investigated sample, is described by the two α and γ indices that, in principal, reflect a different information on the microstructural rearrangement of investigated samples.

Aims of this work were: 1) to measure by means of MR diffusion based techniques the two parameters α and γ in a collection of samples characterized by different microstructural rearrangement, i.e. different geometric dimension in ordered beads samples, and different degrees of ordered samples; 2) to assess the type of microstructural information which can be derived from α and γ; 3) to assess whether an interplay exists between α and γ.

**Materials and Methods:** styrene beads suspensions (Microbeads AS, Norway) in water at high “sphere packing” were used to investigate anomalous diffusion of water. Beads characterized by mean diameters of 0.05, 6.0, 10, 15, 20, 30, 40, 80 and 140 micrometers, were used to produce phantoms in which water can probe microstructures dimension typically observed in biological tissues. Specifically, six 10mm capillaries were filled with mono-dispersed beads in de-ionized water and Tween 20 (samples: 0.005μm, 6μm, 10μm, 15μm, 20μm, 30μm), while two other capillaries were filled with poly-dispersed beads to obtain samples at different degrees of disorder. One of this was constituted of mixed beads sizes of 140+80+40+10+6 μm. To further increase the disorder, another sample was filled by 140+40+6 μm beads sizes. Finally, one sample with free water was also produced. All measurements were performed on a Bruker 9.4T Avance system, operating with a micro-imaging probe (10 mm internal diameter bore) and equipped with a gradient unit characterized by a maximum gradient strength of 1200 mT/m, and a rise time of 100 μs. A spectroscopic bipolar PGSTE with δ=4.4ms, g=0.10T/m (i.e. k=22481m$^{-1}$) TR=2.5s and 48 values of Δ in the range (0.020-1.0)s was used for collecting data to fit with equation [1] and for extracting the α value. *Vice-versa*, a spectroscopic bipolar PGSTE with Δ/δ=80/4.4ms, TR=2.5s and 48 gradient amplitude steps g from 0.026 to 1.02T/m was used to collect data fitting with the function [2], to obtain a measure of the γ value.

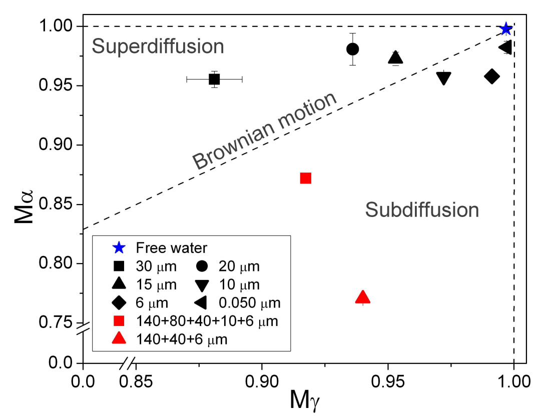


**Fig.1** Mean α (Mα) versus Mean γ (Mγ) graph for ordered samples including monodispersed beads in water (black symbols) and for disordered samples filled by polydispersed beads at different sizes in water (red symbols). Blue star indicates the control sample with free water. Dashed line represents the Brownian (or Gaussian) diffusion region.

**Results:** Mean values of α and γ measured along x, y and z axes, for all nine samples investigated, are displayed in Fig.1. As expected, Mγ and Mα of free water sample are both equal to 1. Mγ increases as beads sizes decrease. Conversely Mα does not depend on beads sizes. Finally, Mα decreases as the degree of the disorder increases, while Mγ does not discriminate between ordered (black points in Fig. 1) and disordered (red points in Fig. 1) samples.

**Discussion:** Experimental data illustrated in Fig. 1, demonstrate that anomalous diffusion indices α and γ reflect some additional microstructural information which cannot be obtained using conventional diffusion procedures based on Gaussian diffusion. Specifically, Mα and Mγ measurements are not correlated to each other. As a consequence they provide different types of information on the microstructural media in which water diffuses. Mα can provide information on the degree of order and/or disorder within the investigated systems. Indeed, the six monodispersed samples constituted by an ordered distribution of equal size beads are characterized by an equal value of Mα. Conversely, the disordered samples including beads with different sizes are characterized by lower values of Mα. Mγ values show an exquisite sensitivity to discriminate the pore sizes due to packing beads in which water diffuses. This observation, confirms our recent findings obtained from brain investigations in vivo [3]. However, in Mα versus Mγ graph, the scattering of the ordered samples points from subdiffusion to superdiffusion zones depending on beads size, needs further investigations.

**Conclusion:** This work experimentally challenged the prediction of the theory illustrated by Metzler et al [5] which is based on CTRW model. α and γ indices were measured (by PGSTE technique) and correlated each other for the first time. Compared to methods based on conventional diffusion, the new approach we propose here, provides some additional information on the microstructural rearrangements of media in which water diffuses. In particular, Mα shows a peculiar ability to reflect the degree of structural disorder, and might provide a new source of contrast different from that of conventional diffusion approaches, when applied to the investigation of biological tissues.

**References:**[1] Özarslan E et al. JMR 2006;183:315-323. [2] Assaf Y, Cohen Y. JMR 1998; 131:69-85. [3] De Santis et al. MRM 2010 in press.
[4] Stejskal EO, Tanner JE. J Chem Phys 1965;42:288–292. [5] Metzler R, Klafter J. Phys Rep 2000;339:1-77.