Multi-compartment T2 relaxometry model with application to multiple sclerosis

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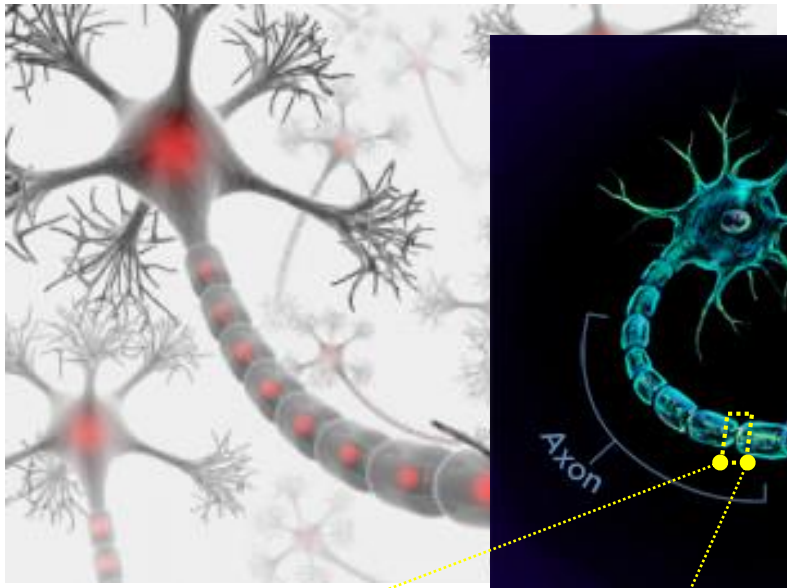
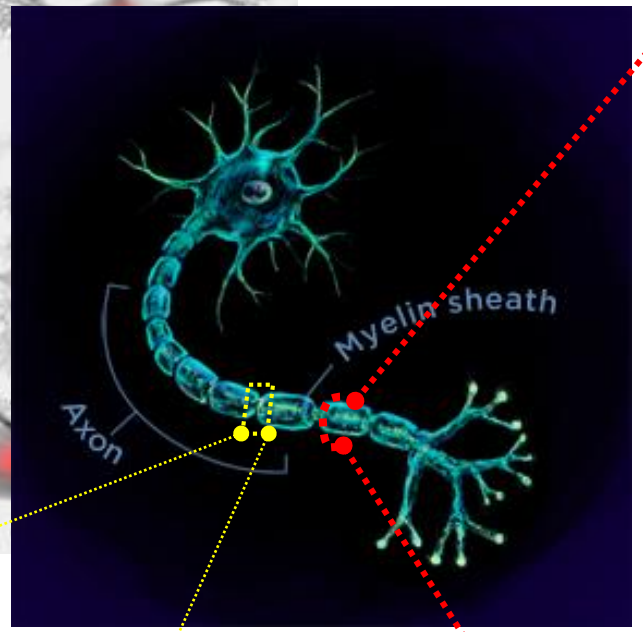
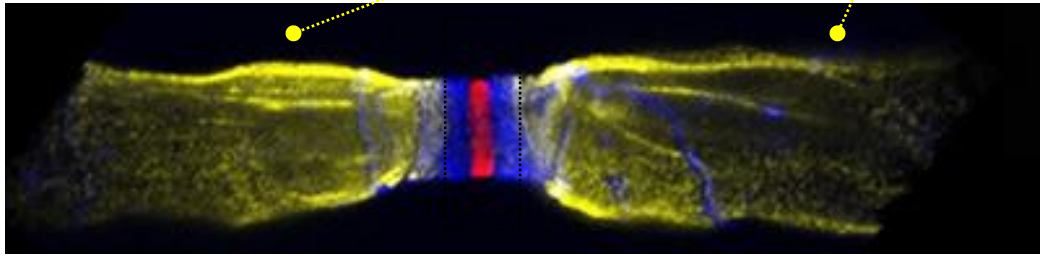
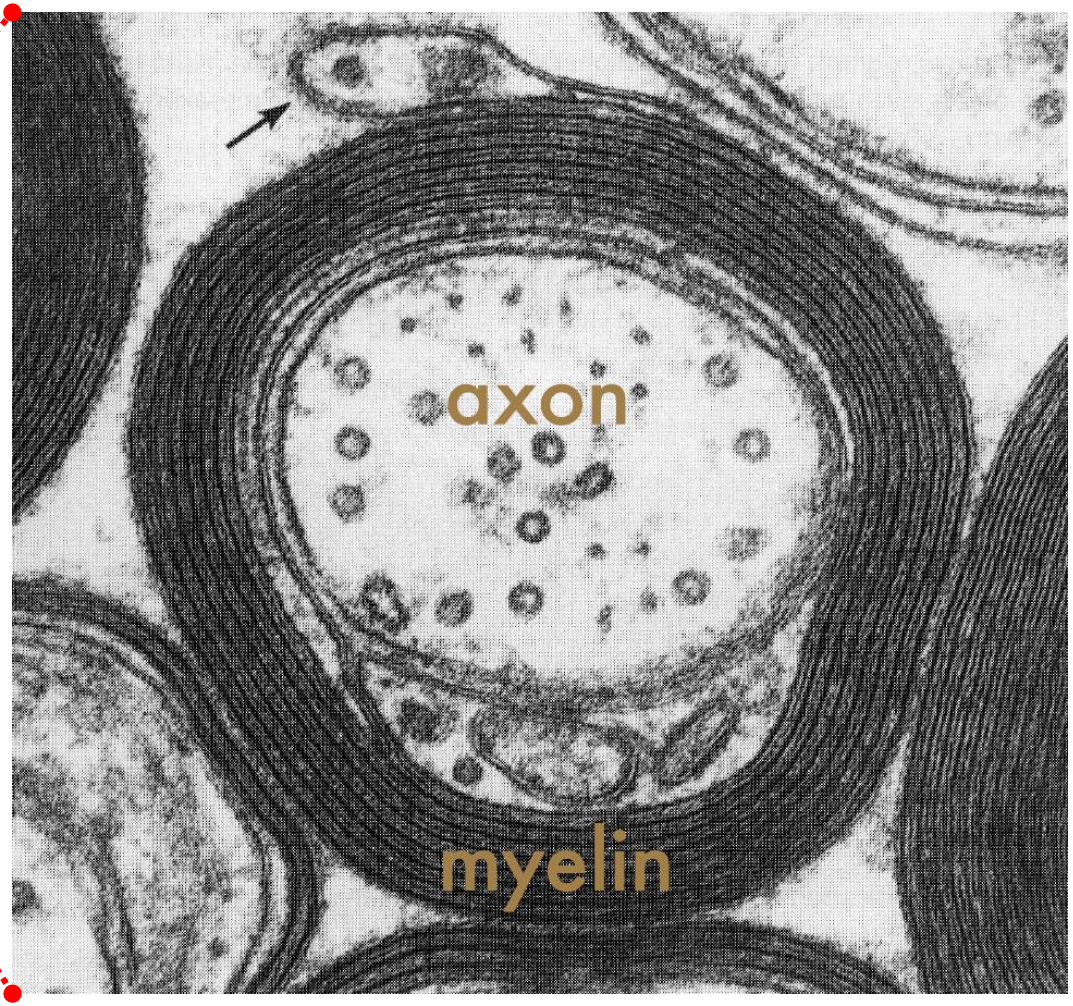
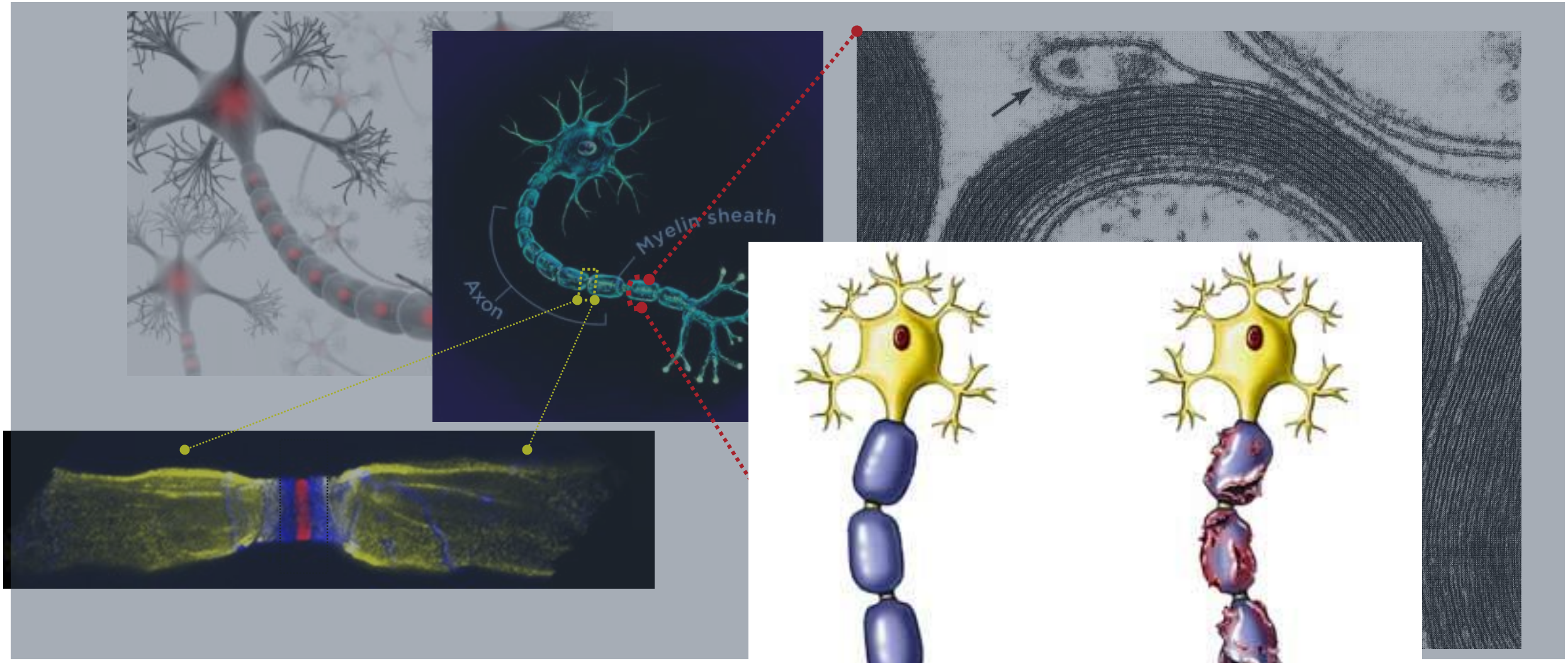



Myelin sheath
Axon




axon
myelin



Neuron with myelin sheath

Neuron with damaged myelin sheath

How can it be tracked at very beginning?

Multiple T2 compartments in white matter

Diffusion MRI
Multi-compartment models

Provides information

No information

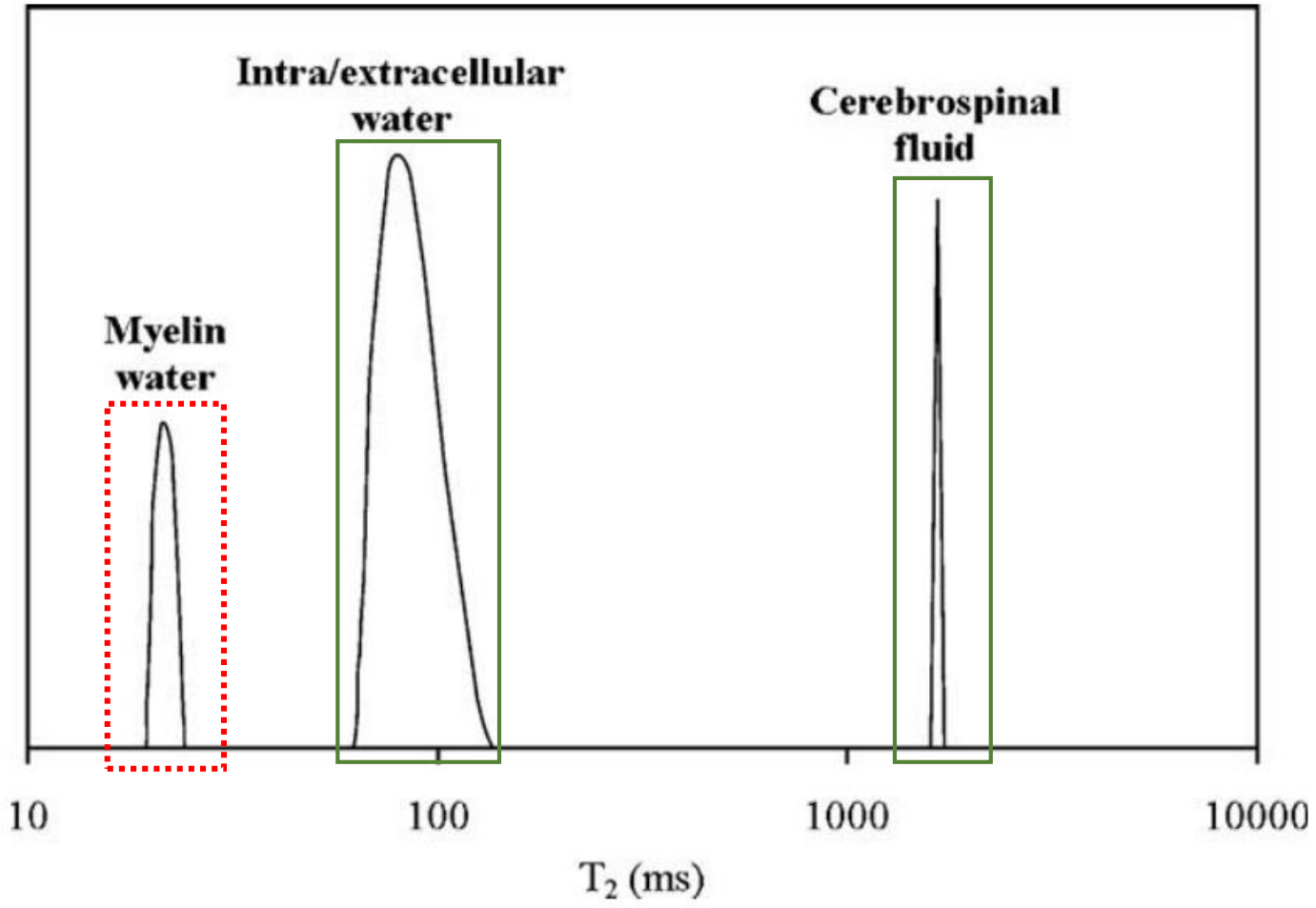


Fig. 2. An example of a T_2 distribution of human white matter in vivo with labeled regions corresponding to compartments of white matter. χ^2 was kept within 2–2.5% of its nominal value.

MacKay, Alex, et al. "Insights into brain microstructure from the T2 distribution." Magnetic resonance imaging 24.4 (2006): 515-525.

Multi-Compartment Model

Multi-Compartment Image Model

$$\langle Image_{Voxel} \rangle = \langle short - T2 \rangle + \langle medium - T2 \rangle + \langle high - T2 \rangle$$

Short-T2
Myelin and highly myelinated axons

- White matter lesions in MS show demyelination in MS
- A change in short-T2 water fraction might indicate re-myelination.

Medium-T2
Intra and extra-cellular fluids

- Intracellular: unmyelinated axons and glia
- Extracellular: interstitial and extra cellular

High-T2
Free water

- Cerebrospinal fluids
- Edema regions

Table 1
T1 and T2 Relaxation Times Estimates for Myelin (my), Myelinated axon (ma), and Mixed (mx) Water Pools in White Matter*

Reference	B_0 (T)	T1 (msec)			T2 (msec)		
		my	ma	mx	my	ma	mx
3-pool model[a]	1.9	350 (.17)	850 (.53)	2800 (.30)	10 (.17)	40 (.53)	130 (.30)
Koenig et al. (3)	1.0	200 (.15)	680 (.85)				
Stanisz et al. (15)[b]	1.5	463 (.32)	970 (.68)		22	176	
Whittall et al. (14)	1.5	718			70		
MacKay et al. (13)[c]					10–55 (.16)	>55 (.84)	
Stewart et al. (22)[d]	2.1				10 (.04)	92 (.96)	
Vavasour et al. (16)[e]	1.5				20	80	120
Does and Gore (19)[f]	4.7	938 (.19)	1328 (.47)	1845 (.34)	12 (.19)	33 (.47)	105 (.34)

*Pool assignment by order of relaxation times.
[a]Pool fractions in parenthesis. Values for 3-pool model are for FWM.
[b]Data from bovine optic nerve.
[c]Three T2 components appear in graphs (Fig. 2 and 5), but pool fractions not given.
[d]Data from brain CNS tissue of Hartley guinea pig.
[e]Data from Fig. 1. Pool fractions not given.
[f]Data from Fig. 5 in rat trigeminal nerve acquired at 4.7 T.

Lancaster, Jack L., et al. "Three-pool model of white matter." *Journal of Magnetic Resonance Imaging* 17.1 (2003): 1-10.

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Myelin water fraction (popularly looked at measure) is a relative measure.
Hence shall be studied in relation to the other compartment water fractions.

Method

Signal model

- Multicomponent model

$$s(t_i) = \sum_j w_j \ \exp(-t_i / T_{2_j})$$

- Multi-compartment model

$$s(t_i) = M_0 \sum_{j=1}^{n} w_j \int_{T_2} f_j(T_2; p)\, EPG(T_2, \Delta TE, i, B_1)\, dT_2$$

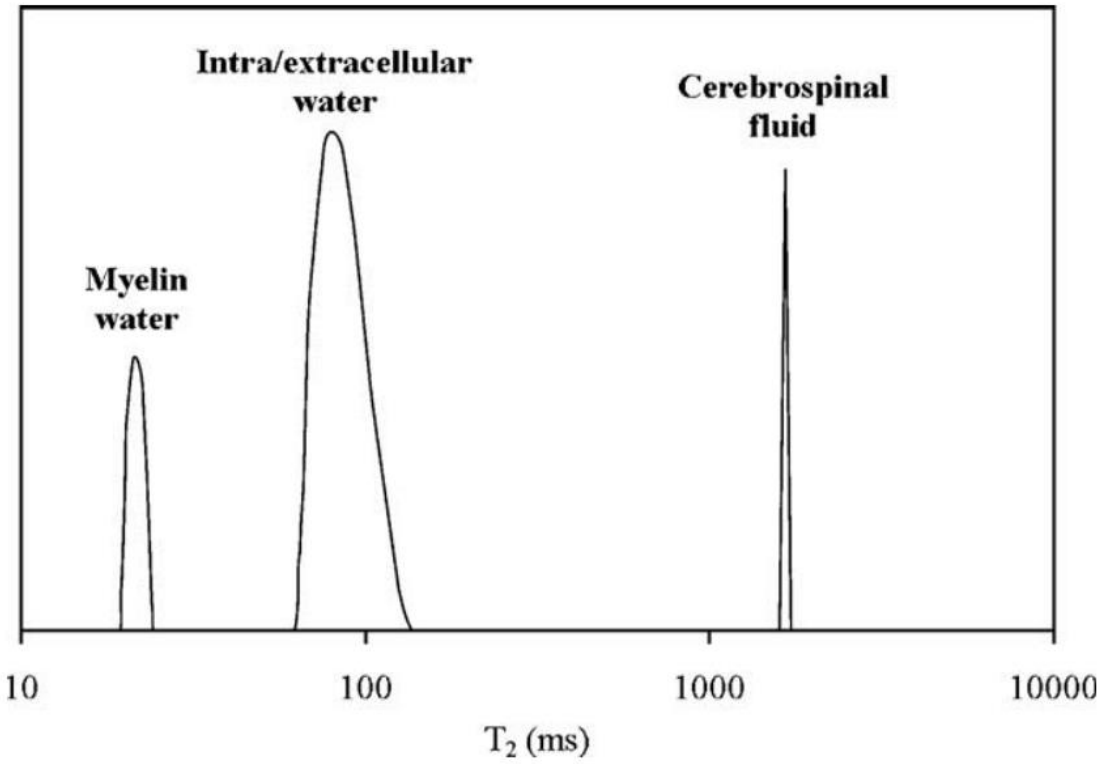
Decay response for sequences with multiple refocusing pulses at certain flip angles

Weights are estimated

Model for each compartment

estimated

Choice of compartment model



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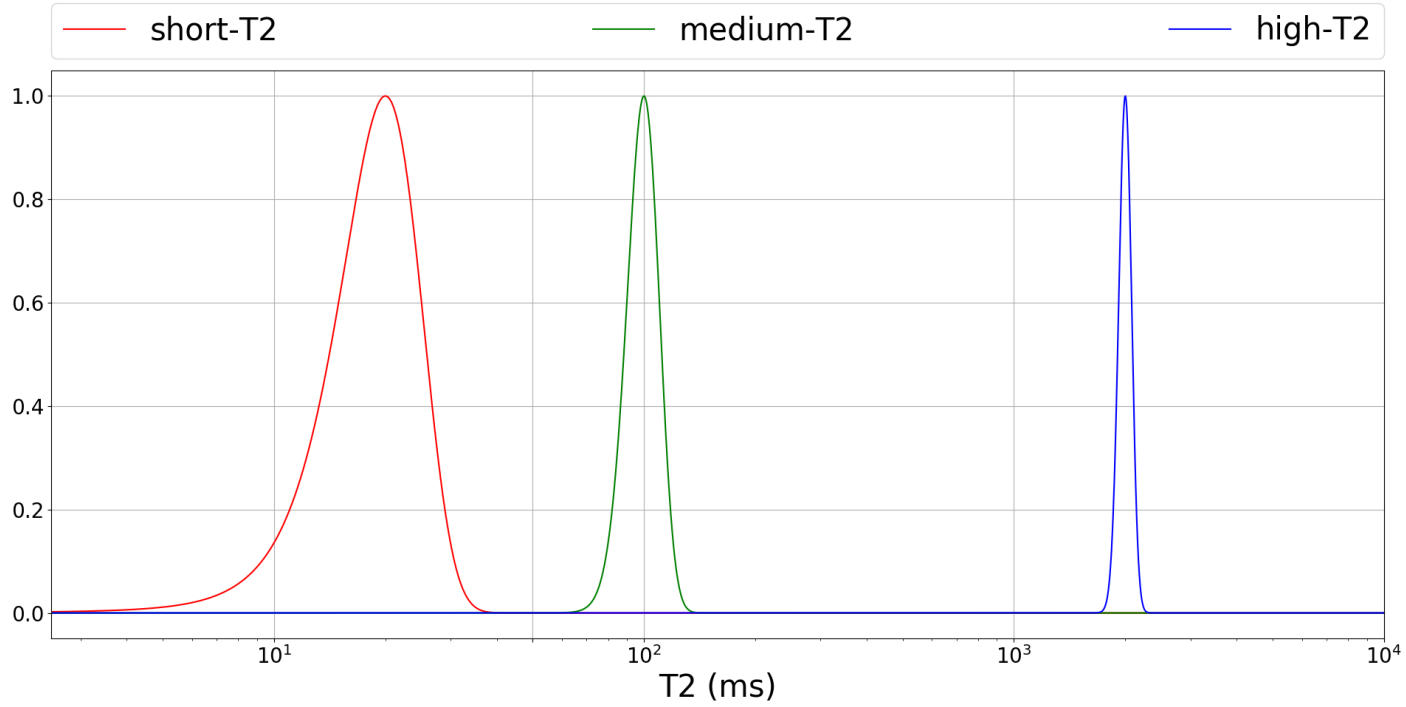


** PDF values are not normalized for viz*

PDF parameters chosen for this study:

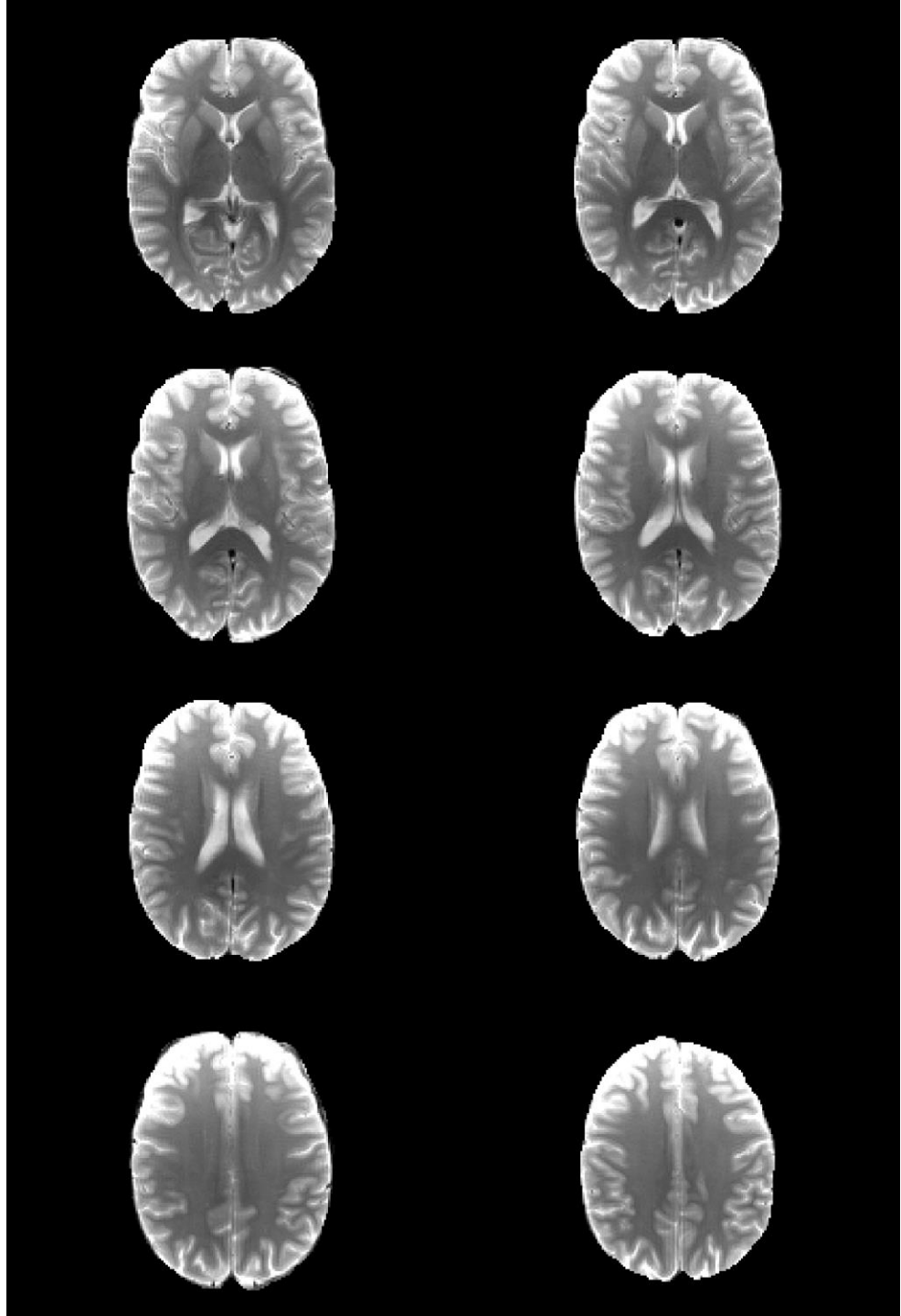
Compartment	Gaussian PDF mean	Gaussian PDF standard deviation
Short-T2	20.0	5.0
Medium-T2	100.0	10.0
High-T2	2000.0	80.0

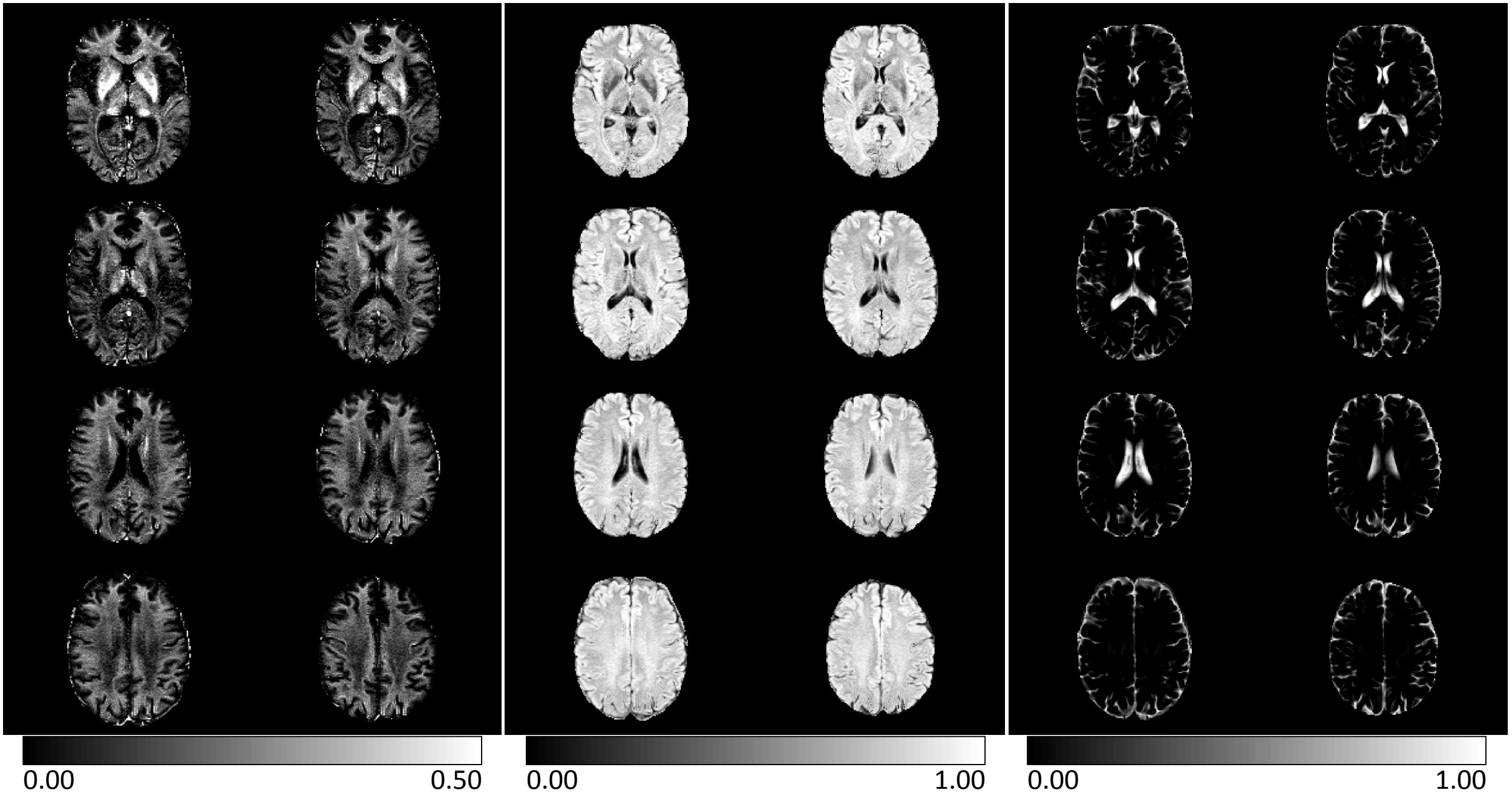
Healthy volunteer

Acquisition details: TE = 9ms / 32 echoes /

TR = 3720ms / 1.33mm x 1.33mm /

Slice thickness = 4mm / Slice spacing = 4mm




Short-T2
Medium-T2
High-T2
0.00
0.50
0.00
1.00
0.00
1.00

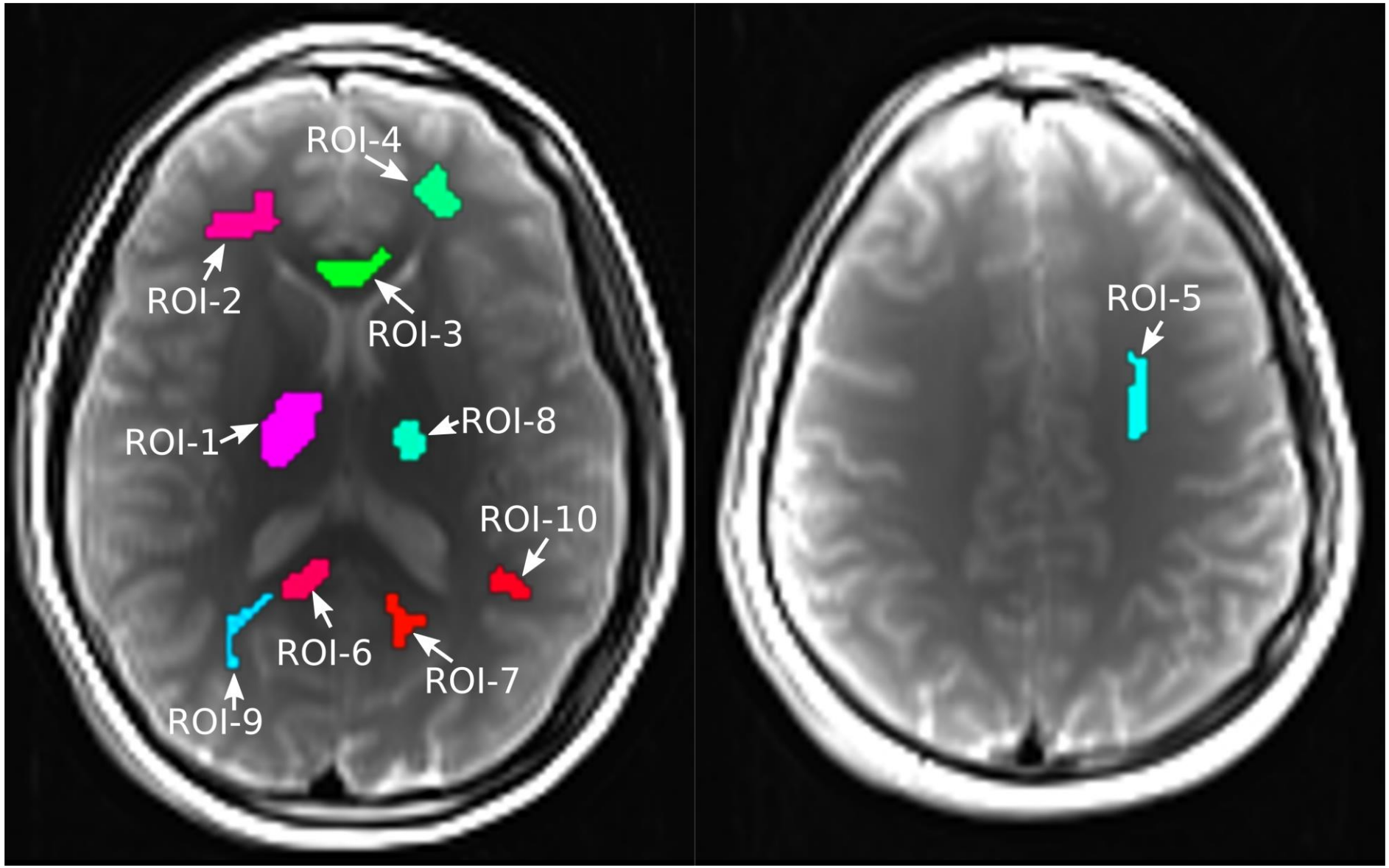
Test retest experiments for healthy volunteers

Reproducibility test

Number of healthy controls = 5

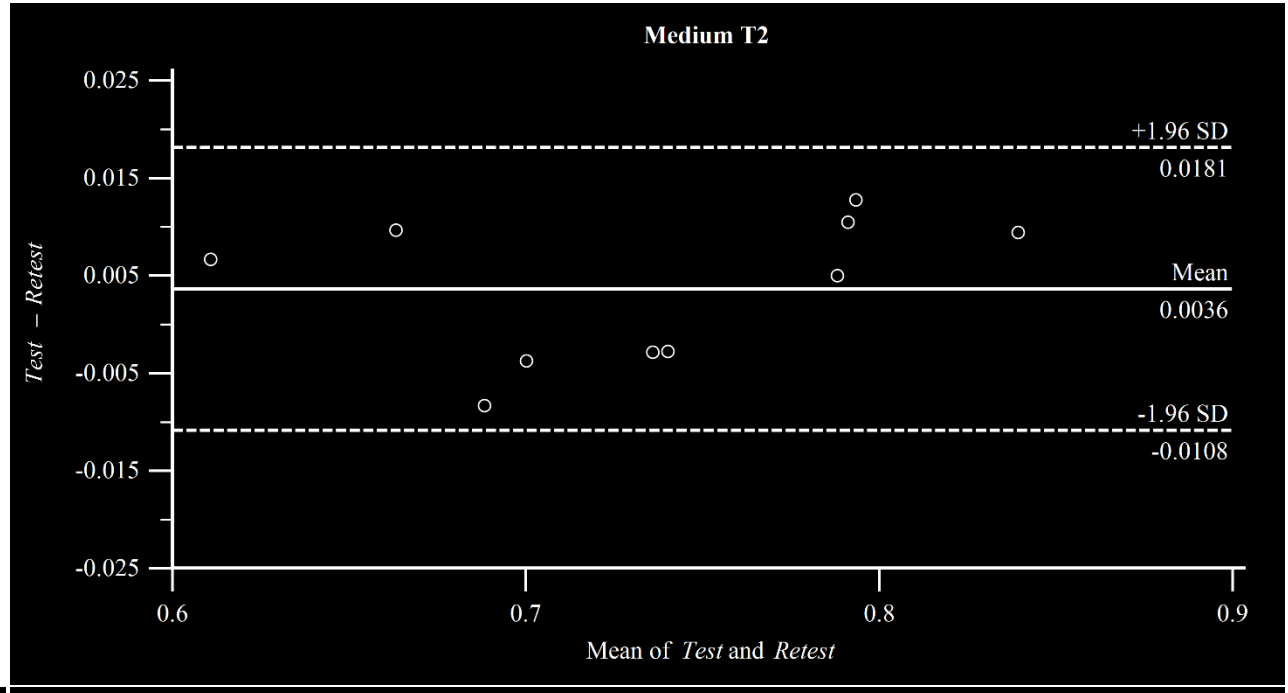
TE = 9ms / TR = 2000ms / 32 echoes

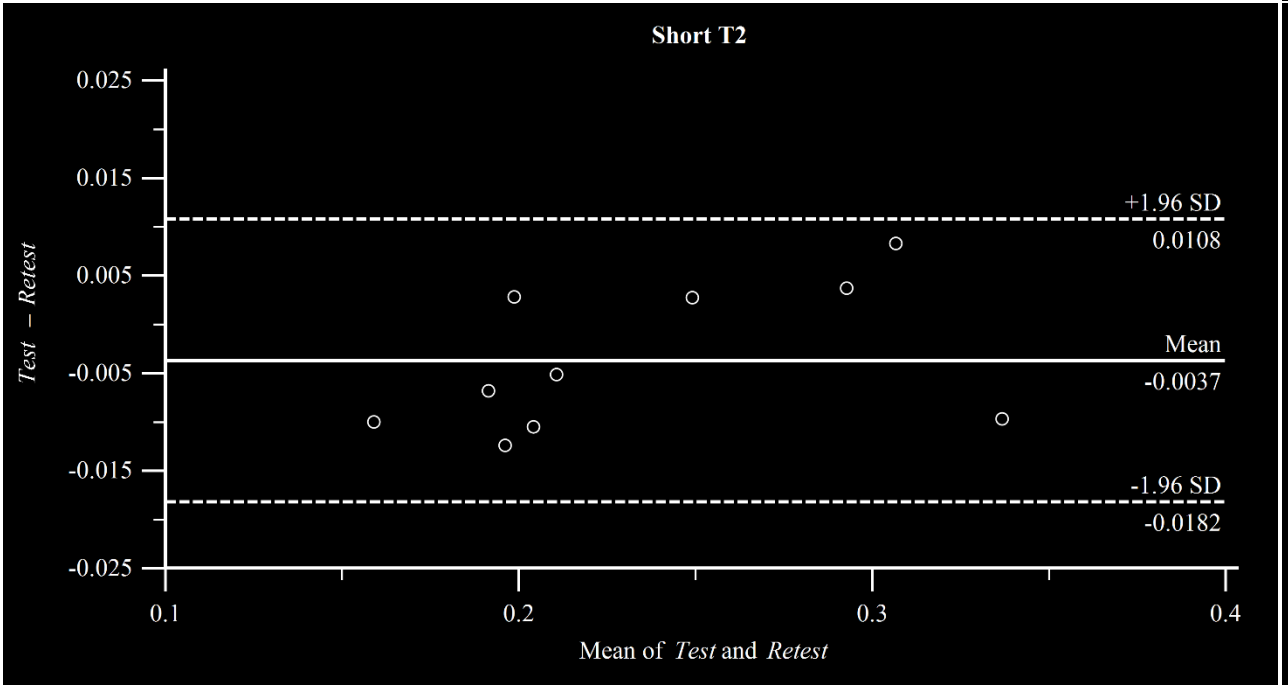
ROIs evaluated

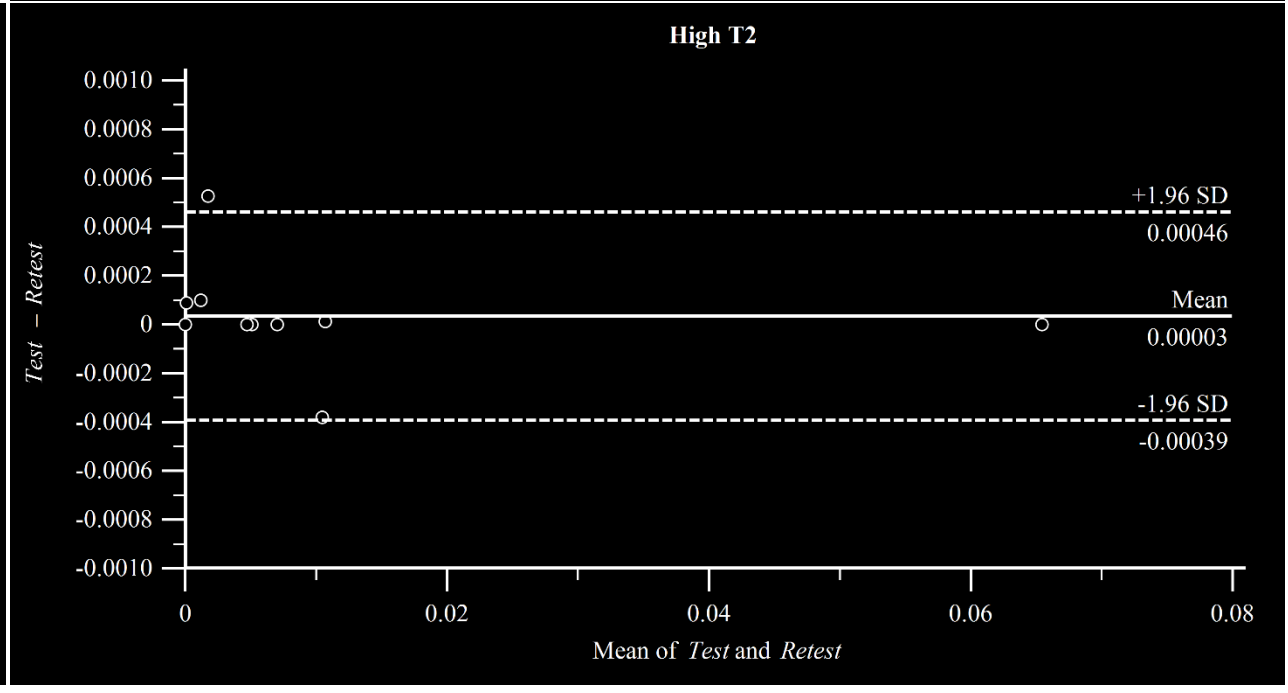


Bland Atman plots

- Plot between:
  - Difference in estimated values of test and retest
  - Mean of the estimations from test and retest
- Lower mean difference suggests high repeatability
- The empirical limits of agreement for estimated values are obtained as $1.96 \times \sigma$







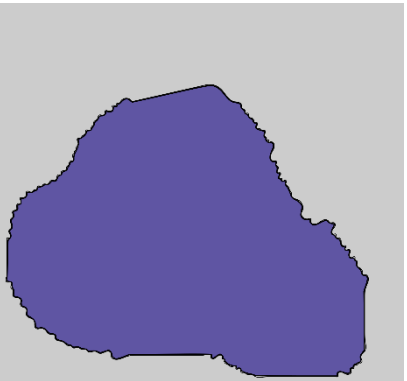
Multiple Sclerosis study

- 10 MS patients – median age of 28.0; 5 male and 5 female MS patients
- 3 year follow-up study
- All patients demonstrated clinically isolated syndrome (CIS) condition
- MS therapy administered after month-3

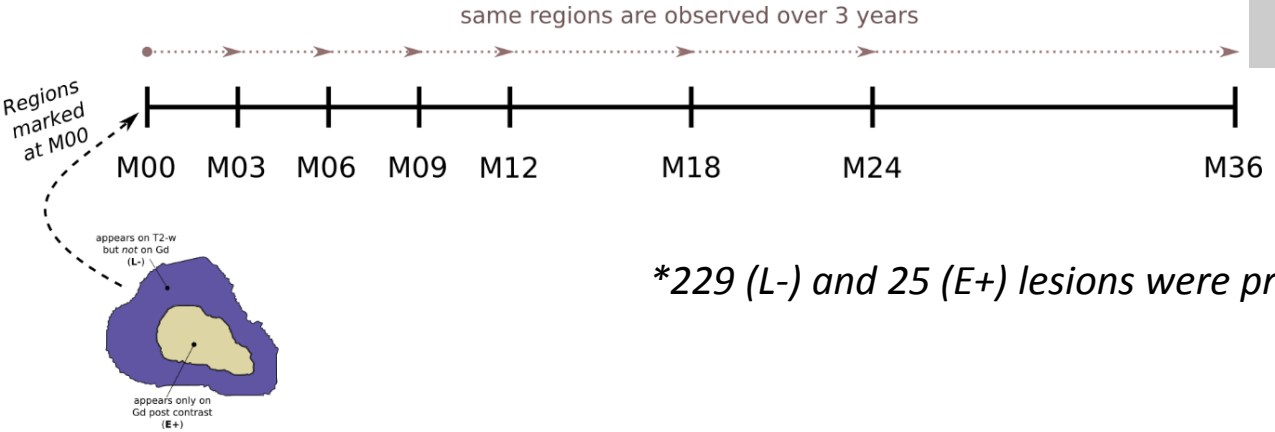
Lesion regions studied

Comparison done for (L-) and (E+) lesions

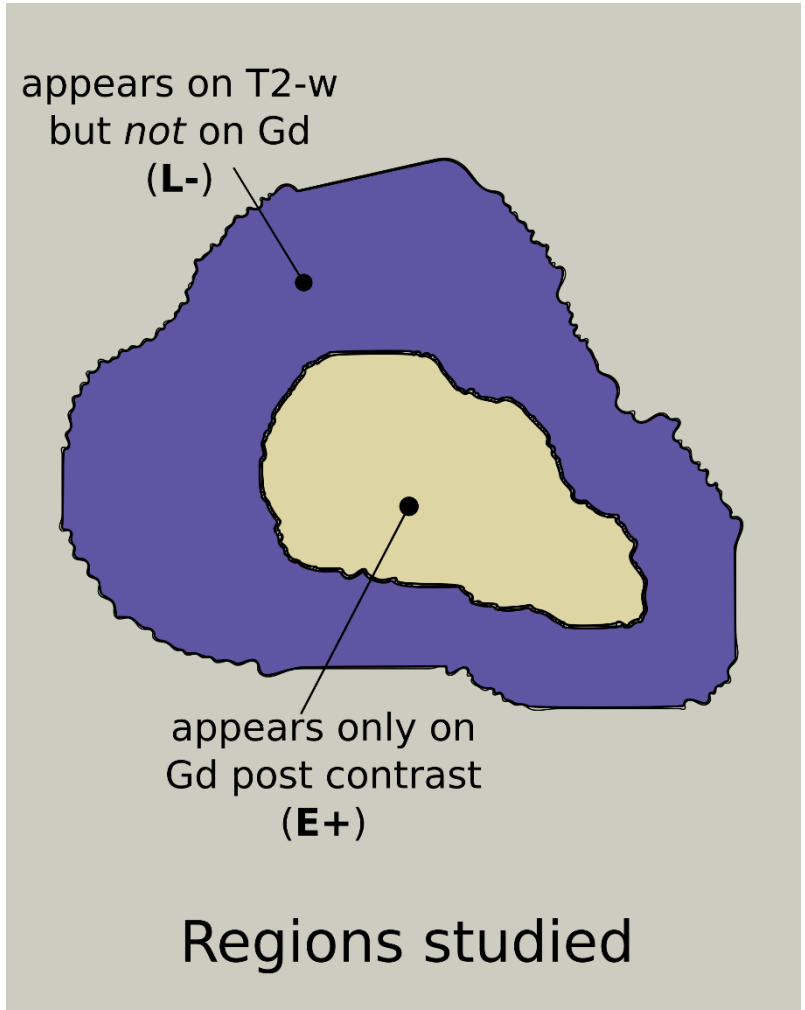
(E+)	Appears only on Gd scans. These are the regions of the lesion undergoing active blood brain barrier breakdown.
(L-)	Appears on T2-w scans but not on the Gd scan. These are later stage lesions as compared to (E+)



MS lesion on T2-w MRI



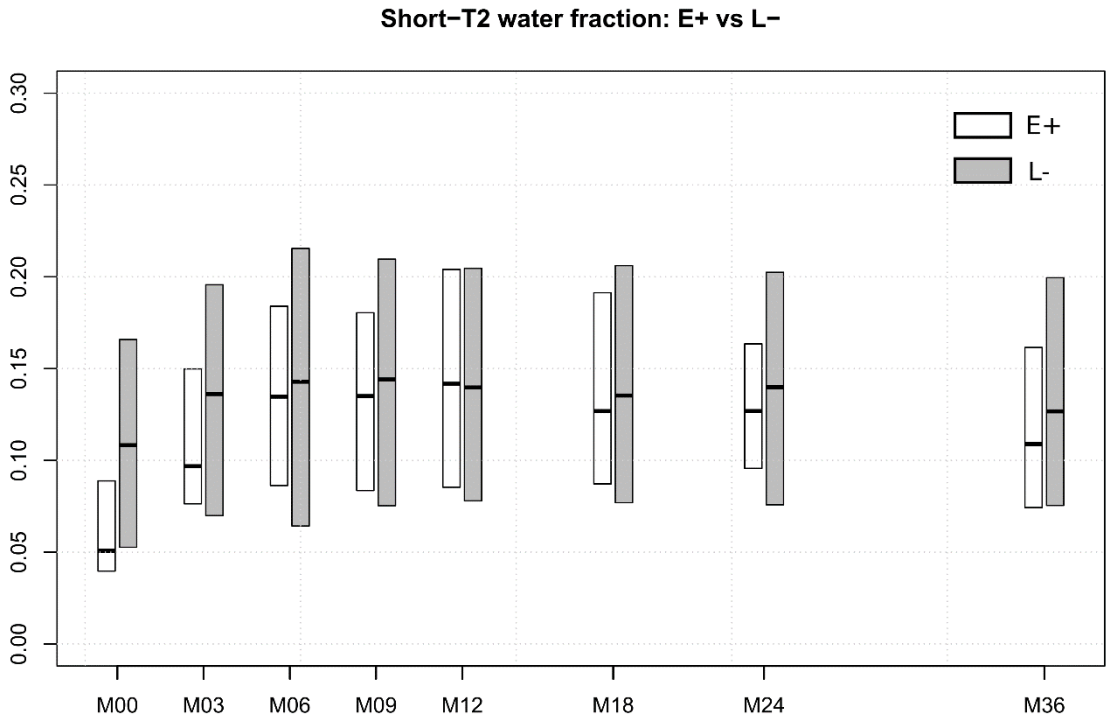
**229 (L-) and 25 (E+) lesions were present in the patients*

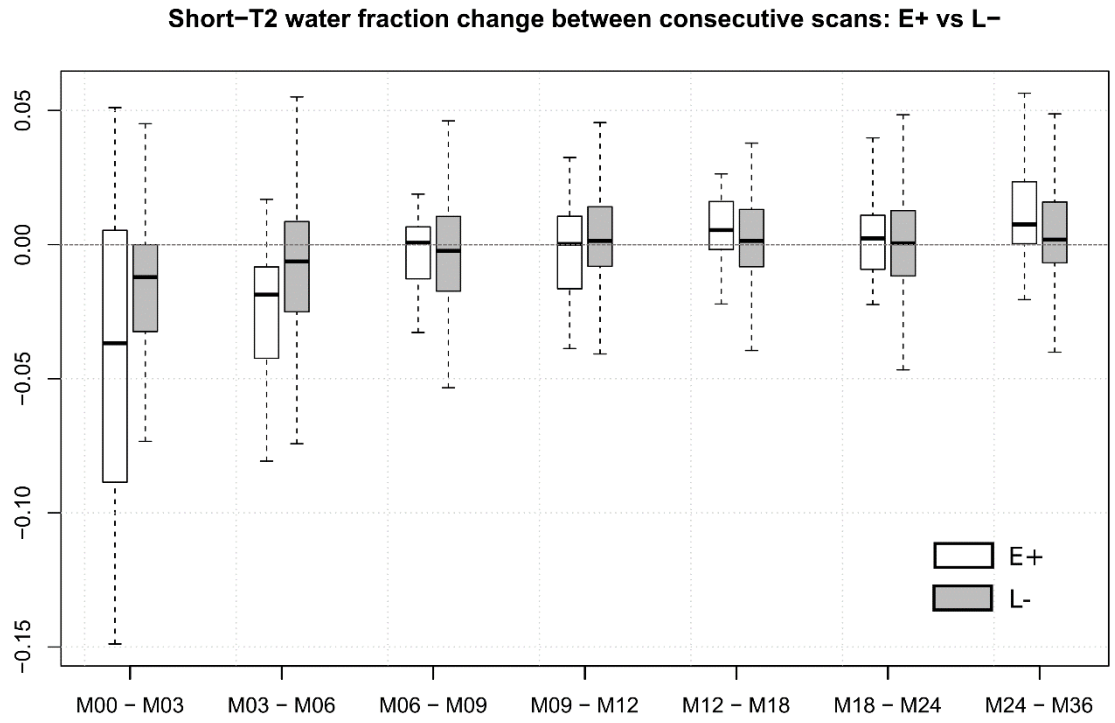


Data acquisition

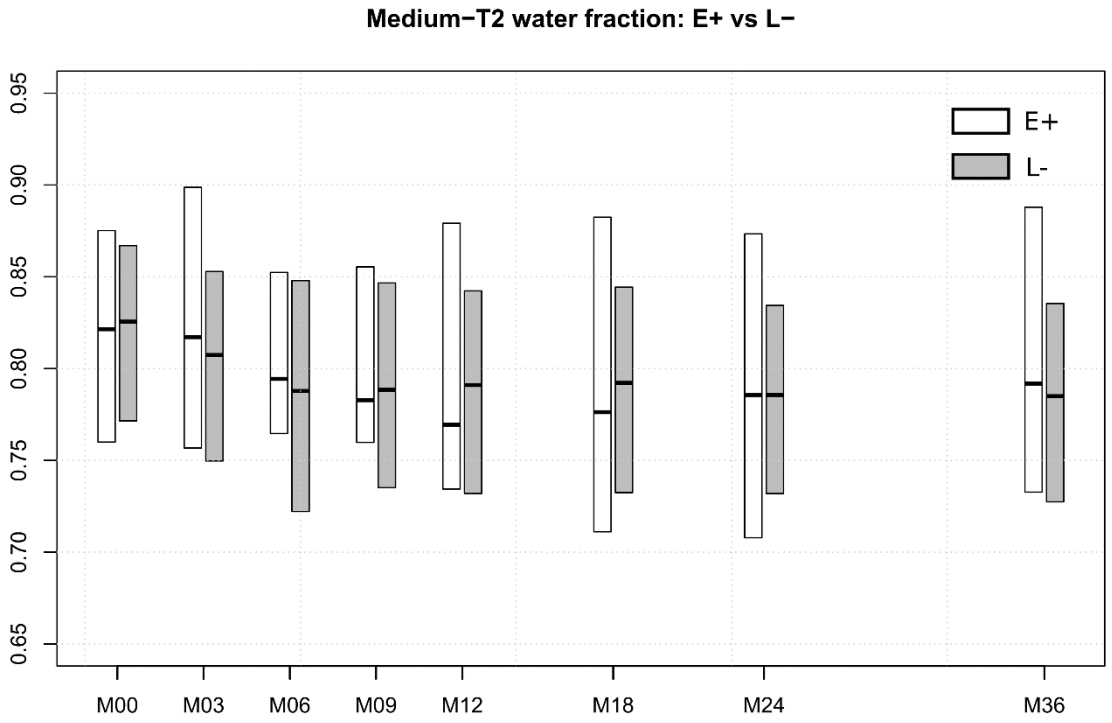
- T2 relaxometry
  - 3T MRI scanner, first TE = 13.8ms, ΔTE = 13.8ms, TR = 4530ms, n_{echoes} = 7, voxel dimension = 1.3 x 1.3 x 3mm^3, slice spacing = 3mm
    Acquisition time ~7 minutes.
- T1 SE Gd scan
  - TE = 8.4ms, TR = 500ms, flip angle = 70^o, voxel dimension = 1.3 x 1.3 x 3mm^3, slice spacing = 3mm, 0.1mmol/kg gadopentetate dimeglumine.

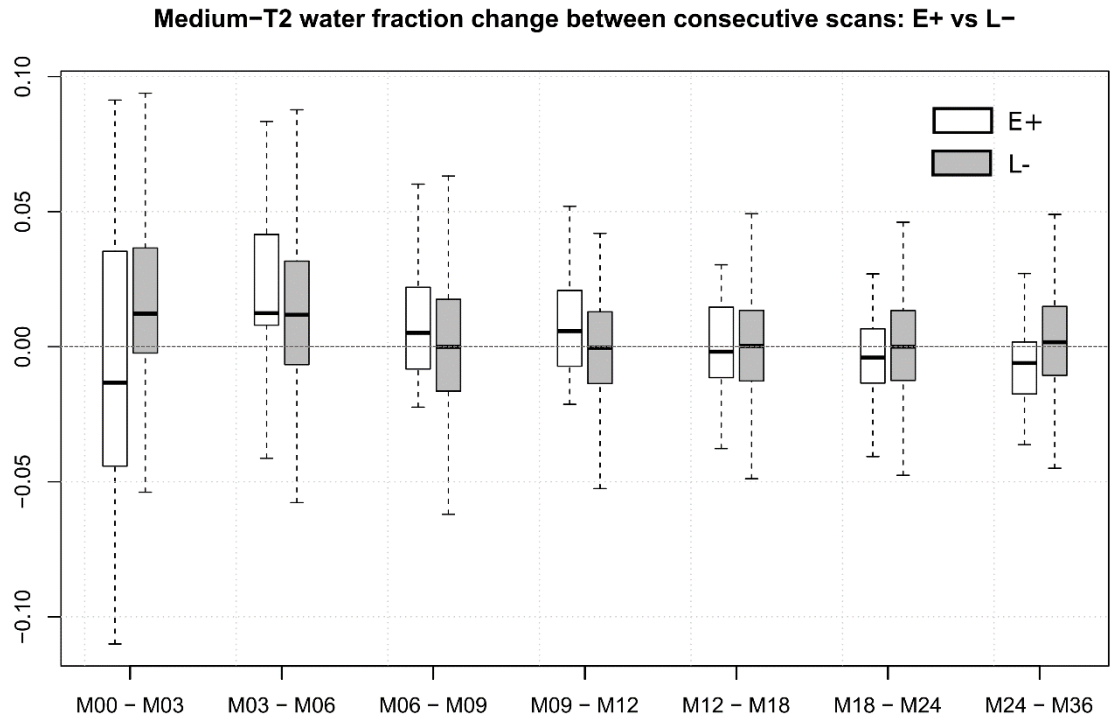
(L-) vs. (E+): short-T2 water fraction evolution



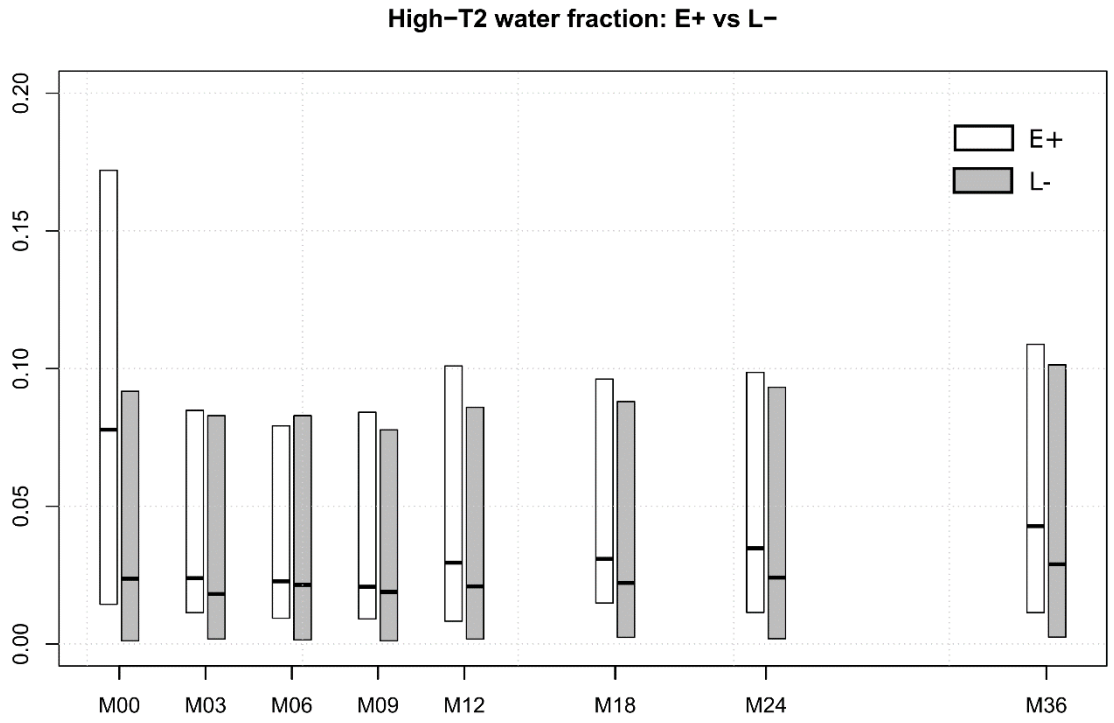


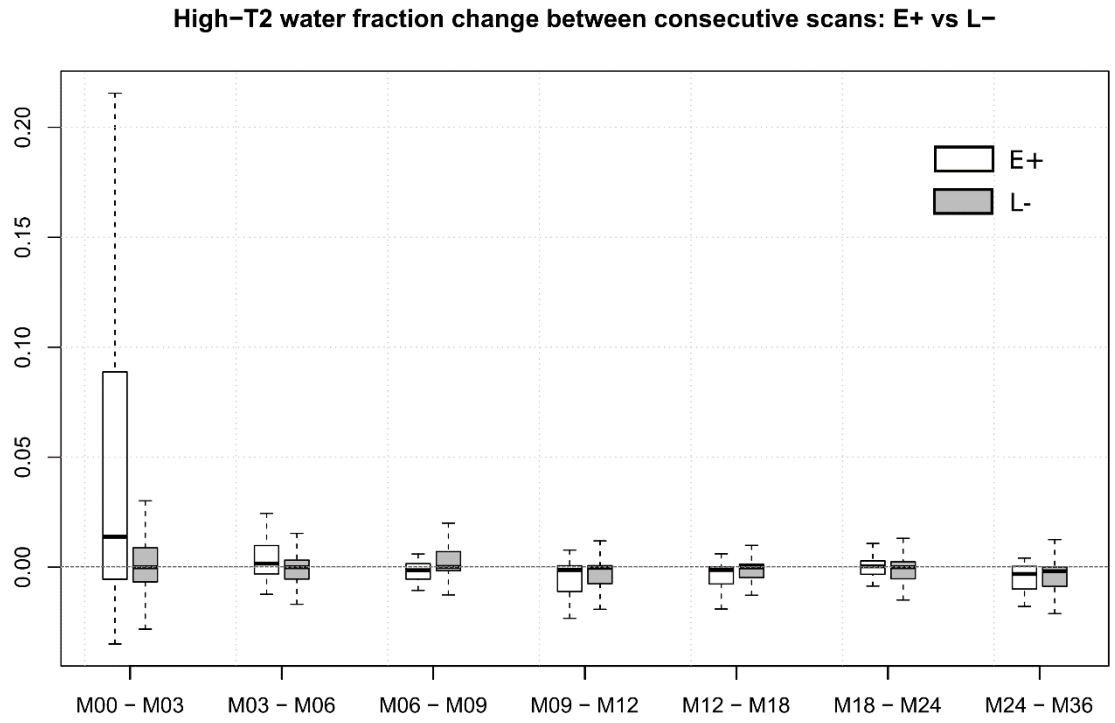
(L-) vs. (E+): medium-T2 water fraction evolution





(L-) vs. (E+): high-T2 water fraction evolution





Conclusion

- Simple and effective tissue multi-compartment model to obtain microstructure information.
- Test retest experiments show that the estimation is repeatable.
- A 3-year study on CIS MS patients show that the trend of the estimated microstructure information are in confirmation with the broad understanding of pathology of MS lesions.
    - Evaluations done for early and late MS lesions.

Questions