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Author(s)	Oppong, Philip Kyeremeh Jnr
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氏名 Oppong Philip Kyeremeh Jnr
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Performance of MRI Indices in Evaluating Myelin and Brain Injury following Whole-Brain Radiotherapy
(ミエリン及び全脳放射線治療後の脳損傷の評価におけるMRI指標の成績)

Chapter 1. Exploring the Sensitivity of MRI indices in Myelin Assessment Across Spinal Cord Regions

Background/Objectives: Multiple magnetic resonance imaging (MRI) indices are effective for noninvasive myelin assessment; however, their relative sensitivities have not been directly compared. This study aimed to identify the most sensitive MRI index for characterizing myelin composition in the spinal cord's gray matter (GM) and white matter (WM).

Methods: Quantitative MRI indices sensitive to myelin, including myelin water fraction (MWF), magnetization transfer ratio (MTR), the signal ratio between T1 and T2-weighted images (T1W/T2W), fractional anisotropy (FA), mean diffusivity (MD), T1 and T2 relaxation times, and T1 ρ relaxation time in the rotating frame, were calculated from ex vivo MRI of a deer cervical spinal cord. Additionally, electrical conductivity (σ) was evaluated for myelin sensitivity. The mean values of these indices were compared across GM and WM columns using repeated measures analysis of variance (ANOVA) and post hoc Bonferroni tests or Friedman tests with post hoc Wilcoxon tests, to identify the differences in myelin distributions, as revealed by histological analysis. Relationships among the indices were examined using Spearman's rank-order correlation analysis. Corrected $p < 0.05$ was considered statistically significant.

Results: All indices, except σ , showed significant variations between GM and all WM columns. MWF, FA, MD, and T2 exhibited significant differences in two of the three WM columns, while MTR, σ , T1, and T1 ρ showed significant differences in one WM column compared to the other. Correlation analysis revealed moderate to very strong relationships among most indices.

Conclusions: MRI indices varied in their sensitivity to myelin across spinal cord regions. A strategic combination of multiple indices may enhance the accuracy of myelin characterization.

Chapter 2. Diffusion Tensor Imaging Radiomics for Assessing Acute and Early Delayed Brain Parenchyma Microstructural Alterations Associated with Whole Brain Radiotherapy

Background/Objectives: Variation in white matter (WM) alterations following WBRT has been suggested. However, imaging biomarkers capable of detecting acute and early delayed WBRT-induced WM microstructural changes remain less characterized. This study aimed to assess regional disparities in WM changes associated with the acute and early delayed phases of WBRT-induced changes, and to explore their associations with neurocognitive function.

Methods: MRI, including diffusion tensor imaging (DTI), was conducted before WBRT as baseline and repeated immediately after WBRT, 1.5 months, and 4 months post-WBRT. List recognition neuropsychological testing (of the repeatable battery for the assessment of neuropsychological status) was administered to assess delayed memory performance before WBRT (as baseline), and 4 months post-WBRT. Eighteen histogram and 24 gray-level co-occurrence matrix (GLCM) features were extracted from WM regions of interest (ROIs) across four DTI indices. Redundant features were removed through intercorrelation analysis based on Pearson's correlation with a threshold of $r > 0.7$. Evaluation of WBRT-induced changes among features was conducted using one-sample t-tests with statistical significance set at uncorrected $p < 0.05$. Pearson's correlation analysis was used to evaluate the associations of DTI-radiomics with delayed memory performance, with statistical significance set at uncorrected $p < 0.01$.

Results: A significant increase in the 10th percentile and decrease in the 90th percentile of axial diffusivity (AD) in the left anterior limb of internal capsule (ALIC-L) were observed immediately post-WBRT. At 1.5 months, a significant decrease in kurtosis of AD and an increase in GLCM difference variance of FA within the left posterior limb of internal capsule were observed. A significant decrease in GLCM cluster tendency and an increase in difference variance of MD were observed in the left and right superior corona radiata, respectively. Correlation analysis revealed strong and moderate positive associations between skewness of FA in the right superior longitudinal fasciculus and the 90th percentile of RD in left superior corona radiata at 1.5 months post-WBRT, with delayed memory scores at 4 months. Conversely, the 10th percentile of FA in the body of corpus callosum showed a strong negative correlation with delayed memory performance at the same time point.

Conclusion: DTI-radiomics revealed significant regional changes, enabling the delineation of WM susceptibility and its associations with delayed memory performance.