Assessment of Upper Extremity Function and Performance Fatigability in Multiple Sclerosis Using Sensor-Based Features Derived from the Smartphone-Based Pinching Test

JS Graves,1 M Elantkowski,2 Y-P Zhang,2 F Dondelinger,2 F Lipsmeier,2 C Bernasconi,2 X Montalban,3 L Midaglia,3,4 M Lindemann2

1Department of Neurosciences, University of California San Diego, San Diego, CA, USA; 2F. Hoffmann-La Roche Ltd, Basel, Switzerland; 3Department of Neurology–Neuroimmunology, Centre d’Esclerosi Múltiple de Catalunya (Cemcat), Hospital Universitari Vall d'Hebron, Barcelona, Spain; 4Department of Medicine, Autonomous University of Barcelona, Barcelona, Spain

Clinical Trial Registration Number: NCT02952911

Presented at the 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) Amsterdam, The Netherlands and virtual | 26–28 October 2022

https://bit.ly/3C5f9lj
The authors would like to thank all patients who participated in this trial, their families and the study investigators. They also thank the following colleagues at F. Hoffmann-La Roche Ltd for their contributions and support to the study: Jan Beckmann, Sandro Fritz, Nicholas Pierce Heinemeier, Sven Holm, Timothy Kilchenmann, Lito Kriara, Bernd Laub, Grégoire Pointeau, Cedric Simillion, Jens Schjodt-Eriksen, Jörg Sprengel and Mattia Zanon.

**JS Graves** has received research support from Biogen, EMD Serono, Novartis and Sanofi; has received speaking honoraria from Bristol Myers Squibb, Bayer and Alexion; and served on advisory boards for Genentech and Bayer.

**M Elantkowski, Y-P Zhang** and **F Lipsmeier** are employees of F. Hoffman-La Roche Ltd.

**F Dondelinger** was an employee of and is a shareholder in F. Hoffmann-La Roche Ltd; he is currently employed by Novartis.

**C Bernasconi** is a contractor for F. Hoffmann-La Roche Ltd.

**X Montalban** has received speaking honoraria and travel expenses for participation in scientific meetings; has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years with Actelion, Alexion, Bayer, Biogen, Celgene, EMD Serono, Genzyme, Immunic, MedDay, Merck, Mylan, Nervgen, Novartis, Roche, Sanofi-Genzyme, Teva, TG Therapeutics, Excemed, MSIF and NMSS.

**L Midaglia** has nothing to disclose.

**M Lindemann** is a consultant to F. Hoffmann-La Roche Ltd via Inovigate.
Floodlight Pinching Test

The Pinching Test

- A remote, smartphone sensor-based assessment for sensitive, quantitative, and frequent measures of UE function in MS
- Investigated during the 24-week Floodlight PoC study involving 76 MS and 25 healthy participants (NCT02952911)\(^1\)

**Objective:** Analyse characteristics of the **pinching** (touchscreen measures), **IMU-based** (smartphone acceleration and orientation) and **fatiguability** (performance difference) features of the Pinching Test

### Pinching features
- UE impairment
- Finger coordination
- Pinching smoothness and precision
- Muscle weakness, spasticity or tremor
- Range of motion or pinching precision

### IMU-based features
- Muscle weakness
- Hand coordination
- Tremor

### Fatiguability features
- Difference between 1\(^{\text{st}}\) and 2\(^{\text{nd}}\) halves of test

---

MS, multiple sclerosis; PoC, Proof-of-Concept; UE, upper extremity.
Methods and demographics

- The following analyses of the pinching, IMU-based and fatiguability features were conducted:
  - Test–retest reliability (ICC)
  - Agreement with gold standard clinical outcomes (Spearman’s rank correlation with 9HPT, EDSS and MSIS-29 arm items)
  - Known-groups discriminant validity (AUC)
  - Shared information between Pinching Test features (repeated-measures correlation)

- Based on the strength of signal, features were aggregated by the median (all features) or SD (fatiguability features)

<table>
<thead>
<tr>
<th></th>
<th>HC n=18</th>
<th>PLwMS n=67</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>6 (33)</td>
<td>45 (67)</td>
</tr>
<tr>
<td>Age, mean years (SD)</td>
<td>35.0 (8.9)</td>
<td>39.3 (7.8)</td>
</tr>
<tr>
<td>Diagnosis, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RRMS</td>
<td></td>
<td>60 (89.6)</td>
</tr>
<tr>
<td>PPMS</td>
<td></td>
<td>3 (4.5)</td>
</tr>
<tr>
<td>SPMS</td>
<td></td>
<td>4 (6.0)</td>
</tr>
<tr>
<td>Time since diagnosis, mean years (SD)</td>
<td></td>
<td>9.1 (6.4)</td>
</tr>
<tr>
<td>EDSS score, mean (SD)</td>
<td></td>
<td>2.4 (1.4)</td>
</tr>
<tr>
<td>9HPT time (dominant hand), mean seconds (SD)</td>
<td>18.7 (2.0)</td>
<td>22.3 (4.7)</td>
</tr>
</tbody>
</table>

9HPT, Nine-Hole Peg Test; AUC, area under the curve; HC, healthy control; ICC, intraclass correlation coefficient; IMU, inertial measurement unit; MSIS-29, 29-Item Multiple Sclerosis Impact Scale; PLwMS, people living with multiple sclerosis; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SD, standard deviation; SPMS, secondary progressive multiple sclerosis.
Pinching and IMU-based features showed moderate-to-good test–retest reliability.

---

**Fatiguability features (SD aggregation)**

- # performed pinches
- # successful pinches
- Successful AF
- Two-finger AF
- Pinch time
- Gap time
- DT asynchrony
- DL asynchrony
- 1st points distance
- Last points distance
- Finger path length
- Finger velocity
- Finger path ratio

**Fatiguability features (median aggregation)**

- # performed pinches
- # successful pinches
- Successful AF
- Two-finger AF
- Pinch time
- Gap time
- DT asynchrony
- DL asynchrony
- 1st points distance
- Last points distance
- Finger path length
- Finger velocity
- Finger path ratio

---

*Features were aggregated by computing the median or SD feature value across two-week windows; at least three valid individual assessments were required for each two-week window. Acc, accelerometer; AF, attempts fraction; DL, double lift; DT, double-touch; ICC(2,1), intraclass correlation coefficient (second model, first type); IMU, inertial measurement unit; SD, standard deviation.
Fatiguability features: Spearman’s correlation analyses and known-group validity

### A. Spearman’s rank correlations

<table>
<thead>
<tr>
<th>Clinical anchor</th>
<th># performed pinches</th>
<th># successful pinches</th>
<th>Successful AF</th>
<th>Two-finger AF</th>
<th>Pinch time</th>
<th>Gap time</th>
<th>DT asynchrony</th>
<th>DL asynchrony</th>
<th>1st points distance</th>
<th>Last points distance</th>
<th>Finger path length</th>
<th>Finger velocity</th>
<th>Finger path ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>9HPT dominant hand</td>
<td>0.59</td>
<td>0.58</td>
<td>0.67</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDSS</td>
<td>0.59</td>
<td>0.63</td>
<td>0.69</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSIS-29 arm items</td>
<td>0.53</td>
<td>0.63</td>
<td>0.69</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

###ii. Known-groups discriminant validity

<table>
<thead>
<tr>
<th>Clinical anchor</th>
<th># performed pinches</th>
<th># successful pinches</th>
<th>Successful AF</th>
<th>Two-finger AF</th>
<th>Pinch time</th>
<th>Gap time</th>
<th>DT asynchrony</th>
<th>DL asynchrony</th>
<th>1st points distance</th>
<th>Last points distance</th>
<th>Finger path length</th>
<th>Finger velocity</th>
<th>Finger path ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>9HPT dominant hand</td>
<td>0.59</td>
<td>0.58</td>
<td>0.52</td>
<td>0.61</td>
<td>0.70</td>
<td>0.64</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDSS</td>
<td>0.59</td>
<td>0.63</td>
<td>0.54</td>
<td>0.61</td>
<td>0.53</td>
<td>0.54</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSIS-29 arm items</td>
<td>0.53</td>
<td>0.58</td>
<td>0.52</td>
<td>0.61</td>
<td>0.53</td>
<td>0.54</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### B. Known-groups discriminant validity

<table>
<thead>
<tr>
<th>Clinical anchor</th>
<th># performed pinches</th>
<th># successful pinches</th>
<th>Successful AF</th>
<th>Two-finger AF</th>
<th>Pinch time</th>
<th>Gap time</th>
<th>DT asynchrony</th>
<th>DL asynchrony</th>
<th>1st points distance</th>
<th>Last points distance</th>
<th>Finger path length</th>
<th>Finger velocity</th>
<th>Finger path ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>9HPT dominant hand</td>
<td>0.59</td>
<td>0.63</td>
<td>0.64</td>
<td>0.61</td>
<td>0.60</td>
<td>0.51</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDSS</td>
<td>0.59</td>
<td>0.63</td>
<td>0.64</td>
<td>0.61</td>
<td>0.60</td>
<td>0.51</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSIS-29 arm items</td>
<td>0.53</td>
<td>0.58</td>
<td>0.52</td>
<td>0.61</td>
<td>0.53</td>
<td>0.54</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**AUC**

- **AUC** colour bar only applies to data with a statistically significant difference (p<0.05).
- **PLwMS** were classified as having normal or abnormal 9HPT times at baseline, with the threshold for abnormal 9HPT being the mean plus two SDs of the dominant-hand normative data of HCs (Erasmus L-P, et al. J Neurosci Methods 2001;108:25–37).
- 9HPT, Nine-Hole Peg Test; Abnorm, abnormal; AF, attempts fraction; AUC, area under the curve; DL, double lift; DT, double touch; EDSS, Expanded Disability Status Scale; HC, healthy control; MSIS-29, 29-item Multiple Sclerosis Impact Scale; Norm, normal; PLwMS, people living with multiple sclerosis; SD, standard deviation.

---

6
Pinching and IMU-based features: Spearman’s correlation analyses and known-group validity

A

i. Spearman’s rank correlations

- # performed pinches
- # successful pinches
- Successful AF
- Two-finger AF
- Pinch time
- Gap time
- DT asynchrony
- DL asynchrony
- 1st points distance
- Last points distance
- Finger path length
- Finger velocity
- Finger path ratio

Clip performance coefficient

AUC

B

i. Spearman’s rank correlations

- Acc magnitude, kurtosis
- Pinch duration
- Pinch gaps
- Whole test
- Orientation stability

Clinical anchor

9HPT dominant hand
EDSS
MSIS-29 arm items

AUC

ii. Known-groups discriminant validity

- 9HPT, Nine-Hole Peg Test; Abnorm; abnormal; Acc; accelerometer; AF; attempts fraction; AUC; area under the curve; DL; double lift; DT; double-touch; HC; healthy control; IMU; inertial measurement unit; kurt, kurtosis; MSIS-29, 29-item Multiple Sclerosis Impact Scale; Norm, normal; PLwMS, people living with multiple sclerosis; SD, standard deviation.

AUC colour bar only applies to data with a statistically significant difference (p<0.05).

PLwMS were classified as having normal or abnormal 9HPT times at baseline, with the threshold for abnormal 9HPT being the mean plus two SDs of the dominant-hand normative data of HCs (Erasmus L-P, et al. J Neurosci Methods 2001;108:25–37).

9HPT, Nine-Hole Peg Test; Abnorm, abnormal; Acc, accelerometer; AF, attempts fraction; AUC, area under the curve; DL, double lift; DT, double-touch; HC, healthy control; IMU, inertial measurement unit; kurt, kurtosis; MSIS-29, 29-item Multiple Sclerosis Impact Scale; Norm, normal; PLwMS, people living with multiple sclerosis; SD, standard deviation.
Most features capture unique information

- Number of performed pinches correlated with pinch time, gap time, finger velocity (faster = more pinches)
- Double-touch asynchrony correlated with gap time (unexpected, could be related to cerebellar dysfunction)
- The two IMU-based features correlated (horizontalness and orientation stability) as could be expected

The low number of correlations suggested that the features may capture different aspects of pinching.
Conclusions

• In PLwMS with mild, relapsing disease, **pinching-related fatiguability features** showed discriminant validity for impairment

• **Pinching features** best differentiated PLwMS-Normal from PLwMS-Abnormal, implying that greater levels of functional impairment lead to worse test performance

• **IMU-based features** showed ample test–retest reliability, but not a strong association with UE impairment

• Future work should explore the utility of all Pinching Test features in more advanced MS and for detecting MS progression

IMU, inertial measurement unit; MS, multiple sclerosis; PLwMS, people living with multiple sclerosis; UE, upper extremity.