Methodology matters: characterization of glioma through advanced MR imaging

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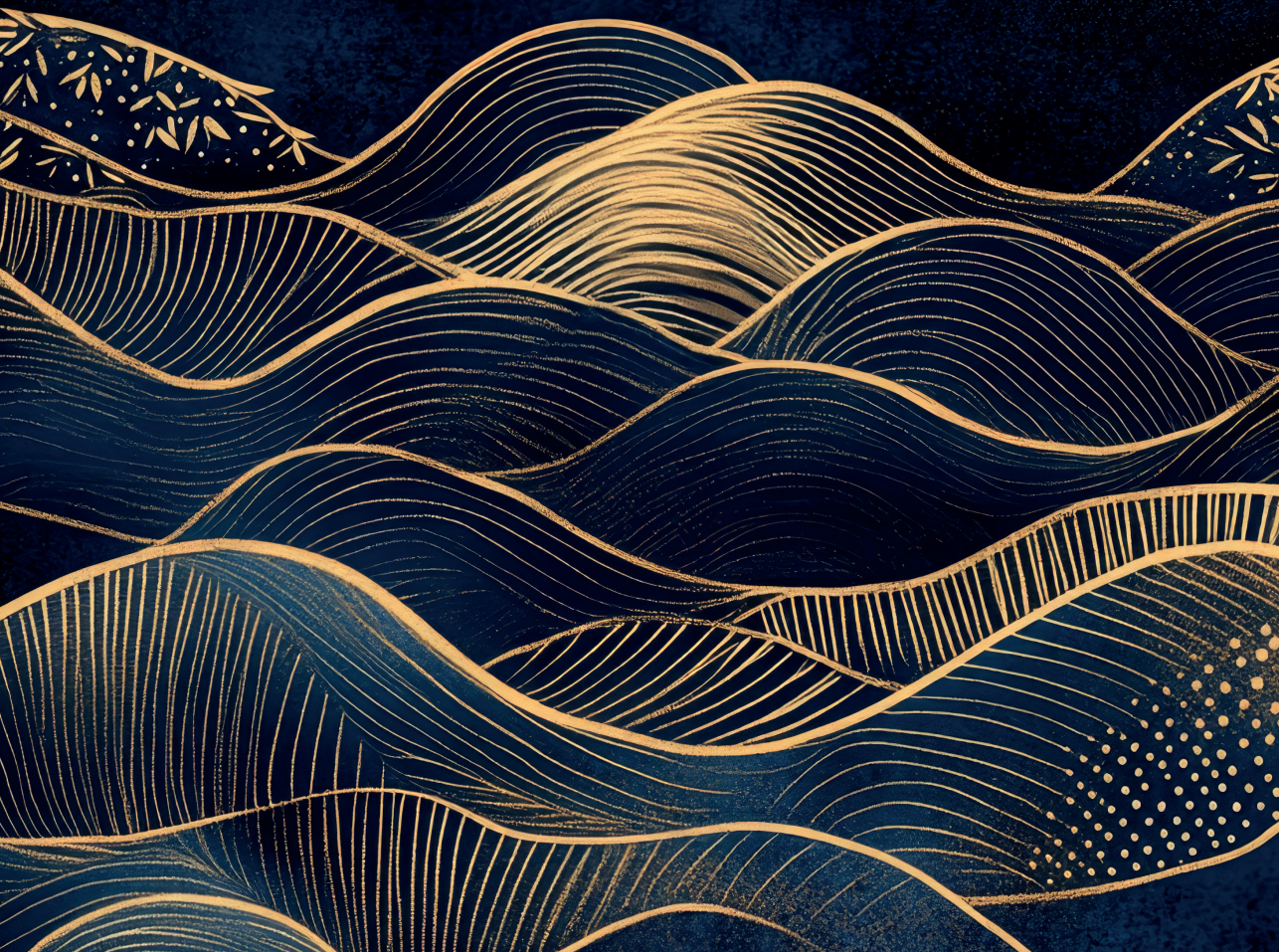
9 Summary



9.1 Summary in English

This thesis explored advanced MRI modalities and their applications to obtain improved characterization of glioma. A substantial focus was put on optimizing CEST imaging and analysis. The optimization work presented in this thesis was performed on healthy individuals, whereas the application of it was done in a pilot study with glioma patients. The work with these patients included a broad protocol allowing to understand the added value of CEST compared to its more traditional clinical imaging counterparts.

Chapter 2 provided a comprehensive review of various Chemical Exchange Saturation Transfer (CEST) imaging modalities that were researched and applied in glioma imaging, discussing their potential clinical implications. Amide Transfer Proton (APT)-CEST emerges as the most extensively studied contrast, and the chapter highlights the promising results achieved to date. However, it also addressed significant challenges to clinical implementation, particularly the need for broader validation and consensus on acquisition parameters. The chapter further explored newer CEST modalities, such as amine and glucose CEST, in the context of pre-operative glioma imaging.

Chapter 3 presented the initial methods optimization, focusing on Variable Delay Multipulse (VDMP)-CEST for *in vivo* human brain imaging. The aim was to separate signals from different CEST pools based on their exchange rates while mitigating effects from magnetization transfer contrast (MTC). Slow-exchanging amides and relative Nuclear Overhauser Effect (rNOE) were successfully distinguished from fast-exchanging amines after Magnetization Transfer Contrast (MTC) correction. The chapter identified the optimal acquisition parameters, such as B_1 amplitude and mixing time, for effective imaging of each CEST pool.

In Chapter 4, the focus shifted to fast-exchanging amines. Both 2 and 3 parts per million (ppm) amine pools have been shown to be present in the human brain, and so the goal was to optimize acquisition parameters to maximize sensitivity to these pools. The study also sought to correlate the 2 ppm and 3 ppm amine pools with creatine and glutamate, respectively. Unexpectedly, the findings revealed that glutamate contributes significantly to the 2 ppm amine pool.

Chapter 5 investigated the application of CEST imaging in gliomas, specifically examining the value of the 2 ppm CEST pool for non-invasive characterization of enhancing and non-enhancing glioma lesions. The CEST signal was analyzed using different methods, consistently revealing differences between enhancing and non-enhancing lesions when compared to contralateral healthy tissue. These findings suggest that the 2 ppm pool could serve as a valuable non-invasive tool for distinguishing between these regions in glioma patients.

The second part of this thesis explored the use of common radiological tumor characteristics, as well as ultra-high field MR imaging, to address current challenges in clinical decision making in patients with glioma.

Chapter 6 compared the extension, volume, and shape complexity of T_2 hyperintense areas

between clinical MRI and high-resolution 7T scans. The high-quality 7T images revealed T_2 hyperintense areas that were not visible on clinical MRI. Additionally, tumor volume and shape complexity were significantly larger and more intricate on 7T scans. These results suggest that 7T imaging could provide more detailed tumor information, potentially improving clinical decision-making and treatment planning by better assessing tumor extension, size, and shape complexity.

In the final part, Chapter 7 investigated whether common radiological tumor characteristics can be utilized to group patients and whether these sub-groups show different behavior according to their progression and survival. Using structural and perfusion data scored from MR images three months post-radiotherapy, four distinct MRI phenotypes could be identified sharing similar tumor perfusion characteristics. Their recurrence rates and overall survival were assessed based on progression status at nine months post-radiotherapy. While the phenotypes appeared to be predictive of overall survival, they did not prove to be useful in differentiating between true and pseudo-tumor progression.