Glucose assessment on a clinical 3 T MRI scanner using a customized multi-shot CEST-MultiFLASH sequence

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INTRODUCTION:

The standard diagnostic procedure for acute renal allograft rejection (AR) after kidney transplantation is currently an invasive kidney biopsy as non-invasive imaging methods have yet to be clinically established. However, studies in animal models have demonstrated that glucose weighted chemical exchange saturation transfer (glucoCEST) can also be used to assess AR. [1] The aim of this study is to develop a suitable CEST sequence on a clinical MR scanner both on phantoms and humans and to establish a glucoCEST contrast analysis pipeline which can be easily integrated into the clinical routine.

METHODS:

The developed multi-shot CEST-MultiFLASH sequence combines a CEST preparation module followed by several 2D FLASH modules for imaging, scanning the k-space non-linearly and representing an accelerated version of the sequence presented in Ref. [2]. All measurements were performed on a 3 T PET/MRI (Siemens Biograph mMR VE11P) using a 6-channel mMR body coil and a 24-channel mMR spine coil. Standard parameters for the CEST module were 5 Gaussian saturation pulses with 100 ms pulse width and 1 ms inter-pulse delay, 129 CEST frequencies between ±8.1 ppm, 4 reference measurements at ±32.5 ppm and 32 measured k-lines per shot; parameters for the FLASH part were TE/TR/α 3.5ms/10ms/15°, acq. Matrix 256×256, voxel size 1.56×1.56×5mm³. For phantom solutions glucose was dissolved in DPBS puffer solution within a concentration range between 0 and 100 mM. Area under the curve (AUC) and full-width half-max (FWHM) maps of the MTR-spectra (magnetization transfer ratio) were calculated using custom software, with further data analysis performed using Fiji ImageJ and OriginPro.

RESULTS:

In the MTR-spectrum, it is evident that the distinct glucose resonances at 0.6, 1.3, 2.2 and 2.9 ppm cannot be separated spectrally (Fig. 1). Nevertheless, the FWHM shows a dependence on the glucose concentration x in the form $y = A_1 + (A_2 - A_1)/(1 + 10^{(\log(x_0)-x)p})$ and the AUC in the form $y = A_1 - A_2 \exp(-kx)$, where A_1, A_2, x_0, p and k denote free parameters. A higher B1 field leads to an improved sensitivity for glucose (Fig. 2), but technical limitations of the clinical PET/MRI used prevent a further beneficial increase of the B1 field. A reduction of the number of saturation pulses leads to a decrease in saturation, as well as a switch from a Gaussian to a Sinc pulse.

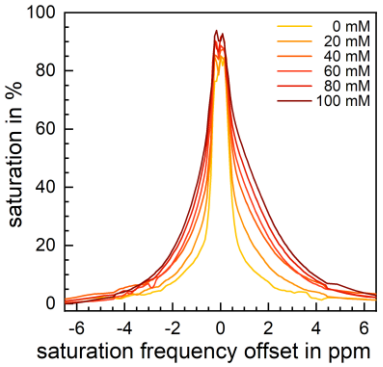

Fig 1: MTR-spectrum at varying glucose concentrations (B1 field: 5 × 1 µT).

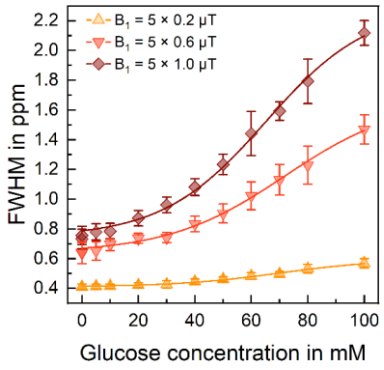

Fig 2: Dependency of the FWHM on the glucose concentration for different B1 saturation fields.

DISCUSSION:

The use of FWHM as a quantification marker represents an evaluation method that is easy to integrate into the clinical routine and does not require complex post-processing. Additionally, it enables a significant reduction in the CEST offset frequencies that need to be sampled, as a lower sampling rate has only a minor effect on the measured FWHM. Reducing the frequencies from 129 to just 31 leads to a noticeable reduction in measurement time for clinical patients taking only around 6 min for a MTR-spectrum. The first measurement in a patient with suspected AR of the transplant kidney demonstrated that the developed sequence could acquire high-quality images without disturbing respiratory artifacts, even without any respiratory triggering.

CONCLUSION:

The single-slice multi-shot CEST-MultiFLASH sequence enables the acquisition of a CEST spectrum from the kidney with measurement times ranging from 5 to 10 min. The FWHM and AUC of the CEST spectrum show a monotonically continuous dependence on glucose concentration, providing an easy-to-use method for detecting changes in glucose metabolism. The next step is to investigate the sequence in kidney transplant patients with suspected AR.

REFERENCES:

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2. Krähling T, *et al*. 23rd Ann. Meet. Ger. Chapter Int. Soc. Magn. Reson. Med. 2021.