

MS Journal Appendix for MRI methodology

Hardware	
Field strength	3T
Manufacturer	Siemens
Model	Centers 01, 02 and 03: MAGNETOM Verio (VB17); Centers 04 and 05: MAGNETOM Skyra (VD13)
Coil type (e.g. head, surface)	head and surface
Number of coil channels	12, 32

Brain acquisition sequence	
Type (e.g. FLAIR, DIR, DTI, fMRI)	3D FLAIR
Acquisition time	5min
Orientation	Sagittal
Alignment (e.g. anterior commissure/poster commissure line)	
Voxel size	1x1x1.1
TR	5000
TE	399
TI	1800
Flip angle	
NEX	1
Field of view	256x256
Matrix size	256x256
Parallel imaging	Yes
If used, parallel imaging method: (e.g. SENSE, GRAPPA)	GRAPPA 2
Cardiac gating	No
If used, cardiac gating method: (e.g. PPU or ECG)	
Contrast enhancement	No

Brain acquisition sequence	
Type (e.g. FLAIR, DIR, DTI, fMRI)	3D T1
Acquisition time	4:30
Orientation	Sagittal
Alignment (e.g. anterior commissure/poster commissure line)	
Voxel size	1x1x1
TR	1900
TE	2.26
TI	900
Flip angle	9
NEX	1
Field of view	256x256

Matrix size	256x256
Parallel imaging	Yes
If used, parallel imaging method: (e.g. SENSE, GRAPPA)	GRAPPA 2
Cardiac gating	No
If used, cardiac gating method: (e.g. PPU or ECG)	
Contrast enhancement	Both (pre and post Gd)

Brain acquisition sequence	
Type (e.g. FLAIR, DIR, DTI, fMRI)	Axial T2
Acquisition time	2:12
Orientation	Axial
Alignment (e.g. anterior commissure/poster commissure line)	AC-PC
Voxel size	0.7x0.7x3
TR	6530
TE	9.4/84
TI	
Flip angle	150
NEX	1
Field of view	220x220
Matrix size	320x320
Parallel imaging	Yes
If used, parallel imaging method: (e.g. SENSE, GRAPPA)	GRAPPA 2
Cardiac gating	No
If used, cardiac gating method: (e.g. PPU or ECG)	
Contrast enhancement	No

Spinal cord acquisition sequence	
Type (e.g. FLAIR, DIR, DTI, fMRI)	Axial T2*W MEDIC
Acquisition time	twice 4min
Orientation	Axial, Perpendicular to the cord
Alignment (e.g. anterior commissure/poster commissure line)	C1-C3 and C4-C7 (2 acquisitions)
Voxel size	0.7x0.7x3
TR	849
TE	23
TI	
Flip angle	30

NEX	2
Field of view	180x180
Matrix size	256x256
Parallel imaging	Yes
If used, parallel imaging method: (e.g. SENSE, GRAPPA)	GRAPPA 2
Cardiac gating	No
If used, cardiac gating method: (e.g. PPU or ECG)	
Contrast enhancement	No

Spinal cord acquisition sequence	
Type (e.g. FLAIR, DIR, DTI, fMRI)	Sag T2
Acquisition time	3min each
Orientation	Sagittal
Alignment (e.g. anterior commissure/poster commissure line)	2 acquisitions : Cervical and Dorsal
Voxel size	0.9x0.7x2.5
TR	3000
TE	68
TI	
Flip angle	180
NEX	3
Field of view	260x260
Matrix size	384x75%
Parallel imaging	Yes
If used, parallel imaging method: (e.g. SENSE, GRAPPA)	GRAPPA 2
Cardiac gating	No
If used, cardiac gating method: (e.g. PPU or ECG)	
Contrast enhancement	No

Spinal cord acquisition sequence	
Type (e.g. FLAIR, DIR, DTI, fMRI)	Sag PSIR
Acquisition time	2:37s each
Orientation	
Alignment (e.g. anterior commissure/poster commissure line)	2 acquisitions : Cervical and Dorsal
Voxel size	0.8x0.8x2.5
TR	4585ms
TE	9.8ms
TI	400ms

Flip angle	160
NEX	1
Field of view	260x260
Matrix size	320x320
Parallel imaging	Yes
If used, parallel imaging method: (e.g. SENSE, GRAPPA)	GRAPPA 2
Cardiac gating	No
If used, cardiac gating method: (e.g. PPU or ECG)	
Contrast enhancement	No

Spinal cord acquisition sequence	
Type (e.g. FLAIR, DIR, DTI, fMRI)	MT imaging
Acquisition time	2x7min
Orientation	Axial
Alignment (e.g. anterior commissure/poster commissure line)	Perpendicular to the cord
Voxel size	0.7x0.7x3
TR	38
TE	3.57
TI	
Flip angle	23
NEX	
Field of view	230x230
Matrix size	320x320
Parallel imaging	Yes
If used, parallel imaging method: (e.g. SENSE, GRAPPA)	GRAPPA
Cardiac gating	No
If used, cardiac gating method: (e.g. PPU or ECG)	
Contrast enhancement	No

Spinal cord acquisition sequence	
Type (e.g. FLAIR, DIR, DTI, fMRI)	3D T1 MPRAGE
Acquisition time	4:12s
Orientation	Sagittal
Alignment (e.g. anterior commissure/poster commissure line)	
Voxel size	1x1x1
TR	1800
TE	2.79

TI	900
Flip angle	9
NEX	1
Field of view	250x250
Matrix size	256x256
Parallel imaging	Yes
If used, parallel imaging method: (e.g. SENSE, GRAPPA)	GRAPPA
Cardiac gating	No
If used, cardiac gating method: (e.g. PPU or ECG)	
Contrast enhancement	No

Image analysis methods and outputs	
Brain Lesions	
Type (e.g. Gd-enhancing, T2-hyperintense, T1-hypointense)	T2-hyperintense
Analysis method	Brain lesion loads were estimated using the command <i>animaPatientToGroupComparison</i> based on intensity comparisons to a control atlas from the T2, FLAIR and PD brain volumes. All the results were visually checked and manually corrected when necessary (AK, 11 segmentations were edited).
Analysis software	Anima (https://github.com/Inria-Visages/Anima-Public/wiki)
Output measure (e.g. count or volume [ml])	Brain lesion volume
Spinal cord lesions	
Type (e.g. Gd-enhancing, T2-hyperintense, T1-hypointense)	T2-hyperintense
Analysis method	Focal spinal cord lesions were defined as abnormal areas of increased signal change that could be demarcated from the surrounding tissue on axial T2* images. Sagittal T2 weighted images and sagittal PSIR images were used to help lesion identification but the final delineation was manually performed by an expert (JM) on the axial T2* images.
Analysis software	none
Output measure (e.g. count or volume [ml])	Cervical spinal cord lesion location, count and volume
Cross sectional area	
Type (e.g. whole brain, grey matter, white matter, spinal cord)	Spinal cord
Analysis method	Mean cross sectional area (CSA) on cervical level C2-C3 were estimated using the <i>sct_propseg</i> command on the T1 3D cord images.
Analysis software	Sct (https://sourceforge.net/p/spinalcordtoolbox/wiki/tools/)

Output measure (e.g. absolute tissue volume in ml, tissue volume as a fraction of intracranial volume, percentage change in tissue volumes)	Spinal cord cross sectional area (mm ²)
MTR measurement	
Type (e.g. whole brain, grey matter, white matter, spinal cord, normal-appearing grey matter or white matter)	Spinal cord MTR
Analysis method	First, the quality of each MT0/MT1 pair of images was visually checked by an expert (BC), to verify signal, contrast, absence of motion, and other types of artifacts. To correct for participant motion between MT0 and MT1 imaging, the MT1 image was rigidly and nonlinearly registered to the MT0 image using the <i>animaDenseSVFBMRegistration</i> command. Registration parameters are chosen so that smooth deformations are favored (elastic regularization factor=5). The MTR map was then computed as $MTR=100 \cdot (MT0-MT1)/MT0$.
Analysis software	Anima (https://github.com/Inria-Visages/Anima-Public/wiki)
Output measure	MTR maps
Cord segmentation and vertebrae levels labeling	
Type (e.g. whole brain, grey matter, white matter, spinal cord, normal-appearing grey matter or white matter)	Spinal cord MT0
Analysis method	The whole cord (WC) was segmented using the <i>sct_propseg</i> command on the MT0 image. The method was initialized by a set of seven manually selected points along the cord between C1 and C7. Then, the vertebrae were automatically labeled using the <i>sct_label_vertebrae</i> command. The method was initialized by selecting the axial slice that passed through the center of the C3C4 disc.
Analysis software	Sct (https://sourceforge.net/p/spinalcordtoolbox/wiki/tools/)
Output measure	Spinal cord mask and vertebrae labels
Alignment of lesion mask on MTR frame	

Type (e.g. whole brain, grey matter, white matter, spinal cord, normal-appearing grey matter or white matter)	Spinal cord DP and T2*w
Analysis method	Due to the shorter cover of T2*w volumes with respect to MT0 volumes, we performed a non-symmetric registration with the T2*w volumes as the reference and the MT0 volume as the moving volume using the <i>animaDenseSVFBMRegistration</i> command. Once the deformation estimated, it was algebraically inverted and applied to the cord lesion mask that was thus map to the anatomical frame of the MT0 volume.
Analysis software	Anima (https://github.com/Inria-Visages/Anima-Public/wiki)
Output measure	Cord lesion mask on MTR anatomical frame

Other analysis details:

Mean MTR extraction on ROI : Mean MTR for each ROI were extracted from R 3.4.3.

Statistical analysis: Statistical analyses were performed with R 3.4.3 and packages lme4, nlme and emmeans. Plots were generated using the ggplot2 package.