**Supplementary material to Megna R, et Al. “Brain tissues volumes and relaxation rates in multiple sclerosis. Implications for cognitive impairment”**

**Relaxation rate calculation**

Details of the relaxation rate calculation procedures are provided in previous works [1–3]

All relaxation rates are calculated according to the general formula of the signal intensity in the transverse steady state for conventional spin-echo images[4], applied to single echo:

 (1) $S=K∙PD∙\frac{1-2e^{-(TR-\frac{TE}{2})∙R1}}{1+e^{-TR∙(R2+R1)}}∙e^{-TE∙R2}$

and double echo sequences:

(2) $S=K∙PD∙\frac{1-2e^{-\left[TR-\frac{TE1+TE2}{2}\right]∙R1}+2e^{-TR-\frac{TE1}{2}∙R1}-e^{-TR∙R1}}{1+e^{-TR∙(R2+R1)}}∙e^{-TE∙R2}$

Where S is the signal intensity, PD is proton density, TR is repetition time, TE is echo time, with and TE2 being the echo times of the first and second echo of the double-echo sequence, respectively, and K is a constant depending essentially on the scanner and on experimental conditions.

From these equations, R2 maps from the ratio of the signals in the PD- and T2-weighted volumes, and of the R1 maps from the ratio of the signals in the PD- and T1-weighted volumes, can be calculated. In particular, R2 is calculated from the ratio of the signals of the PD- and T2-weighted volumes according to the formula

(3) $\frac{S\_{TE2}}{S\_{TE1}}=\frac{e^{-TE\_{2}∙R2}}{e^{-TE\_{1}∙R2}}$

while for R1 calculation, a lookup table of the R1 values generating each couple of signals in the PD- and T2-weighted volumes is preliminarily generated, according to the formula

(4) $\frac{S\_{TE1}}{S\_{TE2}}=\frac{1-e^{-R1∙TR1}(2e^{R1∙\frac{TE}{2}}-1)}{1-e^{-R1∙TR2}(2e^{R1∙\frac{TE}{2}}-1)}$

Note that both calculations are independent of PD and K, provided K does not change across sequences (as is the case within the same MRI study, while if sequences are acquired in separate sessions, different receiver gains are applied and rate calculations are not possible).

**References**

1. Alfano B, Brunetti A, Ciarmiello A, Salvatore M (1992) Simultaneous display of multiple MR parameters with “quantitative magnetic color imaging.” J Comput Assist Tomogr 16:634–640 . doi: 10.1097/00004728-199207000-00025

2. Alfano B, Brunetti A, Arpaia M, et al (1995) Multiparametric display of spin-echo data from MR studies of brain. J Magn Reson Imaging 5:217–25

3. Alfano B, Brunetti A, Covelli EM, et al (1997) Unsupervised, automated segmentation of the normal brain using a multispectral relaxometric magnetic resonance approach. Magn Reson Med 37:84–93 . doi: 10.1002/mrm.1910370113

4. Bakker CJ, de Graaf CN, van Dijk P (1984) Derivation of quantitative information in NMR imaging: a phantom study. Phys Med Biol 29:1511–25