

Multi-center (mono-vendor) longitudinal conventional and quantitative spinal cord MRI in Multiple Sclerosis at 3 Tesla - The EMISEP Study: First results

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The EMISEP Study : First results

Multi-center (mono-vendor) longitudinal conventional and quantitative spinal cord MRI in Multiple Sclerosis at 3 Tesla

Funding : French Ministry of Health 2012 Elise Bannier - <u>elise.bannier@irisa.fr</u> CHU Rennes, Unité/Projet Visages team.irisa.fr/visages/emisep









Neurinfo

Multiple sclerosis (MS) is an often disabling disease of the central nervous system affecting the brain and the spinal cord.

Especially, walking impairment is considered by the patients as the main cause of disability (Hobart et al., 2003).

However, there is a huge heterogeneity in disability progression between patients.

There is a need to identify prognostic factors at the individual level to guide therapeutic decisions.



« Clinico-Radiological paradox »

Barkhof et al. 1999

MRI and Multiple Sclerosis – What about Spinal Cord MRI?



Can spinal cord involment more directly explain motor and sensitive impairment and predict disease evolution ?



> 75 % of spinal cord images show lesions, more frequently in the cervical than thoracic cord (*Ikuta et al. 1976, Nijeholt et al. 1998, Bot et al. 2002, Eden et al. 2018*)



Eden et al. ISMRM 2018

Correlation with impairment

- Weak : Focal lesions (Kidd et al. 1993, Nijeholt et al. 1998)
- Stronger with quantitative imaging
 - Atrophy (Daams et al. 2014, Kearney et al. 2014)
 - Diffusion and MT imaging (Zackowski et al. 2009, Oh et al. 2013)

Prognosis

Spinal cord focal lesions have an impact on patient
prognosis (Brownlee et al, 2016, Arrambide et al. 2018)
No long term quantitative studies

Relies on improved image quality for lesion and quantitative imaging (Wheeler-Kingshott 2014, Stroman 2014)

MRI and Multiple Sclerosis – Study design

EMISEP



13 centers initially
3 scanner change
<1 inclusion (2 GE scanners)
→ 7 centers included patients
5 Siemens, 1 Philips scanner

MRI and Multiple Sclerosis – What about Spinal Cord MRI?



Clinical follow up EDSS, 6min, 8 meter, 9 holes peg test Auto questionnaires MSWS12, Qualiveen Quantitative : Strength and vibration Imaging protocol

- Whole cord
 - Sag T2 TSE and PSIR TSE
- Cervical cord
 - Axial 2D T2* ME GRE C1-C3 and C4-
 - $C7 \rightarrow lesion$
 - Sag 3D T1 \rightarrow atrophy
 - Ax 3D GRE with and without MT \rightarrow MTR
 - Sag 30 dir Diffusion
- Brain (OFSEP French MS Cohort protocol)
 - Sag 3D T1 pre Gd
 - Sag 3D FLAIR
 - Ax DP/T2 or 3D T2
 - Ax 30 Dir Diffusion
 - Sag 3D T1 post Gd

MRI and Multiple Sclerosis – Inclusions



81 patients were included between 2014 and 2017
46 healthy controls
to date >18 months follow-up

Magnetization Transfer Ratio

Healthy Controls reproductibility study Intra-subject Between-subject Between-scanner

Patient study at M0

Diffusion imaging

Distortion correction (Snoussi, ISBI 2019) Lesion location (Chouteau, ECTRIMS 2018)

Lesion imaging

PSIR vs T2 TSE (Rojat et al, JFR 2018)

Article 1

Measurement of Magnetization Transfer Ratio (MTR) from Cervical Spinal Cord: Multicenter Reproducibility and Variability

Combes, Monteau, JMRI 2018

| | IRM 1 (Siemens Verio) | IRM 2 (Siemens Verio) | IRM 3 (Siemens Verio) | IRM 4 (Siemens Skyra) | IRM 5 (Siemens Prisma) | Total |
|------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|------------------------------|-------|
| # subjects | 4 | 20 | 5 | 5 | 20 | 44 |
| # scans | 4 | 20 | 5 | 5 | 30 | 64 |
| | | Betwee Betwee | en scanner en session | | | |

Imaging details 3D GRE, 52 3mm slabs, 0.7mmx0.7mm in-plane resolution, TR/TE=38/3.57ms, 23°, water excitation and GRAPPA 2 MT0 : no prepulse MT1 : with vendor MT prepulse (Gaussian, 1200Hz off-resonance)

Processing (Benoît Combès, Post-Doc)

Registration of MT1 to MT0 using the Anima toolbox (v2.3)* MTR map computation Whole cord segmentation Vertebra labeling Atlas registration GW/WM segmentation (>0.8)









Boxplots of mean MTR measurements in gray matter (GM) and white matter (WM) for each level between C1 and C7 and for C4-C6.

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Variation coefficient = (standard deviation / mean) x 100

Global variation coefficient of 3% (0.9 pu) is compatible with the detection of 1pu MTR Variations between 2 groups (45 per group, type I error= 0.05 and type II error= 0.10)

These results show that it is possible to use cervical cord MTR in multicenter studies

Yet

This was evaluated on a single vendor Inhomogenous MTR along the cord The investigation in longitudinal studies remains challenging

Article 2

Focal and diffuse cervical spinal cord damage in patients with early relapsingremitting MS: A multicentre magnetization transfer ratio study

Combes, Kerbrat, Multiple Sclerosis Journal 2018

Goals

Quantify MTR changes in early RRMS patients in comparison with healthy controls Describe spatial distribution within and outside lesions Correlate MTR measurements with clinical scores









MTR (C4-C6) is significantly lower in patients versus controls considering the normal appearing spinal cord (lesion excluded) and the whole spine



In the sagittal plane



In the axial plane













Correlation with clinical scores

| | EDSS | Pyramidal | 8m | 6 minutes | 12 MSWS |
|---------------------|------------|------------|------------|------------|----------------|
| | | EDSS | | | |
| MTR | -0.21 | -0.27 | -0.08 | 0.13 | -0.12 |
| | (p = 0.14) | (p = 0.05) | (p = 0.57) | (p = 0.36) | (p = 0.39) |
| Cord Lesion | 0.26 | 0.28 | 0.00 | -0.26 | 0.30 |
| volume | (p = 0.06) | (p = 0.03) | (p = 1.00) | (p = 0.05) | (p = 0.03) |
| CSA | 0.08 | 0.01 | 0.04 | -0.04 | -0.06 |
| | (p = 0.58) | (p = 0.92) | (p = 0.75) | (p = 0.79) | (p = 0.67) |
| Brain lesion | 0.15 | 0.12 | -0.12 | -0.11 | 0.07 |
| volume | (p = 0.27) | (p = 0.38) | (p = 0.37) | (p = 0.43) | (p = 0.63) |

Diffuse and focal spinal cord burden can be measured at the beginning of the disease, and is correlated with lesion load

Longitudinal data needs to be processed to investigate whether initial burden can predict disability at 1, 2, 3 and 5 years.





MTR from Cervical Spinal Cord: Longitudinal data – Ongoing work

A particular case



MTR from Cervical Spinal Cord: Longitudinal data

A particular case



MTR from Cervical Spinal Cord: Longitudinal data

Whole cord MTR change between M12 and M0 in a group of 39 patients





...ongoing work

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