Online Resource 2. Reliability of kinetic parameter estimates for the 2T4k\_V8\_k4 model

For $K_1$, $k_2$ and $V_8$ a cut-off of 25% was used and for $k_3$ and $k_4$ a cut-off of 50%. Higher values are highlighted.

A) %SE for $K_1$

|                      | MS1 | MS2 | MS3 | MS4 | MS5 | Mean | HC1 | HC2 | HC3 | HC4 | HC5 | Mean |
|----------------------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|------|
| Frontal cortex       | 5.5 | 10.5| 12.4| 12.6| 10.4| 10.3 | 7.6 | 8.4 | 10.4| 11.9| 13.2| 10.3 |
| Orbitofrontal cortex | 6.6 | 13.7| 14.1| 14.1| 12.2| 12.1 | 9.0 | 10.7| 10.9| 12.3| 16.9| 12.0 |
| Paracentral cortex   | 5.8 | 10.2| 11.4| 11.0| 9.9 | 9.7  | 7.4 | 8.4 | 9.8 | 10.8| 12.0| 9.7  |
| Parietal cortex      | 6.4 | 8.7 | 10.6| 10.0| 8.9 | 8.9  | 6.4 | 7.6 | 8.2 | 10.8| 10.9| 8.8  |
| Temporal cortex      | 5.1 | 9.2 | 11.9| 10.6| 8.6 | 9.1  | 6.2 | 8.9 | 8.4 | 11.6| 10.7| 9.2  |
| Occipital cortex     | 4.6 | 8.8 | 8.8 | 7.2 | 5.9 | 7.1  | 4.1 | 7.1 | 6.6 | 8.4 | 6.8 | 6.6  |
| Cingulate cortex     | 9.9 | 15.2| 12.9| 15.6| 13.8| 13.5 | 10.2| 11.2| 13.1| 13.9| 17.5| 13.2 |
| Thalamic GM          | 10.4| 10.8| 10.1| 8.8 | 10.6| 10.1 | 3.8 | 7.1 | 14.1| 11.4| 11.2| 9.5  |
| Putaminal GM         | 5.3 | 12.7| 13.3| 11.2| 12.4| 11.0 | 6.4 | 14.3| 10.8| 19.2| 12.5| 12.6 |
| Caudate nucleus GM   | 6.2 | 10.9| 13.0| 13.8| 11.0| 11.0 | 9.2 | 15.0| 15.7| 12.2| 13.3| 13.1 |
| Hippocampal GM       | 8.3 | 13.9| 15.0| 18.5| 14.3| 14.0 | 12.0| 19.2| 12.5| 20.3| 16.7| 16.1 |
| Cerebellar GM        | 3.6 | 5.6 | 7.6 | 5.7 | 5.6 | 5.6  | 5.8 | 5.1 | 5.2 | 8.8 | 6.1 | 6.2  |
| Cerebellar WM        | 6.0 | 5.2 | 6.7 | 6.1 | 6.2 | 6.0  | 7.1 | 6.5 | 7.1 | 11.1| 8.0 | 8.0  |
| Brainstem WM         | 8.1 | 7.9 | 10.3| 8.2 | 14.3| 9.8  | 15.1| 9.8 | 9.8 | 13.1| 9.5 | 11.5 |
| Non-lesional WM      | 6.6 | 9.6 | 8.7 | 8.0 | 8.6 | 8.3  | 8.4 | 9.1 | 9.5 | 11.5| 10.6| 9.8  |
| T2 MS lesions        | 6.4 | 11.0| 4.8 | 5.5 | 7.7 | 7.7  |     |     |     |     |     | 7.1  |
| Enhancing MS lesions | 8.0 | 19.4| 4.5 | 4.2 | 9.0 |     |     |     |     |     |     |      |

[^1]^CJSMW139 in multiple sclerosis. EJNMMI. Corresponding author: m.hagens1@vumc.nl
### B) %SE for $K_2$

|                  | MS1 | MS2 | MS3 | MS4 | MS5 | Mean | HC1 | HC2 | HC3 | HC4 | HC5 | Mean |
|------------------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|------|
| Frontal cortex   | 6.9 | 13.4| 15.9| 15.6| 13.8| 13.1 | 9.9 | 9.5 | 12.9| 13.9| 15.0| 12.2 |
| Orbitofrontal cortex | 8.3 | 18.2| 18.4| 17.5| 16.3| 15.7 | 11.6| 12.4| 13.4| 14.2| 19.2| 14.2 |
| Paracentral cortex| 7.4 | 13.3| 14.9| 13.9| 13.2| 12.5 | 9.7 | 9.7 | 12.1| 12.8| 13.7| 11.6 |
| Parietal cortex  | 8.0 | 11.3| 13.8| 12.5| 11.7| 11.5 | 8.2 | 8.8 | 10.2| 12.5| 12.2| 10.4 |
| Temporal cortex  | 6.5 | 12.0| 15.6| 13.4| 11.5| 11.8 | 8.3 | 10.5| 10.7| 13.7| 12.3| 11.1 |
| Occipital cortex | 5.7 | 11.2| 11.5| 9.0 | 7.8 | 9.0  | 5.2 | 8.3 | 8.3 | 9.8 | 7.7 | 7.9  |
| Cingulate cortex | 12.8| 19.5| 17.0| 19.8| 18.6| 17.5 | 13.7| 13.1| 16.2| 16.4| 20.8| 16.0 |
| Thalamic GM      | 12.7| 12.8| 12.6| 10.4| 13.4| 12.4 | 4.7 | 8.0 | 17.0| 13.2| 12.3| 11.0 |
| Putaminal GM     | 6.6 | 15.6| 16.0| 13.2| 15.6| 13.4 | 8.2 | 15.5| 13.1| 21.6| 13.3| 14.3 |
| Caudate nucleus GM| 7.4 | 13.1| 15.4| 16.9| 14.1| 13.4 | 11.0| 16.0| 18.7| 14.1| 14.7| 14.9 |
| Hippocampal GM   | 10.7| 17.6| 19.7| 24.6| 19.6| 18.4 | 16.5| 23.5| 16.7| 25.4| 19.7| 20.4 |
| Cerebellar GM    | 4.5 | 6.9 | 9.4 | 6.9 | 7.2 | 7.0  | 6.1 | 5.6 | 6.4 | 9.8 | 6.6 | 7.1  |
| Cerebellar WM    | 9.3 | 8.2 | 10.4| 9.1 | 9.8 | 9.4  | 11.7| 9.4 | 11.2| 16.3| 10.8| 11.9 |
| Brainstem WM     | 11.9| 12.1| 15.1| 11.9| 22.0| 14.6 | 25.1| 13.3| 15.3| 19.0| 12.7| 17.1 |
| Non-lesional WM  | 10.7| 14.9| 14.4| 12.6| 14.8| 13.5 | 14.4| 13.5| 15.6| 17.8| 14.8| 15.2 |
| T2 MS lesions    | 10.8| 20.8| 9.4 | 9.7 | 14.9| 13.1 |     |     |     |     |     |     |
| Enhancing MS lesions | 14.3| 39.2| 9.0 | 8.5 | 8.5 | 17.8 |     |     |     |     |     |     |

[$^{11}$C]SMW139 in multiple sclerosis. EJNMMI. Corresponding author: m.hagens1@vumc.nl
### C) %SE for K3

| Region                  | MS1  | MS2  | MS3  | MS4  | MS5  | Mean | HC1  | HC2  | HC3  | HC4  | HC5  | Mean |
|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|
| Frontal cortex          | 13.2 | 22.3 | 20.4 | 21.2 | 17.2 | 18.9 | 17.1 | 20.5 | 21.4 | 29.8 | 21.1 | 22.0 |
| Orbitofrontal cortex    | 15.0 | 33.7 | 24.6 | 21.6 | 22.6 | 23.5 | 19.8 | 27.1 | 23.4 | 31.0 | 27.4 | 25.7 |
| Paracentral cortex      | 14.2 | 19.1 | 19.2 | 19.2 | 15.9 | 17.5 | 16.0 | 18.1 | 18.9 | 27.9 | 19.0 | 20.0 |
| Parietal cortex         | 14.9 | 16.6 | 17.1 | 16.0 | 14.2 | 15.8 | 13.1 | 15.7 | 15.7 | 25.8 | 15.7 | 17.2 |
| Temporal cortex         | 12.6 | 21.8 | 21.0 | 19.1 | 16.3 | 18.2 | 15.6 | 21.7 | 19.6 | 31.0 | 17.5 | 21.2 |
| Occipital cortex        | 11.0 | 16.4 | 14.4 | 11.6 | 10.0 | 12.7 | 8.0  | 12.4 | 12.6 | 16.9 | 9.4  | 12.1 |
| Cingulate cortex        | 24.1 | 35.9 | 23.6 | 31.3 | 26.1 | 28.2 | 23.8 | 29.9 | 30.4 | 40.7 | 31.4 | 31.2 |
| Thalamic GM              | 31.7 | 25.9 | 18.6 | 19.5 | 23.4 | 23.8 | 13.9 | 25.6 | 39.9 | 53.9 | 22.8 | 31.2 |
| Putaminal GM             | 18.0 | 36.7 | 22.2 | 20.5 | 26.1 | 24.7 | 23.6 | 43.2 | 33.7 | 68.1 | 24.7 | 38.7 |
| Caudate nucleus GM       | 15.1 | 24.4 | 17.7 | 25.9 | 18.9 | 20.4 | 20.5 | 32.5 | 32.1 | 33.5 | 19.6 | 27.6 |
| Hippocampal GM           | 19.5 | 38.4 | 27.3 | 38.1 | 30.6 | 30.8 | 35.8 | 55.5 | 36.4 | 74.6 | 34.2 | 47.3 |
| Cerebellar GM            | 9.3  | 13.1 | 11.1 | 9.3  | 9.5  | 10.4 | 11.3 | 10.8 | 12.4 | 26.5 | 9.3  | 14.1 |
| Cerebellar WM            | 18.7 | 15.6 | 18.9 | 18.0 | 17.2 | 17.7 | 22.8 | 21.2 | 19.8 | 35.0 | 17.6 | 23.3 |
| Brainstem WM             | 23.5 | 27.2 | 25.3 | 20.9 | 35.2 | 26.4 | 51.5 | 29.1 | 29.1 | 48.0 | 21.1 | 35.8 |
| Non-lesional WM          | 18.7 | 22.6 | 25.4 | 24.7 | 23.2 | 22.9 | 21.1 | 25.5 | 22.7 | 30.5 | 21.9 | 24.3 |
| T2 MS lesions            | 18.9 | 38.5 | 26.4 | 24.0 | 24.1 | 26.4 | 24.0 | 24.0 | 24.0 | 24.0 | 24.0 | 24.0 |
| Enhancing MS lesions     | 39.3 | 128.3| 28.5 | 35.7 | 58.0 | 58.0 | 58.0 | 58.0 | 58.0 | 58.0 | 58.0 | 58.0 |

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### Table: %SE for VB

|                      | MS1  | MS2  | MS3  | MS4  | MS5  | Mean | HC1  | HC2  | HC3  | HC4  | HC5  | Mean |
|----------------------|------|------|------|------|------|------|------|------|------|------|------|------|
| Frontal cortex       | 6.5  | 9.9  | 10.5 | 8.9  | 9.5  | 9.1  | 5.1  | 6.2  | 8.0  | 8.3  | 8.5  | 7.2  |
| Orbitofrontal cortex | 7.9  | 14.7 | 11.9 | 11.6 | 11.4 | 11.5 | 6.6  | 8.1  | 9.1  | 9.6  | 11.8 | 9.0  |
| Paracentral cortex   | 7.2  | 9.1  | 9.7  | 8.1  | 9.0  | 8.6  | 5.2  | 6.1  | 8.0  | 7.6  | 7.8  | 6.9  |
| Parietal cortex      | 7.5  | 8.7  | 8.8  | 7.4  | 7.7  | 8.0  | 4.6  | 5.3  | 6.3  | 6.8  | 6.9  | 6.0  |
| Temporal cortex      | 7.0  | 9.5  | 10.7 | 8.3  | 8.0  | 8.7  | 4.6  | 6.4  | 6.9  | 8.5  | 7.7  | 6.8  |
| Occipital cortex     | 5.0  | 8.4  | 6.1  | 4.4  | 4.2  | 5.6  | 2.6  | 4.2  | 4.5  | 5.0  | 4.0  | 4.1  |
| Cingulate cortex     | 12.1 | 13.0 | 10.8 | 11.7 | 12.1 | 11.9 | 6.3  | 7.6  | 10.5 | 8.4  | 11.8 | 8.9  |
| Thalamic GM          | 13.7 | 9.9  | 7.4  | 8.8  | 10.4 | 10.0 | 3.4  | 5.5  | 13.8 | 8.9  | 7.5  | 7.8  |
| Putaminal GM         | 7.6  | 13.0 | 11.6 | 9.5  | 12.5 | 10.8 | 5.4  | 11.7 | 12.5 | 15.2 | 10.4 | 11.0 |
| Caudate nucleus GM   | 8.5  | 12.4 | 11.5 | 11.2 | 9.6  | 10.6 | 7.8  | 14.1 | 16.8 | 10.4 | 8.7  | 11.6 |
| Hippocampal GM       | 10.7 | 14.9 | 15.6 | 13.0 | 15.0 | 13.8 | 10.0 | 13.9 | 11.8 | 12.6 | 11.4 | 11.9 |
| Cerebellar GM        | 5.0  | 6.3  | 5.9  | 4.4  | 4.7  | 5.3  | 4.4  | 3.8  | 4.4  | 5.3  | 4.7  | 4.5  |
| Cerebellar WM        | 8.6  | 6.9  | 8.2  | 6.9  | 6.8  | 7.5  | 6.5  | 5.7  | 7.4  | 8.2  | 7.3  | 7.0  |
| Brainstem WM         | 14.5 | 11.4 | 11.2 | 9.8  | 14.5 | 12.3 | 11.9 | 9.4  | 10.8 | 10.2 | 8.8  | 10.2 |
| Non-lesional WM      | 10.2 | 10.6 | 10.8 | 9.2  | 10.0 | 10.2 | 6.7  | 8.2  | 9.2  | 9.2  | 8.8  | 8.4  |
| T2 MS lesions        | 11.2 | 15.2 | 10.2 | 8.5  | 8.6  | 10.7 |      |      |      |      |      |      |
| Enhancing MS lesions | 17.7 | 26.1 | 10.3 | 12.6 |      | 16.7 |      |      |      |      |      |      |

Abbreviations: GM = grey matter, HC = healthy control, MS = multiple sclerosis patient, SE = standard error, WM = white matter