Therapeutic applications of technology in Parkinson’s disease

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Disclaimers

• I am employed by Medtronic, Inc.

• Medtronic has a financial interest in Functional Neuromodulation, a company that I will discuss today, and I am a Board of Directors’ observer

• Some potential uses of DBS discussed today are under development or are in the investigational phase only, and are not currently approved for clinical use or commercialization in the US.

• DBS therapy is not for everyone. DBS Therapy requires brain surgery which could have serious or even fatal complications. Other complications can occur and may require additional surgery. Medtronic DBS Therapy may cause worsening of some symptoms. For additional safety information, please refer to Indications, Safety and Warnings at www.http://professional.medtronic.com/pt/neuro/dbs-md/ind
Functional brain restoration defined:

Modulation, repair or replacement of brain structures by precise delivery of stimulation, medication or cells to treat disordered brain function.
What can we learn from Cardiac Resynchronization Therapy?

- Therapy: Pacing and Shock algorithms
- Diagnosis: Fluid Status Monitoring
- Patient Management: Remote monitoring system provide fast and easy remote device follow-up

**How Remote Monitoring Works**

Clinic schedules dates for the patient to send information from their device to the clinic.

Device information is sent automatically (for wireless devices, such as ICDs), usually while the patient sleeps.

Device information is sent automatically from the remote monitor to a secure computer server.

The clinic reviews the device information on a secure website.

Note: For non-wireless devices (such as pacemakers), information is sent manually from the patient’s device.
What can we learn from Diabetes?

- **Therapy:** Threshold Suspend, which automatically stops insulin delivery when sensor glucose values reach a preset low threshold.
- **Diagnosis:** Continuous blood glucose monitoring
- **Patient Management:** Patient and Physician reporting on trends

CareLink® Personal Therapy Management Software

CareLink Personal software is a convenient online tool that brings together critical information from your diabetes-monitoring devices, including Medtronic insulin pumps, continuous glucose monitoring systems, and more than 25 of the most popular blood glucose meters.
What can we learn from Pain Management?

- Therapy: Adaptive Stim automatically adjusts stimulation based on the patient's needs and preferences in different body positions
- Diagnosis: AdaptiveStim Diary provides objective data regarding patient activity
Sensors and Connected Care

1. Patient Screening and Diagnosis
2. 24/7 patient optimized therapy
   – Responsive Therapy
   – Automatic therapy adjustment
3. Improved patient self management
4. Remote patient monitoring
5. Remote patient management
6. Automatic quantification of outcomes to prove value to payers
7. Scientific discovery
   – Large patient datasets
   – Rare events
Challenge: Many qualified DBS candidates do not have access to the therapy

Of the estimated 1,000,000+ Americans with PD

110,000
Are potential candidates for DBS Therapy

only 24%
receive an implant

We are all striving for the best in patient care which involves making therapies more accessible.

MDT data on file PAA
Misconception: Patient is not yet a candidate for DBS or DBS may not provide the expected outcome

TECHNOLOGY SOLUTION = Quantifying symptom fluctuation for DBS application

Technology Goal

• Improve patient selection and identify “DBS-ready” patients
• Confidence in decision with objective measures
• Reduce physician burden and simplify patient follow-up

Sensor-based Quantification

Objective Assessments

Impact to Practice

• Patient selection for DBS
• Therapy optimization
• Quantification of therapeutic benefit

**Study Title:**
Evaluation of the Parkinson’s KinetiGraph Data Logger (PKG) as a tool to measure motor fluctuations and support the DBS eligibility assessment of Parkinson’s disease patients.

**Study Objective:**
To evaluate whether the GKC algorithm can differentiate DBS ready from DBS not-ready patients as assessed during the visit at the clinical site by the DBS specialist.

**Study Design:**
Prospective, dual-center, non-interventional, post-market release clinical study.

**Primary endpoint:**
Percentage of agreement on DBS eligibility classification between DBS specialists assessment and GKC assessment.

**Sites:** Prof. Moro (Grenoble, France) and Prof. Volkmann (Würzburg, Germany).

**Patients:** 36 evaluable patients.

**Device:**
- PKG Data logger (PKG) is a CE mark device.
- Manufactured by Global Kinetics Corporation (GKC).
Brain sensing

Animation of brain activity sensing built into a commercial Activa DBS system (like a CRDM device that measures electrophysiology)*

*Investigational Use Only, Not for U.S. Commercial Sale

Disclosure: Innovations discussed are in development or investigational only and not approved by the FDA.
VIM DBS induces adenosine release in ET patients


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TECHNOLOGY SOLUTION = Medtronic Integrated technology
Physiological Brain Modulation enabled by sensing technology and algorithms – Activa PC+S

Why sensing?
• Basic understanding of Neuroscience
• Serendipitous discovery
• Monitoring of disease progression and therapy effectiveness
• Programming guidance
• Automated Programming
• Patient personalized stimulation

Biomarker identification through sensing and closed loop systems are expected to reduce patient management burden and may lead to automated programming

Data file courtesy of Bronte-Stewart, Stanford; interpretation by Medtronic.

Sensing Research Status:
• A number of physician-sponsored studies ongoing globally
• Numerous devices implanted across a range of disease states/conditions
• Several manuscripts in progress

Potential long-term impact:
Closed-loop stimulation to deliver patient personalized stimulation

Disclosure: Innovations discussed are in development or investigational only and not approved by the FDA.
Initial efforts towards closed loop systems based on LFP sensor

 Disclosure: Innovations discussed are in development or investigational only and not approved by the FDA.
Synchronized LFPs and kinematic recordings during continuous wrist flexion-extension before and during HF DBS using a wearable angular velocity sensor

REST REPETITIVE WRIST FLEXION-EXTENSION REST

HF DBS 3V

Data are courtesy of Bronte-Stewart, MD

Miller Koop et al SfN 2013/Bronte-Stewart Lab

Disclosure: Innovations discussed are in development or investigational only and not approved by the FDA.
Synchronized STN LFP and angular velocity recordings using wearable sensors

Continuous > 8 min neural and kinematic recordings from a sensing neurostimulator in freely moving PD people. Wearable sensors detect when person moving or stationary.

Quinn et al under review

Disclosure: Innovations discussed are in development or investigational only and not approved by the FDA.
Novel Pulses: From High Frequency Stimulation to Novel Patterns

**Today:** High frequency continuous stimulation

**Tomorrow:** Temporal or Waveform modulation to potentially improve therapy outcomes

**Temporal modulation, e.g.:**
- Pseudorandom
- Burst
- Stochastic

**Waveform modulation, e.g.:**
- Square-biphasic
- Non-square
- Arbitrary

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Disclosure: Innovations discussed are in development or investigational only and not approved by the FDA.
**Novel Pulses: Feasibility data from Duke**

**Improve Efficacy**

- Strong correlation between symptom reduction and suppression of oscillatory activity across patterns of DBS.

**and Reveal Mechanisms**

- ~60% improvement in symptom reduction.

Data file courtesy of Warren Grill, Ph.D.

Technology Solution = Anatomical field shaping
Potentially better patient outcomes from personalized stimulation

**Traditional DBS**
*Circumferential Stimulation*

- Current spreads into adjacent structures especially if lead position is not perfect
- Side effects limit amount of stimulation that can be applied\(^1\)
- Limited data available from lead in final placement

**Future DBS**
*Field Shaping*

- Current can be moved away from adjacent structures and focused on target structures
- Potential for higher stimulation with fewer side effects\(^2\), leading to better therapy
- Potential to augment interoperative data with directionally-sensed LFP

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TECHNOLOGY SOLUTION = Auto optimization of programming

Tools provided to today’s optometrist:
- **Autorefractor**
  - Automated starting point
  - Patient exam, “subjective refraction”
  - Effective prescription

Tools provided to today’s neurologist:
- **Manual protocol**
  - Predict the tissue stimulated by a given DBS setting
  - Conduct smart search to find highest scoring DBS settings
  - Software identifies lead location in patient’s brain

Can we make an “autorefractor” for the neurologist?
- Assign a “score” based on tissue stimulated (target vs side-effect)
- Automated starting point tailored to this patient

Disclosure: Innovations discussed are in development or investigational only and not approved by the FDA.
Given patient’s anatomy and lead location, prototype algorithm suggests DBS parameter settings:

**Top-scoring parameter settings**
(out of > 90,000 possibilities)

**Search completed (on laptop PC) in 19.485 seconds**

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