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**Modeling Lesion-level Spatial Association Between MWF and QSM**

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**Introduction:**

Quantitative susceptibility mapping (QSM) is an advanced magnetic resonance imaging (MRI) technique used for characterizing patterns of iron deposition and demyelination in Multiple Sclerosis (MS) lesions. Myelin Water Fraction (MWF) imaging is a quantitative MRI biomarker for myelin and can also be used to assess the extent of myelin damage within lesions. Previous research has explored the association between MWF and QSM, but did not account for the spatial correlation of lesions. This study seeks to examine the association between iron-associated inflammation and myelin damage using both modalities while accounting for the spatial lesion correlation to better characterize the underlying mechanisms of lesion progression.

**Objectives/Aims:**

To explore the connection between myelin damage and inflammation using MWF and QSM, while considering spatial correlations within lesions.

**Methods:**

This study analyzed 169 new T1-weighted gadolinium-enhancing lesions from 37 MS patients who were followed longitudinally up to a period of four years. To model the association between MWF and QSM while accounting for the spatial correlation among voxels, regression with Gaussian spatial correlation structure was performed. Models’ performances were compared using the Akaike Information Criterion (AIC). The parameter confidence intervals were calculated using a spatial neighborhood bootstrap framework to preserve spatial correlations among voxels.

**Results:**

Models that accounted for the spatial correlation among voxels had a significantly lower AIC compared to a non-spatially adjusted regression model (p<.05). The proposed non-parametric neighborhood bootstrapping framework was an effective method of quantifying the uncertainty of the association between MWF and QSM.

**Conclusion:**

This study demonstrated improved model performance when the spatial correlations among voxels are accounted for. For MS lesions, nearby voxels are more likely to have similar iron deposition or demyelination events compared to voxels that are farther apart. The proposed statistical method could potentially be used to monitor treatment effectiveness and to predict spatial progression of lesion inflammation, thereby identifying patients at high risk of developing more severe symptoms.