Medtronic
Engineering the extraordinary

BrainSense™ technology:*

Clinician case study on uncovering suboptimal programming

Data presented represents the experience, results, and recommendations of one clinician's use with the Percept™ PC device. Results in other case studies may vary.

" The LFP data retrieved from BrainSense™ helped me quickly uncover that the patient was overstimulated on the right hemisphere. I used Event LFP Captures and Live Streaming to inform my therapy decisions. These features of BrainSense™ technology allowed me to achieve optimal programming for the patient in just 3 visits. As a result, the therapy is improving the patient's symptoms more efficiently and offers treatment optimization for a better quality of life."
– Dr. Okeanis Vaou

Patient background snapshot

- A 66-year-old man diagnosed with Parkinson's disease due for a neurostimulator replacement.
- Patient had limited mobility due to Parkinson's disease and was sub-optimally controlled at his prior DBS therapy settings. The patient was wheelchair-bound and suffered from rigidity, dyskinesia, and severe motor fluctuations throughout the day.
- The patient and family decided to move forward with the decision to replace with Percept™ PC neurostimulator, with BrainSense™ technology.

Clinician and patient goals

- Gain objective data and insights about the patient's disease state and current fluctuations.
- Optimize therapy by helping to reduce rigidity, dyskinesia, and severe motor fluctuations throughout the day.
- Figure 1 shows initial patient therapy configurations after replacement, with interleaving on right hemisphere.

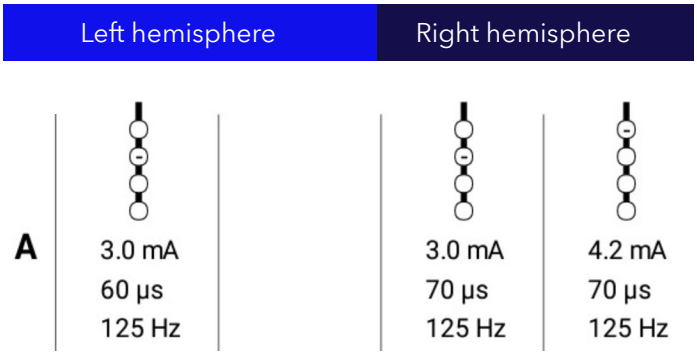


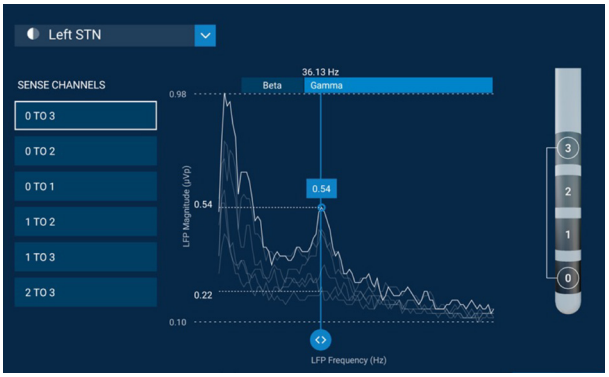
Figure 1

Initial BrainSense™ SetUp

In the Post Anesthesia Care Unit (PACU), post implant. BrainSense™ Survey & new therapy group set up.

Observations:

- BrainSense™ Survey was conducted to identify peaks. A peak of 0.54uVp at 36.13 Hz was identified and confirmed in BrainSense™ SetUp for chronic sensing (Figure 2). BrainSense™ Survey helped to identify local field potential (LFP) peaks that may be good signals of interest for tracking in BrainSense™ Streaming when adjusting medication or stimulation therapy.
- BrainSense™ Survey identified a clear Gamma Peak 0.59uVp at 68.36 Hz which correlates the underlying disease state symptoms of dyskinesia (Figure 2).



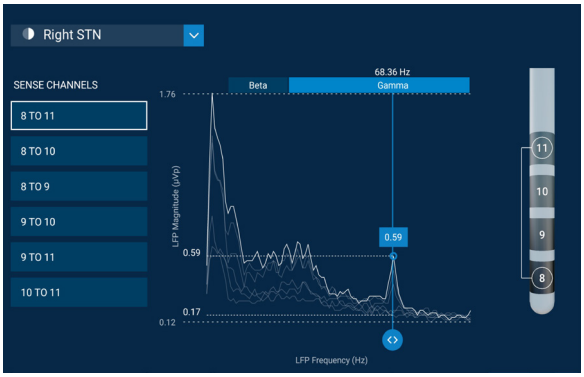


Figure 2

* The sensing feature of the Percept™ PC system is intended for use in patients receiving DBS where chronically-recorded bioelectric data may provide useful, objective information regarding patient clinical status. Signal may not be present or measurable in all patients. Clinical benefits of brain sensing have not been established.

All data for this case study was provided by Dr. Okeanis Vaou under a Data Access Agreement.
The information presented is from a single patient.

Actions taken:

- Created Group B (labeled: BrainSense™ group) where interleaving was removed so that left and right hemispheres would be conducive to sensing. Group A was still accessible to patient if they needed to revert to their original therapy (Figure 3).
- BrainSense™ Events (LFP Snapshots) were set up for "Dyskinesia" and "OFF Time" and the caregivers could record the future events.

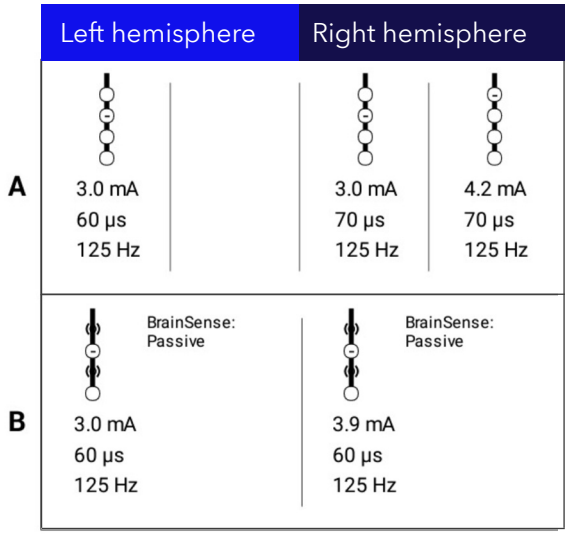


Figure 3: Group A with original therapy settings and Group B with BrainSense™ compatible settings and interleaving removed.

First programming session
2 weeks after initial BrainSense™ SetUp.
BrainSense™ Timeline and BrainSense™ Events used to observe symptoms and modify therapy.

Patient input:

- Patient complained of rigidity & severe dyskinesia and was utilizing the programmer to track these most bothersome symptoms.
- Tried multiple times to go back to Group A (original therapy settings) but felt increased dyskinesia and rigidity on this setting.
- Attempt to change in Groups on 7/15 and 7/16 is noted in green on Timeline (Figure 4).

Figure 4

Clinician observations and actions:

- The BrainSense™ Timeline view showed high frequency band fluctuations in the left and right STN (Figure 4).
- Stimulation adjustments were made to the right STN by changing original settings of 3.9 mA and 60 us to 3.0 mA and 30 us Left STN also had a decrease in pulse width from 60 us to 30 us (Figure 5).
- New BrainSense™ Event of "Medication" was added to existing Events, "Dyskinesia" and "OFF Time", to look for any correlations between medication, frequency band levels, and symptomatic state.

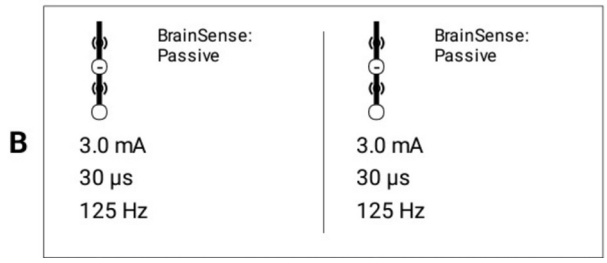


Figure 5

Second programming session
2 weeks post first programming session.
Streaming revealed key information.

Patient input:

The patient and caregivers noted an improvement in overall mobility with decreased severity and frequency of dyskinesias since adjustments made at previous visit. The patient's main complaint was still experiencing some rigidity, especially in right side of the body.

Observations and actions:

When looking at Event Snapshots, some of the programming changes made at first visit seemed to decrease peak power during "Medications," "OFF time," and "Dyskinesias"; therefore, therapy programming was in a better direction, but still could be further optimized.

A decision was made to live-stream using BrainSense™ Streaming, with the beta frequency of interest at 10.74 Hz to assess stimulation relationship to peak power correlating with symptoms of rigidity (Figure 6).

Figure 6

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- While live-streaming and decreasing stimulation amplitude, clinician observed a decrease in bradykinesia as the patient performed the task of hand open-close and an increase in shoulder rigidity /tightness. In addition, secondary observations of improvement were made in the patient's dysarthria and dyskinesia.
- The patient's improvement in symptoms was noted while live streaming, showing suppression in the tracked frequency of 10.74 Hz, corresponding to the patient's main complaint of rigidity.

Key finding:

Review of BrainSense™ Streaming provided objective data which helped the clinician conclude that the patient was experiencing stimulation-induced corticospinal effects due to over-stimulation. The patient had been interpreting these as symptoms of PD, and had been increasing stimulation within physician prescribed limits to try to manage the symptoms with no improvement.

Third programming session
1 week after second programming session.
Key observations after programming to a lower amplitude.

Physician observations:

The patient had noticeable improvement in mobility as he was no longer wheelchair-bound and able to walk unassisted. The patient shared that he was able to walk a mile a day, and was able to return to an engaged lifestyle. The patient experienced decreased bradykinesia, and improved dyskinesias.

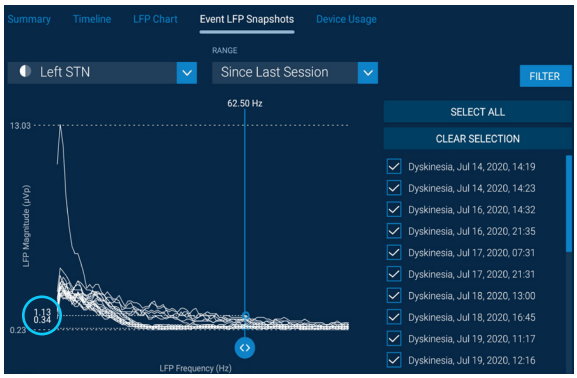
Medtronic's DBS therapy safely and effectively manages tremor, rigidity, and bradykinesia associated with Parkinson's disease. DBS improves quality of life and activities of daily living for Parkinson's patients. It may be a therapeutic option for patients with recent or longer-standing motor complications.[1,2]

Decrease in beta and gamma peak power in LFP captured events (Figures 7 and 8):

Reduction in µVp peak amplitude during events			
	Off Time Events	**Dyskinesia Events**	**Medication Events**
Left STN	No reduction	69%	33%
Right STN	44%	71%	45%

Figure 7 illustrates how using BrainSense™ technology can confirm the presence of gamma activity with the dyskinesias. It further supports the improvement with the programming changes.

Baseline Event LFP Capture Dyskinesia 7.14.20



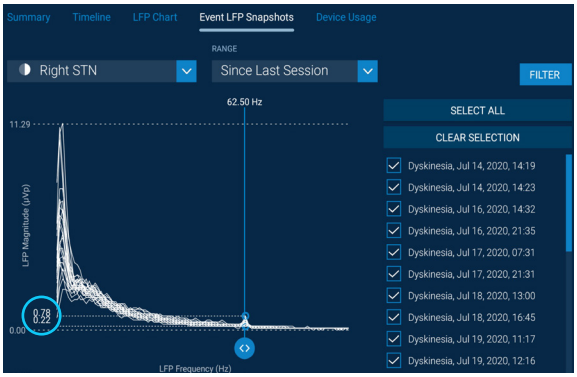
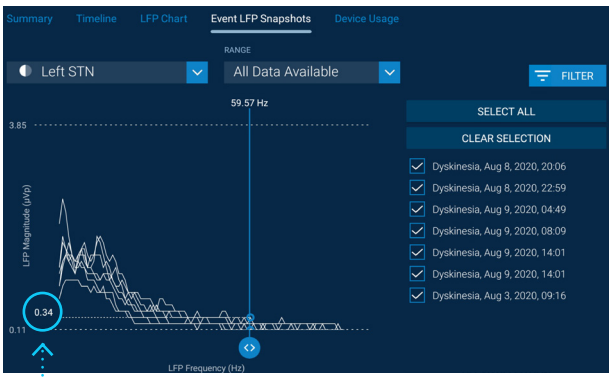
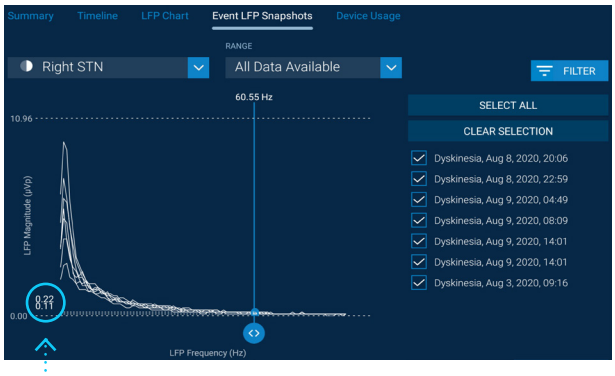


Figure 8

Event LFP Capture Dyskinesia 8.10.20 Visit



69% reduction in uVp



71% reduction in uVp

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Summary of purpose and use of each BrainSense™ feature

BrainSense™ SetUp
In order to use all features of BrainSense™ technology (with the exception of BrainSense™ Survey), the user must first setup LFP sensing using BrainSense™ SetUp, and select a frequency band of interest (approximately 5Hz wide) to track while the patient is out of office.
Use: In-clinic, with approximately 90 seconds measurement for setup.

BrainSense™ Survey
Broad spatial overview of LFP signals measurable from both hemispheres of the patient with stimulation off.
Use: In-clinic, with approximately 90 second measurement duration.

BrainSense™ Events
Once BrainSense™ Setup has been completed, BrainSense™ Events, a.k.a LFP Snapshots, can be recorded at a moment in time, showing the magnitude of the LFP signal over a range of frequencies. The LFP Snapshot is recorded when the patient records an event (eg, 'symptom' or 'medication intake') as configured by the clinician. This is used to assess the occurrence of clinician-defined events, and associated LFP activity with those events.
Use: Outside-clinic, the snapshot is representative of a period of approximately 30 sec after patient marking an event.

BrainSense™ Streaming
Once BrainSense™ Setup has been completed, the user can view the LFP power in a selected frequency band in real-time, by streaming the data to the clinician tablet. This is used to observe changes in the LFP during active stimulation programming or while instructing and observing the patient performing activities. Moreover, Streaming can be used to collect time domain data from the selected channel(s) for offline analysis and signal processing.
Use: In-clinic, with no limit on streaming measurement duration, with or without stimulation.

References:
1. Schüpbach W, Rau J, Knudsen K, Volkmann J, Krack P, Timmermann L, et al. Neurostimulation for Parkinson's disease with early motor complications. EARLYSTIM Study. N Eng J Med. 2013;368:610-226.
2. Follett KA, Weaver FM, Stern M, et al. Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. N Engl J Med. 2010;362(22):2077-91.

Brief Statement:
See the device manual for detailed information regarding the instructions for use, indications, contraindications, warnings, precautions, and potential adverse events. For further information, contact your local Medtronic representative and/or consult the Medtronic website at medtronic.eu.

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