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# In-Vivo Assessment of Cellular Soma and Neurite Density Abnormalities in Multiple Sclerosis Paramagnetic Rim and Core-Sign Lesions

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## Introduction:

In multiple sclerosis (MS), paramagnetic rim lesions (PRLs) and core-sign lesions may underlie different stages of white matter lesion (WML) evolution that are associated with a more severe disease course. By evaluating both soma and neurite properties, soma and neurite density imaging (SANDI) model may provide more specific information about their heterogeneous pathological processes.

## Objectives/Aims:

Using SANDI method based on diffusion-weighted MRI, we characterized*in vivo* the microstructural abnormalities of MS WML showing a paramagnetic rim (i.e., PRLs) or diffuse hypointensity (core-sign lesions) on susceptibility-weighted imaging (SWI) and their clinical relevance.

## Methods:

Forty MS patients and 28 healthy controls (HC) underwent a 3T brain MRI. Using SANDI, the fractions of neurite (fneurite) and soma (fsoma) and size of soma (rsoma) were quantified in PRLs, including their core and rim separately, and core-sign lesions identified on SWI.

## Results:

Among 1811 WMLs, 122 (6.7%) core-sign lesions and 97 (5.4%) PRLs were identified. Compared to HC and MS normal-appearing white matter, all MS WML showed significantly lower fNeurite and fSoma and higher rSoma (FDR-$p<0.001$). Compared to isointense WMLs, core-sign lesions showed a significantly higher fNeurite, and lower fSoma and rSoma (FDR-$p\leq0.001$). Compared to isointense WMLs and core-sign lesions, PRLs showed a significantly lower fNeurite, higher fSoma, and higher rSoma (FDR-$p<0.001$). The core of PRLs showed significantly lower fNeurite, and higher rSoma than their rim (FDR-$p<0.001$). Lower PRL lesion fNeurite ($\beta\leq$-0.006, FDR-$p\leq0.015$) and higher rSoma ($\beta\geq0.032$, FDR-$p\leq0.024$) were significantly associated with a longer disease duration and more severe disability.

## Conclusion:

PRLs are clinically-relevant lesions characterized by significant neurite loss and increase of soma fraction and size, potentially reflecting higher amount of activated microglia and astrogliosis. Core-sign lesions exhibit milder axonal loss and amount of microglia and astrogliosis, supporting their less destructive nature.

## Disclosures:

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