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Measurements of diffusion at short and long diffusion times at 17T in the rat brain *in vivo* and postmortem using OGSE and PGSE methods and a biexponential model

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PURPOSE: Diffusion MRI provides information on obstacles encountered by water molecules, if an adequate model is used. The biexponential model assumes the presence of fast and slow water pools, but their nature has remained elusive. The limitation of most studies carried out on clinical scanners is the necessity of using long diffusion times, resulting in averaging effects. The Oscillating Gradient Spin-Echo (OGSE) approach allows very short diffusion times to be reached. In this work we compare OGSE with standard Pulsed Gradient Spin-Echo (PGSE) method for studying the dependence of the diffusion parameters on the diffusion time.

MATERIALS AND METHODS: Images were obtained for 30 Male Wistar rats at 17.2T (Bruker) using PGSE and OGSE sequences. Diffusion times ranges from 1.9 to 40 ms. 40b values up to 4000 s/mm^2 were acquired to fit data according to: $S(i)/S0 = [f_{fast}*\exp(-bD_{fast}+(1-f_{fast})*\exp(-bD_{slow})]$ using Levenberg-Marquardt algorithm. Data were acquired in vivo and after the animals were sacrificed as a global ischemia model.

RESULTS: An overall ADC decrease with the increase of diffusion time was observed. In alive rats, f_{slow} increased dramatically with the diffusion time from 11% to 39% for 1.9 ms and 40 ms, respectively, while D_{slow} and D_{fast} remained constant. Upon death the f_{slow} became higher and kept increasing with diffusion time.

DISCUSSION: The global ADC decrease with the diffusion time increase, was explained by a dramatic increase of the slow pool fraction, and not by changes in the fast and slow diffusion coefficients. These results rule out the view that the slow and fast fractions correspond to physical compartments, such as the intra- and extra- cellular compartments. Instead, they are more functional in nature, with the slow pool originating from water molecules bound to or interacting with obstacles, such as membrane surfaces. The slow fraction increased also upon death, related to the cytotoxic edema with cell swelling.

CONCLUSION: The OGSE approach has a potential to clarify water intrinsic diffusion mechanisms in tissues. However, for clinical applications, long diffusion times could be more relevant, since while f_{slow} and membrane interactions increase we can better investigate cell swelling, cell proliferation and anisotropy.