Cervical myelopathy patient follow-up after decompressive surgery using diffusion tensor imaging (DTI) and inhomogeneous magnetization transfer (ihMT): preliminary application and results

Manuel Taso[1,2], Olivier M. Girard[3,4], Guillaume Duhamel[3,4], Thorsten Feiweier[5], Pierre-Jean Arnoux[2], Maxime Guye[3,4], Jean-Philippe Ranjeva[3,4], Kathia Chaumoitre[6], Pierre-Hugues Roche[7], and Virginie Callot[3,4]

[1]*CRMBM-CEMEREM UMR 7339, Aix-Marseille Université, CNRS, Marseille, France,* [2]*LBA UMR T 24, Aix-Marseille Université, IFSTTAR, Marseille, France,* [3]*CRMBM UMR 7339, Aix-Marseille Université, CNRS, Marseille, France,* [4]*CEMEREM, Pole d'imagerie médicale, Hopital la Timone, AP-HM, Marseille, France,* [5]*Siemens AG, Healthcare, Erlangen, Germany,* [6]*Service de radiologie, Hopital Nord, Pole d'imagerie médicale, AP-HM, Marseille, France,* [7]*Service de Neurochirurgie,Trauma Center, Hopital Nord, AP-HM, Marseille, France*

TARGET AUDIENCE Basic scientists and clinicians involved in the diagnostic and management of spinal cord (SC) degenerative pathologies

INTRODUCTION Cervical myelopathies (caused by intervertebral disk degeneration among other factors) are a common cause of SC dysfunction, especially in elderly people (1). In clinical practice, although diagnosis highly depends on the presence of T_2-w hyperintensities (2) as well as poor prognosis depending on postoperative T_2-abnormalities persistence (2), both diagnosis and prognosis still lack of objective and quantitative markers of SC tissue impairment and indices of potential postoperative neurological recovery (2). In this study, we propose to perform a longitudinal MR follow-up (pre/post surgery) of patients suffering from cervical myelopathy, using a multimodal quantitative MR protocol combining diffusion tensor imaging (DTI), which has already shown to be more predictive of surgery outcome (3) than the sole presence of T_2 hyperintensity, and inhomogeneous magnetization transfer (ihMT), a recently developed technique presumably myelin-specific (4,5) that bears great potential to characterize white matter (WM) integrity. We investigate whether predictive biomarkers or response criteria could be established from both techniques.

MATERIAL AND METHODS ***MR scanning:*** 2 patients (1M/1F, respective age 59 and 76 y.o.) with cervical myelopathy and 18 controls (7M/11F, mean age 59±5yo) were recruited and examined at baseline (T_0) and 3 months after decompressive surgery (T_3). The neurological deficits were assessed with the modified JOA scale (6) at both T_0 and T_3. MRI was performed at 3T (MAGNETOM Verio, Siemens Healthcare, Germany) using standard head, neck and spine matrix coils. **Anatomical imaging** consisted in a sagittal T_2-w TSE sequence (13 contiguous slices, thickness 2mm) followed by a 3D T_1-w MPRAGE sequence (176 slices, 1mm isotropic resolution) and an axial T_2*-w MEDIC (multi-echo GRE) sequence (ECG-gated, 0.5x0.5x5mm^3, 1 slice per cervical level and one slice at the level of maximal compression, noted C_{max}). **DTI** data were acquired with an ECG-gated monopolar single-shot SE-EPI prototype sequence (30 directions, 2 b-values (0-800 s/mm^2), fat suppression and local B_0 shimming), in the sagittal plane (FOV=266x266 mm^2, 7 contiguous slices, resolution 1.9x1.9x4mm^3) as well as in the axial plane, at C_{max} (FOV 128x128 mm^2, 3 slices, 0.9x0.9x10mm^3). FA, ADC, $\lambda_{//}$ and $\lambda_{\perp}$ were estimated using Siemens Neuro 3D software. **Inhomogeneous Magnetization Transfer imaging** (4,5) was based on a ECG-triggered single-slice HASTE readout (TR=4s) combined with a customized pulsed ihMT preparation (500 Hann-shaped pulses (500µs duration), repeated every 1ms, frequency offset f=7KHz, E_{TR} = 12.1µT².s). The ihMT contrast was generated by combining 4 different MT images according to ihMT=MT(+f)+MT(-f)–MT(+/-f)–MT(-/+f), in both sagittal (FOV 220x220mm^2, resolution 1.7x1.7x4mm^3) and C_{max} axial planes (FOV=172x172mm^2, resolution 0.9x0.9x10mm^3). ECG data were recorded for retrospective filtering (7) before calculation of ihMT ratio (ihMTR=ihMT/M_0) and conventional MTR (MTR=1-MT(+f)/M_0). K-space apodization (hamming function) was used for the ihMT and MT data to reduce Gibbs artifacts within the SC. Total protocol duration was 45 min.


Fig. 1

Post-processing: The T_1-w volume was automatically segmented using PropSeg (8), part of the Spinal Cord Toolbox (http://sourceforge.net/projects/spinalcordtoolbox) (9), and registered to the MNI-Poly-AMU template (10), providing a ROI delineation and labeling of the cervical vertebral levels within the patient's space by inverting the warping field from patient to template (cf. fig. 1). Afterwards, the segmentation of the T_1-w volume was non-linearly registered to both Trace (DTI) and ihMTR maps (both providing exquisite contrasts between SC and adjacent tissues), using the SC toolbox multimodal registration module (7) (ANTs, SyN transform, cross-correlation cost function). The vertebral labeling was then warped to each modality, allowing for a level-specific quantification of the metrics (cf. fig. 3 and 5).

RESULTS AND DISCUSSION: ***Patient 1*** presented with a mJOA of 13/17 at baseline (T_0), with a maximal compression at the C4/C5 disk (cf fig. 2a, 2d). Diffusion metrics (cf. fig. 3b) were close (within STD) to reference values, except for C3/C4 levels, which presented higher $\lambda_{//}$. From C1 to C5, ihMTR was lower than for controls, with maximal impairment at C_{max} and C5 (fig. 2c and 3). MTR was within 10% similar to controls, except at C5. At T_3, the SC presented with a decompression of the antero-posterior diameter (by 20% compared to baseline (fig. 2e). ihMTR (fig. 2h and 3) further decreased below C_{max}, whereas MTR further decreased rostrally with an increase of $\lambda_{\perp}$. These results may suggest a 3-step process, with an already installed demyelination rostrally at T_0 (seen by ihMT), with a continued tissues destructuration at T_3 (seen by MTR and $\lambda_{\perp}$), along with a delayed demyelination below C_{max} at T_3. These observations are in line with the declining neurological function of the patient (mJOA at T_3 of 11/17).

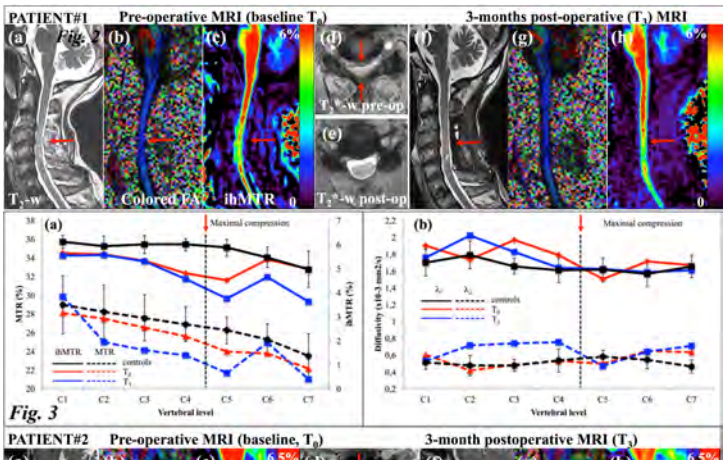

Fig. 3

Patient 2 presented with a C5/C6 disk protrusion into the SC (cf fig. 4a and d, red arrows), with a T_2 hyperintensity covering both C5 and C6 levels. This patient had a baseline mJOA of 13/17, abnormal diffusion mostly below C_{max} and myelin impairment around C_{max}. At T_3, an increase in SC øAP by 4% and restoration of the anterior subarachnoid space is seen and the mJOA was evaluated to 15. Diffusion metrics regressed, drifting more towards reference value at lesion site and caudal to C_{max}, but getting lower than reference rostrally. When considering MT/ihMT metrics, it is worth noting that both metrics go in opposite trends, with an ihMTR diminishing at T_3 rostrally to C_{max} and stabilized around C_{max} (as seen on fig.4h) while the MTR increases along all levels. Knowing that the $\lambda_{\perp}$ also diminishes in the same regions, one could hypothesize demyelination followed by gliosis (while conventional MTR would be sensitive to all macromolecular content, ihMTR would be more specific for myelin (11)).

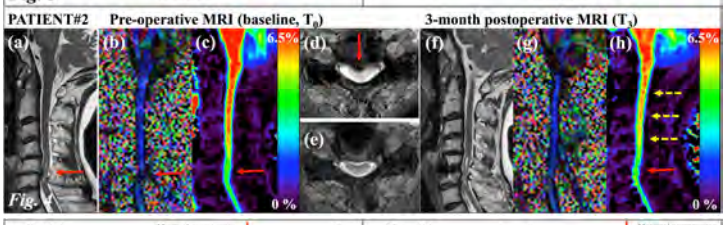

Fig. 4

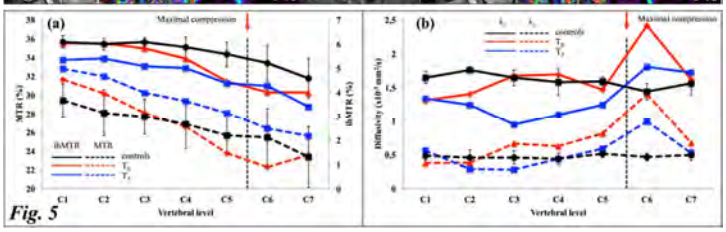

Fig. 5

The 3-month delay post-surgery is of course too early to draw conclusions about final recovery and potential predictive values, however, further answers about patient evolutions and pathophysiological processes will be provided with their 6-months clinical and MR evaluations.

CONCLUSION In this preliminary study, 2 patients were followed using an anatomical/MT/ihMT/DTI multimodal MR protocol bringing complementary information on focal and diffuse tissue integrity and potentially on functional recovery prediction. Seven additional patients have been included at baseline and will be re-explored soon. Further work will also include analyses of axial data using automated processing in order to study region-specific alterations (sensory/motor WM tracts, compressed GM). Combined with multivariate analysis of the collected metrics, the continuity of this work should help determining predictive markers of patient outcome.

REFERENCES (1) Boden et al, J Bone Joint Surg Am 1990; (2) Vedentam et al., Eur Spine J, 2013; (3) Jones et al, AJNR 2012; (4) Varma et al, MRM 2014; (5) Girard et al, MRM 2014; (6) Chile et al, Neurosurgery 1999; (7) Girard et al., ISMRM 2014; (8) De Leener et al, Neuroimage 2014; (9) Cohen-Adad et al, OHBM 2014; (9) http://sourceforge.net/projects/spinalcordtoolbox/, (10) Fonov et al, Neuroimage 2014; (11) Alsop et al., ISMRM 2004.

ACKNOWLEDGMENTS ANR-11-IDEX-0001-C2