in order to compare to the true lesion histopathological segmentation, and determine whether or not it gives better results than FLAIR data.

# Using qMRI to characterize lesioned tissues in MS patients: a longitudinal study

#1622

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## INTRODUCTION

FLAIR sequence from conventional MRI is the most commonly used imaging technique for the diagnosis and follow-up of multiple sclerosis (MS) disease though it has limited histopathological specificity. "Quantitative MRI" (qMRI), as opposed to conventional MRI, provides quantitative measures of brain tissues. With an MPM protocol, 4 parameter maps are constructed (MTsat, PD, R1 and R2*), reflecting tissues physical properties associated to biological features such as water, iron and myelin content [1]. QMRIs have already been used to study brain microstructure evolution with aging [2], or to compare sick and healthy populations in the case of different diseases such as multiple sclerosis (MS) [3] and glioma [4]. Here, we investigate the evolution of those parameters through time in an MS population.

## DATA ACQUISITION & PROCESSING

- 17 MS patients, 11 with relapsing-remitting MS form (RRMS), 6 with a progressive phenotype (PMS).
- All subjects scanned at least twice, with a minimal one year scan interval.
- MRI acquisition (3T Siemens Prisma) methodology as in [3] and qMRI maps estimated with the hMRI toolbox [1].
- Longitudinal registration performed with SPM12 and multi-channel segmentation using the US-with-Lesion (USwL) approach [3,5] with MT, PD, R1 and FLAIR images.
- 4 tissue classes of interest considered: normal-appearing white matter (NAWM), normal-appearing cortical (cNAGM) and deep gray matter (dNAGM) and lesions.
- Median MT, R1 and R2* values from these 4 tissue classes are used to assess the disease evolution for each subject.

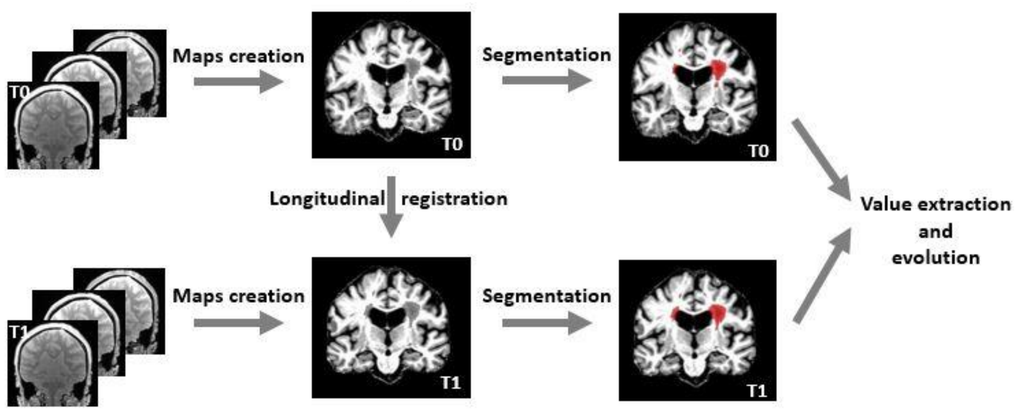


**Fig. 1:** Preprocessing steps

## METHODS

The rate of change in qMRI parameter, i.e. value difference over scan interval, was assessed through a regression model as follows:

$$Y = \beta_0 + \beta_1 X_{age} + \beta_2 X_{v\ init} + \beta_3 X_{status} + \varepsilon$$

Where *Y* is the rate of change for a qMRI parameter and tissue class, $X_{age}$ is the patients' age mid-scanning interval, $X_{v\ init}$ is the parameter value at first scan, $X_{status}$ is a binary variable representing the patient's clinical status (NEDA score [6] for RRMS and CDP [7] for PMS patients), $\beta$ values are the corresponding regression parameters ($\beta_0$ is the intercept), $\varepsilon$ the residuals. Those factors were chosen because they are the most likely to influence the rate of change of different qMRI parameters.

The partial influence on the rate of change of each factor was evaluated with permutation tests on the residuals, following the method from Freedman and Lane [8].

## RESULTS & DISCUSSION

**Fig. 2** shows the evolution of MT and R2* for each subject individually, the rate of change being normalized to a one-year interval for easier comparison. **Table 1** gathers the *p*-values obtained with the permutation tests applied to the $\beta$ parameters of the regression, focused on NAWM and cNAGM (the other tissues not showing any significant results). We choose to investigate only $X_{v\ init}$ and $X_{status}$ because patients' age is not uniformly distributed.

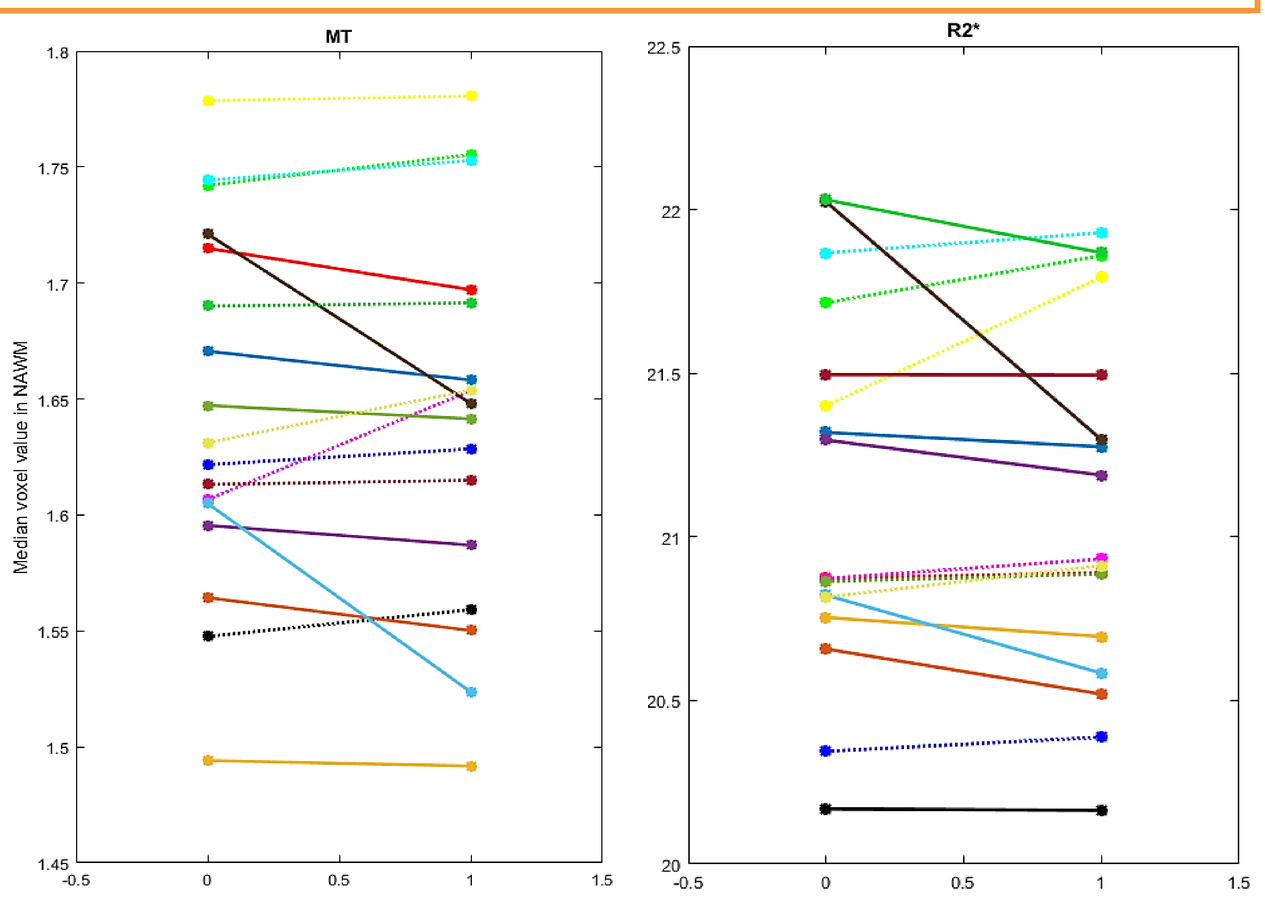


**Fig. 2:** Rate of change of MT (left) and R2* (right) in NAWM normalized for a one-year inteval, each line corresponds to one patient. Dotted lines show an increase in the parameter value

| | | NAWM | | cNAGM | |
|---|---|---|---|---|---|
| | | $X_{v\ init}$ | $X_{status}$ | $X_{v\ init}$ | $X_{status}$ |
| **MT** | *p* | 0.586 | 0.058 | 0.652 | 0.067 |
| | β | -0.12 | 1.04 | -0.10 | 1.09 |
| **R1** | *p* | 0.102 | 0.449 | **0.014** | 0.447 |
| | β | -0.39 | 0.40 | -0.61 | -0.40 |
| **R2*** | p | 0.825 | **0.038** | 0.853 | 0.201 |
| | β | -0.05 | 1.20 | 0.05 | 0.90 |

**Table 1:** Permutations *p*-values for NAWM and cNAGM, evaluating factor partial influence

Results & limitations discussion:

- Despite the limited number of subjects (17), 2 *p*-values are significant at *p<.05* and 2 others are just above this threshold, calling for a broader study to confirm and strengthen these results.
- Patient status is linked to R2* change in NAWM and (almost significantly) to MT change in both NAWM and cNAGM. This points at some remyelinization with better clinical status.
- The initial value seems to have an impact in the R1 change in cNAGM. Patients starting with a smaller value tend to increase in the following years. It could be that R1 expresses myelin content until some point where other factors (gliosis and axonal dysfunction for example) take over.

## CONCLUSION

This longitudinal analysis allowed to highlight two main results: 1. It confirms that qMRI is a useful tool in the study of MS disease, as it helps to understand the brain microstructural changes linked to the condition. 2. Despite the limited number of subjects and low statistical power, those are promising preliminary results on the evolution of qMRI parameters over time in MS disease, which open the doors for further analysis on a larger dataset.

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