QUANTITATIVE DIFFUSION-WEIGHTED IMAGING IN CANCER APPLICATIONS

Abstract

Quantitative magnetic resonance imaging (MRI) quantifies multiple factors utilizing tissue-specific physical units. These quantitative metrics are sensitive to physiological tissue changes and pathologies. In recent years, demand for non-contrast quantitative MRI has grown, such as intravoxel incoherent motion combined with diffusion kurtosis imaging (IVIM-DKI). IVIM-DKI is a diffusion-weighted imaging technique that uses low-to-high diffusion sensitizing gradient strengths (b-value). IVIM-DKI doesn't require contrast agents, ensuring application safety to a wide variety of patients and reducing MRI costs. Although IVIM-DKI is beneficial for clinical studies, it has not yet been widely used in routine clinical practices because of a few technical problems: (i) the signal-to-noise ratio (SNR) of the IVIM-DKI signal is poor, (ii) piecewise simultaneous fitting of parameters result in noisy and unreliable parameter maps, (iii) the diagnostic utility of IVIM-DKI in a various clinical setting at different MRI field strength has not been proven, and (iv) the absence of a standardized protocol for organ-specific imaging leads to prolonged scan times. Thus, this thesis aims to address some of these challenges by proposing novel strategies for improving IVIM-DKI parametric map estimation using parametric reconstruction method validation of the novel model at different MRI field strengths and optimization of b-values for protocol standardization, which can promote the role of IVIM-DKI in the improved quantitative lesion characterization technique in cancer applications.

The first objective was to develop a novel strategy to improve the parameter estimation of IVIM-DKI for producing high-quality parametric maps. To implement this objective, the total three-dimensional total variation (TV) penalty function was utilized in conjunction with non-linear lease square optimization (NLLS) of the IVIM-DKI model (IDTV model). TV is an image-based reconstruction approach that corrects for NLLS error and adaptively removes any abrupt changes in the map while preserving the edges. Two models were implemented for the estimation of diffusion coefficient (D), perfusion coefficient (D*), perfusion fraction (f), and kurtosis (k) using either: (1) standard model and (2) IDTV model. Experimental simulation

results showed accurate and high-quality IVIM-DKI parameter maps, particularly at low signal-to-noise ratios in simulations. Additionally, TV regularization was resilient to changes in SNR, resulting in less error and bias in IVIM-DKI parameter maps.

The second objective was to examine the clinical usefulness of IVIM-DKI analysis using the IDTV model in prostate mass characterization at different MRI field strengths (1.5T and 3T). The IDTV model resulted in enhanced parameter estimation with minimal error at 1.5T and 3T. Furthermore, compared to the standard model at 3T, the IDTV model at 1.5T resulted in lower parameter estimate error and higher-quality parametric reconstruction. D, f, and k estimated with the IDTV model showed higher diagnostic performance than the standard model. Hence, IVIM-DKI might play an essential role in prostate lesion diagnosis when paired with the IDTV model.

The third objective was to assess the efficacy of IVIM-DKI analysis with the IDTV model and machine learning-based multi-parametric texture analysis in characterizing pancreatic masses. Perfusion fraction was found to out-perform the diffusion measures (ADC and D) in discriminating pancreatic adenocarcinoma (PDAC) from the pancreatic neuroendocrine tumor (pNET). Whole-volumetric texture analysis of individual or combination IVIM-DKI parameters with machine learning-based classification of pancreatic masses can help with the non-invasive characterization of pancreatic lesions.

The fourth objective was to optimize the b-value for IVIM and IVIM-DKI analyses by combining different b-values. IVIM and IVIM-DKI signals were modeled utilizing the IVIM model with the TV method (BE+TV model) and the IDTV model, respectively. The experimental findings of simulation and clinical data demonstrated that the BE+TV and IDTV models were resistant to b-value combinations. Furthermore, both models were robust to any number and combination of b-values, and they improved the quality of all parametric maps at low SNR. The BE+TV approach significantly enhanced the quality of D and f maps. The IDTV model, on the other hand, improved the quality of D, f, and k maps. The acquisition of IVIM and IVIM-DKI with optimal 8 b-values may be employed for faster acquisition times and high-quality parameter maps with comparable accuracy as 13b-values using the standard model with less acquisition time.

Finally, this thesis concluded by using an IVIM-DKI model with an optimized b-value for diagnosing malignant lymph nodes compared to fluorodeoxyglucose-positron emission tomography with computed tomography (FDG-PET/CT) imaging. The preliminary findings

revealed that the IDTV model outperformed PET imaging in identifying benign and malignant lymph nodes in lymphoma and further classifying lymphoma subtypes. In diagnosing malignant lymph nodes, IVIM-DKI parameters showed higher diagnostic performance than ADC and PET parameters. IVIM-DKI can potentially be used for lymph node evaluation in lymphoma and is comparable to PET imaging.