# Clinical Feasibility of a Wearable, Conformable Sensor Patch to Monitor Motor Symptoms in Parkinson's Disease

Babak Boroojerdi[1], Kasper Claes[2], Roozbeh Ghaffari[3], Nikhil Mahadevan[4], Michael Markowitz[4], Katie Melton[4], Briana Morey[3], Christian Otoul[2], Shyamal Patel[3], Jake Phillips[3], Ellora Sen-Gupta[3], Oliver Stumpp[5], Daljit Tatla[4], John A. Wright Jr[3], Nirav Sheth[3]

1. UCB Pharma, Monheim am Rhein, Germany; 2. UCB Pharma, Brussels, Belgium; 3. MC10, Inc, Lexington, MA, USA; 4. UCB Pharma, Raleigh, NC, USA; 5. UCB Medical Devices, Bulle, Switzerland

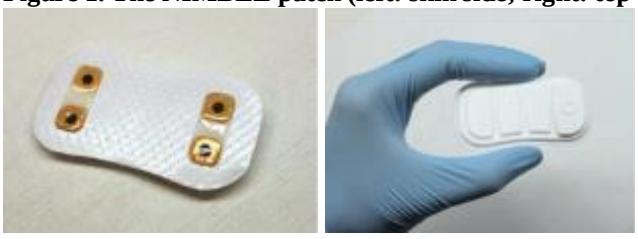
## Objective

A two-part pilot study (PD0028) to evaluate the safety, tolerability and clinical feasibility of the prototype NIMBLE system sensor patch, as an objective and continuous measure of motor symptoms in patients with Parkinson's disease (PD).

## Background

- In current clinical practice, the assessment of motor symptoms in patients with PD involves assessment of patient historical data, patient diaries and neurological assessments performed by physicians.
- The United Parkinson's Disease Rating Scale (UPDRS) is the most commonly used scale in the clinical assessment of PD, but is subject to biased reporting of historical information, and the short duration of routine neurological assessments performed in the clinic may not accurately reflect motor impairments experienced by patients in everyday life.
- Tools are needed that provide more objective, quantitative and continuous symptom assessments.
- The NIMBLE patch was developed by MC10, Inc. (Lexington, MA, USA) as a biosensor patch to record motor activity in patients with PD. The NIMBLE patch consists of an accelerometer and an electromyograph (EMG) sensor embedded into a flexible, conformable patch designed to measure and record patterns in movement and muscle activity (**Figure 1**).
- The NIMBLE patch was used in a clinical study (PD0028) sponsored by UCB Biosciences (Raleigh, NC, USA). Part 1 of this study evaluated the feasibility of the patch to accurately capture movement at various body sites during Movement Disorder Society (MDS)-UPDRS assessment in six participants. Part 2 (reported here) explored the feasibility of applying the patch to the most appropriate body sites identified in Part 1 to record a subset of motor symptoms in-clinic and at-home.

**Figure 1. The NIMBLE patch (left: skin side; right: top side)**



The NIMBLE patch is a wearable, conformable electronic sensor, which is approximately 7 cm in length, 4 cm in width, 0.6 cm thick and weighs 12 g. The patch records physiological data. The sensor, rechargeable sensor battery and electrodes are encapsulated in medical grade silicone. A separate adhesive sticker attaches the silicone capsule to the skin.

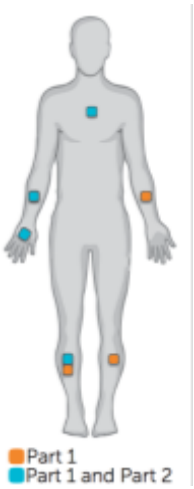
## Methods

### Eligibility

Participants were male or female, aged ≥18 years with PD, at Hoehn & Yahr (HY) stage II-IV in the 'on' state during screening, had troublesome motor fluctuations, and were on a stable levodopa dose of ≥200 mg for at least 4 weeks before study enrollment.

**Design**

- Part 2 of the study involved a 3-day observation period in which participants stayed in-clinic on Days 1-2, were discharged on the afternoon of Day 2, continued as outpatients until the afternoon of Day 3, and had a safety follow-up on Day 6.
- Patches were applied to the chest, shin, forearm and back of hand (for the latter three sites, patches were placed on the side of the body most affected by PD motor symptoms) on Day 1.
- From Days 1-3, participants used a software application 'Diary APP' to document medicine intake, sleep and PD symptoms.
- On the morning of Day 2, new patches were applied to the shin and forearm (and other sites if needed), and a subset of UPDRS III tasks completed twice (60 and 30 minutes) before levodopa intake, repeated every 30 minutes after levodopa intake for up to a total of seven sets.
- At least 1 hour after the motor assessments were completed, the NIMBLE patches were removed, new patches applied, and the participant was discharged.
- On Day 3, participants performed one set of motor assessments listed on the Diary APP in the morning before levodopa intake and at least two sets (30 minutes apart) after levodopa intake. Participants were instructed to also complete additional motor activities when symptoms changed from 'on' to 'off', or vice versa.




**Outcomes**

Primary Variables

- Recognizable patterns in motor symptoms obtained from the NIMBLE patch output, translated via algorithms into measures of PD symptoms.
- UPDRS scores in relation to NIMBLE patch output.

Secondary Variables

- Adhesiveness of the NIMBLE patch up to 24 hours.
- Participant and investigator feedback regarding the user-friendliness of the NIMBLE patch.
- Participant feedback regarding their experience with the NIMBLE patch and with the data derived from the NIMBLE patch.

**Safety**

- Occurrence of device-emergent adverse events (DEAEs) and device deficiencies.
- Skin tolerability assessments.

**Statistical Analyses**

- Multiple algorithms were developed by MC10 to translate raw output from the patch (from in-clinic and at-home assessments) into data relating to PD motor symptom severity that could be analyzed (ie predicted scores).
- Motor symptoms were also assessed independently in-clinic by participants' neurologists (ie observed scores).
- The Safety Set (SS) consisted of all participants for whom at least one patch was applied for any period of time. The Full Analysis Set (FAS) consisted of all participants for whom the patch was applied for a total of ≥24 hours.
- All analyses were descriptive.

## Results

### Baseline Demographics and Participant Disposition (SS)

- In Part 1, six participants started and completed the study (66.7% male; mean ± standard deviation [SD] age: 60.7 ± 9.5 years; HY: II [50.0%]-III [50.0%]).
- In Part 2, 21 participants (57.1% male; mean ± SD age: 65.0 ± 7.0 years) with low symptomatology (HY: II [66.7%]-III [33.3%]) started (including two participants from Part 1) and 19 (90.5%) completed the study. Two participants were lost to follow-up.

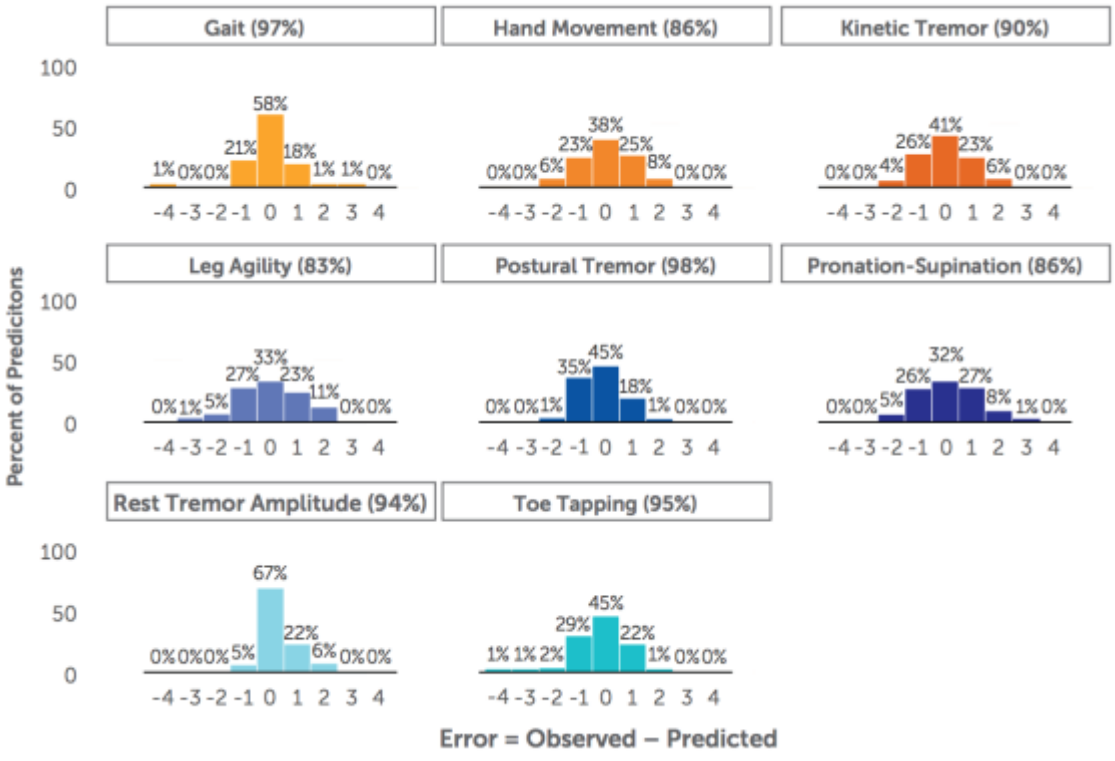
### Algorithm Training Methods

- Part 1 algorithms were trained using data from the six participants in Part 1.
- Part 1 algorithms were further improved by including the in-clinic data from the 21 participants in Part 2 in the training set. These algorithms were subsequently applied to the Part 2 at-home data to produce at-home predictions.
- A leave-one-out method was utilized to assess the performance of the algorithms.

### Accuracy of Part 2 Algorithm from In-Clinic Assessments

- The exact accuracy (error rate of 0) of predicted vs observed scores was 44.9% and the overall predicted score was within a ±1 range (error rate of -1 to 1) 91% of the time (**Figure 2**).
- The exact accuracy of each individual activity varied, ranging from 32% (pronation-supination) to 67% (rest tremor amplitude). All assessments other than rest tremor amplitude (67%) and gait (58%) had <50% exact accuracy.

**Figure 2. Error distribution of Part 2 algorithm across UPDRS III subset activities performed in-clinic (FAS)[a]**




[a]The error was defined as the difference between the observed (neurological assessment) and the predicted (Part 2 algorithms leveraging patch data) scores, and ranged from -4 to +4 with the value 0 corresponding to an exact match between these two scores.

**In-Clinic Motor Assessment Scores**

- The average correlation coefficient between observed and predicted scores in-clinic was 0.471; rest tremor amplitude and toe-tapping algorithms had the highest correlations (**Table 1**).

**Table 1. Part 2: Correlation between in-clinic predicted and observed motor symptom severity scores across UPDRS III subset activities (post- hoc exploratory analysis; FAS)**

| Activity | Number of assessments | Correlation coefficient | p-value[a] | Accuracy and clinician score distribution[b] |
|---|---|---|---|---|
| Rest tremor amplitude | 143 | 0.746 | 0.0002 | 0 1 2 3 |
| Toe-tapping | 139 | 0.709 | 0.0005 | 0 1 2 3 4 |
| Postural tremor | 141 | 0.477 | 0.034 | 0 1 2 3 |
| Kinetic tremor | 137 | 0.437 | 0.054 | 0 1 2 3 |
| Leg agility | 133 | 0.320 | 0.182 | 0 1 2 3 4 |
| Hand movements | 146 | 0.291 | 0.201 | 0 1 2 3 |
| Pronation-supination | 140 | 0.213 | 0.367 | 0 1 2 3 4 |
| Gait | 138 | 0.164 | 0.489 | 0 1 3 |
| Average (all activities) | 140 | 0.471 | 0.031 | 0 1 2 3 4 |

Accuracy
1.00 0.75 0.50 0.25 0.00

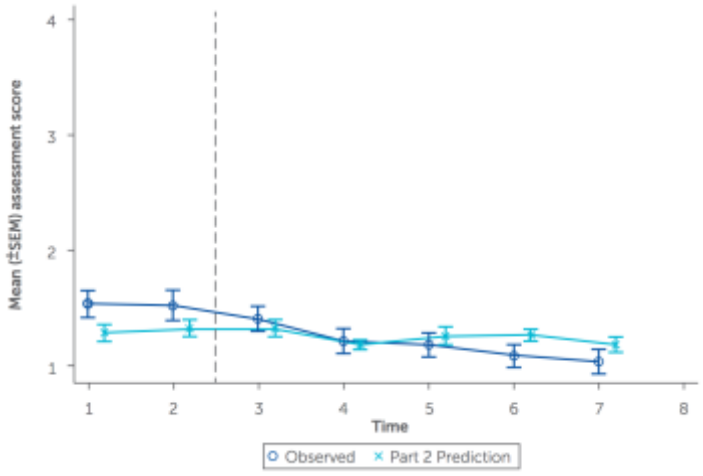
[a]Test of significance by Pearson coefficient correlation

[b]The relative representation of clinician scores for each activity (0-4 UPDRS score, displayed below graphic), colored by the accuracy of predicting that score. Algorithms were more accurate for scores with more assessments. No 4s were observed for hand movement, kinetic tremor, postural tremor, and rest tremor amplitude, and no 2s were observed for gait.

**Motor Assessment scores in Relation to Treatment**

- In-clinic predicted and observed scores were similar before and after levodopa intake (**Figure 3**).

**Figure 3. Part 2: In-clinic mean motor assessment scores over time for the average of eight UPDRS II subset activities (FAS)**




Dashed line indicates levodopa intake

**Participant Feedback (SS)**

- Participants found the patch easy to use, not too painful to detach, and felt that it did not interfere with daily activities or sleep. They were very satisfied with the usage training provided and not embarrassed to wear the patch in public (**Table 2**).
- In addition, overall, participants found the information gathered from the patch to be valuable and found the Diary APP to be a useful tool and easy to use.

**Table 2. Part 2: Summary of participant feedback on NIMBLE patch use (SS)**

| Item | Part 2 N=21 |
|---|---|
| 1. Use difficulty, mean (SD) | 6.1 (1.2) |
| 2. NIMBLE patch usage training, mean (SD) | 6.3 (0.7) |
| 3. Removal pain, mean (SD) | 1.3 (2.3) |
| 4. Interference with daily activities, mean (SD) | 4.3 (0.8) |
| 5. Interference with sleep, mean (SD) | 4.6 (0.7) |
| 6. Embarrassment from patch in public, mean (SD) | 4.4 (1.0) |
| 7. Data helped participants to manage their medication dosing, n (%) | 17 (81.0) |
| 8. Data helped participants to better communicate with their neurologist, n (%) | 15 (71.4) |
| 9. Found Diary APP easy to use, n (%) | 18 (85.7) |
| 10. Would use Diary APP to record and display information on their symptoms, n (%) | 16 (76.2) |

For items 1, 2, 4, 5 and 6, a higher score (range 1 to 7 for Items 1 and 2, and 1 to 5 for Items 4, 5 and 6) indicates a favorable result; for item 3, a higher score (range 1 to 10) indicates a worse result.

**Safety and Adhesiveness (SS)**

- The patch was well tolerated in Part 2, with one participant (4.8%) reporting two DEAEs: application site irritation (moderate intensity) and application site pain (mild intensity).
- The patch also had good adhesiveness (**Table 3**).

**Table 3. Part 2: Overall study device exposure and patch adhesiveness (SS)**

| | Part 2 (N=21) |
|---|---|
| Total device application duration (hours)[a] | |
| Mean (SD) | 43.55 (1.97) |
| Patch adhesiveness score, # (%)[b,c] | |
| 0 or 1 (defined as overall adhesion success) | 207 (97.2) |
| 2, 3 or 4 (defined as overall adhesion fail) | 6 (2.8) |

[a]Calculated as the sum of the longest individual patch application time
[b]Data are number (%) of patches. Twenty-one participants wore 221 patches: eight adhesion scores were not recorded (4%). Thus, percentage is calculated using denominator of 213 patches
[c]Adhesiveness scores ranged from 0 (≥90% adhered [essentially no lift off the skin]) to 4 (0% adhered – device detached [patch completely off skin])

## Conclusions

- The NIMBLE patch technology was demonstrated to be feasible for measuring the severity of PD motor symptoms.
- Participants found the NIMBLE patch easy to use and the information gathered to be a valuable tool in the management of their PD symptoms.
- The NIMBLE patch was safe and well tolerated.
- The correlation between predicted and observed motor PD motor symptom severity can be expected to improve with algorithm refinement after further studies in larger groups of participants with a greater range

of symptom severity.

## Acknowledgements

The authors thank the participants who contributed to the study. The study was funded by UCB Pharma, Brussels, Belgium. The authors acknowledge Nicole Meinel, PhD, CMPP (Evidence Scientific Solutions, London, UK) for writing assistance, which was funded by UCB Pharma (Brussels, Belgium), and Cédric Laloyaux, PhD, Strategic Publication Lead Neurology (UCB Pharma, Brussels, Belgium) for publication coordination.

Babak Boroojerdi, Michael Markowitz, Katie Melton, Briana Morey, Shyamal Patel, Oliver Stumpp, Christian Otoul, John A Wright, Jr, and Nirav Sheth designed the study. Katie Melton, Briana Morey, Ellora Sen-Gupta and John A Wright, Jr were involved in data collection. Oliver Stumpp and MC10 authors defined technical specifications for the patch. Kasper Claes, Michael Markowitz, Christian Otoul and MC10 authors contributed to data analysis. All authors contributed to data interpretation. All authors were involved in the critical review/revision of poster drafts and approved the final version.

Babak Boroojerdi, Kasper Claes, Michael Markowitz, Katie Melton, Christian Otoul, Oliver Stumpp and Daljit Tatla are employees of UCB Pharma. Michael Markowitz receives UCB stock units from his employment. Roozbeh Ghaffari, Nikhil Mahadevan, Briana Morey, Jake Phillips, Ellora Sen-Gupta and John Wright are employees of MC10, Inc. Nirav Sheth and Shyamal Patel are former employees of MC10, Inc.