Internal gradients affect the γ value arising from Anomalous Diffusion stretched exponential model

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Introduction:
The departure from purely mono-exponential decay (S(b)=S(0)exp(-bD), due to PFG (Pulse field gradient) signal as a function of the b-value increasing observed in biological tissues, prompted the search for alternative models to characterize anomalous dynamics of water diffusion. Several approaches have been proposed in the last years, including the so-called anomalous diffusion stretched exponential model, in which γ is the stretch parameter arising from fitting the stretched function $S(b)=S(0)\exp(-(bD)^{\gamma})$ to PFG data. Although this is an empirical approach, the stretched exponential method has been already used to investigate healthy human brains, showing the ability of γ maps to discriminate between different brain structures on the basis of their microstructural complexity[1-3]. However, the exact meaning of the γ parameter still needs to be fully understood, especially with respect to its ability to discriminate between different tissues for which no significant differences in Mean diffusivity (MD) can be observed.
In this work we investigated the γ parameter by means of both Spectroscopic and Imaging version of Pulse gradient Stimulated Echo (PGSTE) sequence in controlled phantoms comprised of monodispersed and polydispersed micro beads in water solution. Specifically, we tested the influence of the internal gradient (G_{int}) due to the magnetic susceptibility difference between diffusing water and obstacles, with respect to the capability of the γ parameter to discriminate between structures characterized by different geometrical dimensions.

Materials and Methods:
Phantoms used in spectroscopic experiments: styrene beads (Microbeads AS, Norway) characterized by mean diameters of 6.0, 10, 15, 20, 30, 40, 80 and 140 micrometers were used to perform phantoms in which water molecules probe microstructures with the dimensions typically observed in biological tissues. Eight 8mm capillaries were filled with monodispersed beads in de-ionized water and Tween 20. The magnetic susceptibility difference $\Delta\chi_m$ between polystyrene micro-beads and water is approximately equal to 1.6 in SI.
Phantom used in imaging experiments: Microcapillaries with 0.7mm inner diameter were filled with distilled water (two capillaries), with styrene 6 μm beads monodispersed in water (five capillaries). These eight microcapillaries were immersed in a 8mm NMR tube containing 10μm packed beads in water (see Fig. 1a).
All measurements were performed using 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 PGSTE sequence (with Δ/δ=40/4.4ms, diffusion gradients g along x,y and z axis, TR=3s, NS=8) using 32 gradient amplitude steps from 0.6 to 180 mT/m was used to obtain Mγ. Moreover a spectroscopic Spin Echo (SE) sequence (TR=1.5s, NS=8) with N=64 data points (corresponding to 64 echoes refocusing every 2ms from 1ms to 125 ms) was used to extract G_{int} from SE decay as previously described [4].
An imaging version of PGSTE sequence with Δ/δ=40/4.4ms, diffusion gradients along x axis, TR=3s, slice thickness 1mm, FOV=8 mm, and 10 values of g from 28 to 224 mT/m (i.e. b values range from 500 to 6500 s/mm2, plus b=0) was used to obtain γ maps along x axis. T2*w images at different TE were also collected.

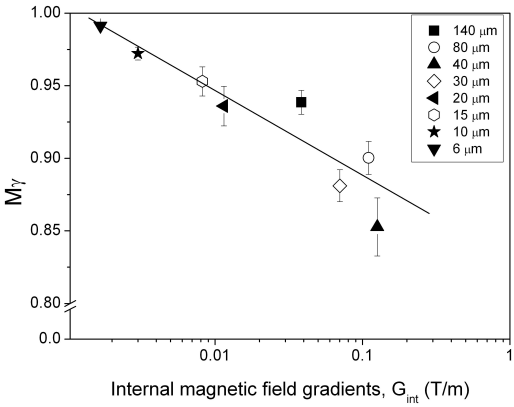

Fig. 1 Mean γ values (Mγ) vs internal magnetic field gradient strenght G_{int} in T/m for eight different styrene suspension of monodispersed beads characterized by the sizes displayed in the right side insert.

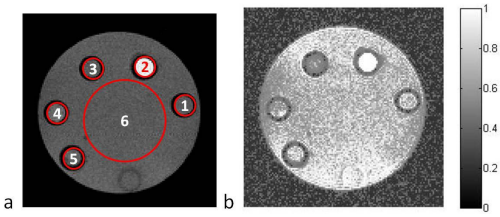

Fig.2 T2*-w image (a) and γ map (b) of the phantom characterized by different microstructural rearrangement. Capillaries marked in red from 1 to 5 are filled with microbeads of 6μm (1), free water (2), mixed microbeads (3), 6μm beads (4) and 10 μm beads. Moreover ROI 6 indicates 10 μm beads zone. Mean γ values measured in these ROIs are equal to: 0.71(1), 0.98(2), 0.56(3), 0.70(4), 0.77(5), 0.76(6).

Results: Mγ as a function of G_{int} for all the investigated phantoms is displayed in Fig. 1 (in logarithmic scale). The graph clearly shows that Mγ strongly depends on G_{in} measured by SE sequence. Specifically the higher the internal gradient, the lower the Mγ value. Moreover, each phantom characterized by mono-dispersed micro beads with a well defined diameter, can be identified by a well defined Mγ value. T2*-w image and γ map of an heterogeneous phantom are shown in Fig. 2a and Fig. 2b respectively. As expected γ-image contrast is different from that of T2*image. In particular, γ value is approximately equal to 1 in free water capillaries, while it assumes different values lower than 1 in each phantom zone characterized by a different beads size (see figure 2).

Discussion:
This work has investigated the dependence of γ stretch exponent parameter on internal gradients. Experimental results displayed in Figs. 1 and 2 demonstrate, for the first time, that γ value depends on the strength of the internal gradients which are present at the interface of regions with different magnetic susceptibility. Specifically, as γ value quantifies the departure from the purely monoexponential decay of water diffusion in heterogeneous systems, our findings highlight a strong correlation between the increase of G_{int} strength and the increase of anomalous diffusion behavior of diffusing protons.

Conclusion:
Spectroscopic and Imaging data illustrated here, propose a new interpretation for the γ parameter arising from Anomalous Diffusion stretched exponential model [1-3]. Specifically, we suggest that the ability of γ to discriminate between different brain structures on the basis of their microstructural rearrangement, can be due to its ability to probe differences in magnetic susceptibility, at a microscopic scale.

References:
[1] Bennet KM et al. MRM 2006;56:235-240. [2] Zhou, XJ et al. MRM 2010;63:562-569**.** [3] De Santis et al. MRM 2010 in press. [4] De Santis et al. Phys Med Biol 2010;55(19):5767-5785.