

# Implementation of mobile technology in clinical management of Parkinson's disease: opportunities & challenges

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# General considerations about mobile technology in PD management

# Three types of markers needed to understand Parkinson's

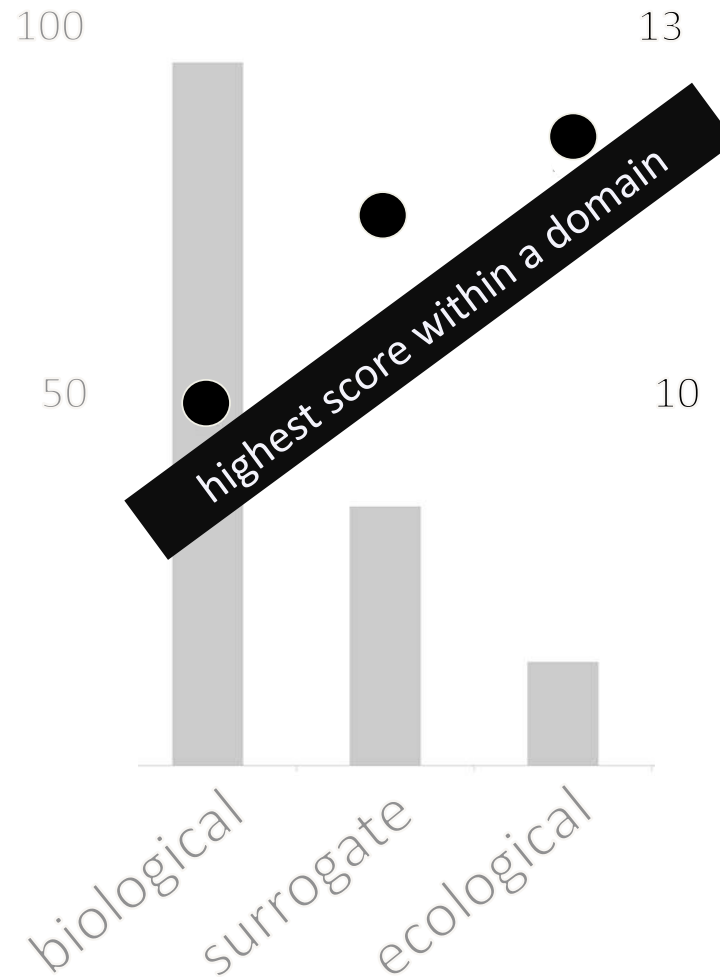
biological  
markers

surrogate  
markers

ecological  
markers



# Surrogate and ecological markers are more important for QoL than biological markers



A large proportion of PD patients have an enormous drive to contribute to research, and to learn more about their PD

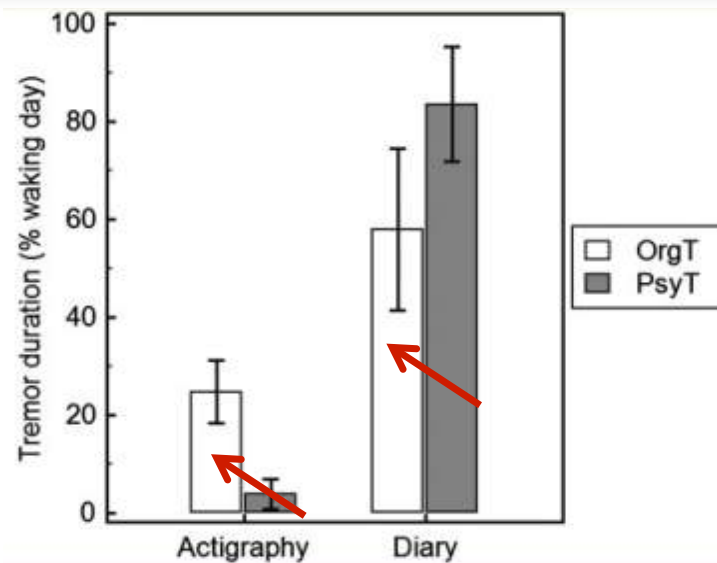


# Patient-reported outcomes (PROs) have limitations

**Diaries** are mostly reported in **binary terms**, depend on **motivation**, have **recall bias**, rely on patients' **perception**

## Believing is perceiving: mismatch between self-report and actigraphy in **organic** tremor

Isabel Pareés, Tabish A. Saifee, Panagiotis Kassavetis, Maja Kojovic, Ignacio Rubio-Agusti, John C. Rothwell, Kailash P. Bhatia and Mark J. Edwards

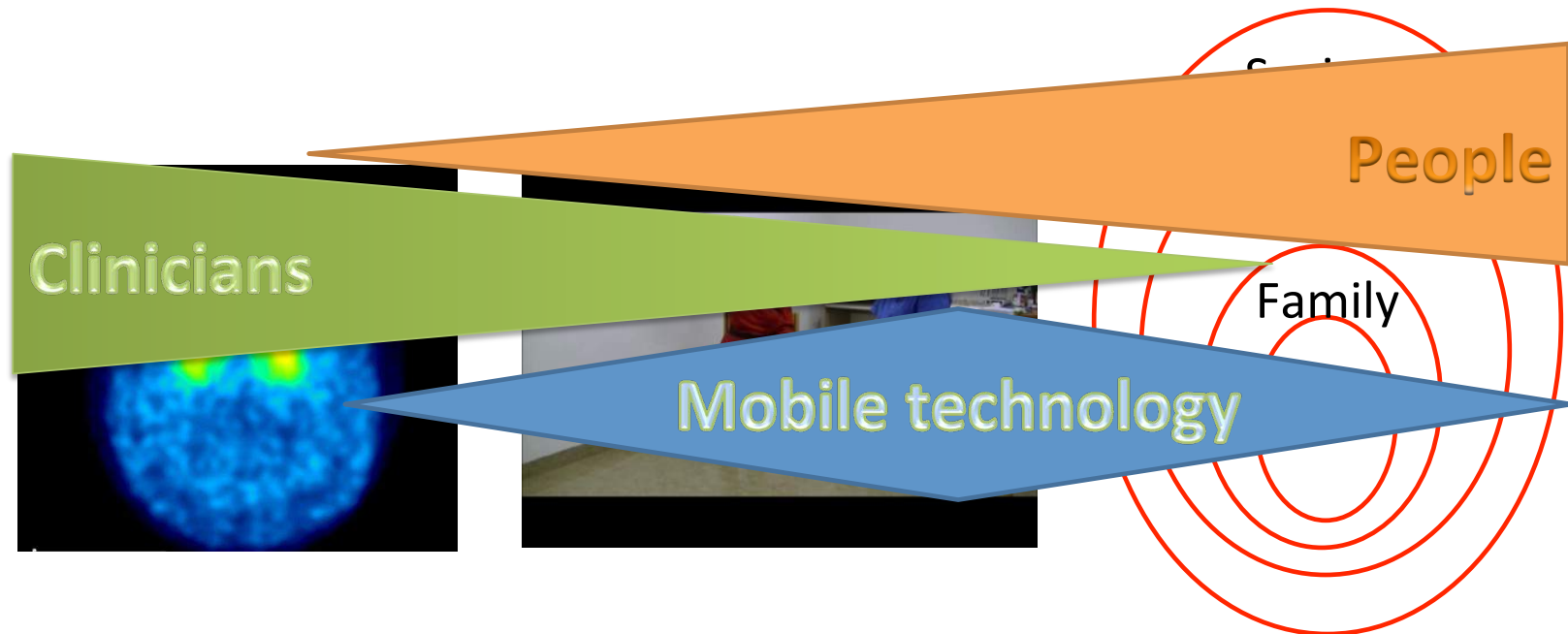


# Three types of markers needed to understand Parkinson's

biological  
markers

surrogate  
markers

ecological  
markers



derived / adapted from the ICF model of the WHO, 2001

## Surrogate and ecological markers

**... are absolutely necessary to get a whole picture of Parkinson's disease.**



# EMA and FDA: Huge interest in mobile technology development



funded by FDA and Duke University

## **VALIDATING AND QUALIFYING NOVEL ENDPOINTS GENERATED BY MOBILE TECHNOLOGY IN CLINICAL TRIALS**

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### **DRAFT SUMMARY AGENDA**

Multi-Stakeholder Expert Meeting to be held September 29 - 30, 2016

DoubleTree by Hilton Hotel Silver Spring  
8727 Colesville Rd, Silver Spring, MD 20910

# Main outcomes

- Currently no FDA-approved mobile technology-based tool to assess PD symptoms
- Financing and IP aspects not clarified
- Actual proposals for scientists, clinicians and trialists:
  - Use new measures in clinical trials along existing measures
  - Observational > predictive > treatment trials could be a good sequence
  - Do not matter too much about „clinically meaningful changes“
  - Accept new validation pathways
  - Build algorithm and raw data platforms

Actual situation of mobile technology in PD

## Advances in Sensor and Wearable Technologies for Parkinson's Disease

Álvaro Sánchez-Ferro, MD, MSc <sup>1,2</sup> and Walter Maetzler, MD <sup>3,4\*</sup>



## REVIEW

### New Methods for the Assessment of Parkinson's Disease (2005 to 2015): A Systematic Review

Álvaro Sánchez-Ferro, MD, MSc,<sup>1,2\*</sup> Morad Elshehaby, MD, MSc,<sup>3,4</sup> Catarina Godinho, PhD,<sup>5,6,7</sup> Dina Salkovic, MD, MSc,<sup>3,4</sup>  
Markus A. Hobert, MD,<sup>3,4</sup> Josefa Domingos, MSc,<sup>5,7</sup> Janet MT. van Uem, MSc,<sup>3,4</sup> Joaquim J. Ferreira, MD, PhD,<sup>5,7,8</sup> and  
Walter Maetzler, MD<sup>3,4</sup>

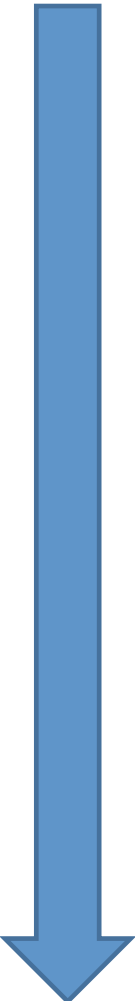
**TABLE 1.** New technologies for the assessment of Parkinson's disease (NAM-PD) published during the past decade (2005-2015) by disease domain

| Domain   | Number of references<br>describing the NAM-PD<br>(% of all included) |
|--|--|
| Motor  | 504 (85.7)   |
| Axial features   | 212 (36.1)   |
| Bradykinesia   | 126 (21.4)   |
| Tremor   | 81 (13.8)  |
| Speech   | 42 (7.1)   |
| Activity   | 32 (5.4)   |
| Rigidity   | 11 (1.9)   |
| Nonmotor <sup>a</sup>                                    | 24 (4.1)   |
| Cognition  | 12 (2.0)   |
| Sleep  | 9 (1.5)  |
| ANS  | 2 (0.3)  |
| Neuropsychiatric features                                | 1 (0.2)  |
| Smell  | 0 (0.0)  |
| Treatment complications                                  | 20 (3.4)   |
| Miscellaneous  | 40 (6.8)   |
| Total, included in the results                           | 588  |
| Not included in the full evaluation process <sup>b</sup> | 260  |
| Total number of references evaluated                     | 848  |

|   |                   |                        |                                |                           |                                |                               |                               |
|---|-------------------|------------------------|--------------------------------|---------------------------|--------------------------------|-------------------------------|-------------------------------|
| pilot form (Responses)  |                   |                        |                                |                           |                                |                               |                               |
| File Edit View Insert Format Data Tools Add-ons Help Last edit was made 13 days ago by Álvaro Sánchez Ferro |                   |                        |                                |                           |                                |                               |                               |
| Comments Share  |                   |                        |                                |                           |                                |                               |                               |
| Timestamp   |                   |                        |                                |                           |                                |                               |                               |
|   | AJ                | AK                     | AL                             | AM                        | AN                             | AO                            | AP                            |
| 1   | Accuracy measured | Sensitivity (%)        | Sensitivity > 80% (0: N; 1: 1) | Specificity (%)           | Specificity > 80% (0: N; 1: 1) | Positive predictive value (%) | Negative predictive value (%) |
| 29  | Yes               | 73.10%                 | 0                              | 81.60%                    | 1                              | uk                            | uk                            |
| 30  | Yes               | 73.1                   | 0                              | 81.6                      | 1                              | uk                            | uk                            |
| 31  |                   |                        |                                |                           |                                |                               |                               |
| 32  | Yes               | uk                     |                                | uk                        |                                | uk                            | uk                            |
| 33  |                   |                        |                                |                           |                                |                               |                               |
| 34  |                   |                        |                                |                           |                                |                               |                               |
| 35  | Yes               | uk                     |                                | uk                        |                                | uk                            | uk                            |
| 36  |                   |                        |                                |                           |                                |                               |                               |
| 37  | Yes               | 100 (for detecting PD) | 1                              | 80-100 (for detecting PD) | 1                              | uk                            | uk                            |
| 38  | Yes               | 88%                    | 1                              | 86%                       | 1                              | uk                            | uk                            |
| 39  | Yes               | 100%                   | 1                              | 94%                       | 1                              | uk                            | uk                            |
| 40  | Yes               | 97.7%                  | 1                              | 75.5%                     | 0                              | uk                            | uk                            |

<http://bit.ly/pd-technologies>

# Technology readiness levels (TRL) are generally low



|   |
|---|
| TRL 1 – basic principles observed                                 |
| TRL 2 – technology concept formulated                             |
| TRL 3 – experimental proof of concept                             |
| TRL 4 – technology validated in lab                               |
| TRL 5 – technology validated in relevant environment              |
| TRL 6 – technology demonstrated in relevant environment           |
| TRL 7 – system prototype demonstration in operational environment |
| TRL 8 – system complete and qualified                             |
| TRL 9 – actual system proven in operational environment           |

N = 42 (out of 848)

**System approved for PD management: N=0**

# Prerequisites for implementation in PD management

1. Provide valid, accurate and clinically relevant results
2. Contribute to an ecologically effective therapeutic decision (QoL)
3. Offer a target range
4. Allow easy and repetitive / continuous use

Examples from other areas of medicine: blood pressure, HbA1c

Feature assessment with mobile technology  
relatively close to clinical implementation in PD

- Akinesia
- Dyskinesia
- Motor fluctuations
- Gait impairment, freezing
- Physical inactivity



# Who will benefit most of mobile technology?

- Most PD patients
- PD patients with limited access to specialists
- PD patients with a predominant motor phenotype
- Young PD patients
- Clinicians and allied health professionals

# What are the main challenges?

- Systems under control of a regular body, or „leave the data with the patient“?
- Financing and IP rights of the development not clarified
- Reporting matters
- Patients and clinicians must know what to do with the data
- Validation process → next talk by Jochen Klucken

# Limitations of LAB-validated algorithms to serve as gold standard for data obtained in naturalistic environment

## PD Disease State Assessment in Naturalistic Environments using Deep Learning

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Keele University, UK

**Lynn Rochester**

Institute of Neuroscience  
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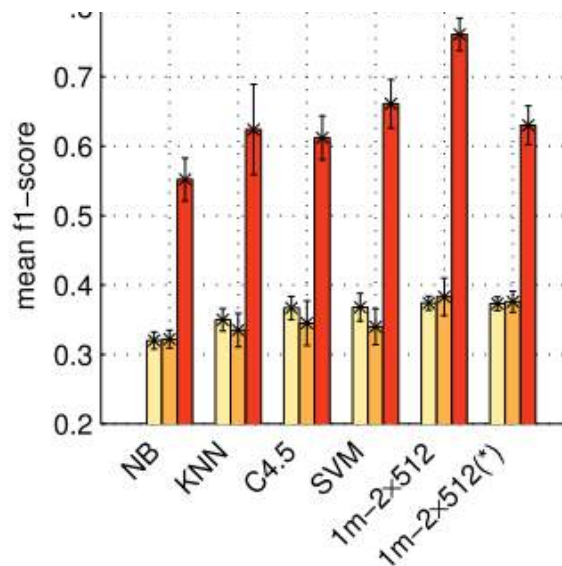
**Thomas Plötz**

Culture Lab, Digital Interaction Group  
Newcastle University, UK

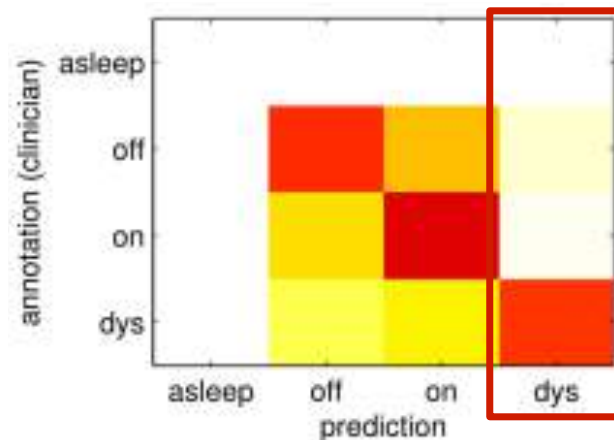
- **Participants:** 34 PD patients H&Y 1-4
- **Paradigm:**
  - LAB assessment of **off, on, and dyskinesia** once / hour over 4 h duration, videotaped, rated by clinician
  - HOME assessment of **off, on, dyskinesia, asleep** once / hour over 7 days with a diary
  - Both LAB and HOME phase also assessed with a sensor at each wrist

# Lab-validation is „an incredibly poor model for naturalistic behaviour”

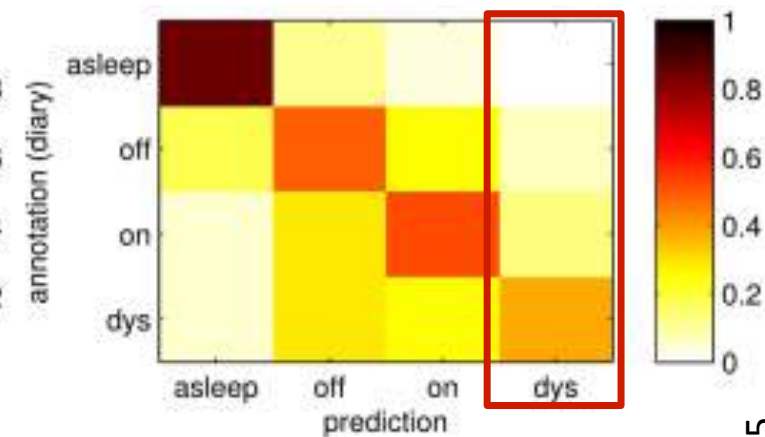
Training on LAB-based dataset



LAB-based dataset



HOME-based dataset



- we need home-based validation datasets
- machine learning techniques promising

# Machine Learning for Large-Scale Wearable Sensor Data in Parkinson's Disease: Concepts, Promises, Pitfalls, and Futures

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<sup>3</sup>*Interdepartmental Program in Bioinformatics, University of California at Los Angeles, Los Angeles, California, USA*

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**ABSTRACT:** For the treatment and monitoring of Parkinson's disease (PD) to be scientific, a key requirement is that measurement of disease stages and severity is quantitative, reliable, and repeatable. The last 50 years in PD research have been dominated by qualitative, subjective ratings obtained by human interpretation of the presentation of disease signs and symptoms at clinical visits. More recently, "wearable," sensor-based, quantitative, objective, and easy-to-use systems for quantifying PD signs for large numbers of participants over extended durations have been developed. This technology has the potential to significantly improve both clinical diagnosis and management in PD and the conduct of clinical studies. However, the large-scale, high-dimensional character of the data captured by these wearable sensors requires sophisticated signal processing and machine-learning algorithms to transform it into scientifically

and clinically meaningful information. Such algorithms that "learn" from data have shown remarkable success in making accurate predictions for complex problems in which human skill has been required to date, but they are challenging to evaluate and apply without a basic understanding of the underlying logic on which they are based. This article contains a nontechnical tutorial review of relevant machine-learning algorithms, also describing their limitations and how these can be overcome. It discusses implications of this technology and a practical road map for realizing the full potential of this technology in PD research and practice. © 2016 International Parkinson and Movement Disorder Society

**Key Words:** machine learning; artificial intelligence; data science; wearables; digital sensors

# Hypothesis-driven algorithms: example turning

>2000 turns under daily-like activity, against video observation (ICC 0.92)

In PD patients under medication OFF-condition

→ sensitivity 0.92, specificity 0.89, accuracy 0.92

In PD patients under medication ON-condition

→ sensitivity 0.92, specificity 0.78, accuracy 0.83

In older adults

→ sensitivity 0.94, specificity 0.89, accuracy 0.92

# Conclusion

- Potential of mobile technology for management of PD extremely high
- Huge interest from all stakeholders, including patients, clinicians and companies such as Google
- Challenges:
  - Financing and IP aspects not clarified
  - Data and algorithms platforms to be developed
  - Validation of algorithms: machine learning and hypothesis-driven algorithms complementary

Thank you