In-depth evaluation and development of post-processing methods for 2D-glucoCEST in breast cancer

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ABSTRACT (max. 2000 characters (including spaces), no paragraphs)

A key hallmark of breast cancer is the switch to aerobic glycolysis that is commonly imaged with [^{18}F]-FDG PET. However its use may be limited by the elevated radiation burden especially during treatment monitoring. GlucoCEST is a promising radiation-free alternative that quantifies glucose metabolism based on magnetization transfer between glucose and water protons. Usually, evaluation is done using the MTR asymmetry (Magnetization transfer ratio) that calculates the difference in raw signal intensity on opposite sides of the CEST spectrum, but is affected by field-related artefacts. We show that fit-based quantification combined with T_1 correction stabilizes the glucoCEST quantification. Female athymic BALB/c nude mice (n=54) were inoculated with breast cancer cells of luminal A, Her2+ and triple-negative molecular subtypes. MRI and simultaneous [^{18}F]-FDG PET imaging was performed using a 9.4T Bruker BioSpec 94/30 USR system combined with a Bruker PET insert. CEST images were acquired with a RARE-based sequence. After baseline measurement, a 2D-glucose challenge was injected to amplify CEST signals that reveal areas with elevated metabolic rates. Endogenous solutes amide and amine, prevalent in highly proliferating tissues, were also evaluated. MTR asymmetries, Lorentzian fit amplitudes, MTR Rex and AREX (Apparent exchange-dependent relaxation, correcting for T_1) parameter maps were generated using MATLAB code written in-house. MTR asymmetry maps were prone to noise which underlined their unreliability. Lorentzian-fit-based maps however successfully showed viable tumor tissue at the periphery while revealing a hypoxic core. AREX corrects for multiple other chemical exchanges and T_1 and was least influenced by artefacts. This research reveals the limitations of the conventional MTR asymmetry. Instead, other quantifications, like AREX assessed in this study, are needed to establish glucoCEST as a valuable radiation-free alternative for imaging glucose metabolism.