MSMilan2023
9th Joint ECTRIMS-ACTRIMS Meeting
11–13 October 2023 | Milan, Italy

**Abstract Number:** [1389]

**Abstract Title: Quantitative Myelin imaging is associated with Eomesodermin expressing CD4+ Th-cells in secondary progressive multiple sclerosis**

**Abstract Category:** Imaging and non-imaging biomarkers - 27 - MRI & PET

**Preferred Presentation Type:** Oral or poster presentation

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**Introduction:**
Demyelination and brain atrophy increase in progressive forms of multiple sclerosis (MS), although the relationships at the cellular level with quantitative magnetic resonance imaging (MRI) parameters are not known. In secondary progressive multiple sclerosis (SPMS) higher frequencies of Eomesodermin expressing (Eomes+) CD4+Th-cells are associated with disability progression and predict disease worsening.
**Objectives/Aims:**
To analyze the association of quantitate myelin fraction with Eomes+Th-cells in SPMS and RMS
**Methods:**
30 relapsing (RMS) and 42 SPMS patients received a quantitative multislice, multiecho, multisaturation delay acquisition sequence (QRAPMASTER) on a 1.5 Tesla MRI scanner for brain segmentation und myelin quantification. Myelin and brain volumes as fractions of intracranial volume (Myelin volume fraction: MVF, brain parenchymal fraction: BPF) were estimated. Peripheral blood mononuclear cells (PBMCs) were isolated and frequencies of Eomes+Th-cells were analyzed using flow cytometry (BD FACS-Canto TMII).
**Results:**
In SPMS intracranial MVF and BPF (mean values, SDs) were significantly ($p<0,001$) lower compared to RMS [MVF: 8.5%(±1.4%) vs. 9.1%(±0.8%), BPF: 75%(±4.6%) vs. 80%(±5.5%)]. Frequencies of Eomes+Th-cells (median values, IQRs) were significantly ($p<0,001$) increased in SPMS compared to RMS [2.21% (IQR:1.29,3.25) vs. 1,85% (IQR:0.96,2.82)]. Proportion of Eomes+Th-cells correlated with intracranial MVF($R^2$: 0.298, r:-0.598) and BPF in SPMS patients (age as covariate, $p<0,001$) but not in RMS.
**Conclusion:**
Confirming recent literature, Eomes+Th-cells were increased in patients with SPMS compared to RMS. Quantitative synthetic MRI revealed reduced myelin and global brain volume fractions in SPMS compared to RMS, whereby a correlation of MVF with Eomes+Th-cells could be demonstrated only in SPMS. It could be hypothesized that Eomes+Th-cells mediated processes might be in part associated with the extent of myelin loss in SPMS.

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9th Joint ECTRIMS-ACTRIMS Meeting
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**Abstract Number:** [1700]

**Abstract Title: Serum-Neurofilament light chain levels in secondary progressive multiple sclerosis are associated with grey matter destruction characterized by relaxation rates**

**Abstract Category:** Imaging and non-imaging biomarkers - 27 - MRI & PET

**Preferred Presentation Type:** Oral or poster presentation

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**Introduction:**
In multiple sclerosis (MS) patients the association of serum Neurofilament light chain (sNfl) values with grey matter (GM) pathology, namely atrophy, is well known. However, the underlying mechanisms leading to GM changes in different MS disease courses have not been established. Quantitative magnetic resonance imaging (MRI) parameters like relaxation rates provide biophysical measures of the microstructural tissue changes.

**Objectives/Aims:**
To analyze the association of relaxation rates of GM with sNfl in secondary progressive (SPMS) and relapsing (RMS) MS.

**Methods:**
RMS(n=20), SPMS(n=27) patients and Control subjects (CS, n=24) received quantitative synthetic MRI using a multiecho acquisition of saturation recovery pulse sequence on a 1.5 Tesla scanner to quantify relaxation rates (R1 and R2) and for GM segmentation. In patients, sNfl measurement using the Simoa HD-X analyzer by Quanterix was performed.

**Results:**
sNfl in RMS (mean=33.1 pg/ml ±24.3) and SPMS (mean=32.5 pg/ml ±29.3) showed no significant group difference. GM fraction (%of intracranial volume) was significantly ($p<0.001$) lower in RMS(mean=45.9±2.5) and SPMS(mean=45.2±3.9) compared to CS(mean=50.2±2.0). R1 and R2 in GM($sec^{-1}$) were significantly ($p<0.001$) decreased in RMS(R1 mean=0.77±0.03/ R2 mean=10.3±0.3) and SPMS(R1 mean=0.78±0.02/ R2 mean=10.3±0.3) compared to HC(R1 mean=0.8±0.02/ R2 mean=10.7±0.2). In SPMS, sNfl correlated with R1($r=-0.46, p<0.016$) and R2($r=-0.43, p<0.025$) in GM, but not in RMS.

**Conclusion:**
While the extent of GM atrophy and reduction of GM relaxation rates were equally pronounced in both SPMS and RMS, no significant difference was found between SPMS and RMS with respect to sNfl. The exclusive association of sNfl with R1 and R2 in GM in SPMS implies that GM damage in SPMS corresponds to axonal degeneration, whereas in RMS several factors coming together may influence GM pathology. This suggests that the sNfL levels in RMS and SPMS are based on different forms of tissue affection and therefore have to be evaluated in the context of disease course.

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