

Postmortem quantitative MRI disentangles histological lesion types in multiple sclerosis

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Methods

The TE of the 3D-EPI sequence was adapted to postmortem conditions and amounted to 35ms. We compared QSM maps obtained with 3D EPI with QSM maps obtained with multi-echo gradient echo acquisition, which has been performed on 10 echoes (the shortest ones being 7.30ms), in $n = 76$ regions of interest. The results obtained for 76 regions of interest (lesions and NAWM) showed that there is a high correlation between the QSM values obtained with the two methods ($r = 0.68$, $p < 0.0001$), which is why we judge the QSM map obtained with single echo 3D-EPI images with TE = 35 ms as adequate to study also myelin properties.

Fig. S1: full image slice of each MRI method

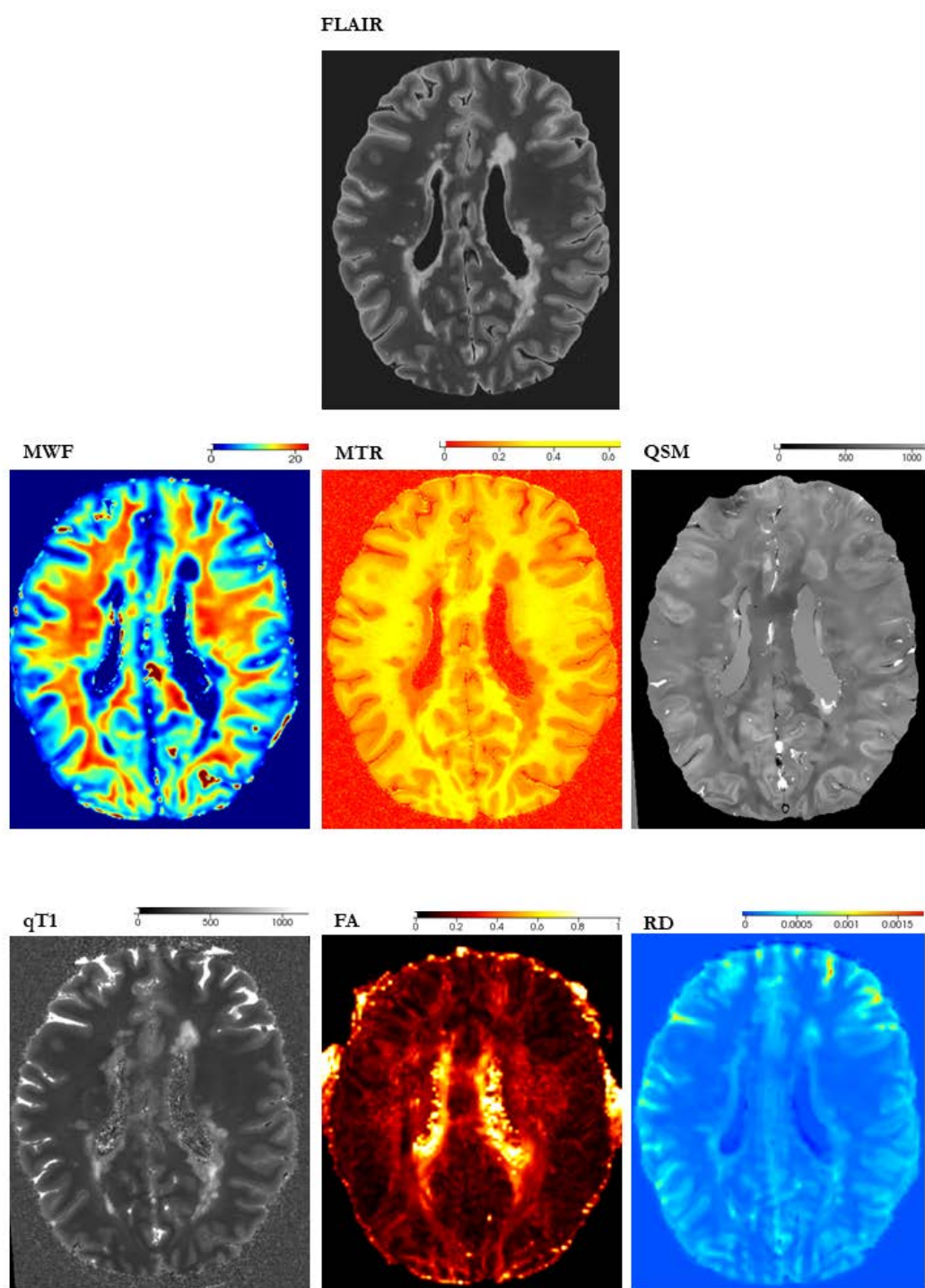


Fig. S2: Brain slab and corresponding 3D EPI image.

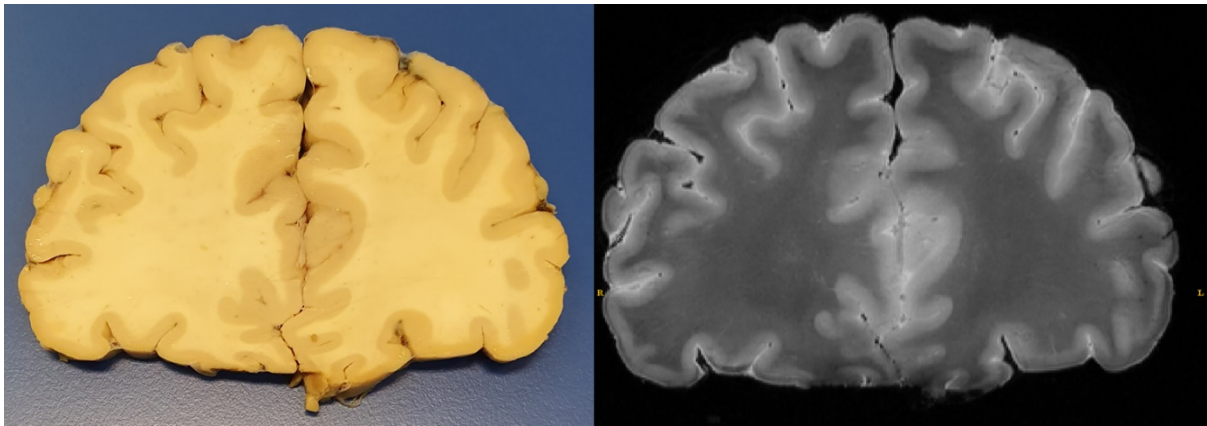


Fig. S3: Example of WML and NAWM segmentation on digitized histological slices and on the corresponding EPI 3D images.

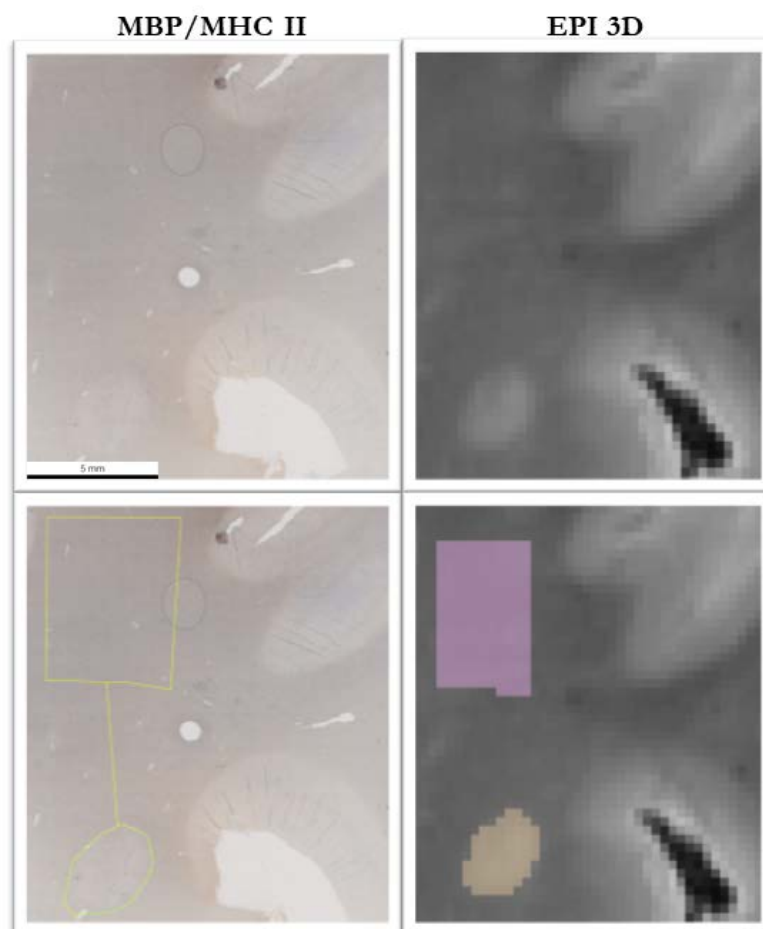
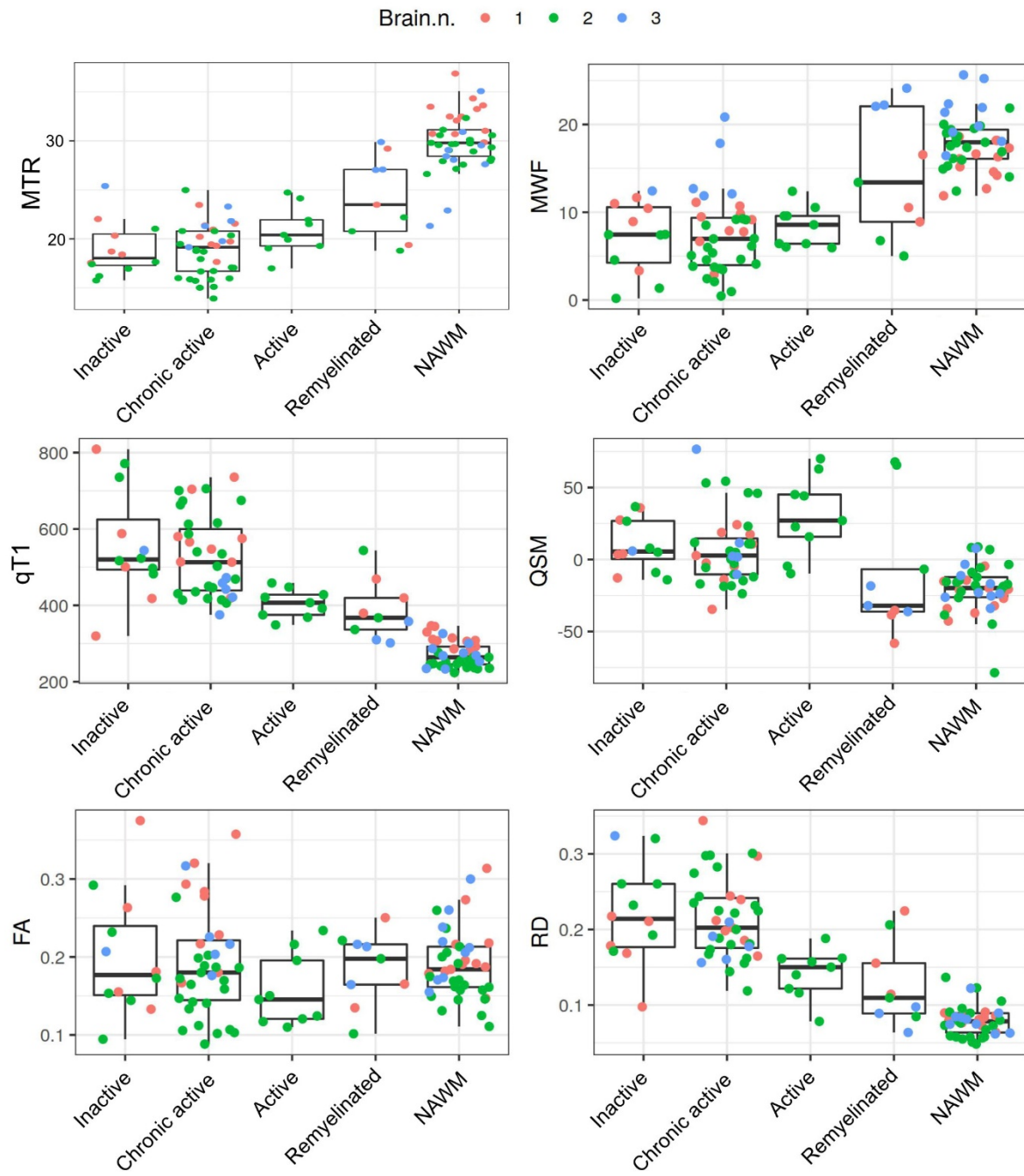


Fig. S4. MRI measures by type of lesions.



Tables S1-4. Association between qMRI and histology measures – linear regression models.

A: model including sampling location as covariate (NAWM vs. lesion).

B: model including sampling location as covariate (NAWM vs. lesion) and interaction term between the MRI measure and lesion (qMRI:NAWM (vs. lesion)). In this model, the estimate for the MRI measure indicates the association with histology measure in lesions only, whereas the interaction term indicates if this association differs in the NAWM.

Table S1. Association between qMRI and Mean MBP (IHC)

A.

Variable	Estimate	CI	p
MTR	0,01	[-0.04,0.06]	0,7386
NAWM (vs lesion)	0,02	[0.01,0.02]	<0.001
MWF	0,00	[0.00,0.00]	0,00376
NAWM (vs lesion)	0,01	[0.01,0.02]	< 0.001
qT1	-0,00002	[-0.00004,-0.00000]	0,0221
NAWM (vs lesion)	0,01388	[0.00926,0.01851]	<0.001
QSM	0,0000	[-0.0001,0.0000]	0,141
NAWM (vs lesion)	0,0167	[0.0133,0.0201]	<0.001
FA	0,02	[-0.01,0.05]	0,173
NAWM (vs lesion)	0,02	[0.02,0.02]	<0.001
RD	-0,05	[-0.08,-0.02]	0,00384
NAWM (vs lesion)	0,01	[0.01,0.02]	< 0.001

B.

Variable	Estimate	CI	p
MTR	0,08	[0.02,0.14]	0,0115
NAWM (vs lesion)	0,06	[0.04,0.09]	<0.001
MTR:NAWM (vs lesion)	-0,18	[-0.27,-0.09]	<0.001
MWF	0,00	[0.00,0.00]	0,0114
NAWM (vs lesion)	0,01	[-0.00,0.03]	0,0608
MWF:NAWM (vs lesion)	0,00	[-0.00,0.00]	0,9021
qT1	-0,00002	[-0.00003,0.00000]	0,09228
NAWM (vs lesion)	0,03335	[0.01352,0.05293]	0,00133
qT1:NAWM (vs lesion)	-0,00007	[-0.00013,-0.00000]	0,05116
QSM	0,0000	[-0.0001,0.0000]	0,224
NAWM (vs lesion)	0,0165	[0.0125,0.0205]	<0.001
QSM:NAWM (vs lesion)	0,0000	[-0.0002,0.0001]	0,827
FA	0,01	[-0.03,0.04]	0,735
NAWM (vs lesion)	0,01	[-0.00,0.02]	0,132
FA:NAWM (vs lesion)	0,05	[-0.01,0.11]	0,122
RD	-0,05	[-0.08,-0.01]	0,00824
NAWM (vs lesion)	0,02	[0.00,0.03]	0,00870
RD:NAWM (vs lesion)	-0,03	[-0.14,0.09]	0,65516

Table S2: Association between qMRI and mean LFB.**A.**

Variable	Estimate	CI	p
MTR	0,15	[-0.05,0.36]	0,1561
NAWM (vs lesion)	0,02	[-0.00,0.04]	0,0851
MWF	0,00	[-0.00,0.00]	0,69047
NAWM (vs lesion)	0,03	[0.02,0.05]	< 0.001
qT1	0,0000	[-0.0000,0.0001]	0,406
NAWM (vs lesion)	0,0429	[0.0239,0.0610]	<0.001
QSM	-0,0002	[-0.0004,0.0001]	0,153
NAWM (vs lesion)	0,0305	[0.0184,0.0434]	<0.001
FA	-0,02	[-0.11,0.08]	0,70333
NAWM (vs lesion)	0,04	[0.03,0.05]	< 0.001
RD	0,00	[-0.15,0.14]	0,9697
NAWM (vs lesion)	0,04	[0.02,0.05]	<0.001

B.

Variable	Estimate	CI	p
MTR	-0,04	[-0.28,0.21]	0,7781
NAWM (vs lesion)	-0,11	[-0.22,-0.00]	0,0596
MTR:NAWM (vs lesion)	0,49	[0.09,0.90]	0,0236
MWF	0,00	[-0.00,0.00]	0,74938
NAWM (vs lesion)	0,00	[-0.04,0.05]	0,91640
MWF:NAWM (vs lesion)	0,00	[-0.00,0.00]	0,17674
qT1	0,0000	[-0.0001,0.0001]	0,649
NAWM (vs lesion)	-0,0125	[-0.0901,0.0624]	0,749
qT1:NAWM (vs lesion)	0,0002	[-0.0001,0.0004]	0,152
QSM	0,0000	[-0.0003,0.0003]	0,8743
NAWM (vs lesion)	0,0255	[0.0121,0.0393]	0,0012
QSM:NAWM (vs lesion)	-0,0005	[-0.0011,0.0001]	0,0832
FA	-0,03	[-0.13,0.08]	0,64908
NAWM (vs lesion)	0,03	[-0.01,0.07]	0,15976
FA:NAWM (vs lesion)	0,03	[-0.18,0.23]	0,80187
RD	-0,01	[-0.16,0.14]	0,9034
NAWM (vs lesion)	0,03	[-0.01,0.07]	0,1775
RD:NAWM (vs lesion)	0,07	[-0.36,0.50]	0,7592

Table S3: Association between qMRI and mean NF.**A**

Variable	Estimate	CI	p
MTR	170,08	[-612.93,997.73]	0,672
NAWM (vs lesion)	0,91	[-86.95,84.38]	0,983
MWF	8,46	[0.81,16.34]	0,0338
NAWM (vs lesion)	-51,63	[-125.72,20.02]	0,1649
qT1	0,03	[-0.26,0.32]	0,851
NAWM (vs lesion)	23,39	[-49.66,97.62]	0,537
QSM	-0,10	[-1.15,0.93]	0,852
NAWM (vs lesion)	14,13	[-35.22,62.88]	0,576
FA	767,48	[320.33,1245.04]	0,00126
NAWM (vs lesion)	17,78	[-17.35,52.93]	0,32764
RD	-408,78	[-942.40,124.32]	0,141
NAWM (vs lesion)	-27,35	[-95.64,40.87]	0,438

B.

Variable	Estimate	CI	p
MTR	677,52	[-369.96,1770.94]	0,2074
NAWM (vs lesion)	333,83	[-128.65,802.24]	0,1705
MTR:NAWM (vs lesion)	-1283,90	[-3068.52,468.82]	0,1629
MWF	8,68	[0.83,16.71]	0,0342
NAWM (vs lesion)	-30,69	[-248.70,188.34]	0,7871
MWF:NAWM (vs lesion)	-1,29	[-13.77,10.98]	0,8406
qT1	0,03	[-0.26,0.33]	0,837
NAWM (vs lesion)	-53,84	[-369.94,249.36]	0,730
qT1:NAWM (vs lesion)	0,29	[-0.82,1.45]	0,606
QSM	-0,39	[-1.57,0.78]	0,523
NAWM (vs lesion)	28,59	[-27.96,84.61]	0,331
QSM:NAWM (vs lesion)	1,25	[-1.25,3.74]	0,337
FA	897,02	[399.30,1421.06]	<0.001
NAWM (vs lesion)	111,76	[-47.68,273.51]	0,184
FA:NAWM (vs lesion)	-490,86	[-1315.47,322.01]	0,251
RD	-433,25	[-971.20,103.05]	0,126
NAWM (vs lesion)	-81,27	[-241.37,76.37]	0,326
RD:NAWM (vs lesion)	658,36	[-1078.90,2421.44]	0,469

Table S4: Association between qMRI and mean GFAP.**A.**

Variable	Estimate	CI	p
MTR	13,33	[0.72,246.33]	0,0861
NAWM (vs lesion)	0,25	[0.18,0.35]	<0.001
MWF	1,01	[0.99,1.04]	0,289
NAWM (vs lesion)	0,29	[0.22,0.37]	<0.001
qT1	1,00	[1.00,1.00]	0,477
NAWM (vs lesion)	0,29	[0.22,0.39]	<0.001
QSM	1,00	[0.99,1.00]	0,0303
NAWM (vs lesion)	0,28	[0.23,0.35]	<0.001
FA	0,84	[0.16,4.35]	0,842
NAWM (vs lesion)	0,32	[0.26,0.38]	<0.001
RD	0,23	[0.03,1.65]	0,152
NAWM (vs lesion)	0,27	[0.21,0.36]	<0.001

B.

Variable	Estimate	CI	p
MTR	22,67	[0.53,965.77]	0,109
NAWM (vs lesion)	0,35	[0.07,1.73]	0,207
MTR:NAWM (vs lesion)	0,26	[0.00,101.35]	0,664
MWF	1,03	[1.00,1.05]	0,0359
NAWM (vs lesion)	0,75	[0.34,1.70]	0,4983
MWF:NAWM (vs lesion)	0,94	[0.90,0.99]	0,0183
qT1	1,00	[1.00,1.00]	0,552
NAWM (vs lesion)	0,37	[0.11,1.27]	0,120
qT1:NAWM (vs lesion)	1,00	[0.99,1.00]	0,696
QSM	1,00	[0.99,1.00]	0,0988
NAWM (vs lesion)	0,27	[0.21,0.35]	<0.001
QSM:NAWM (vs lesion)	1,00	[0.99,1.01]	0,5388
FA	2,97	[0.45,19.39]	0,2648
NAWM (vs lesion)	0,75	[0.37,1.49]	0,4142
FA:NAWM (vs lesion)	0,01	[0.00,0.39]	0,0142
RD	0,14	[0.02,1.00]	0,057
NAWM (vs lesion)	0,15	[0.08,0.30]	<0.001
RD:NAWM (vs lesion)	745,10	[0.70,794576.50]	0,070

MTR = magnetization transfer ratio, MWF = myelin water fraction, qT1 = quantitative T1, QSM = quantitative susceptibility mapping, FA = fractional anisotropy, RD = radial diffusivity. NAWM = normal appearing white matter. CI = confidence interval, p = p value.