Supplementary Table 2. T1-weighted spherical mean diffusion tensor (T1-SMDT) model fitting based on artificial neural networks.

Signal model	$s(b,\mathrm{TI},\mathrm{TS}) = \frac{\sqrt{\pi}}{2}\, s_0 \left| 1 - e^{-\frac{\mathrm{TI}}{T_1}} - \left(1 - e^{-\frac{\mathrm{TS}}{T_1}}\right) e^{-\frac{\mathrm{TI}}{T_1}} \right| e^{-b d_\perp} \frac{\mathrm{erf}\left(\sqrt{b(d_\parallel - d_\perp)}\right)}{\sqrt{b(d_\parallel - d_\perp)}}$ b: b-value; TS: saturation time (delay saturation-inversion); TI: inversion time (delay inversion-excitation)
Tissue parameters	s_0 (apparent proton density): fitting range [0.5; 5.0] T_1 (longitudinal relaxation time): fitting range [100; 4000] ms $d_\parallel$ (parallel fibre diffusivity): fitting range [0.01; 3.20] $\mu m^2\ ms^{-1}$ $d_\perp$ (perpendicular fibre diffusivity): parametrised as $d_\perp = k\, d_\parallel$, fitting range for k [0.00; 0.99]

DNN implementation	• The DNN is built of a cascade of hidden layers (here 7), each consisting of a linear matrix operation followed by ReLU activation, with $\mathrm{ReLU}(x) = \max(0, x)$
	• The DNN features N input neurons (as many as the number of input measurements per voxel) and 4 output neurons, which map the 4 tissue parameters:
	  ○ for fully-sampled signals we use $\{32, 28, 24, 20, 16, 12, 8, 4\}$ neurons;
	  ○ for 16-measurement sub-protocols we use $\{16, 14, 13, 11, 9, 7, 6, 4\}$ neurons;
	  ○ for 8-measurement sub-protocols we use $\{8, 7, 7, 6, 6, 5, 5, 4\}$ neurons;
	  ○ for 4-measurement sub-protocols we use $\{4, 4, 4, 4, 4, 4, 4, 4\}$ neurons
	• The i-th output neuron activation u_i, defined in the range $0 \le u_i \le u_{max}$, is mapped to the i-th tissue parameter p_i as
	$p_i = \frac{2}{1 + e^{-\alpha_i \left(\log(\mathrm{softplus}(u_i)) - \log(\log(2))\right)}} - 1,$
	where α_i is a learnable scaling factor and $\mathrm{softplus}(x) = \log(1 + e^x)$
	• Output MRI signals are calculated from tissue parameters p_i with the equation above

DNN training	• Input measurements $\{s(b_n, \mathrm{TI}_n, \mathrm{TS}_n) \mid n = 1, \ldots, N\}$ from each voxel are normalised by computing $a(b_n, \mathrm{TI}_n, \mathrm{TS}_n) = s(b_n, \mathrm{TI}_n, \mathrm{TS}_n) \,/\, \max_n \left(s(b_n, \mathrm{TI}_n, \mathrm{TS}_n)\right)$ • The DNN is optimised by backpropagating the ℓ^2-norm of the error (i.e. mean squared error, MSE) between ground truth MRI measurements and signal prediction • Optimisation is performed with ADAM on synthetic MRI signals for 50 epochs (learning rate of 10^{-4}; one update per mini-batch of 100 voxels) for sub-protocols, repeating the training 10 times with different random DNN initialisations • Synthetic MRI signals are computed for uniformly distributed tissue parameters within the ranges reported above, adding Rician noise with $SNR = \frac{s_0}{\sigma_{\mathrm{noise}}}$ within the range $[10; 100]$. We use 80,000 voxels as training set and 20,000 as validation set. Note that parameter s_0 in the model T1-SMDT is strongly T2-weighted (unlike in the HM-MRI model): as a consequence, SNR calculated with respect to s_0 is expected to be lower in T1-SMDT than HM-MRI for the same σ_{noise} • The DNN providing the minimum validation loss is deployed