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Study of Tumour Intracellular pH (pHi) in a Rat Model of Glioblastoma Using CEST-MRI

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Introduction: The non-invasive chemical exchange saturation transfer (CEST) MRI method measures pHi with high spatial and temporal resolution. In CEST, exchangeable protons on proteins can be selectively excited and detected through the transfer of magnetization to bulk water; the rate of which is pH-dependent. We have previously developed a CEST-MRI technique, amine and amide concentration-independent detection (AACID), to measure absolute tissue pH that is heavily weighted to the intracellular compartment. The AACID value is inversely related to tissue pH. This study is focused on the change in tumour pHi over time in a rat C6 glioma model.
Methods: C6 glioma cells were injected into the right frontal lobe of fifteen rats. CEST-MRI was performed at baseline, 7-11 days, and 14-16 days post-implantation on a 9.4T MRI. CEST images were acquired at saturation frequencies from 1.2-6.6 ppm to create CEST spectra for each pixel in the image, AACID maps were then produced.
Results: The average AACID values at day 0 were similar to the values in contralateral tissue at days 7-11 and days 14-16 post-implantation. The AACID value was significantly lower in the tumour compared to the contralateral region at day 7-11. At day 7-11, the average AACID value was 4.8% lower in the tumour compared to the contralateral side indicating a 0.24 higher pH. Surprisingly, at day 14-16 the average tumour AACID value was no longer significantly different than the contralateral region.
Discussion: The difference between tumour pH and contralateral pH is expected to increase over time in this model. However, this was not observed. One potential explanation is the temporal stability of the AACID CEST measurement and the emergence of an altered physiological state within the contralateral tissue as tumours increase. Future work will explore different MRI acquisition sequences and coils to improve temporal stability.

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