Remote Assessment of Disease and Relapse in Central Nervous System Disorders (RADAR-CNS)

Matthew Hotopf (KCL)
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Introduction

- Remote measurement technologies (RMT) could predict/avert negative outcomes by providing real-time information on current clinical state and predicting future deterioration.
- RADAR-CNS will develop and test transformative platform of RMT in three CNS diseases: epilepsy; multiple sclerosis (MS); and depression.
- The ultimate goal is to improve patient outcomes through remote assessment.
Original vision

RADAR PROGRAMME OFFICE
COORDINATION & DATA SHARING

RADAR TOPIC 1
CNS

FUTURE RADAR TOPIC
A Data Challenge

Molecular Biological Data
= 380M

Clinical data
= 0.1 micron

Thanks to Ken Kubota and Michael J Fox Foundation
The traditional approach

a. Clinical practice

- Sporadic presentations to GP
- Episode of specialist care
- Sporadic presentations to GP

Lots of unstructured data, with incomplete measurement of outcomes & risk factors. Time points related to clinical state

b. Research

- Detailed baseline assessment
- Scheduled follow up visits at regular intervals

Snapshots of clinical outcomes, incomplete data, inefficiently used
Prediction of seizure likelihood with a long-term, implanted seizure advisory system in patients with drug-resistant epilepsy: a first-in-man study


<table>
<thead>
<tr>
<th>Patient</th>
<th>Estimated monthly seizure rate at enrolment</th>
<th>Mean monthly seizure rate during study</th>
<th>Mean monthly seizure rate captured by intracranial electroencephalography</th>
<th>Spearman’s rank correlation coefficient (r)</th>
<th>p</th>
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<tr>
<td>Patient 1</td>
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</table>

We eliminated outliers 1.5 times or more outside the IQR, which resulted in zero values for some patients with infrequent seizures.

Table 4: Seizure rates before and during the study, by patient
Example of 24 Hours of Ambulatory Data in Parkinson's Disease

Activity Level vs. Medication Intake

- Sleeping according to patient's diary
- Patient in OFF according diary

Thanks to Ken Kubota and Michael J Fox Foundation
1. Build a data collection, management, modelling and visualisation infrastructure. Including:
   • Generic RMT platform for active and passive RMT (aRMT/pRMT)
   • Data management pipeline, processing and analysis to identify bio-signatures
   • Data visualisation platform presenting user-friendly data for patients and clinicians.
   • Maximal interoperability with health systems e.g. electronic health records (EHRs) and patient health records.
   • Acceptable privacy protections to maximise patient confidence and acceptability.
2. Devise clinical studies using observational prospective designs to:
   • Test the acceptability of RMT
   • Determine added value of RMT to conventional markers of disease outcomes
   • Detect changes in disease state,
   • Changes in disease state due to drug effects
   • Prediction of change in disease state.
3. Engage stakeholders to maximise real world use of RMT and produce relevant and important questions to inform clinical study design.

- Prioritise clinical endpoints of greatest relevance to patients, ensure RMT is use-friendly and acceptable.
- Test measures to ensure maximal adherence.
- Identify the priorities of clinicians and healthcare funders.
- Engage with regulators to identify key issues likely to be raised in relation to market authorisation of actionable bio-signatures.
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RADAR-CNS Governance

IMI2 JU
innovative medicines initiative

Academic Lead
KCL - Matthew Hotopf

EFPIA Lead
JPNV - Vaibhav Narayan

Management Team
Matthew Hotopf (KCL), Vaibhav Narayan (JPNV), Jane Rhodes (Biogen) and Inez Myin-Germeys (KU Leuven);
One non-voting representatives each of Lygature and JPNV

Steering Committee
Two co-leads (EFPIA/Academia) per WP

WP01 WP02 WP03 WP04 WP05 WP06
WP07 WP08 WP09 WP10 WP11

General Assembly
One representative per participant

Scientific Advisory Board
Independent Ethics Advisor
Patients Advisory Board
RADAR-CNS Work Packages

Cluster A

Cluster B

Cluster C

Cluster D

Translation

WP02: Patient Involvement
KCL & MSD

WP03: Clinical Harmonisation
KU Leuven & HLU

WP04: Epilepsy
KCL & UCB

WP05: Multiple Sclerosis
USR & Biogen

WP06: Depression
KCL & HLU

WP07: Devices & Platform
KCL & Biogen

WP08: Data Integration,
analyis & bio-signatures
UNI PASSAU & JPNV

WP09: Clinical Pathways
UN & JPNV

WP10: Regulation
Lygature & Biogen

Cluster A

Cluster A

Cluster A

Cluster A

Cluster A

Cluster A
**Scientific Advisory Board:** Ken Kobuta, Norman Sartorius, Tom Insel

The SAB advise on a **high standard of research and monitor the main progress of the Action**

**Patients Advisory Board:** representatives of
- Italian MS Society
- MS Society
- Epilepsy Action
- GAMIAN
- Netherlands Knowledge Center of Anxiety and Depression

The PAB provide a focus of **expertise in patient experience**, and offer a natural vehicle for **patient engagement** in the Action’s activities

**Ethics Advisor:** Felicity Callard

The IEA advise on a in a non-binding way on: **ethical issues and good clinical practices guidelines** and will contribute to the researchers’ awareness of ethical issues
• WP02: Patient Involvement
  • Til Wykes (KCL) / Peter Gamble (Merck)
  • WP02 provides information on requirements of patient stakeholders
• WP09: Clinical Pathways
  • Michael Craven (UN) / Claudia Tamasy (JPNV)
  • WP09 focuses on the requirements of clinical stakeholders with respect to integration of RMT into care pathways in European healthcare systems.
• WP10: Regulation
  • Andre Broekmans (Lygature) / Steve Dew (Biogen)
  • WP10 focuses on the requirements of both medical device regulators and medicinal product regulators.
• WP07: Devices and Platform
  • Richard Dobson (KCL) / Shoibal Datta (Biogen)
  • WP07 will build an end-to-end system for RADAR-CNS clinical work-packages supporting pRMT and aRMT measurement and feedback using mobile and web technologies.

• WP08: Data integration, analysis and biosignatures
  • Björn Schuller (UNI PASSAU) / Anthony Rowe (JPNV)
  • WP8 will enable analysis of the collected data to understand the association between RMT and remission, relapse, and recurrence of the CNS disorders and to classify and predict the disease status.
• WP03: Clinical Harmonisation
  • Inez Myin-Germeys (KU LEUVEN) / Michiel Ringkjøbing-Elema (Lundbeck)
  • WP03 provides an overarching assessment and analysis scheme across clinical disorders, combining aRMT and pRMT.

• WP04: Epilepsy
  • Mark Richardson (KCL) / Nancy van Osselaer (UCB)
  • WP04 aims to evaluate the utility of multi-parametric RMT in people with epilepsy

• WP05: Multiple Sclerosis
  • Giancarlo Comi (USR) / Bernd Kieseier (Biogen)
  • WP05 aims to evaluate the utility of multi-parametric RMT in people with MS to improve characterisation of its clinical presentation, depression and gait disturbance.

• WP06: Depression
  • Matthew Hotopf (KCL) / Hans Eriksson (Lundbeck)
  • WP06 aims to evaluate the utility of multi-parametric RMT in people with depression.
**Passive Streams**

Stressful life event  
Antipsychotic discontinuation  
Disruption of sleep schedules  
Substance misuse  

Insomnia  
Sleep deprivation  

Sleep & circadian rhythm disturbance  

Worsening psychosis

Measured by optical wrist-worn sensor  
Autonomic dysfunction  

Measured by smartphone symptom questionnaire  
Increased motor variability  

Measured by wrist-accelerometry

**Question**: can physiological signals such as sleep patterns, motor activity and heart rate variability serve as useful early-signs of relapse in psychosis?
Motor activity
Mean heart rate
Battery charge
Mobile data upload

Automated real-time analysis
Intuitive visualisations

Care team
Patient

Relapse prevention
Improved self-management

Wearable device
Smartphone sensors

Welcome to SleepSight
Questionnaire
Help
Settings

Mobile data upload

Hearing and seeing things
- I have heard voices
  - not at all: 5/7
  - very much
- I have found it difficult to concentrate on other things
  - not at all: 4/7
  - very much

Active
Passive

Symptom questionnaire

Improve self-management
Relapse prevention

Wearable device
Smartphone sensors

Automated real-time analysis
Intuitive visualisations

Care team
Patient

Relapse prevention
Improved self-management

Wearable device
Smartphone sensors

Automated real-time analysis
Intuitive visualisations

Care team
Patient

Relapse prevention
Improved self-management
Acceptability - findings

Wear-time: 88%
Sleep diary: 89%
Symptom diary: 86%