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<b>Auteurs:</b> Authors:	Lisa Eunyoung Lee, Julien Cohen-Adad, Irene M. Vavasour, Melanie Guenette, Katherine Sawicka, Neda Rashidi-Ranjbar, Nathan W. Churchill, Akash Chopra, Adelia Adelia, Pierre-Louis Benveniste, Anthony Traboulsee, Nathalie Arbour, Fabrizio Giuliani, Larry D. Lynd, Scott B. Patten, Alexandre Prat, Alice Schabas, Penelope Smyth, Roger Tam, Yunyan Zhang, Simon J. Graham, Mojgan Hodaie, Anthony Feinstein, Shannon Kolind, Tom A. Schweizer, & Jiwon Oh
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**Supplemental Table 1** Relationships between MTR and clinical outcome measures in the normal-appearing (non-lesional) cervical spinal cord regions of interest using multiple linear regression models for RIS, RRMS, and PPMS with unadjusted  $p < 0.1$ .

Group	Clinical Outcome	Region of Interest	Regression Coefficient ( $\beta$ )	95% CI	P-Value	R <sup>2</sup>
RIS	EDSS	Gray Matter	0.10	-0.02, 0.22	0.09	0.23
	MDT	Gray Matter	0.61	0.06, 1.15	<b>0.03</b>	0.24
RRMS	EDSS	Whole Spinal Cord	-0.08	-0.15, 0.00	0.05	0.04
		White Matter	-0.09	-0.16, -0.02	<b>0.01</b>	0.06
		Dorsal Columns	-0.07	-0.13, 0.00	0.05	0.05
		Lateral Funiculi	-0.08	-0.14, -0.01	<b>0.02</b>	0.05
		Ventral Funiculi	-0.04	-0.09, 0.00	0.08	0.04
PPMS	EDSS	White Matter	-0.24	-0.50, 0.02	0.07	0.10
		Dorsal Columns	-0.32	-0.54, -0.09	<b>0.01</b>	0.21
	WST	Dorsal Columns	-0.48	-1.01, 0.04	0.07	0.11
	MDT	Ventral Funiculi	-0.56	-1.09, -0.03	<b>0.04</b>	0.13

P-values were not adjusted for multiple testing given the exploratory nature of this analysis. Significant unadjusted p-values are bolded.

**Supplemental Table 2** Relationships between CSA and clinical outcome measures in multiple linear regression models for RIS, RRMS and PPMS.

Group	Clinical Outcome	Regression Coefficient ( $\beta$ )	95% CI	Unadjusted P-Value	Adjusted P-Value	R <sup>2</sup>
RIS	EDSS	0.01	-0.03, 0.05	0.66	0.66	0.15
	WST	-0.02	-0.05, 0.02	0.44	0.66	0.16
	MDT	-0.05	-0.24, 0.13	0.57	0.66	0.13
RRMS	EDSS	-0.01	-0.03, 0.01	0.43	0.65	0.03
	WST	-0.03	-0.05, -0.01	0.01	<b>0.03</b>	0.05
	MDT	-0.02	-0.10, 0.07	0.70	0.70	0.07
PPMS	EDSS	0.00	-0.06, 0.07	0.92	0.94	0.01
	WST	0.05	-0.17, 0.28	0.65	0.94	0.03
	MDT	0.01	-0.21, 0.23	0.93	0.94	0.02

P-values were adjusted for multiple testing using the false discovery rate method. Significant adjusted p-value is bolded.

**Supplemental Table 3** Relationships between MTR and clinical outcome measures in multiple regression models for RIS, RRMS and PPMS.

Group	Clinical Outcome	Region of Interest	Regression Coefficient ( $\beta$ )	95% CI	Unadjusted P-Value	Adjusted P-Value	R <sup>2</sup>
RIS	EDSS	Whole Spinal Cord	-0.17	-0.34, 0.00	0.05	0.19	0.21
		White Matter	-0.14	-0.31, 0.03	0.09	0.25	0.20
		Gray Matter	-0.17	-0.32, -0.01	0.04	0.18	0.22
		Dorsal Columns	-0.10	-0.22, 0.01	0.07	0.22	0.20
		Lateral Funiculi	-0.13	-0.30, 0.04	0.13	0.29	0.19
		Ventral Funiculi	-0.02	-0.14, 0.11	0.81	0.85	0.15
		Corticospinal Tracts	-0.09	-0.23, 0.04	0.18	0.29	0.18
	WST	Whole Spinal Cord	-0.18	-0.34, -0.01	0.03	0.18	0.23
		White Matter	-0.18	-0.33, -0.02	0.03	0.18	0.23
		Gray Matter	-0.11	-0.26, 0.05	0.17	0.29	0.18
		Dorsal Columns	-0.08	-0.19, 0.03	0.16	0.29	0.18
		Lateral Funiculi	-0.16	-0.32, 0.00	0.04	0.18	0.22
		Ventral Funiculi	-0.13	-0.25, -0.01	0.03	0.18	0.23
		Corticospinal Tracts	-0.09	-0.22, 0.04	0.18	0.29	0.18
MDT	Whole Spinal Cord	-0.22	-1.02, 0.57	0.58	0.76	0.13	

RRMS		White Matter	-0.24	-0.99, 0.52	0.53	0.74	0.13
		Gray Matter	-0.06	-0.79, 0.68	0.88	0.88	0.12
		Dorsal Columns	-0.28	-0.79, 0.24	0.28	0.43	0.14
		Lateral Funiculi	-0.15	-0.89, 0.60	0.70	0.83	0.12
		Ventral Funiculi	0.09	-0.48, 0.65	0.75	0.83	0.12
		Corticospinal Tracts	-0.11	-0.74, 0.51	0.71	0.83	0.12
	EDSS	Whole Spinal Cord	-0.11	-0.18, -0.05	<0.01	<b>0.01</b>	0.08
		White Matter	-0.10	-0.16, -0.04	<0.01	<b>0.01</b>	0.08
		Gray Matter	-0.09	-0.15, -0.03	<0.01	<b>0.02</b>	0.07
		Dorsal Columns	-0.07	-0.13, -0.02	0.01	<b>0.02</b>	0.06
		Lateral Funiculi	-0.11	-0.16, -0.05	<0.01	<b>0.01</b>	0.08
		Ventral Funiculi	-0.04	-0.08, 0.01	0.09	0.18	0.04
WST	Corticospinal Tracts	-0.07	-0.13, -0.02	0.01	<b>0.03</b>	0.06	
	Whole Spinal Cord	-0.06	-0.14, 0.01	0.10	0.18	0.03	
	White Matter	-0.06	-0.13, 0.01	0.09	0.18	0.03	
	Gray Matter	-0.04	-0.12, 0.03	0.23	0.40	0.03	
	Dorsal Columns	-0.04	-0.10, 0.03	0.25	0.40	0.02	
	Lateral Funiculi	-0.07	-0.14, 0.00	0.05	0.15	0.04	

		Ventral Funiculi	-0.02	-0.07, 0.03	0.41	0.45	0.02	
		Corticospinal Tracts	-0.06	-0.12, 0.01	0.10	0.18	0.03	
	MDT	Whole Spinal Cord	-0.11	-0.39, 0.16	0.41	0.45	0.07	
		White Matter	-0.09	-0.35, 0.17	0.50	0.51	0.07	
		Gray Matter	-0.14	-0.40, 0.12	0.30	0.42	0.07	
		Dorsal Columns	-0.10	-0.32, 0.12	0.37	0.45	0.07	
		Lateral Funiculi	-0.12	-0.37, 0.13	0.34	0.45	0.07	
		Ventral Funiculi	0.06	-0.12, 0.25	0.51	0.51	0.07	
		Corticospinal Tracts	-0.12	-0.36, 0.11	0.30	0.42	0.07	
	PPMS	EDSS	Whole Spinal Cord	-0.27	-0.42, -0.12	<0.01	<b>&lt;0.01</b>	0.25
			White Matter	-0.27	-0.41, -0.12	<0.01	<b>&lt;0.01</b>	0.26
			Gray Matter	-0.19	-0.34, -0.04	0.01	<b>0.02</b>	0.15
			Dorsal Columns	-0.22	-0.35, -0.09	<0.01	<b>0.01</b>	0.22
Lateral Funiculi			-0.25	-0.39, -0.11	<0.01	<b>&lt;0.01</b>	0.25	
Ventral Funiculi			-0.14	-0.26, -0.02	0.02	<b>0.03</b>	0.13	
Corticospinal Tracts			-0.23	-0.37, -0.08	<0.01	<b>0.01</b>	0.20	
WST		Whole Spinal Cord	-0.89	-1.42, -0.37	<0.01	<b>0.01</b>	0.24	
		White Matter	-0.83	-1.34, -0.33	<0.01	<b>0.01</b>	0.24	

		Gray Matter	-0.76	-1.27, -0.26	<0.01	<b>0.01</b>	0.21
		Dorsal Columns	-0.54	-1.04, -0.05	0.03	<b>0.04</b>	0.13
		Lateral Funiculi	-0.75	-1.25, -0.26	<0.01	<b>0.01</b>	0.21
		Ventral Funiculi	-0.72	-1.09, -0.35	<0.01	<b>&lt;0.01</b>	0.29
		Corticospinal Tracts	-0.63	-1.14, -0.12	0.02	<b>0.03</b>	0.16
	MDT	Whole Spinal Cord	-0.56	-1.15, 0.03	0.06	0.07	0.10
		White Matter	-0.59	-1.16, -0.02	0.04	0.05	0.12
		Gray Matter	-0.31	-0.86, 0.24	0.27	0.27	0.05
		Dorsal Columns	-0.61	-1.14, -0.08	0.03	<b>0.04</b>	0.14
		Lateral Funiculi	-0.36	-0.92, 0.20	0.20	0.21	0.06
		Ventral Funiculi	-0.47	-0.88, -0.06	0.02	<b>0.04</b>	0.14
		Corticospinal Tracts	-0.41	-0.97, 0.16	0.16	0.17	0.07

P-values were adjusted for multiple testing using the false discovery rate method. Significant adjusted p-values are bolded.

**Supplemental Table 4** Relationships between MTR and clinical outcome measures with age, sex, MRI system vendor type, and normalized brain volume as co-variates in multiple linear regression models for RRMS and PPMS with adjusted  $p < 0.1$ . No relationships reached an adjusted  $p < 0.1$  for RIS.

Group	Clinical Outcome	Region of Interest	Regression Coefficient ( $\beta$ )	95% CI	Unadjusted P-value	Adjusted P-Value	R <sup>2</sup>
RRMS	EDSS	Whole Spinal Cord	-0.10	-0.16, -0.03	<0.01	<b>0.02</b>	0.06
		White Matter	-0.09	-0.15, -0.03	<0.01	<b>0.02</b>	0.05
		Gray Matter	-0.09	-0.14, -0.03	<0.01	<b>0.02</b>	0.05
		Dorsal Columns	-0.06	-0.11, -0.01	0.02	0.09	0.04
		Lateral Funiculi	-0.09	-0.14, -0.03	<0.01	<b>0.02</b>	0.06
PPMS	EDSS	Whole Spinal Cord	-0.23	-0.38, -0.08	<0.01	<b>0.02</b>	0.29
		White Matter	-0.22	-0.37, -0.08	<0.01	<b>0.02</b>	0.29
		Gray Matter	-0.17	-0.31, -0.03	0.02	<b>0.04</b>	0.23
		Dorsal Columns	-0.17	-0.31, -0.03	0.02	<b>0.04</b>	0.23
		Lateral Funiculi	-0.22	-0.35, -0.09	<0.01	<b>0.01</b>	0.32
		Corticospinal Tracts	-0.20	-0.33, -0.06	0.01	<b>0.02</b>	0.27
	WST	Whole Spinal Cord	-0.85	-1.40, -0.29	<0.01	<b>0.02</b>	0.25
		White Matter	-0.79	-1.32, -0.25	<0.01	<b>0.02</b>	0.24
		Gray Matter	-0.73	-1.24, -0.21	0.01	<b>0.02</b>	0.22
		Lateral Funiculi	-0.72	-1.22, -0.21	0.01	<b>0.02</b>	0.23

		Ventral Funiculi	-0.69	-1.09, -0.30	<0.01	<b>0.01</b>	0.29
		Corticospinal Tracts	-0.59	-1.11, -0.07	0.03	0.05	0.17

P-values were adjusted for multiple testing using the false discovery rate method. Significant adjusted p-values are bolded.

**Supplemental Table 5** Relationships between MTR and clinical outcome measures with age, sex, MRI system vendor type, and disease duration as co-variates in multiple linear regression models for RRMS and PPMS with adjusted  $p < 0.1$ . No relationships reached an adjusted  $p < 0.1$  for RIS.

Group	Clinical Outcome	Region of Interest	Regression Coefficient ( $\beta$ )	95% CI	Unadjusted P-Value	Adjusted P-Value*	R <sup>2</sup>
RRMS	EDSS	Whole Spinal Cord	-0.11	-0.18, -0.05	<0.01	<b>0.01</b>	0.08
		White Matter	-0.10	-0.16, -0.04	<0.01	<b>0.01</b>	0.08
		Gray Matter	-0.09	-0.15, -0.03	<0.01	<b>0.02</b>	0.07
		Dorsal Columns	-0.07	-0.13, -0.02	0.01	<b>0.02</b>	0.07
		Lateral Funiculi	-0.10	-0.16, -0.05	<0.01	<b>0.01</b>	0.09
		Corticospinal Tracts	-0.07	-0.13, -0.02	0.01	<b>0.03</b>	0.06
PPMS	EDSS	Whole Spinal Cord	-0.28	-0.42, -0.14	<0.01	<b>&lt;0.01</b>	0.35
		White Matter	-0.27	-0.41, -0.14	<0.01	<b>&lt;0.01</b>	0.36
		Gray Matter	-0.20	-0.35, -0.06	0.01	<b>0.01</b>	0.24
		Dorsal Columns	-0.23	-0.36, -0.11	<0.01	<b>&lt;0.01</b>	0.33
		Lateral Funiculi	-0.25	-0.38, -0.12	<0.01	<b>&lt;0.01</b>	0.34
		Ventral Funiculi	-0.15	-0.26, -0.04	0.01	<b>0.02</b>	0.23
		Corticospinal Tracts	-0.23	-0.37, -0.10	<0.01	<b>&lt;0.01</b>	0.30
	WST	Whole Spinal Cord	-0.89	-1.43, -0.36	<0.01	<b>&lt;0.01</b>	0.25
		White Matter	-0.84	-1.35, -0.32	<0.01	<b>0.01</b>	0.24
		Gray Matter	-0.76	-1.28, -0.25	<0.01	<b>0.01</b>	0.21

		Dorsal Columns	-0.54	-1.05, -0.04	0.04	0.05	0.13
		Lateral Funiculi	-0.76	-1.26, -0.26	<0.01	<b>0.01</b>	0.21
		Ventral Funiculi	-0.72	-1.10, -0.34	<0.01	<b>&lt;0.01</b>	0.29
		Corticospinal Tracts	-0.63	-1.15, -0.11	0.02	<b>0.03</b>	0.16
	MDT	Whole Spinal Cord	-0.55	-1.15, 0.04	0.07	0.08	0.11
		White Matter	-0.59	-1.16, -0.01	0.05	0.06	0.12
		Dorsal Columns	-0.60	-1.14, -0.06	0.03	<b>0.04</b>	0.14
		Ventral Funiculi	-0.46	-0.88, -0.05	0.03	<b>0.04</b>	0.14

P-values were adjusted for multiple testing using the false discovery rate method. Significant adjusted p-values are bolded.

**Supplemental Table 6** Relationships between MTR and clinical outcome measures with age, sex, MRI system vendor type, and use of disease-modifying therapy as co-variates in multiple linear regression models for PPMS with adjusted  $p < 0.1$ .

Clinical Outcome	Region of Interest	Regression Coefficient ( $\beta$ )	95% CI	Unadjusted P-Value	Adjusted P-Value*	R <sup>2</sup>
EDSS	Whole Spinal Cord	-0.29	-0.44, -0.14	<0.01	<b>&lt;0.01</b>	0.28
	White Matter	-0.28	-0.43, -0.14	<0.01	<b>&lt;0.01</b>	0.29
	Gray Matter	-0.20	-0.35, -0.05	0.01	<b>0.02</b>	0.16
	Dorsal Columns	-0.24	-0.38, -0.11	<0.01	<b>&lt;0.01</b>	0.26
	Lateral Funiculi	-0.26	-0.40, -0.12	<0.01	<b>&lt;0.01</b>	0.27
	Ventral Funiculi	-0.15	-0.27, -0.03	0.02	<b>0.03</b>	0.15
	Corticospinal Tracts	-0.23	-0.38, -0.09	<0.01	<b>&lt;0.01</b>	0.22
WST	Whole Spinal Cord	-0.92	-1.45, -0.38	<0.01	<b>&lt;0.01</b>	0.25
	White Matter	-0.87	-1.38, -0.35	<0.01	<b>&lt;0.01</b>	0.24
	Gray Matter	-0.77	-1.28, -0.25	<0.01	<b>0.01</b>	0.21
	Dorsal Columns	-0.57	-1.09, -0.06	0.03	0.05	0.14
	Lateral Funiculi	-0.77	-1.28, -0.27	<0.01	<b>0.01</b>	0.22
	Ventral Funiculi	-0.74	-1.12, -0.36	<0.01	<b>&lt;0.01</b>	0.30
	Corticospinal Tracts	-0.64	-1.16, -0.12	0.02	<b>0.03</b>	0.16
MDT	White Matter	-0.54	-1.14, 0.05	0.07	0.09	0.13
	Dorsal Columns	-0.57	-1.13, -0.00	0.05	0.06	0.14
	Ventral Funiculi	-0.44	-0.86, -0.03	0.04	0.05	0.15

P-values were adjusted for multiple testing using the false discovery rate method. Significant adjusted p-values are bolded.