Dynamic Imaging of D-Glucose at 7T: First Experiments in Human Brain

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Target audience: Those interested in chemical exchange saturation transfer (CEST) and perfusion imaging with contrast agents.

Purpose: Recently, D-glucose has shown potential as a biodegradable contrast agent that can be detected using CEST MRI (glucoCEST)[1-3], T1ρ-based[4,5] or T2-based[6] relaxation approaches. Glucose derivatives detectable by CEST have also been suggested.[7,8] To gain information regarding the uptake of glucose and hence the tissue perfusion properties, time resolved dynamic images are required. In the present work, we developed dynamic glucose enhanced (DGE) imaging using CEST MRI and demonstrated the feasibility of this method on healthy volunteers and a brain tumor patient.

Method: The study was conducted on 4 healthy consented volunteers and a patient later diagnosed with a non-enhancing anaplastic astrocytoma. Subjects received a D50 glucose ampule (25 g Dextrose in 50 ml water sterile solution, Hospira) infused intravenously over 1-2 min in one arm. (No complication in all subjects.) Their Blood glucose level was monitored at 0.5, 1, 1.5, 2, 3, 5, 7, 10, 15, 20, 30, 45, and 60 min post infusion by sampling the venous blood from the other arm and measuring it using a blood analyzer (Radiometer).

Subjects were scanned on a 7T Philips MRI scanner. The saturation was achieved using a train of 32 sinc-gauss pulses, B1 = 1.96 μT, with each pulse 50 ms long and separated by 35 ms delays. The images were acquired using a single-shot turbo gradient echo with TR (between each echo)/TE/FA = 5 ms/1.48 ms/30°. A single slice with 6 mm thickness across a FOV of 224×224mm^2 with 3×3 mm^2 in plane resolution was acquired. The time for acquiring each dynamic image was 5.3 s, 70 dynamics were acquired. The glucose infusion started at 90 s during the dynamic scan.

Results and Discussion: An 8-17% change in water saturation fraction due to the effect of glucose infusion was detected in the arterial blood. Arterial input functions (AIFs) in healthy volunteers are shown in **Fig. 1. Fig. 2** shows the T2-FLAIR and the post-contrast T1w images of the tumor patient performed at 3T prior to surgery. **Fig. 3** shows DGE difference images. It can be seen that tumor rim and vessel rich areas enhance strongly. The dynamic response curves of several regions of interest (anterior cerebral artery, tumor core, lateral tumor rim, and contralateral white matter) are shown in **Fig. 4.** The venous glucose concentration measured independently with the glucose analyzer is also plotted and compared with the AIF, showing similar changes. Interestingly, the signal in the tumor rim changed by approximately 5% after glucose infusion and the changes persisted even when the arterial blood level started to decrease. As a first approach in relating the dynamic glucose images to tissue perfusion, an area-under-the-curve (AUC) image over a post perfusion-start period of 280 s was calculated and shown in **Fig. 5.** No contrast was visible in the tumor core, most likely indicating poor tissue perfusion.

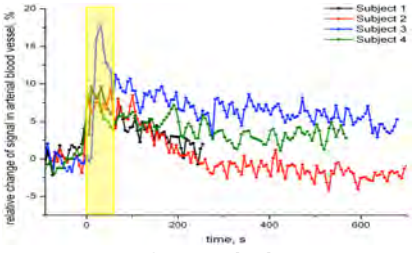

Fig. 1 AIFs of 4 normal subjects.

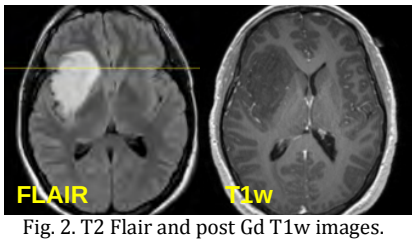

Fig. 2. T2 Flair and post Gd T1w images.

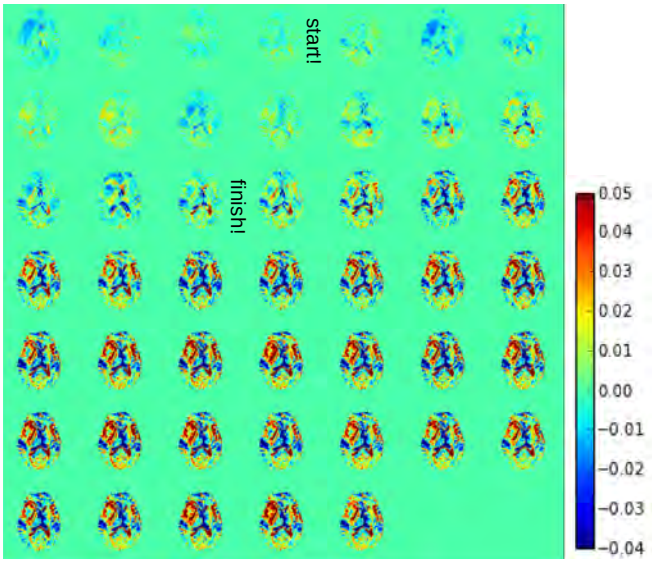

Fig. 3. Dynamic difference images of glucose. The pre- infusion images were averaged to generate a baseline image; the images show the difference between the baseline and each dynamic scan.

Conclusion: Using dynamic glucoCEST imaging, it was possible to detect water signal changes in the human brain induced by infusion of D-glucose. The signal changes are expected to be due to glucose uptake in the vessels and the brain and tumor tissue areas, which are related to the kinetics of perfusion, as well as glucose transport and metabolism. These observations support the use of D-glucose as an MRI contrast agent in humans. While first animal studies were only published less than two years ago, this agent could be translated to human testing quickly because of its previous approval for glucose tolerance testing.[9]

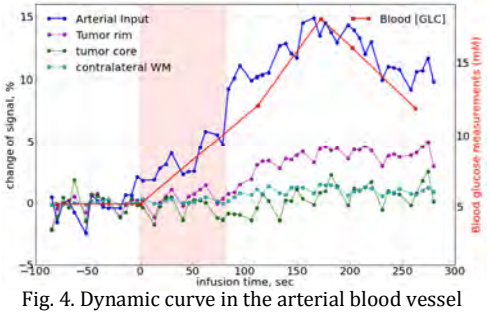

Fig. 4. Dynamic curve in the arterial blood vessel and several ROIs (left scale), alongside with independently measured venous blood glucose level (right scale).

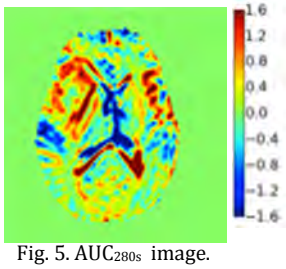

Fig. 5. AUC_{280s} image.

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