Probing the vitality of yeast suspensions by Double Diffusion Weighted MRI

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Target audience: Researchers interested in diffusion MRI or in water exchange in biological systems.

Purpose: The aim of this work was to test double diffusion weighted imaging as a means to determine apparent exchange rates and to evaluate its ability to monitor the vitality of cell suspensions as a first step towards application in vivo.

Introduction: The Filter Exchange Imaging (FEXI) sequence has recently been introduced as a new approach in diffusion weighted MRI [1,2]. It allows one to measure a new functional tissue parameter, namely the Apparent Exchange Rate AXR. The AXR can be considered a measure for the exchange rate between intra- and extracellular water, which is directly related to the integrity of the cell membranes. The technique thus holds great promise for diagnostic and treatment monitoring purposes in diseases affecting the cell membrane (e.g. brain tumors [3]).

Material and Methods: A schematic representation of the developed pulse sequence is shown in Fig.1. A first diffusion weighting with constant b-value (b_f) serves as a low pass filter suppressing the fast diffusing part of the signal. Its effect on the ADC is described by the filter efficiency $\sigma = 1 - ADC(t_m = 0)/ADC_{eq}$. During the variable mixing time t_m, the apparent diffusion coefficient (ADC) returns to its equilibrium value (ADC_{eq}): $ADC(t_m) = ADC_{eq}(1 - \sigma e^{-AXR\, t_m})$.
To verify this method, bottle phantoms filled with mixtures of yeast and water in different concentrations were used (mass ratio yeast/water = 1/1; 1/2; 1/3). For these phantoms, the AXR was determined at various days over a period of three weeks with different values for the filter strength (b_f = 0, 900 and 1500 s/mm²). Images were acquired at 1.5 T (Magnetom Avanto, Siemens Healthcare, Erlangen) for three diffusion directions, with TE_f =60 ms, TE=80 ms, Δ_f=Δ=26.38 ms, δ_f =δ=22.96 ms and an in plane resolution of 3.75x3.75 mm². For the analysis, the directions and afterwards the signal in a region of interest were averaged.

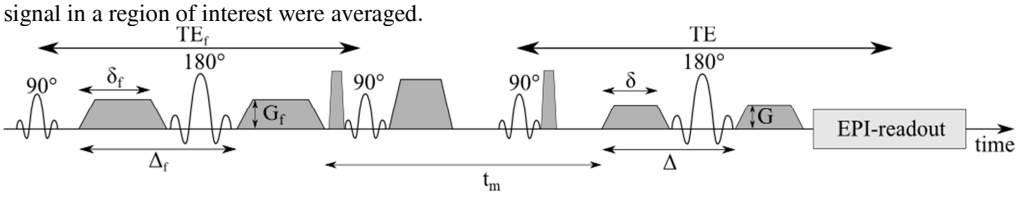

Fig.1: Schematic representation of the used FEXI-sequence. The additional filter block before the standard diffusion sequence allows to gain information about water exchange.

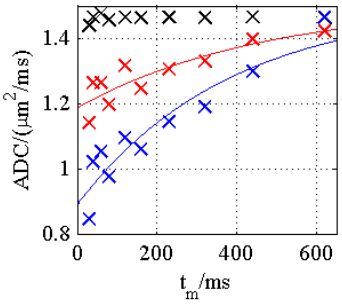

Fig.2: ADC vs t_m measured for different filter values in the 1/1 phantom. Black: b_f=0 s/mm², red: b_f=900 s/mm², blue: b_f=1500s/mm²

Results: The AXR could be detected successfully for all yeast concentrations (Fig.2). The AXR increases slightly for lower concentrations of yeast (Fig.3), but error margins are substantial. The AXR remains approximately constant until an age of two weeks is reached. Then it starts to increase and show higher variations for the 1/2 yeast/water concentration (Fig.4). Remarkably, no such rise is seen in the 1/1 phantom. The filter efficiency σ reaches its peak at the age of 10 days for the 1/2 phantom and continuously decreases afterwards (Fig.5). The maximum of σ is shifted to later times for lower yeast concentrations. Dying of the yeast was visibly observable by a color shift of the yeast solution towards reddish and by the onset of an intense smell of hydrogen sulfide. Those indicators were evolving concurrently with the change of FEXI parameters. The results shown in Fig. 3-5 were acquired with b_f =900 s/mm². This b_f was chosen since it is applicable for potential future in vivo applications.

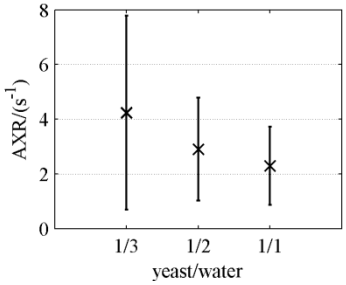

Fig.3: Dependence of the AXR on the yeast concentration (1 day old yeast)

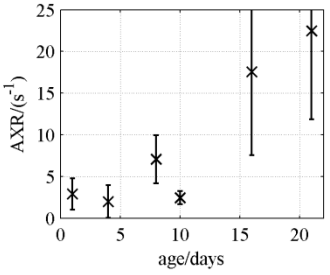

Fig.4: Time evolution of AXR in the 1/2-phantom

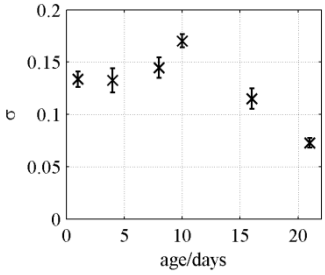

Fig.5: Time evolution of the filter efficiency in the 1/2-phantom

Discussion: The AXR values measured in fresh yeast are above those stated for a yeast/water concentration of 2/1 in [1], which supports the trend suggested by Fig.3. The discovered connection between cell viability and FEXI parameters supports the claim that FEXI holds the potential of obtaining new information on water exchange through membranes. While further experiments on understanding the mechanisms behind the AXR, like the dependence on diffusion time, are necessary, improved hardware and sequence techniques might enable FEXI to become a viable tool for improving the understanding of biological /pathological processes that are related to membrane integrity.

Conclusion: FEXI experiments on yeast suspensions were performed successfully and the FEXI parameters, in particular the filter efficiency, were good indicators of the cell vitality.

References:

[1] Lasič *et al.*MRM 2011;66:356-365.
[2] Callaghan *et al.* J. Chem. Phys.2004; 120:4032-4038
[3] Nilsson *et al.* MRM 2013; 69:1572-1580