On the influence of temperature in dynamic glucose enhanced CEST MRI

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INTRODUCTION:

Dynamic glucose enhanced (DGE) MRI relies on the administration of D-glucose to study changes in the CEST signal over time. Brain tissue temperature fluctuates (~3°C) and may increase by 1.5°C after feeding due to metabolic activity[1]. Thus, it is reasonable to assume a similar temperature change after intravenous D-glucose injection. To our knowledge, the effect of temperature changes on the DGE MRI signal has not yet been investigated. The proton exchange rate (k_{ex}) increases with temperature, making detection of the already fast-exchanging hydroxyl protons in D-glucose more challenging. T_1 is also affected by temperature, influencing the saturation efficiency and thus the DGE MRI signal. Therefore, we aimed to investigate whether the hypointense DGE MRI signal in white matter (WM) observed in DGE MRI experiments at 3 T[2,3] can be attributed to metabolic temperature changes, and to explore other potential effects of temperature on the DGE MRI signal in healthy brain tissue.

METHODS:

For simulations of DGE MRI signal, we considered a 1.5°C temperature increase[1] (37°C at baseline, 38.5°C post-infusion), and brain tissue D-glucose concentration of 1 mM before and 3.75 mM after infusion[4]. According to a prior study[5], the increase in T_1 is 3.4 ms/°C in WM and 17.4 ms/°C in gray matter (GM), while T_2 is unaffected. The averaged k_{ex} for an averaged D-glucose hydroxyl proton pool at 1.4 ppm was estimated at 37°C and at 38.5°C using the Arrhenius equation as described by Yadav et al.[6]. To approximate the effect of temperature on the exchange rate, the ratio $k_{ex}^{38.5°C}/k_{ex}^{37.0°C}$ was used to scale k_{ex} for each hydroxyl pool in the 38.5°C post-infusion situation. Z-spectra at 3 T were simulated without/with D-glucose infusion and without/with temperature-related changes in k_{ex} and T_1 using Bloch-McConnell equations as described previously[2]. The DGE MRI signal difference at 2 ppm were calculated as $\Delta S_{2\,ppm}[\%] = 100 \cdot (S_{base} - S_{post})/S_{base}$, where S_{base} is the pre-infusion and S_{post} is the post-infusion signal intensity.

Table 1. Estimated proton exchange rates and T_1 relaxation rates at two different temperatures.

k_{ex} [s^{-1}] at pH 7.2[7]	37°C	38.5°C
0.66 ppm	2900	3132
1.28 ppm	6500	7020
2.08 ppm	5200	5615
2.88 ppm	14300	15444
$T_{1,WM}$ [ms]	800	805
$T_{1,GM}$ [ms]	1300	1326

RESULTS:

The estimated averaged exchange rates were $k_{ex}^{37.0°C}$= 4808 s^{-1} and $k_{ex}^{38.5°C}$= 5174 s^{-1}, giving $k_{ex}^{38.5°C}/k_{ex}^{37.0°C}$ = 1.08. Exchange rates and T_1 relaxation rates used in the simulations are shown in Table 1. The simulation results are shown in Table 2.

Table 2. Simulated DGE signal difference $\Delta S_{2\,ppm}$ [%] in normal brain tissues without/with D-glucose infusion (*No glc/Glc*), and without/with temperature related changes in k_{ex} and T_1.

Parameter combination		White matter		Gray matter	
k_{ex}	T_1	*No glc*	*Glc*	*No glc*	*Glc*
$k_{ex}^{37.0°C}$	$T_1^{37.0°C}$	0	0.068	0	0.107
$k_{ex}^{38.5°C}$	$T_1^{37.0°C}$	-0.002	0.062	-0.003	0.098
$k_{ex}^{37.0°C}$	$T_1^{38.5°C}$	0.266	0.334	0.781	0.889
$k_{ex}^{38.5°C}$	$T_1^{38.5°C}$	0.264	0.328	0.778	0.879

DISCUSSION:

The work aimed to explore the influence of temperature on the DGE MRI signal and lay the foundation for further studies. This initial exploration suggests that, while the temperature-related increase in the exchange rate is small, its impact on T_1 can amplify the DGE MRI signal difference. At 3 T, and due to the low D-glucose concentration in healthy tissue, $\Delta S_{2\,ppm}$ is small. However, our results indicate that the effect on T_1 from a 1.5°C temperature rise considerably increases $\Delta S_{2\,ppm}$, while the decrease in $\Delta S_{2\,ppm}$resulting from the temperature related increased exchange rate is small and cannot explain the hypointense signal in WM. Still, these complex relationships need further investigation and temperature changes across multiple proton pools may have a larger effect. Additionally, it would also be of interest to examine the influence of temperature at different pH levels, and how temperature changes may affect the DGE MRI signal in brain tumor tissue.

CONCLUSION:

This study suggests that D-glucose infusion related metabolic temperature changes have a substantial effect on the DGE MRI signal in healthy brain tissue, potentially increasing the DGE signal difference at clinical field strength.

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