Infusion duration in dynamic glucose enhanced (DGE) MRI revisited

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INTRODUCTION:

Dynamic glucose enhanced (DGE) CEST MRI can detect signal changes after D-glucose administration[1]. Previously, a slower D-glucose infusion duration was recommended for increased patient comfort without compromising DGE MRI signal in healthy volunteers at 3 T[2]. In tumors, the DGE MRI signal is higher due to blood-brain barrier (BBB) breakdown and a lower pH in the extravascular-extracellular space (EES)[1,3]. Recently, we developed a 3-tissue-compartment model to characterize D-glucose transport, uptake, and metabolism in healthy and tumor brain tissue[3]. This model simulates brain D-glucose concentrations from plasma levels, allowing further investigation of plasma-brain glucose dynamics. In this study, we simulated brain D-glucose concentration curves and corresponding DGE MRI signals to validate our slow infusion recommendation, ensuring that the brain glucose response is fast enough to be captured within typical imaging durations.

METHODS:

In our previous studies[2,5,6], venous plasma D-glucose concentrations $C_p^v(t)$ were measured with a blood gas analyzer after D-glucose infusion of different durations. The $C_p^v(t)$ curves from 27 subjects (16 in the 1-minute (30-90 s) and 11 in the 4-minute infusion group) were averaged. $C_p^v(t)$ were converted to $C_p^a(t)$ and used as input function for numerical simulation of compartmental (blood, EES, intracellular) D-glucose concentrations ($C_b(t), C_e(t), C_c(t)$) in healthy gray matter (GM) and in glioblastoma (GBM). The corresponding Z-spectra were simulated using Bloch-McConnell equations as described previously[3,4], using saturation parameters from prior studies at 7 T[5,6]. DGE signal curves were calculated at 1.2 ppm as $\Delta S = 100 \cdot (S_{base} - S(t))/S_{base}$, where S_{base} is the average pre-infusion signal and $S(t)$ is the signal at each time point.

RESULTS:

Simulated D-glucose concentrations and corresponding DGE MRI signal changes ΔS during infusion are shown in Figure 1. As expected, a slower infusion resulted in a delayed rise in brain D-glucose concentration, concentrations at t=4 min were lower by 16% in GM and 19% in GBM. The difference in DGE MRI signal change is more pronounced (GM 42%, GBM 32% lower). However, similar ΔS magnitudes are reached after t=8 min.

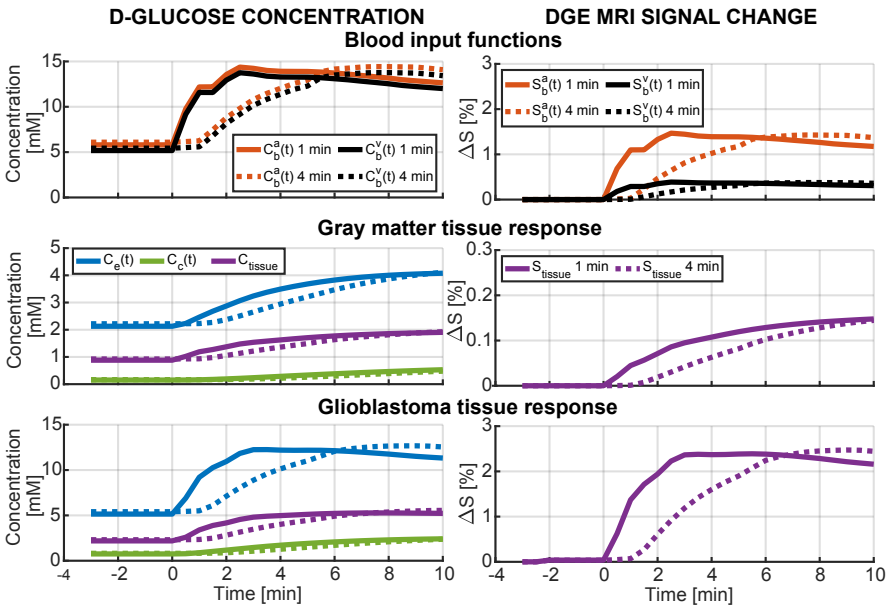

Figure 1. Compartmental and total tissue D-glucose concentration curves and corresponding DGE MRI signal changes ΔS in blood, gray matter, and tumor tissue. T=0 denotes the onset of D-glucose infusion.

DISCUSSION:

Due to facilitated transport across the BBB, D-glucose concentration in GM is delayed compared to blood. With longer infusion durations, we anticipate further delays in brain D-glucose concentration. In tumor, where the BBB is compromised, brain D-glucose rises rapidly, reflecting blood levels. Importantly, and in accordance with previous experimental observations[2], maximum D-glucose concentrations and DGE MRI signals remain unaffected at later time points. Additionally, insulin responses are reduced when infusing slower, potentially leading to higher signal changes at later time points[7].

CONCLUSION:

A slower D-glucose infusion yields comparable signal magnitudes, but with a delayed response compared to faster infusions. Our recommendation of a 4-minute infusion remains unchanged, but we here emphasize the need for imaging to extend at least 10 minutes after the start of the infusion.

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