# Validation of Gluco-Cest Experiments with $^{13}$C-Labeled Glucose Detection *in vivo*

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## Introduction

Novel minimally invasive molecular MRI methods have high potential of being translated rapidly into the clinic for tumor assessment and monitoring of treatment. To accomplish this, we exploit MR contrast based on chemical exchange saturation transfer (CEST) compounds[1,2]. CEST contrast is generated by magnetic labeling of exchangeable protons on exogenous or endogenous agents, followed by a transfer of this magnetic label to bulk water, which allows detection of these agents via cumulative effect on the water signal[3,4]. We also demonstrated that carbohydrates, such as D-glucose, could be used as CEST biomarkers[5]. Tumors generally have high glucose utilization and uptake that can be measured by $^{18}$FDG-PET. Our overall goal is to develop noninvasive MRI glucoCEST method to detect glucose delivery and metabolism in body tumors. In this project we have developed and implemented new method for direct comparison of *in vivo* $^{13}$C MRSI of $^{13}$C-D-glucose and its metabolites[6] with glucoCEST signals generated by the same compound in the same mouse. These data will be used to further understand the origin of glucoCEST signals *in vivo* and to directly validate this new technology.

## Experimental

A new method for interleaved acquisition of proton enhanced $^{13}$C CSI and glucoCEST was implemented on a 21.1T MR system and tested it in $^{13}$C-labeled D-glucose phantoms using a dedicated *in vivo* $^{1}$H/$^{13}$C double-tuned probe. After optimizing the experimental parameters, we performed *in vivo* studies with normal mice that received infusion of $^{13}$C-D-glucose solution (0.5M, total of 0.5ml) via a tail vein catheter. The anesthetized animal was positioned in the probe with the brain centered within the RF coil. *In vivo* GlucoCEST and $^{13}$C/$^{1}$H 2D CSI brain images were acquired before and for ~2h during and after completing the i.v. glucose infusion. After completing of the infusion GdDTPA a standard dynamic DCE-MRI was performed to assess enhancement patterns.

## Results and Discussion

Experimental data for glucoCEST and $^{13}$C CSI of phantoms with sucrose and D-glucose solutions are shown in **Figure 1 A&B** and a typical T2-weighted mouse brain image with overlaid glucoCEST contrast is shown in **Figure 1C.**

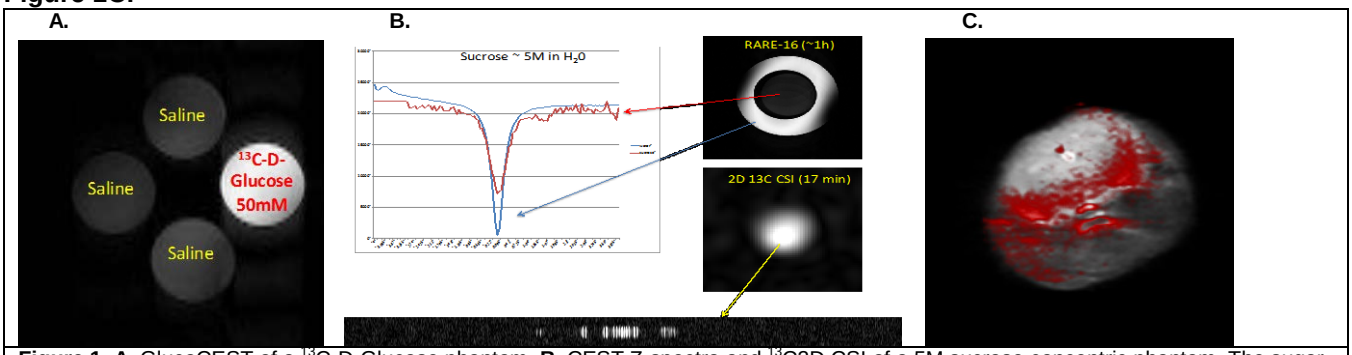


**Figure 1**. **A.** GlucoCEST of a $^{13}$C-D-Glucose phantom. **B**. CEST Z-spectra and $^{13}$C2D CSI of a 5M sucrose concentric phantom. The sugar generates a peak at +1.5ppm from the water resonance. C. MR image of a central slice through a brain superimposed with the difference glucoCEST map acquired at 45 min after the start of $^{13}$C-D-glucose infusion.

## Conclusions

$^{13}$C proton enhanced *in vivo* MR of $^{13}$C-labeled D-glucose on a 21.1T MR system can be used to validate glucoCEST experiments by detecting the same substrate in the same animal using an interleaved acquisition method.

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## References

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