1. Supplementary Materials

1.1. Data collection

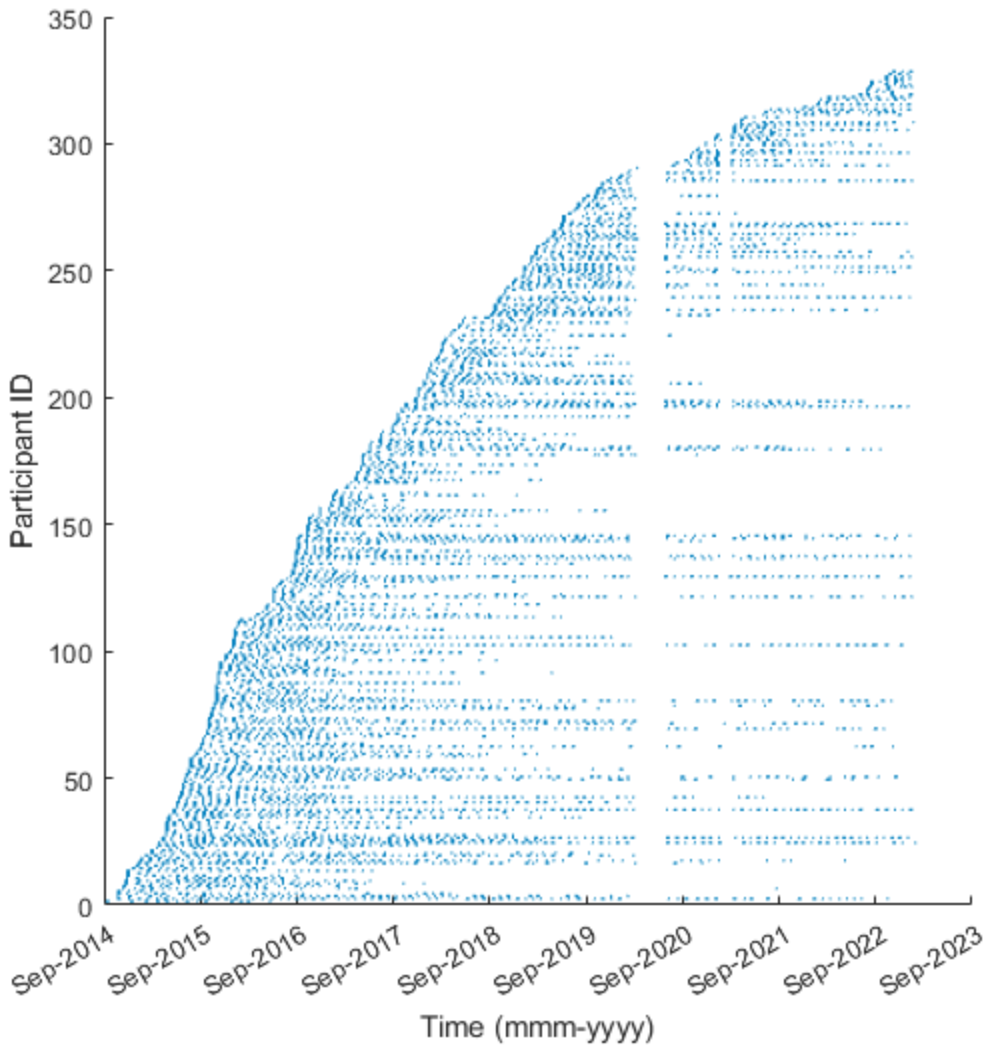

Figure S1. Participant enrollment and data collection in the analyzed dataset.

1.2. Association with ALSFRS-RSE

Table S1. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q1—12 using limb swing-derived outcomes of accelerometry data.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					

	Count	34.80 [33.23, 36.37]	0.079 [0.039, 0.119]	1.08e-04	0.800 [0.748, 0.841]
	Duration	40.30 [38.91, 41.69]	-2.066 [-2.994, -1.138]	1.29e-05	0.781 [0.718, 0.856]
	Intensity	34.34 [33.42, 35.26]	10.42 [8.71, 12.13]	1.36e-32	0.870 [0.845, 0.904]
	Similarity	29.66 [26.78, 32.54]	8.58 [5.66, 11.49]	7.92e-09	0.788 [0.725, 0.861]
Dominant wrist					
	Count	35.13 [33.56, 36.7]	0.067 [0.027, 0.107]	1.02e-03	0.798 [0.731, 0.849]
	Duration	39.55 [38.16, 40.93]	-1.624 [-2.565, -0.683]	7.20e-04	0.792 [0.736, 0.842]
	Intensity	34.30 [33.37, 35.23]	10.04 [8.32, 11.76]	4.05e-30	0.870 [0.824, 0.903]
	Similarity	28.60 [25.49, 31.71]	9.67 [6.49, 12.85]	2.66e-09	0.792 [0.736, 0.842]

Table S2. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q1—3 using limb swing-derived outcomes of accelerometry data.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Count	9.41 [8.87, 9.95]	0.016 [0.004, 0.028]	9.19e-03	0.889 [0.858, 0.916]
	Duration	10.42 [9.98, 10.85]	-0.350 [-0.627, -0.074]	0.013	0.875 [0.843, 0.918]
	Intensity	9.34 [8.97, 9.72]	1.608 [1.208, 2.007]	3.50e-15	0.917 [0.894, 0.936]
	Similarity	8.74 [7.97, 9.52]	1.277 [0.542, 2.012]	6.64e-04	0.871 [0.815, 0.913]
Dominant wrist					
	Count	9.49 [9.00, 9.98]	0.013 [0.002, 0.023]	0.017	0.882 [0.850, 0.918]
	Duration	10.32 [9.90, 10.74]	-0.302 [-0.561, -0.044]	0.021	0.880 [0.846, 0.909]
	Intensity	9.37 [9.01, 9.74]	1.391 [1.042, 1.740]	6.21e-15	0.911 [0.892, 0.932]
	Similarity	8.31 [7.45, 9.16]	1.749 [0.922, 2.576]	3.43e-05	0.876 [0.835, 0.917]

Table S3. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q7—9 using limb swing-derived outcomes of accelerometry data.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Count	7.117 [6.546, 7.687]	0.029 [0.014, 0.043]	9.18e-05	0.813 [0.777, 0.859]
	Duration	9.119 [8.582, 9.657]	-0.751 [-1.107, -0.396]	3.39e-05	0.809 [0.778, 0.842]
	Intensity	6.956 [6.608, 7.304]	3.539 [2.935, 4.144]	2.88e-30	0.866 [0.826, 0.889]
	Similarity	5.159 [4.168, 6.149]	3.214 [2.228, 4.200]	1.74e-10	0.810 [0.772, 0.858]
Dominant wrist					
	Count	7.276 [6.681, 7.872]	0.023 [0.008, 0.038]	2.31e-03	0.816 [0.790, 0.866]
	Duration	8.745 [8.194, 9.296]	-0.514 [-0.877, -0.151]	5.48e-03	0.814 [0.763, 0.851]

	Intensity	6.97 [6.623, 7.317]	3.357 [2.745, 3.969]	8.51e-27	0.871 [0.842, 0.893]
	Similarity	4.977 [3.882, 6.073]	3.386 [2.274, 4.498]	2.49e-09	0.810 [0.766, 0.850]

Table S4. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q10—12 using limb swing-derived outcomes of accelerometry data.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Count	10.34 [9.97, 10.71]	0.015 [0.006, 0.024]	7.23e-04	0.851 [0.802, 0.885]
	Duration	11.31 [11.01, 11.62]	-0.340 [-0.528, -0.152]	3.98e-04	0.838 [0.764, 0.886]
	Intensity	10.43 [10.17, 10.68]	1.356 [1.010, 1.701]	1.68e-14	0.882 [0.852, 0.912]
	Similarity	9.715 [9.024, 10.41]	1.239 [0.558, 1.920]	3.62e-04	0.845 [0.796, 0.889]
Dominant wrist					
	Count	10.46 [10.08, 10.84]	0.012 [0.002, 0.021]	0.013	0.853 [0.805, 0.896]
	Duration	11.2 [10.91, 11.49]	-0.266 [-0.446, -0.085]	3.91e-03	0.846 [0.787, 0.885]
	Intensity	10.43 [10.17, 10.69]	1.305 [0.952, 1.658]	4.75e-13	0.882 [0.828, 0.911]
	Similarity	9.578 [8.945, 10.21]	1.384 [0.766, 2.001]	1.13e-05	0.849 [0.778, 0.896]

1.3. Exercise vs. free-living upper limb movements metrics

Table S5. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q1—12 using limb swing-derived outcomes of accelerometry data for the free-living upper limb movements. Models were estimated using data from days with simultaneous exercise and substantial sensor wear time (>=21 h).

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Count	35.54 [33.42, 37.65]	0.070 [0.017, 0.123]	9.51e-03	0.811 [0.707, 0.889]
	Duration	40.62 [38.36, 42.88]	-1.910 [-3.473, -0.346]	0.017	0.826 [0.739, 0.891]
	Intensity	32.10 [30.36, 33.84]	10.33 [8.15, 12.52]	3.12e-20	0.908 [0.861, 0.943]
	Similarity	31.73 [27.26, 36.19]	6.74 [2.07, 11.40]	4.65e-03	0.792 [0.639, 0.890]
	C_{fe45}	32.71 [31.22, 34.20]	0.004 [0.004, 0.005]	1.47e-24	0.877 [0.819, 0.920]
	C_{sp45}	32.78 [31.22, 34.33]	0.002 [0.002, 0.002]	6.36e-22	0.869 [0.810, 0.915]
	D_{fe45}	43.80 [42.44, 45.15]	-11.02 [-13.26, -8.77]	1.24e-21	0.821 [0.713, 0.912]
	D_{sp45}	44.27 [42.66, 45.87]	-17.27 [-21.64, -12.91]	1.14e-14	0.834 [0.723, 0.915]
Dominant wrist					
	Count	36.40 [34.30, 38.51]	0.037 [-0.016, 0.090]	0.1687	0.813 [0.729, 0.902]
	Duration	39.72 [37.82, 41.62]	-1.415 [-2.644, -0.187]	0.023	0.805 [0.661, 0.885]
	Intensity	32.26 [30.61, 33.90]	9.682 [7.742, 11.623]	2.93e-22	0.899 [0.857, 0.936]
	Similarity	29.23 [25.38, 33.07]	9.456 [5.476, 13.436]	3.33e-06	0.791 [0.616, 0.885]
	C_{fe45}	32.85 [31.40, 34.29]	0.004 [0.004, 0.005]	8.35e-25	0.873 [0.797, 0.923]
	C_{sp45}	32.98 [31.44, 34.52]	0.002 [0.001, 0.002]	2.37e-19	0.866 [0.810, 0.914]
	D_{fe45}	43.25 [42.10, 44.41]	-10.10 [-12.26, -7.94]	9.75e-20	0.865 [0.790, 0.909]
	D_{sp45}	43.78 [42.23, 45.34]	-15.94 [-20.07, -11.82]	4.65e-14	0.847 [0.771, 0.913]

1.4. Association based on fewer limb swings

1.4.1. Association with ALSFRS-RSE Q4—6

Table S6. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q4—6 using accelerometry outcomes quantified from 5 initial limb swings.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	8.61 [8.33, 8.88]	-0.035 [-0.048, -0.021]	7.23e-07	0.774 [0.728, 0.836]
	Intensity	7.77 [7.46, 8.09]	3.107 [2.516, 3.699]	9.16e-25	0.867 [0.835, 0.889]
	Similarity	7.46 [6.87, 8.04]	1.234 [0.712, 1.755]	3.58e-06	0.791 [0.732, 0.834]
Dominant wrist					
	Duration	8.61 [8.34, 8.88]	-0.038 [-0.059, -0.018]	2.77e-05	0.772 [0.735, 0.826]
	Intensity	7.76 [7.43, 8.08]	2.975 [2.414, 3.536]	3.24e-25	0.866 [0.839, 0.890]
	Similarity	7.89 [7.34, 8.46]	0.748 [0.228, 1.268]	4.84e-03	0.787 [0.744, 0.853]

Table S7. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q4—6 using accelerometry outcomes quantified from 10 initial limb swings.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	8.60 [8.36, 8.88]	-0.031 [-0.044, -0.018]	2.82e-06	0.772 [0.729, 0.847]
	Intensity	7.78 [7.46, 8.09]	3.180 [2.582, 3.778]	2.54e-25	0.869 [0.847, 0.895]
	Similarity	7.42 [6.66, 8.18]	1.315 [0.575, 2.054]	4.96e-04	0.798 [0.765, 0.840]
Dominant wrist					
	Duration	8.60 [8.33, 8.87]	-0.031 [-0.050, -0.012]	1.64e-03	0.772 [0.715, 0.827]
	Intensity	7.74 [7.42, 8.06]	3.069 [2.492, 3.645]	2.06e-25	0.869 [0.840, 0.899]

	Similarity	7.36 [6.64, 8.08]	1.359 [0.653, 2.066]	1.63e-04	0.795 [0.749, 0.838]

Table S8. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q4—6 using accelerometry outcomes quantified from 15 initial limb swings.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	8.65 [8.25, 9.06]	-0.041 [-0.252, 0.170]	0.701	0.792 [0.740, 0.833]
	Intensity	7.79 [7.47, 8.11]	3.230 [2.618, 3.842]	5.78e-25	0.873 [0.840, 0.896]
	Similarity	7.11 [6.25, 7.97]	1.677 [0.826, 2.528]	1.13e-04	0.804 [0.762, 0.851]
Dominant wrist					
	Duration	8.63 [8.35, 8.90]	-0.035 [-0.059, -0.011]	4.36e-03	0.778 [0.753, 0.834]
	Intensity	7.75 [7.43, 8.07]	3.086 [2.518, 3.653]	1.99e-26	0.874 [0.853, 0.897]
	Similarity	6.89 [6.02, 7.76]	1.889 [1.012, 2.766]	2.43e-05	0.804 [0.750, 0.841]

Table S9. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q4—6 using accelerometry outcomes quantified from 20 initial limb swings.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	8.68 [8.19, 9.17]	-0.056 [-0.341, 0.229]	0.700	0.803 [0.744, 0.851]
	Intensity	7.83 [7.51, 8.15]	2.981 [2.434, 3.528]	1.64e-26	0.873 [0.843, 0.898]
	Similarity	6.79 [5.84, 7.73]	2.070 [1.117, 3.022]	2.06e-05	0.811 [0.755, 0.855]
Dominant wrist					
	Duration	8.48 [8.07, 8.89]	0.081 [-0.127, 0.288]	0.447	0.794 [0.731, 0.837]
	Intensity	7.76 [7.44, 8.08]	2.906 [2.396, 3.416]	8.07e-29	0.874 [0.845, 0.898]
	Similarity	6.70 [5.81, 7.59]	2.112 [1.206, 3.018]	4.89e-06	0.808 [0.769, 0.854]

1.4.2. Association with ALSFRS-RSE Q1—12

Table S10. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q1—12 using accelerometry outcomes quantified from 5 initial limb swings.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	37.47 [36.79, 38.14]	-0.106 [-0.154, -0.058]	1.48e-05	0.741 [0.685, 0.813]
	Intensity	34.89 [34.01, 35.78]	8.691 [7.104, 10.278]	9.09e-27	0.857 [0.812, 0.887]
	Similarity	34.29 [32.53, 36.05]	3.375 [1.742, 5.007]	5.10e-05	0.759 [0.696, 0.813]
Dominant wrist					
	Duration	37.50 [36.84, 38.17]	-0.144 [-0.220, -0.067]	2.20e-04	0.741 [0.671, 0.806]
	Intensity	34.92 [34.04, 35.81]	8.189 [6.641, 9.738]	4.43e-25	0.853 [0.818, 0.890]
	Similarity	35.56 [33.87, 37.26]	1.962 [0.343, 3.581]	0.017	0.758 [0.669, 0.815]

Table S11. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q1—12 using accelerometry outcomes quantified from 10 initial limb swings.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	37.46 [36.79, 38.13]	-0.095 [-0.142, -0.048]	8.31e-05	0.734 [0.693, 0.819]
	Intensity	34.90 [34.02, 35.78]	8.765 [7.198, 10.333]	7.85e-28	0.857 [0.811, 0.889]
	Similarity	34.26 [31.96, 36.57]	3.545 [1.262, 5.829]	2.34e-03	0.764 [0.672, 0.820]
Dominant wrist					
	Duration	37.46 [36.80, 38.13]	-0.110 [-0.175, -0.046]	7.53e-04	0.731 [0.692, 0.799]
	Intensity	34.88 [34, 35.76]	8.419 [6.852, 9.986]	7.75e-26	0.854 [0.832, 0.887]
	Similarity	33.96 [31.72, 36.21]	3.776 [1.549, 6.003]	8.89e-04	0.763 [0.679, 0.826]

Table S12. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q1—12 using accelerometry outcomes quantified from 15 initial limb swings.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	37.92 [36.78, 39.06]	-0.368 [-1.049, 0.313]	0.289	0.747 [0.684, 0.822]
	Intensity	34.94 [34.06, 35.82]	8.780 [7.228, 10.333]	1.97e-28	0.856 [0.826, 0.888]
	Similarity	33.24 [30.77, 35.71]	4.713 [2.260, 7.165]	1.66e-04	0.762 [0.697, 0.820]
Dominant wrist					
	Duration	37.54 [36.87, 38.20]	-0.122 [-0.196, -0.047]	1.42e-03	0.728 [0.682, 0.805]
	Intensity	34.91 [34.03, 35.78]	8.284 [6.802, 9.767]	8.48e-28	0.852 [0.819, 0.885]
	Similarity	32.50 [29.92, 35.08]	5.425 [2.827, 8.024]	4.30e-05	0.764 [0.706, 0.815]

Table S13. Model intercept and estimated average change associated with a one-point increase in ALSFRS-RSE Q1—12 using accelerometry outcomes quantified from 20 initial limb swings.

Sensor location	Movement biomarker	Intercept [95% CI]	Slope [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	38.21 [36.84, 39.58]	-0.539 [-1.433, 0.355]	0.237	0.746 [0.687, 0.810]
	Intensity	35.07 [34.19, 35.94]	8.186 [6.770, 9.603]	1.32e-29	0.847 [0.814, 0.878]
	Similarity	32.47 [29.67, 35.28]	5.686 [2.867, 8.506]	7.75e-05	0.755 [0.680, 0.809]
Dominant wrist					
	Duration	37.36 [36.27, 38.45]	0.036 [-0.573, 0.646]	0.906	0.736 [0.701, 0.801]
	Intensity	34.95 [34.07, 35.83]	7.909 [6.544, 9.273]	9.23e-30	0.847 [0.817, 0.879]
	Similarity	31.95 [29.35, 34.55]	6.102 [3.451, 8.753]	6.49e-06	0.758 [0.698, 0.816]

1.4.3. Association with time

Table S14. Average baseline and weekly change in ALSFRS-RSE scores and accelerometry outcomes quantified from 5 initial limb swing movements.

Sensor location	Outcome	Baseline estimate [95% CI]	Weekly change estimate [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	1.561 [1.432, 1.690]	0.009 [0.005, 0.014]	1.89e-05	0.201 [0.185, 0.254]
	Intensity	0.685 [0.614, 0.757]	-0.002 [-0.003, -0.001]	7.40e-04	0.870 [0.851, 0.894]
	Similarity	0.921 [0.814, 1.028]	0.001 [-0.001, 0.004]	0.341	0.154 [0.084, 0.244]
Dominant wrist					
	Duration	1.572 [1.455, 1.688]	0.008 [0.004, 0.011]	2.14e-05	0.178 [0.121, 0.252]
	Intensity	0.721 [0.646, 0.796]	-0.002 [-0.003, -0.001]	1.39e-04	0.858 [0.832, 0.888]
	Similarity	0.906 [0.896, 0.916]	-0.001 [-0.001, -0.000]	7.45e-06	0.424 [0.403, 0.515]

Table S15. Average baseline and weekly change in ALSFRS-RSE scores and accelerometry outcomes quantified from 10 initial limb swing movements.

Sensor location	Outcome	Baseline estimate [95% CI]	Weekly change estimate [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	1.564 [1.451, 1.677]	0.007 [0.003, 0.011]	1.48e-04	0.179 [0.135, 0.236]
	Intensity	0.680 [0.609, 0.751]	-0.002 [-0.003, -0.001]	1.47e-04	0.872 [0.851, 0.893]
	Similarity	0.906 [0.894, 0.917]	-0.001 [-0.001, -0.000]	1.62e-06	0.573 [0.525, 0.627]
Dominant wrist					
	Duration	1.595 [1.483, 1.706]	0.005 [0.002, 0.008]	3.54e-04	0.113 [0.086, 0.173]
	Intensity	0.719 [0.643, 0.794]	-0.002 [-0.003, -0.001]	3.94e-05	0.863 [0.827, 0.887]
	Similarity	0.911 [0.900, 0.921]	-0.001 [-0.001, -0.000]	8.24e-08	0.590 [0.525, 0.659]

Table S16. Average baseline and weekly change in ALSFRS-RSE scores and accelerometry outcomes quantified from 15 initial limb swing movements.

Sensor location	Outcome	Baseline estimate [95% CI]	Weekly change estimate [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	1.504 [1.397, 1.611]	0.006 [0.003, 0.010]	1.03e-03	0.136 [0.130, 0.202]

	Intensity	0.673 [0.602, 0.743]	-0.002 [-0.003, -0.001]	4.52e-05	0.871 [0.848, 0.895]
	Similarity	0.907 [0.895, 0.915]	-0.001 [-0.001, -0.001]	4.52e-08	0.610 [0.569, 0.661]
Dominant wrist					
	Duration	1.526 [1.436, 1.615]	0.004 [0.001, 0.006]	1.68e-03	0.061 [0.056, 0.144]
	Intensity	0.712 [0.637, 0.788]	-0.002 [-0.003, -0.001]	1.54e-05	0.863 [0.832, 0.891]
	Similarity	0.913 [0.901, 0.924]	-0.001 [-0.001, -0.001]	1.87e-09	0.631 [0.582, 0.690]

Table S17. Average baseline and weekly change in ALSFRS-RSE scores and accelerometry outcomes quantified from 20 initial limb swing movements.

Sensor location	Outcome	Baseline estimate [95% CI]	Weekly change estimate [95% CI]	*p*-value	R-squared [95% CI]
Non-dominant wrist					
	Duration	1.389 [1.298, 1.480]	0.006 [0.002, 0.010]	5.98e-03	0.139 [0.117, 0.217]
	Intensity	0.667 [0.597, 0.737]	-0.002 [-0.003, -0.001]	3.27e-05	0.869 [0.851, 0.900]
	Similarity	0.902 [0.889, 0.916]	-0.001 [-0.001, -0.001]	7.77e-09	0.644 [0.600, 0.694]
Dominant wrist					
	Duration	1.426 [1.340, 1.511]	0.003 [-0.001, 0.006]	0.102	0.093 [0.088, 0.247]
	Intensity	0.709 [0.635, 0.784]	-0.002 [-0.003, -0.001]	9.41e-06	0.862 [0.837, 0.884]
	Similarity	0.908 [0.896, 0.921]	-0.001 [-0.001, -0.001]	6.13e-10	0.665 [0.612, 0.727]