Redefining MRI:
From Image to Insight

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Plenary Lecture-PhD

PL02

Advancing MRI-based differential assessments of neurodegenerative brains

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Differentiating Parkinsonian disorders, Parkinson's disease, Multiple System Atrophy, and Progressive Supranuclear Palsy, remains difficult in clinical practice because these conditions look very similar in the early stages. Although they share core motor symptoms, their underlying pathology, prognosis, and optimal treatment differ substantially, so getting the diagnosis wrong has real consequences for patients. Current diagnostic criteria still fall short, particularly positive predictive values for PD and MSA, and sensitivity for PSP, leaving a clear need for better imaging biomarkers.

This talk presents a series of MRI-based quantitative approaches developed through a translational pipeline integrating postmortem human brain studies with histological ground truth and clinical MRI. First, we describe a multi-parametric iron MR imaging framework combining T_2, T_2*, and Quantitative Susceptibility Mapping to spatially resolve neuromelanin-iron complexes and labile iron within the post-mortem substantia nigra, offering pathologically grounded markers for PD. Simulation and mass spectrometry cross-validation confirmed that the differential behavior of T_2* and T_2 mismatch reflects the size-dependent magnetic perturbation effects of iron-laden neuromelanin organelles versus deposited ferric iron. Building on this framework, subdivisional analysis of the SN, distinguishing anterior/posterior and rostral/caudal subregions, revealed that myelin-iron interplay creates regionally heterogeneous R_2* and QSM profiles. Combining rostral R_2* with caudal QSM further improved PD diagnostic AUC beyond whole-structure metrics, demonstrating that spatial decomposition of nigral MRI signals captures disease-relevant pathological gradients obscured in global measurements. Second, for PSP, we newly demonstrate that a susceptibility-volume-ratio of the substantia nigra, combined with midbrain and pons volumetry, significantly improves PSP sensitivity. Third, for MSA, we identify the choroid plexus–ventricular axis as a novel early marker: MSA patients exhibit significantly enlarged ChP volume and expanded ventricular morphology relative to PD, with ChP and cerebellar white matter volume together achieving classification accuracy up to 0.92 even in early-stage MSA. A deep learning-based synthetic contrast-enhanced MRI approach may further enable non-invasive ChP segmentation comparable to gadolinium-enhanced imaging.

Collectively, these quantitative MRI biomarkers, targeting distinct pathological epicenters for each condition, offer complementary and potentially additive diagnostic value beyond conventional structural imaging, with direct translational implications for earlier and more accurate Parkinsonism differentiation.

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