2-Deoxy-D-Glucose CESL MRI in Rat Stroke Models

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INTRODUCTION: The disruption of glucose metabolism stands as a pivotal feature in the pathology of stroke.[1] Consequently, methods enabling the visualization of glucose dynamics and distribution hold promise as biomarkers for assessing disease severity and therapeutic efficacy. This study endeavors to establish a novel protocol for evaluating glucose metabolism in a rat stroke model through chemical exchange-sensitive spin-lock (CESL)[2-5] MRI of the glucose analogue 2-deoxy-D-glucose (2DG).

METHODS: 12 male Wistar rats (280-320 g, mean age ~8 weeks) were anesthetized using isoflurane and underwent 90 min filamentous left middle cerebral artery occlusion (MCAO). Directly after reperfusion, rats were imaged at a pre-clinical 7T MRI (BioSpec 70/20 USR, Bruker, Ettlingen, Germany). The protocol consisted of anatomical T2-weighted MRI, diffusion MRI (dMRI) to measure the apparent diffusion coefficient (ADC), FAIR MRI to measure cerebral blood flow (CBF) and a series of 35 2DG-CESL MRI scans (13 spin lock times (TSL), 1:26 min per scan, injection of 1 g/kg 2DG i.v. after scan #5). CESL MR images and a rat atlas were co-registered to the first image and $R_{1\rho}$ maps were generated using a mono-exponential fitting model.

RESULTS: The voxel-wise change of $R_{1\rho}$ after *i.v.* 2DG injection compared to the mean value before injection ($\Delta R_{1\rho}$) shows a clear increase in normal tissue and a decrease in damaged tissue as shown exemplarily for the lesion core (defined on ADC map) in Figure 1A. The quantification results for ADC, CBF and late $\Delta R_{1\rho}$ for the ipsilateral lesion core, hypoperfused tissue (CBF), penumbra (CBF/ADC mismatch), in the most affected anatomical region (striatum) and in the corresponding contralateral regions are shown in Fig. 1B, which allows for a direct comparison of the proposed biomarker $\Delta R_{1\rho}$ with respect to classical MRI biomarkers of stroke.

DISCUSSION: The continuous increase of $R_{1\rho}$ observed in the hemisphere opposite the stroke aligns with previous findings in healthy tissue[2-5], indicating the anticipated accumulation of 2DG, which is metabolically trapped within cells similarly to [18F]Fluorodeoxyglucose. The slight decrease in the ipsilateral ROI is likely due to reduced transport and uptake of 2DG and the simultaneous onset of anatomical changes in the stroke-affected area. The quantitative analysis shows that late $\Delta R_{1\rho}$ might provide additional, valuable information compared to traditional ADC and CBF measurements.

CONCLUSION: We established a protocol combining CESL, FAIR and diffusion MRI in a rat stroke model and could show that CESL MRI of 2DG provides a biomarker of disturbed glucose uptake after stroke with high effect to noise ratios. We expect that 2DG-CESL MRI might be able to validate or falsify newly introduced concepts of defining the penumbra.

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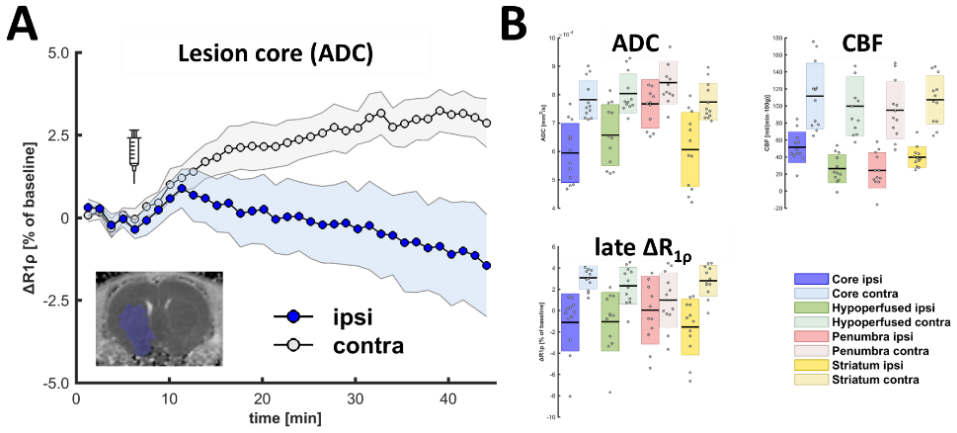

*Figure 1: **A**) 2DG uptake measured via $\Delta R_{1\rho}$ (voxel-wise change of $R_{1\rho}$ compared to mean baseline) in ipsilateral lesion core (ADC) and a mirrored contralateral ROI. Mean values across all (n=12) animals are shown. Shaded area corresponds to 95% CI. **B**) Quantification of ADC, CBF and late $\Delta R_{1\rho}$ (mean of last 5 timepoints) in lesion core (ADC), hypoperfused tissue (CBF), penumbra (CBF/ADC mismatch), the most affected anatomical region (striatum) and corresponding contralateral regions.*