Title: Comparison of Glucose-CEST with Perfusion and Glycolysis Measurement in a C6 Rat Model of Glioma

Trainee Name: Qi Qi

Supervisor(s): Drs. Jonathan D. Thiessen and Ting-Yim Lee

Structured Abstract:

Introduction: Glioblastoma is one of the most aggressive brain tumours. The median survival for patients who are diagnosed with glioma remains approximately 12-15 months regardless of technical advances. Chemical exchange saturation transfer allows us to use endogenous contrast agents to image provide us more biological information relating to the metabolite. Glucose-CEST allows us to use glucose investigate the distribution of glucose the tumour in vivo. However, whether glucose-CEST measurement is more related to perfusion or glycolysis measurement is unknown. Tumour perfusion maps can be derived with computed tomography perfusion (CTP) measurements acquired during a bolus injection of iodinated contrast agent (Isovue). Glucose metabolism can be evaluated with positron emission tomography (PET) and 18F-fluorodeoxyglucose (FDG), a glucose analogue which is phosphorylated in the cell but doesn't go through subsequent steps of glycolysis. In this study, we compared glucose-CEST measurement to perfusion measurements from CTP and glycolysis measurement from FDG-PET to validate if glucose-CEST is a perfusion or glycolysis measurement. Moreover, CEST result can be effect by pH and enable us to measure intracellular pH (pHi) changes. The change in tumour pHi can provide information about tumour cell proliferation and evasion.

Methods: 10^6 C6 glioma cells were implanted in the brains of Wistar rats (n=11) using stereotactic surgery. Tumours were monitored actively using CT starting from Day 7 after the surgery. Glucose metabolism was measured in the tumour using the standardized uptake value (SUV) in PET images acquired 60 minutes after a bolus of FDG (30 ± 2 MBq) 11 to 13 days post-surgery. Glucose CEST measurements were acquired the following day. CEST spectra were acquired on a 9.4 T Agilent MRI using a continuous wave presaturation pulse preceding a series of fast spin-echo images. The maps for areas under the curve (AUC) for MTR asymmetry curve, relative change after glucose infusion and the pHi measurement of AACID were calculated.

Results: Tumour glucose-CEST measurement of %CEST significantly and most strongly correlated with tumour perfusion measurement of blood volume (ρ = 0.82, P = 0.02) followed by the perfusion measurement of permeability surface-area product (ρ = 0.79, P = 0.04). Negative tumour %CEST values were found when AACID values were significantly increased at tumoural and peritumoural regions prior and post glucose infusion.

Discussion: Glucose-CEST measurement of tumour %CEST was significantly correlated with perfusion measurement of blood volume and permeability and surface-area product. No significant correlation was found between tumour %CEST and glycolysis measurement of SUV. pHi measurement of AACID value affected the glucose-CEST measurement, glucose-CEST signal decreased (negative %CEST) when ACCID value significantly increase after glucose infusion.