Mapping Intracellular Exchange Times with Diffusion Weighted Imaging

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Introduction:

Diffusion weighted NMR-experiments over a large range of b-values result in a multi-exponential signal decay for biological samples as cell cultures or organic tissue. The multi-exponentiality reflects structural information on the scale of cell dimension. However, as the signal decay depends on many physiological properties, the interpretation is a complex multi-parametrical problem and the quantification of a single parameter as cellular volume fraction, extracellular tortuosity, membrane permeability, transmembrane water exchange rates etc are difficult. Recently, a method was analyzed that enables the determination of intracellular exchange times τ_{in} [1] and was successfully applied to rat brain tissue [2]. However, a drawback is its poor spatial resolution as it consisted of a localized spectroscopic ^{1}H DW-STEAM sequence on a large volume. Following a study that tries to overcome this restriction [3] in this contribution intracellular exchange maps were obtained by combining this method with imaging techniques. The maps demonstrate that spatial resolution is valuable as they reveal distinct regional differences in τ_{in}.

Materials and Methods:

Experiments were carried out on a Bruker Biospec system 4.7T/40cm. Post mortem measurements were performed on 3 male wistar rats sacrificed by a halothane overdose. The brain was imaged using a U-FLARE sequence. The matrix size was 32x32, FoV 32x32 mm^2, slice thickness 3 mm. Data were acquired with a receiver bandwidth of 10 kHz. The measurement was averaged 30 times with a TR of 3.2 sec. The diffusion weighted module consisted of a stimulated echo with diffusion gradients applied after the 1st and the 3rd RF pulse with duration of 5 ms and a constant amplitude of 67.6 mT/m in 3 directions simultaneously (cg-experiment, cg: constant gradient). The diffusion time t_D was varied from 533 to 953 ms by increasing the mixing time TM between the 2nd and 3rd RF pulse. This results in b-values between 13075 and 23375 s/mm^2. Due to the successive change of TM, a different T_1-relaxation is superposed on each of the 8 diffusion weighted images. This effect was corrected with a supplementary measurement for normalisation which had identical pulse timing but minimum gradients of 5 mT/m necessary for spoiling.

Performing cg-experiments in rat brain over a large range of diffusion times the signal decay converges to a long time limit [1, 2]:

$$D_B \rightarrow 1/q^2\tau_{in}, \qquad [1]$$

where D_B is the apparent intracellular diffusion coefficient which is attributed to the slowly decaying signal component and $q^2 = \gamma^2\delta^2 g^2$ is the effective gradient strength. Thus, for long diffusion times the intracellular water component becomes independent of the intracellular self-diffusion coefficient, but solely depends on the transmembrane water flux. Eq. [1] is applicable only when the extracellular water has no or negligible contribution to the slowly attenuated signal component. According to [2] the experimental setup with gradient strength of $q^2 = 24.5\times10^3$ mm^{-2} used here meets this requirement. Under this condition the signal Ψ obeys the relation $\Psi \sim \exp(-t_D / \tau_{in})$ and τ_{in} can be determined by linear regression from the slope of $\ln\Psi$ as a function of t_D.

Results:

The intracellular exchange times τ_{in} show a distinct regional variation over the brain which is similar in both hemispheres. In cortical areas τ_{in} varies from 220 to 350 ms and is much faster than in sub-cortical white matter areas, where the exchange time is slow with a maximum exchange time of 684± 39 ms in the right and 673± 48 ms in the left hemisphere. Thus, the regional difference of τ_{in} exceeds more than 300%.

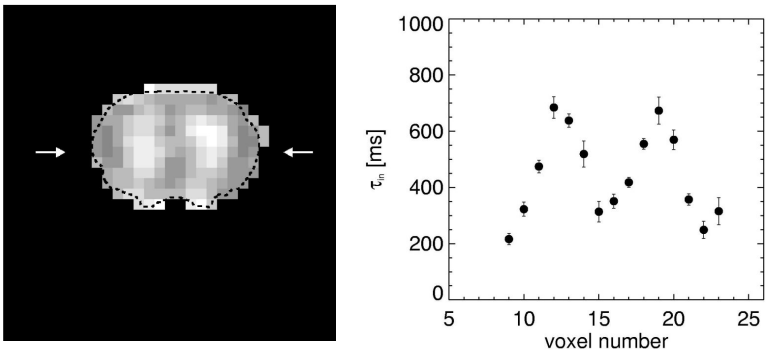

Fig 1: Left: Image of the intracellular exchange times of a post mortem rat brain. Brighter intensities represent slower exchange. The dotted line indicates the contour of the skull. The profile of the voxel row marked with arrows is given in the right plot.

The values are similar to those published in [2] (578 ± 20). There, a voxel was positioned in a sub-cortical area, but as it was of a size of 5x5x5 mm^3 it comprised also regions with shorter exchange times. This might explain why the value given there is smaller. Quirk et al published 550 ± 272 ms. This value was obtained with different NMR technique [4]. The region of interest encompassed parts of the thalamus and striatum and was of such an extension that averaging effects might also explain the lower value found there.

Conclusions:

It is shown that it is possible to combine a diffusion weighted cg-experiment of very large b-values with an imaging technique to acquire maps of transmembrane water flux. The spatial resolution is sufficient to identify distinct regional differences of the exchange times for a rat brain. The maps reveal a strong variation of τ_{in} of more than 300% over the brain. The intracellular exchange observed in cortical areas is fast (220 - 350 ms) while for sub-cortical regions it is slow with a maximum of 680 ms.The results are in agreement with other published values obtained with a lower resolution.

References:

[1] C. Meier et al, MRM 50: 500-509 (2003), [2] C. Meier et al, MRM 50: 510-514 (2003), [3] J. Pfeuffer et al, MRI 16 : 1023-1032 (1998), [4] J. D. Quirk et al, MRM 50 : 493-499 (2003)