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Target Physiology in DBS: Definition and Mapping Using Single Unit Activity and Local Field Potentials

Physiology-Based Targeting to Confirm Targeting in Deep Brain Stimulation Surgery

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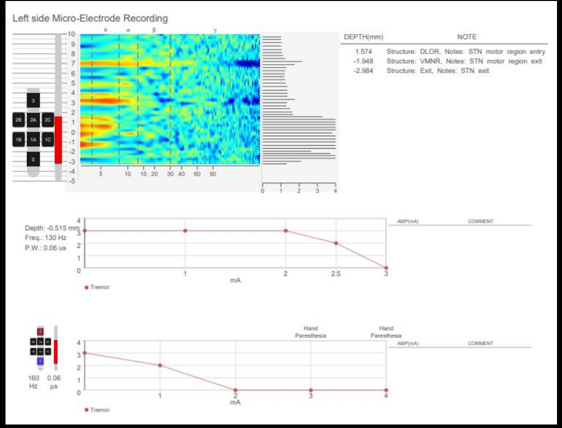
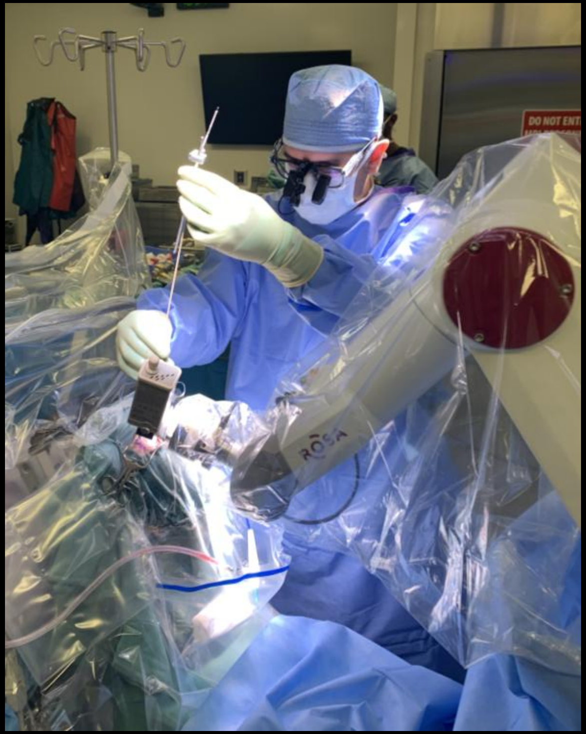
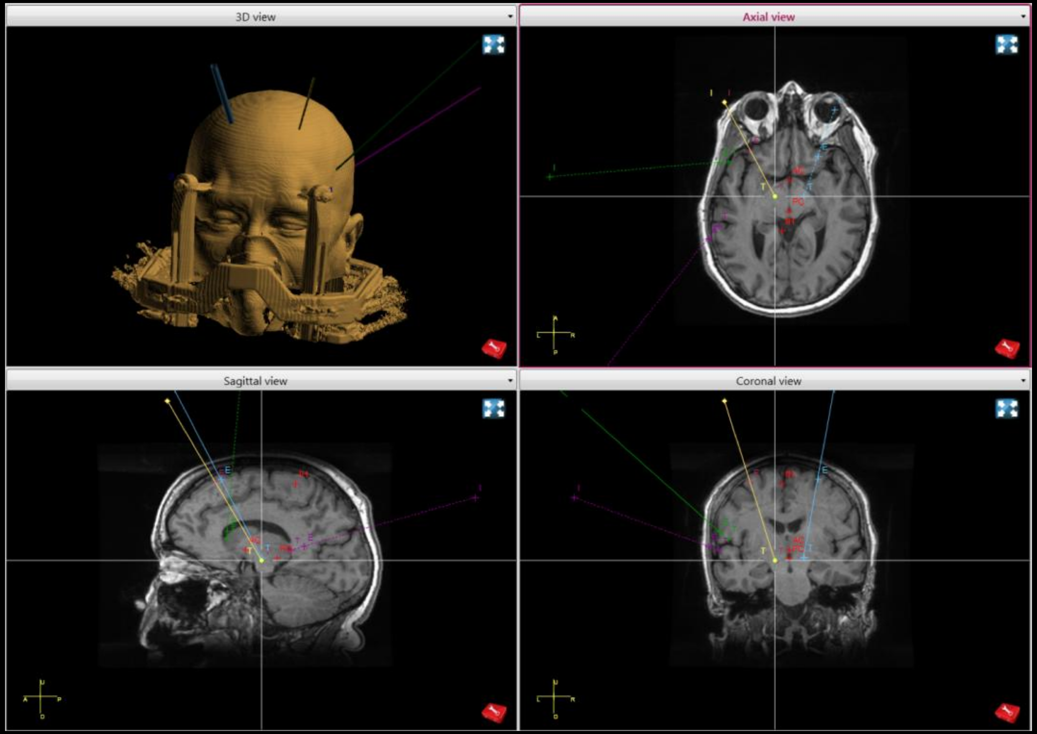
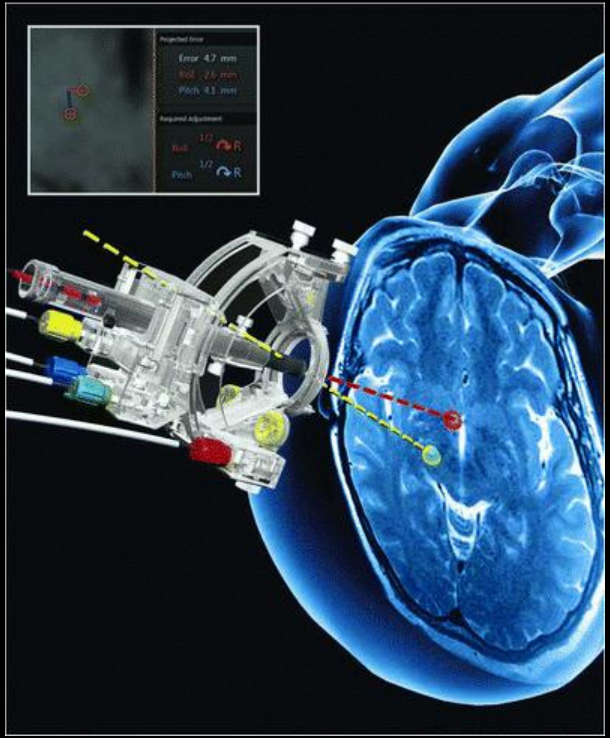
Innovation in Deep Brain Stimulation









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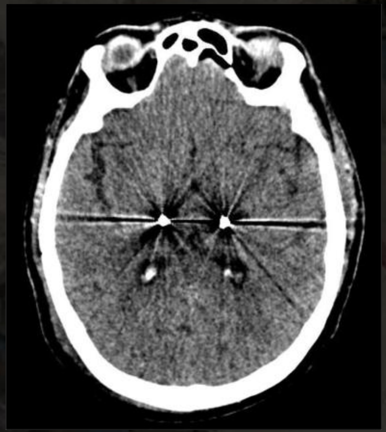
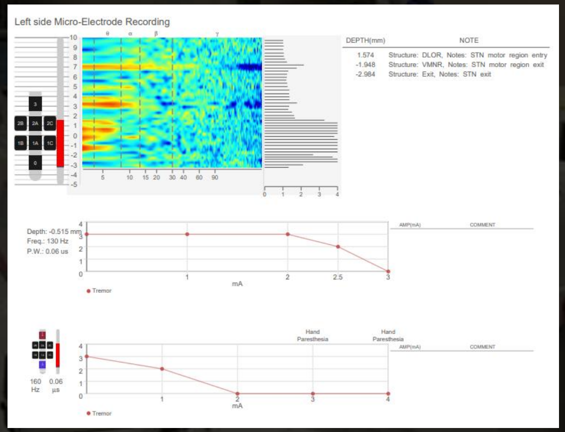
Goals for Deep Brain Stimulation Surgery

1. Accurately Place DBS Leads at the Anatomic and Physiologic Target
2. Verify Clinical Efficacy and Symptom Control in “Awake” DBS Surgery
3. Reduce Potential Off-Target Effects in “Awake” DBS Surgery
4. Maintain Patient Safety and Reduce Adverse Surgical Risks
5. Share Operative Findings With the Neurologist for Effective Programming





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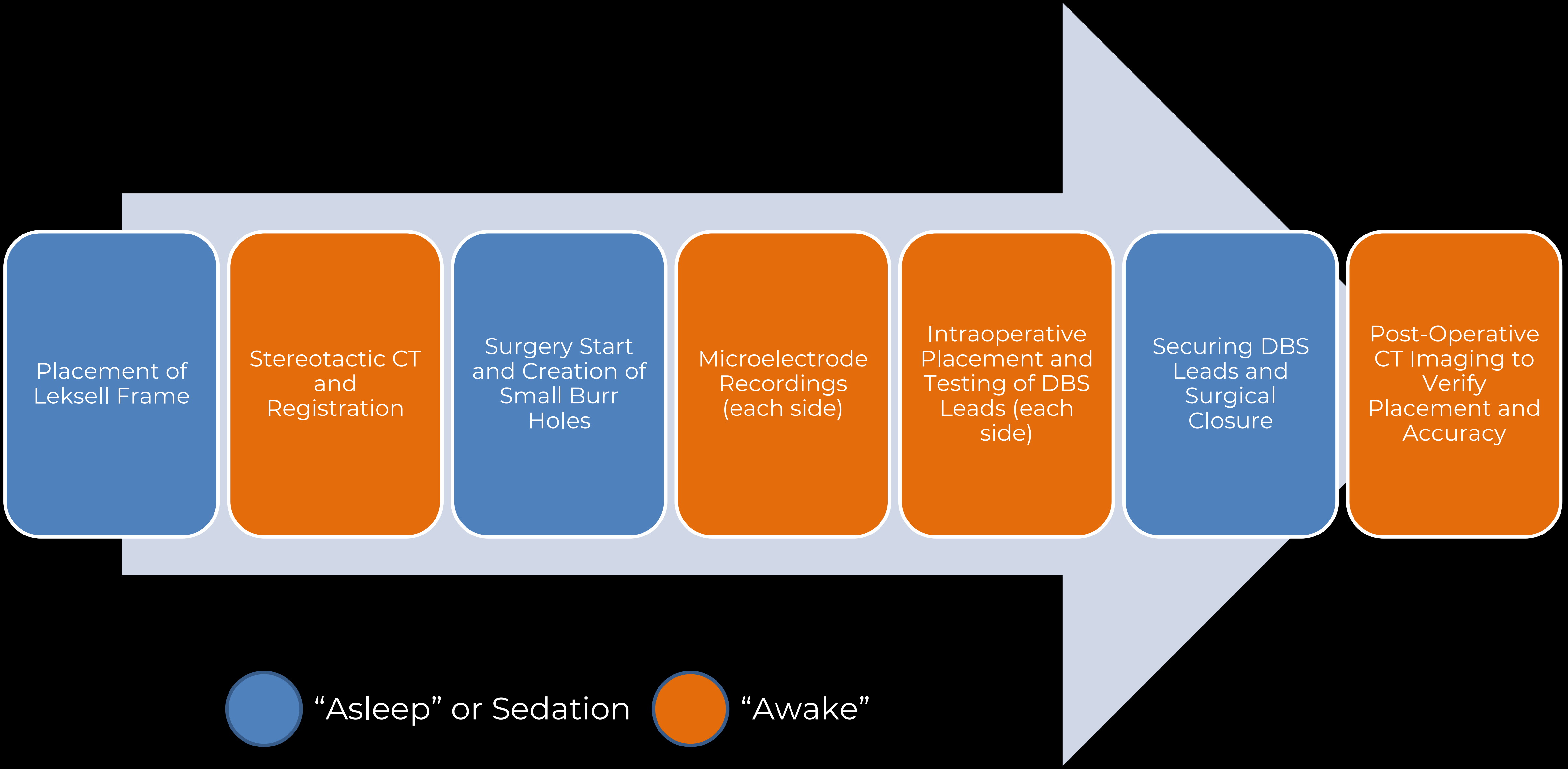
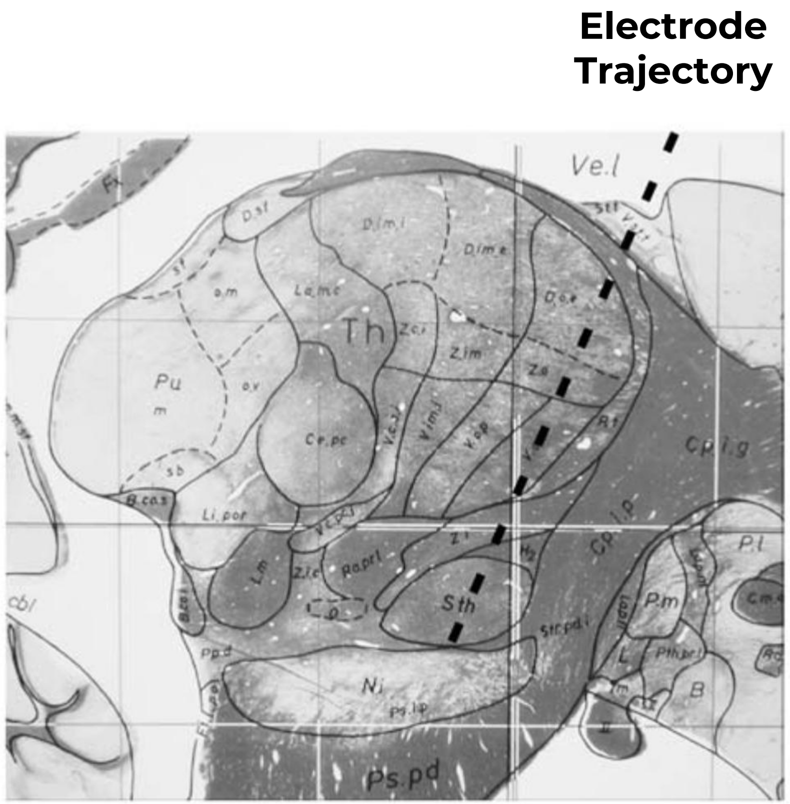
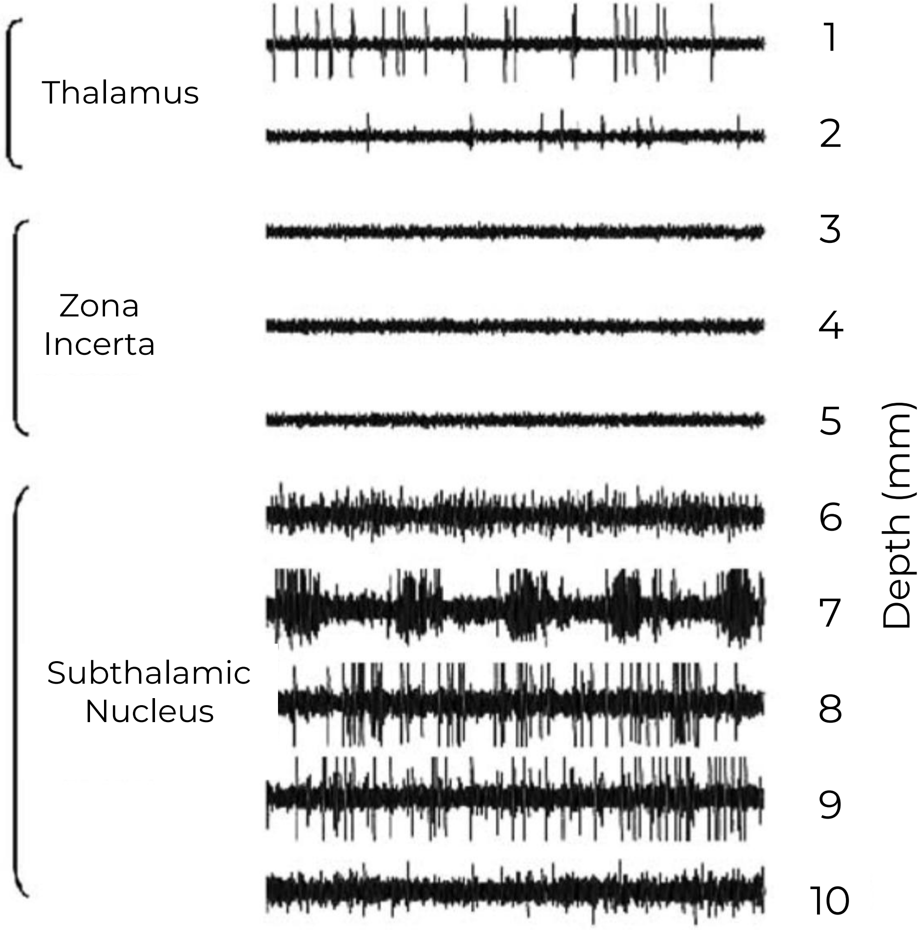
Workflow for “Awake” Stage 1 DBS Surgery



Intraoperative Recordings During DBS Surgery

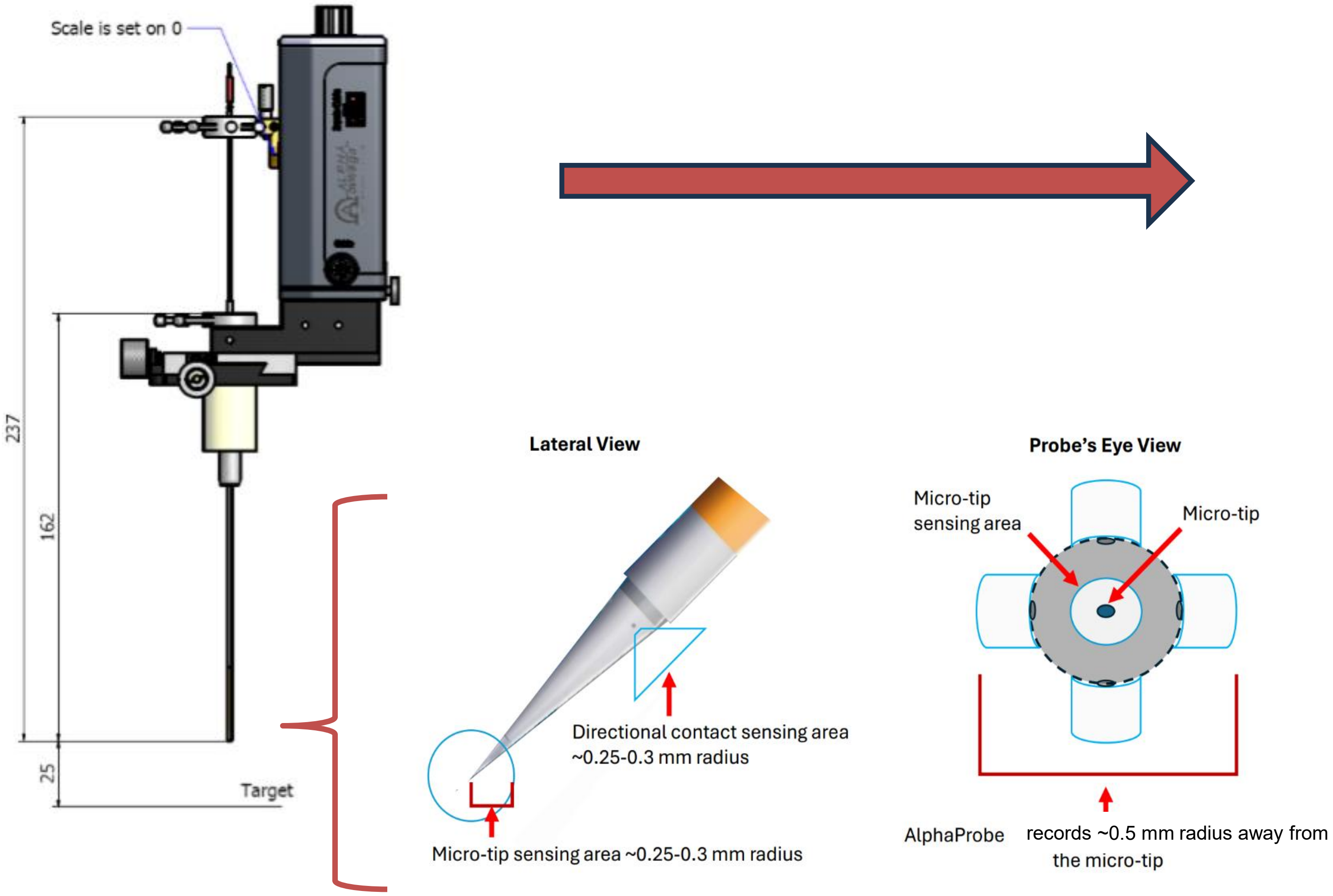


Para-Sagittal Section – 12 mm Lateral



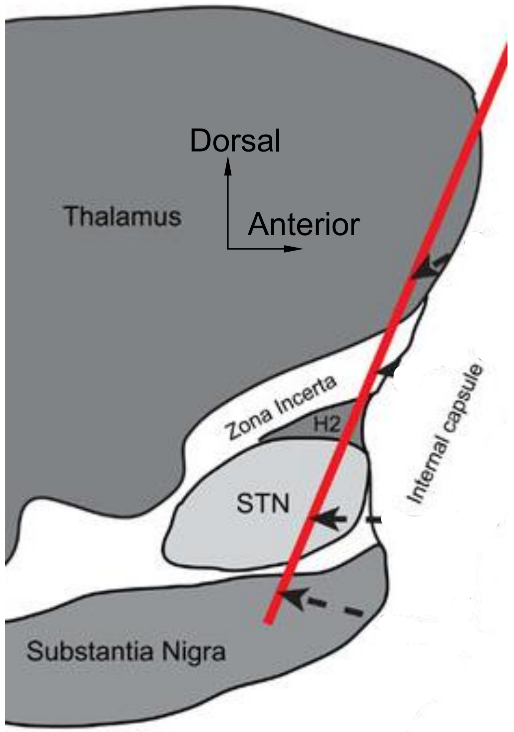
Williams, Z. *et al*. Exp. Brain Res. **2005**, 162, 407.

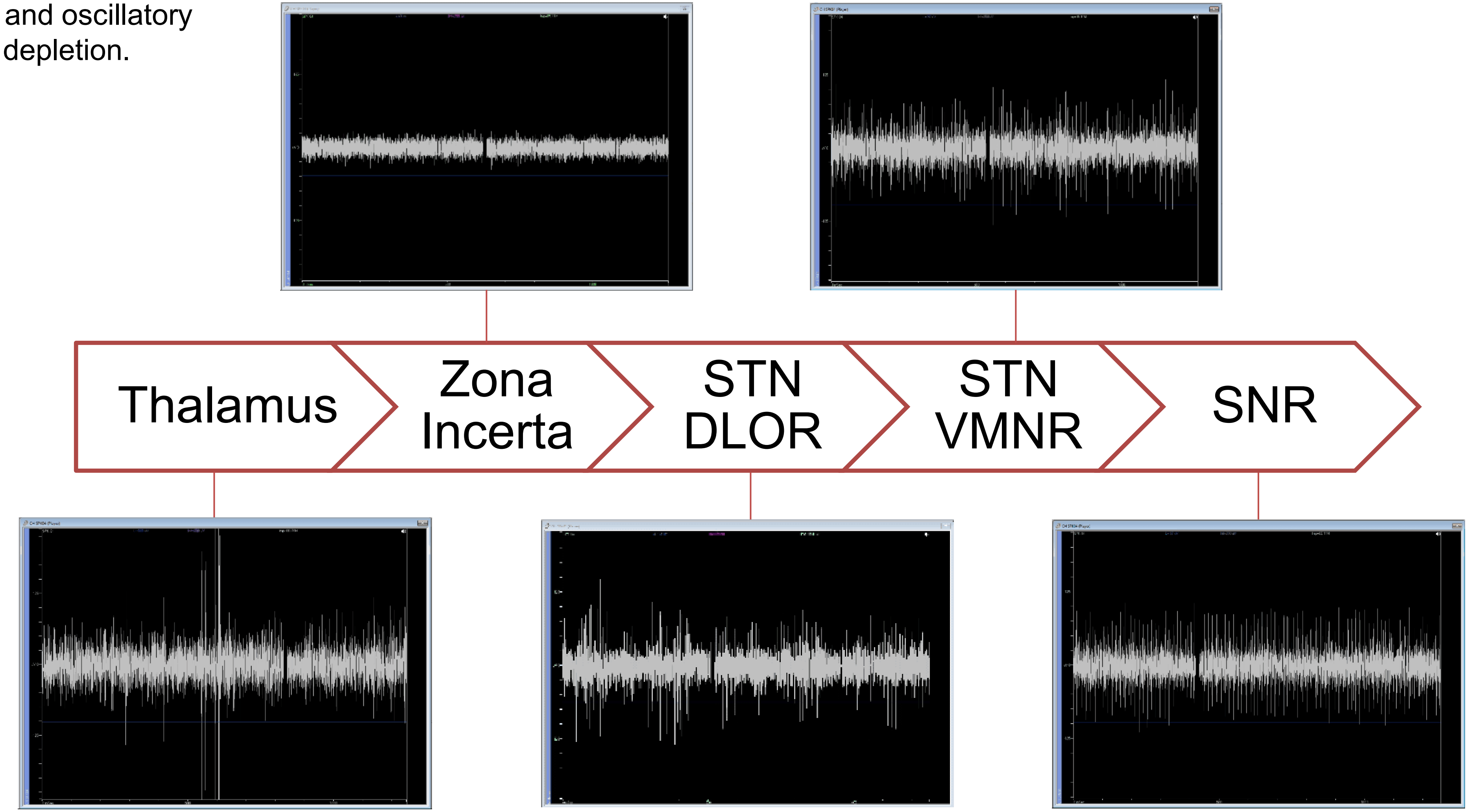
Surgical Setup for Microelectrode Recordings



STN Microelectrode Recordings

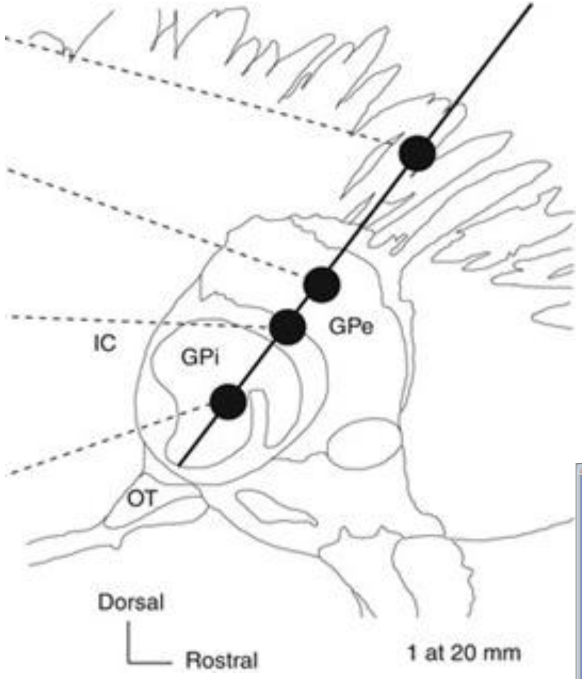
STN and GPi exhibit increased beta (13–30 Hz) synchronization. Bursting and oscillatory firing increase with dopamine depletion.

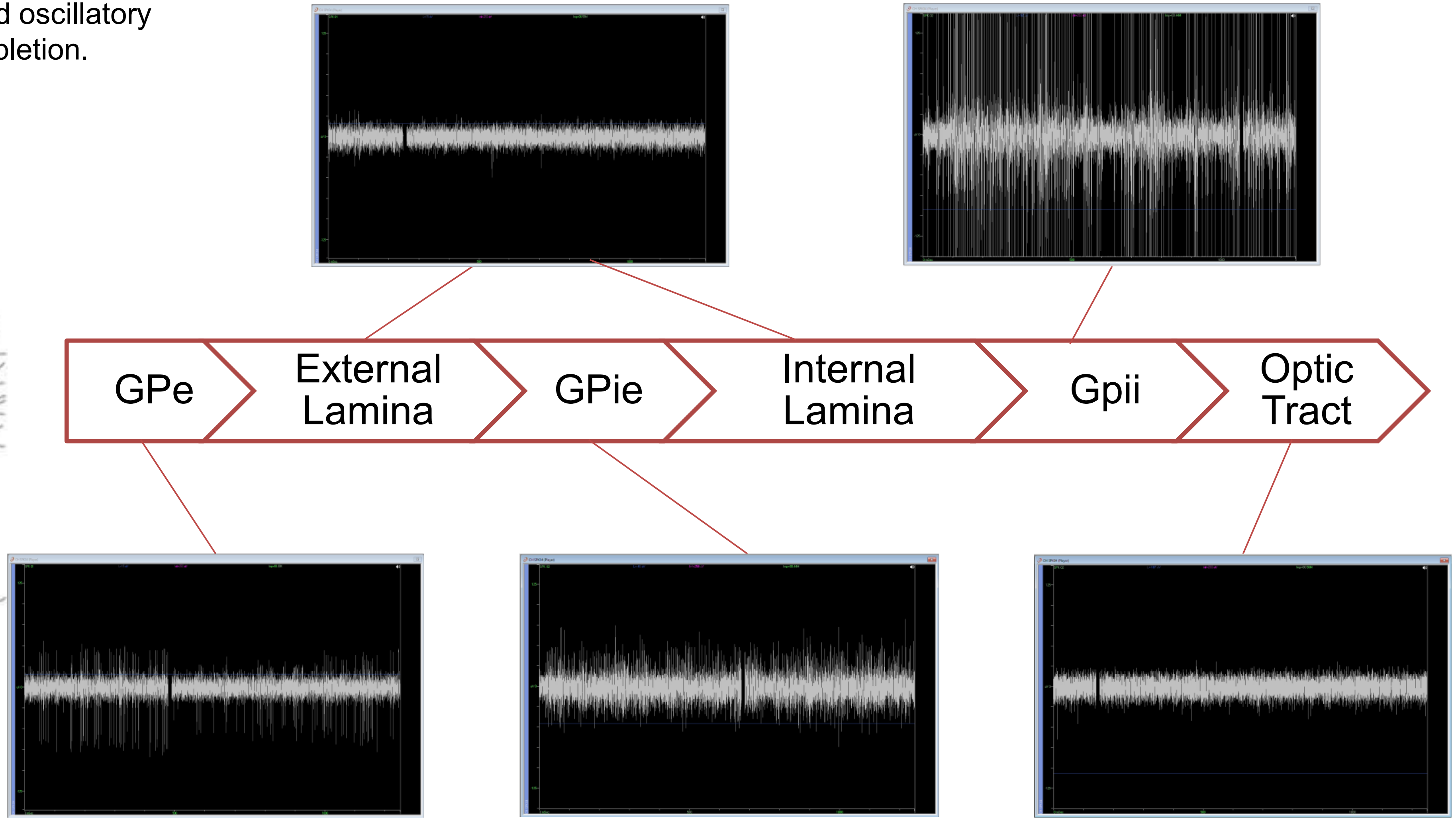




GPi Microelectrode Recordings

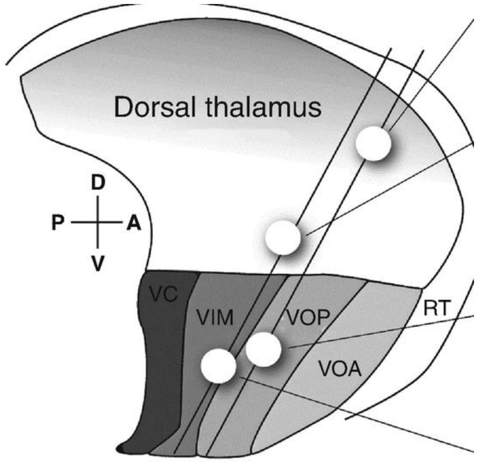
STN and GPi exhibit increased beta (13–30 Hz) synchronization. Bursting and oscillatory firing increase with dopamine depletion.

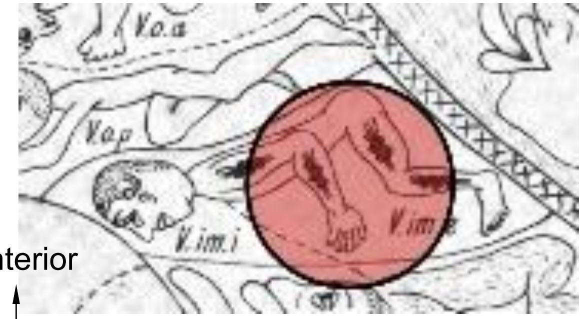




VIM Microelectrode Recordings

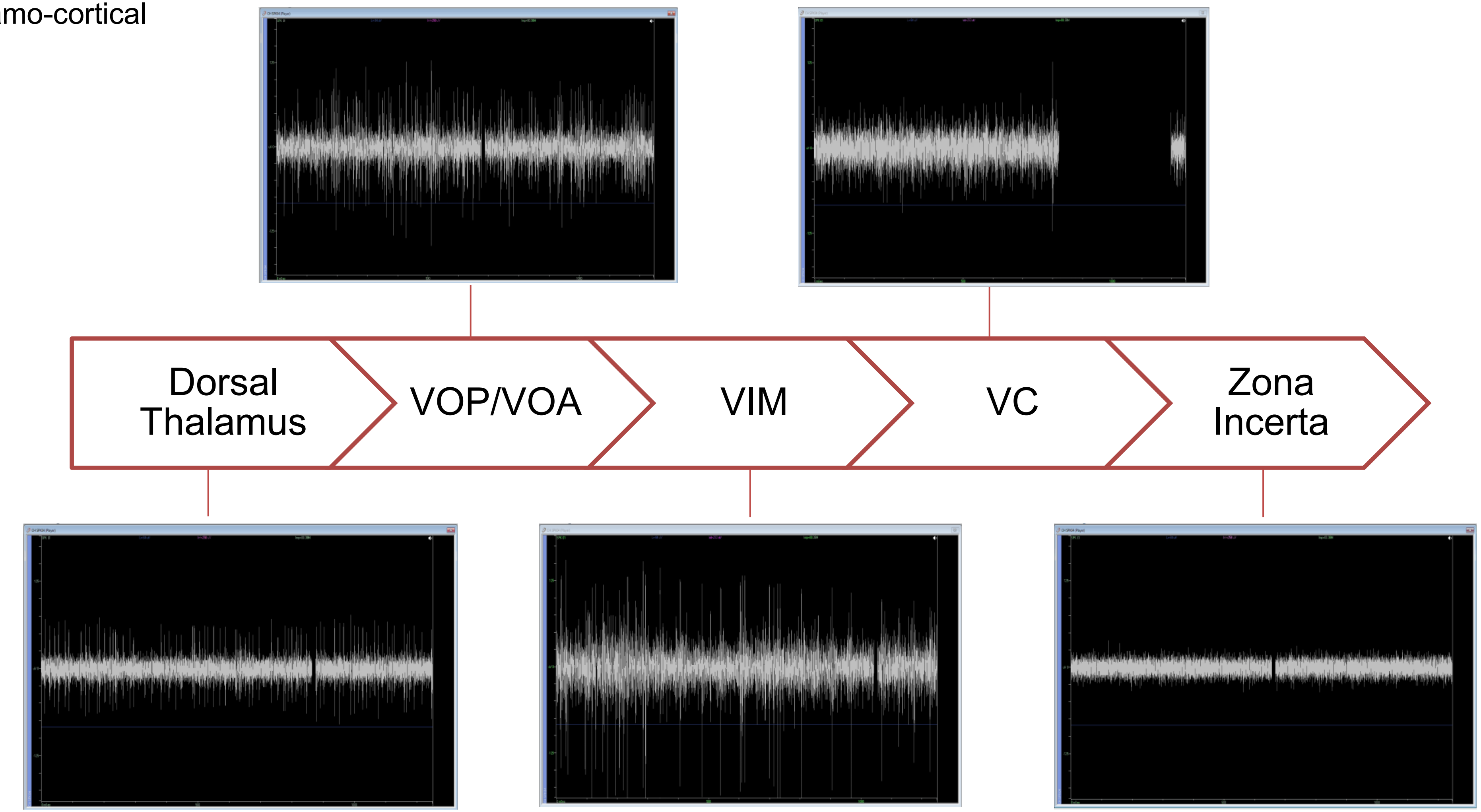
VIM recordings often show tremor-frequency locking (4–12 Hz). Cerebello-thalamo-cortical network oscillations dominate.





Anterior

Lateral



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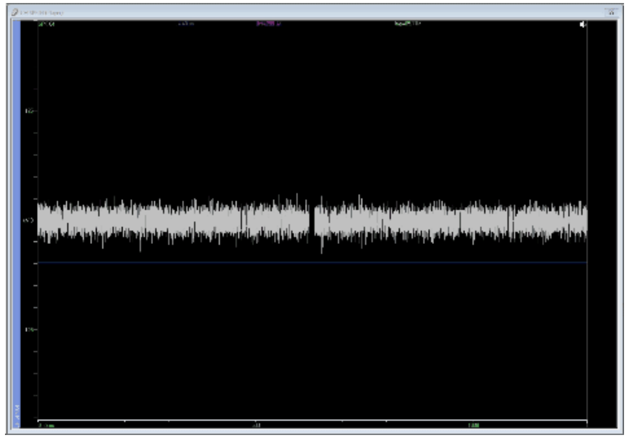
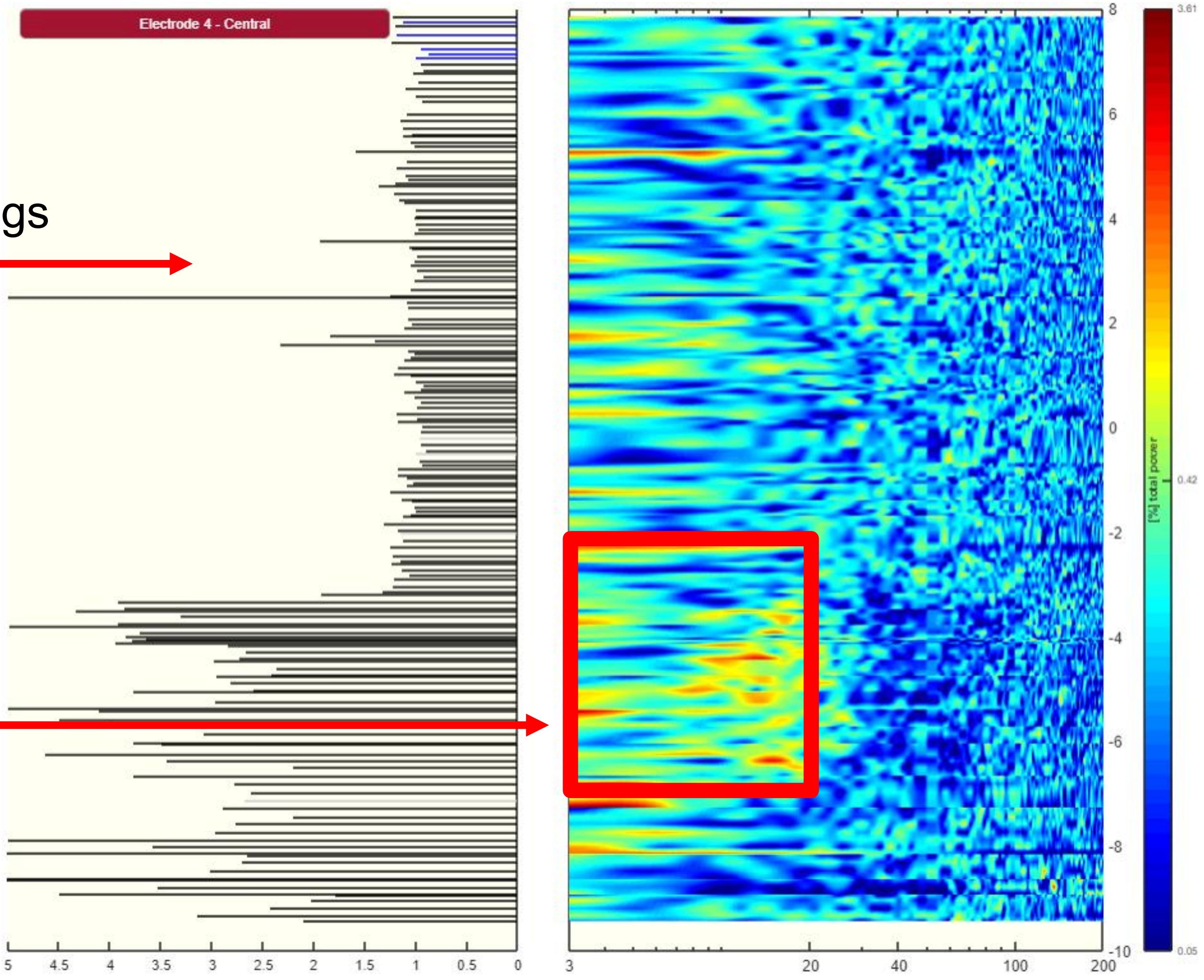
Power Spectral Density (PSD) Plots in MER



Non-active Recordings

Active Recordings

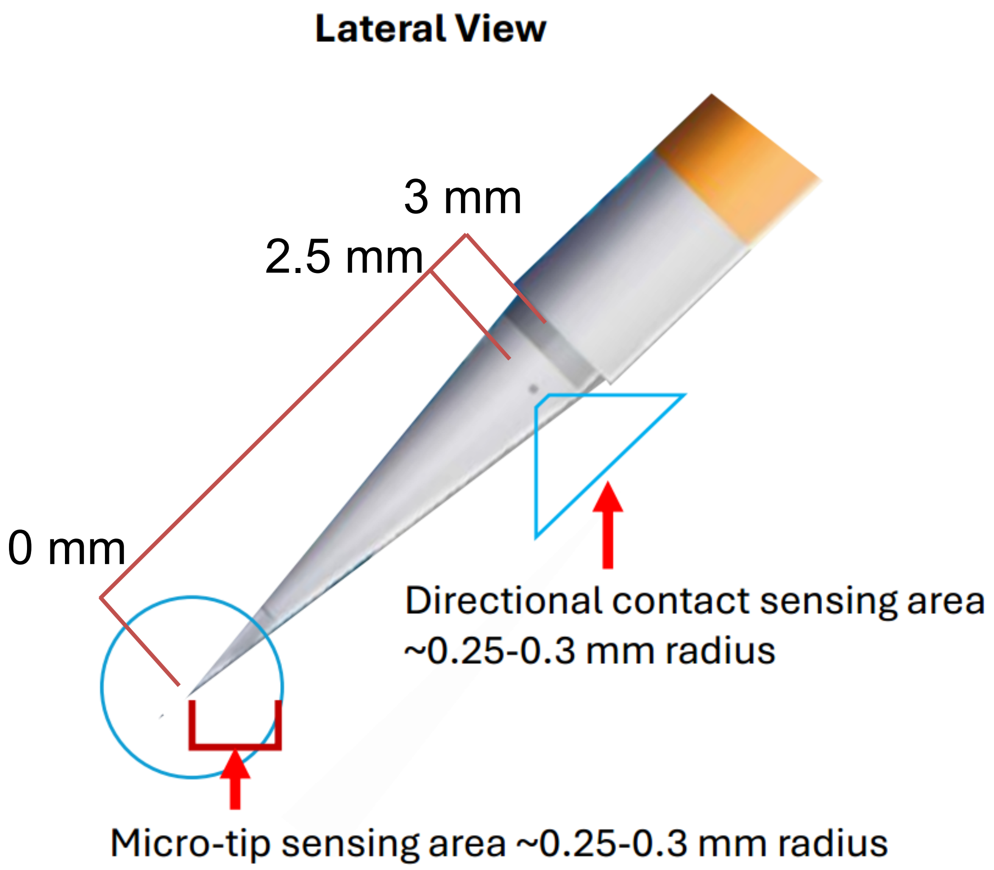
Beta Local Field Potential

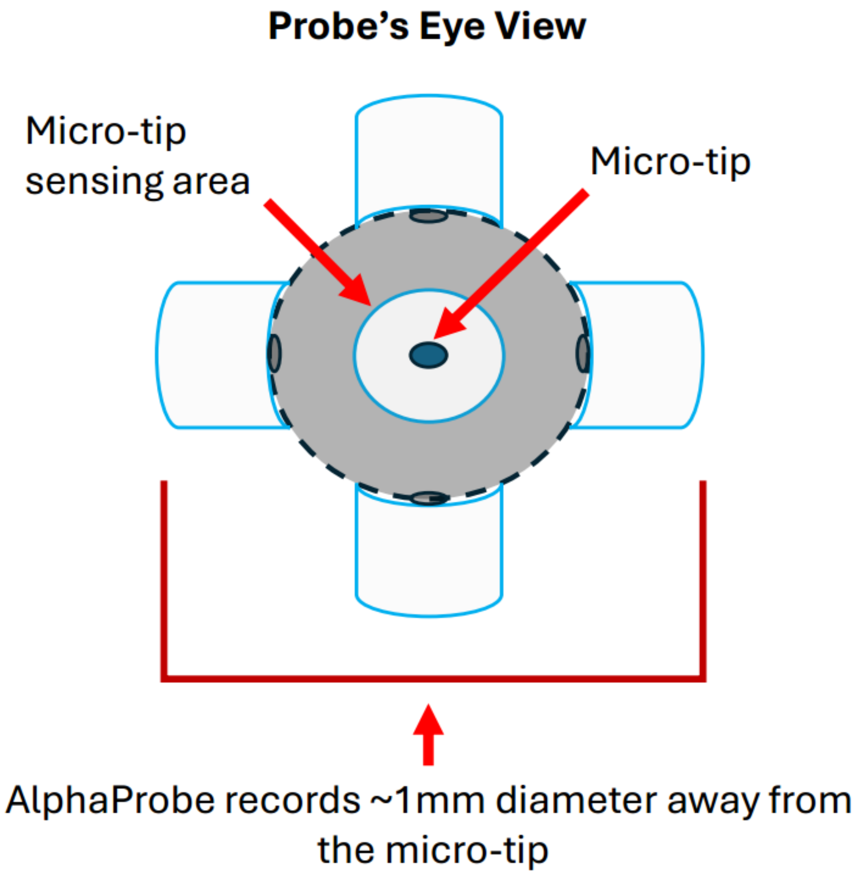


Normalized RMS –
Average activity per site stopped

Frequency (Hz)

Multi-Directional Electrode Probes in MER





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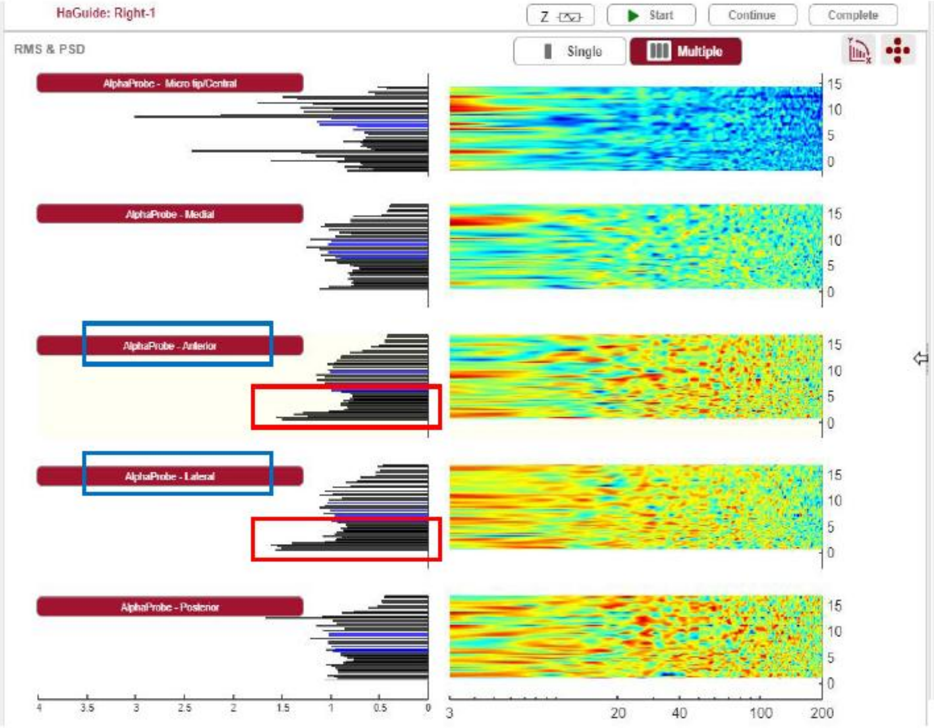
Multi-Directional Electrode Probes in MER

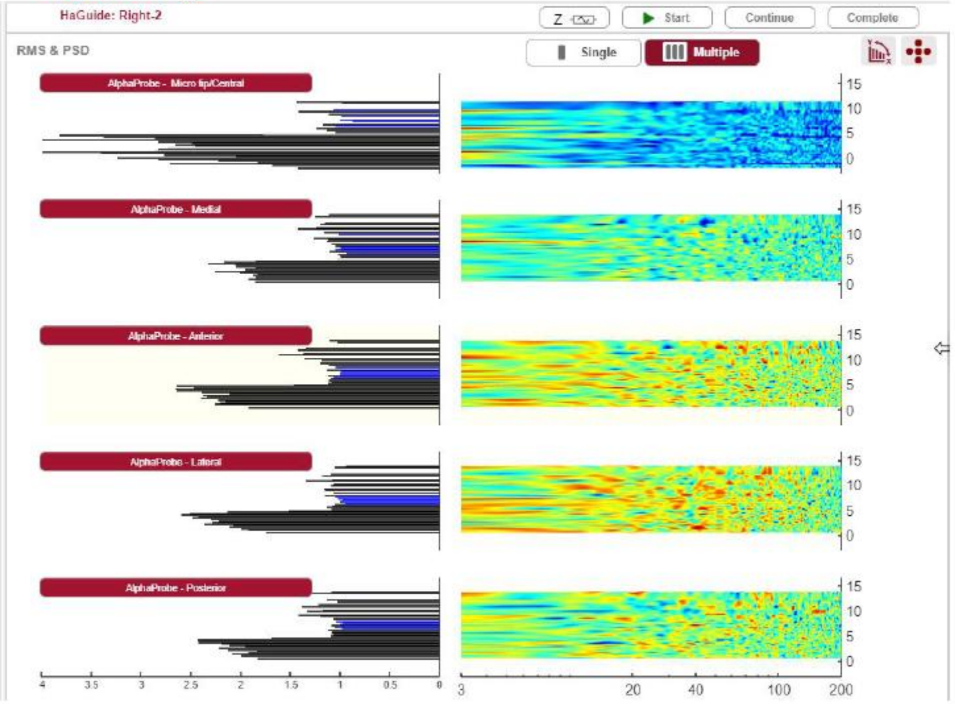
Trajectory 1 – Planned Trajectory

Anterior and Lateral directional contact recordings display greater background and spike activity.



Trajectory 2 – Moved Electrode Lateral – Final Implant

All contacts display a robust background and spike recording.

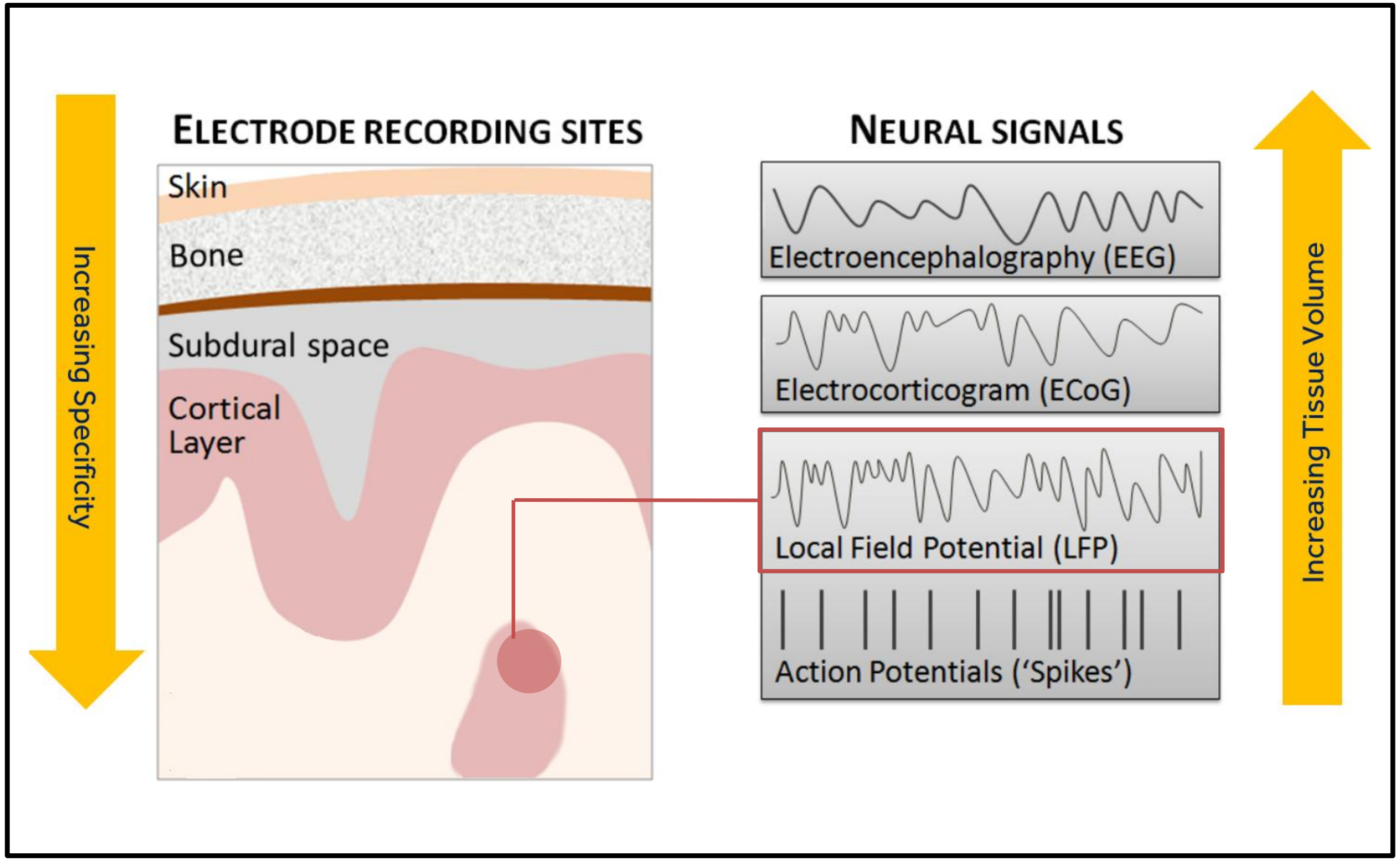


Surgical Benefit: directional anatomy of structure, Informed additional passes, Reduced number of additional passes, Targeted Stimulation testing

Overview of Local Field Potentials (LFPs)

LFPs are biological signals representing the collective and summed activity of large neuronal populations that are recorded via electrodes inserted into the central nervous system

- LFP signals represent the oscillatory and synchronous activity of many neurons
- LFPs can aid in the understanding of brain dynamics in health and in disease



Ganguly. Introduction to Brain-Machine Interfaces. ASNR
http://asnr/files/Ganguly%20Handout.pdf last accessed 07/14/2022

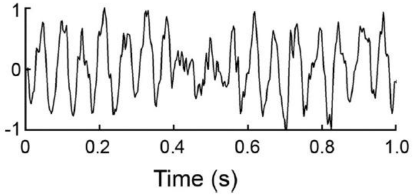
Overview of Local Field Potentials (LFPs)

Microelectrode Recordings (MER)

- Single or multi-unit recordings
- Provides detailed information about neuronal characteristics
- Does not provide a broad picture of how neuronal populations are communicating within a nucleus

LFP Recordings

- Recordings from a much larger population of neurons
- Reveals the presence of neural rhythms or synchronised oscillatory activity

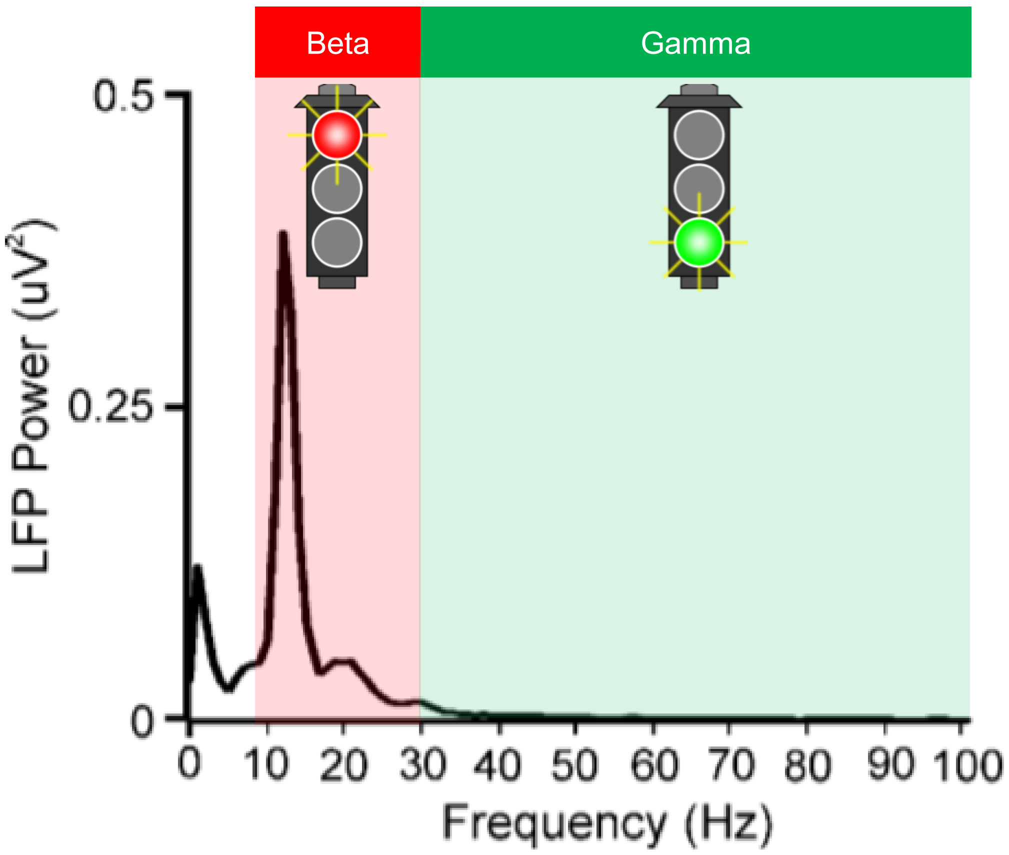


Maling et. al. J. Neurophys. 120, 1932, **2018**.

Overview of Local Field Potentials (LFPs)

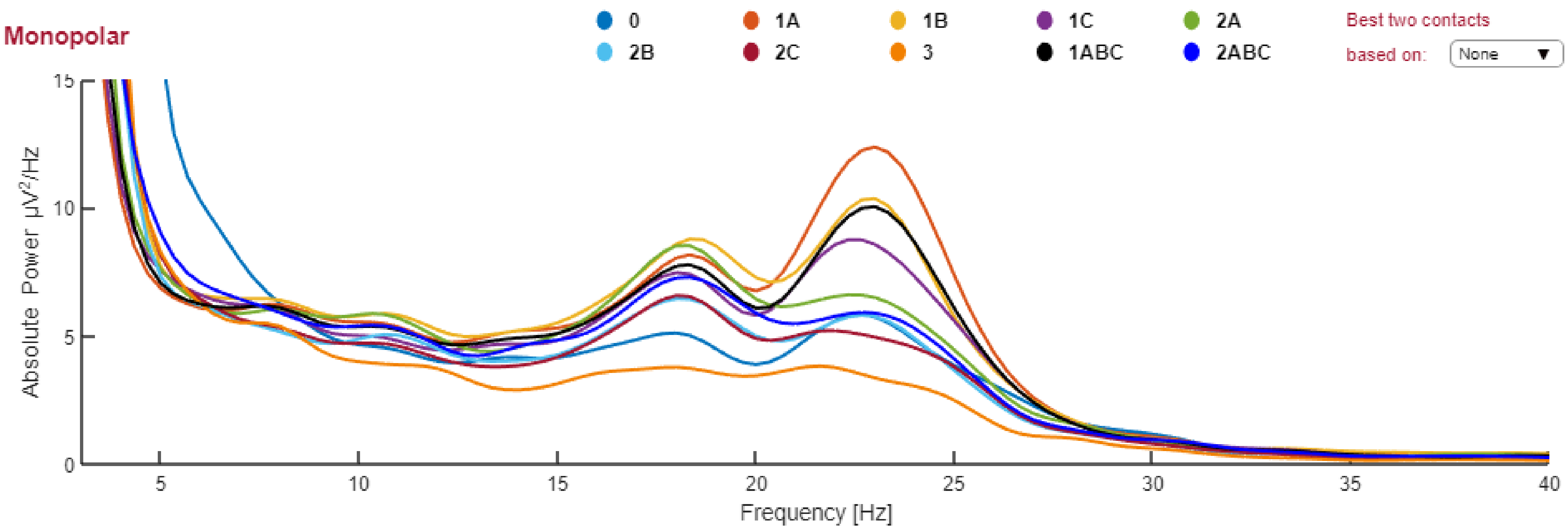
- Persistent hypersynchrony in the beta frequency range is considered an "anti-kinetic" signal

- Persistent hypersynchrony in the gamma frequency range in the basal ganglia is considered a "pro-kinetic" signal

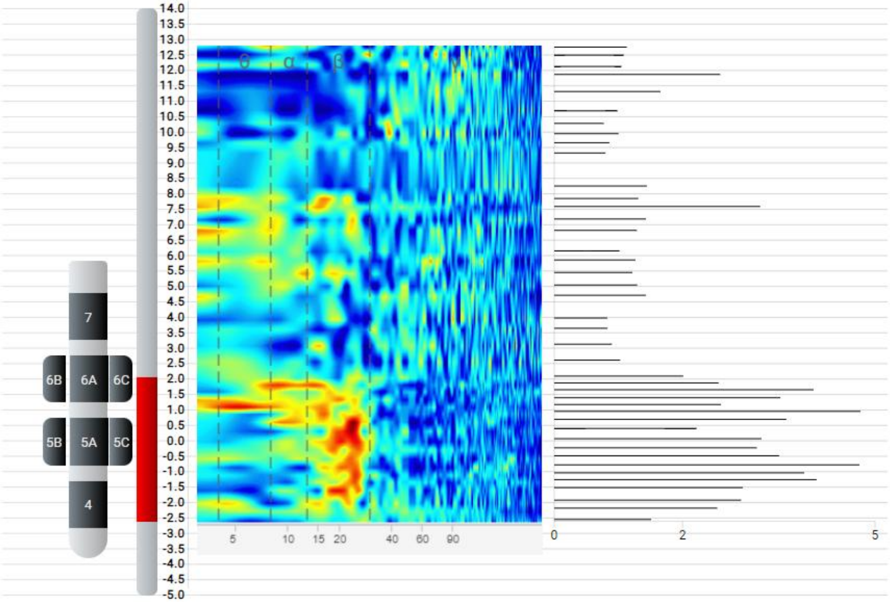


Brown et. al. Clin. Neurophys. 116, 2510, **2005**.

Intraoperative Assessment of LFPs



Incorporating MER and LFPs During DBS Surgery

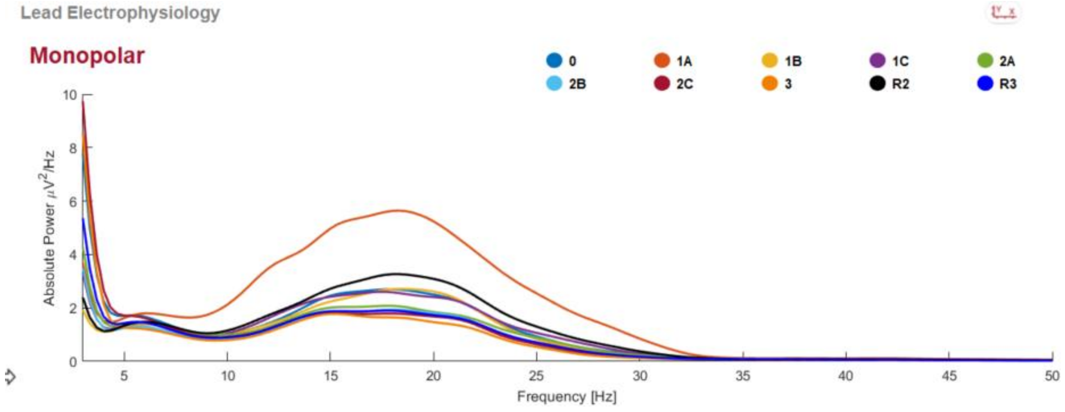


Typical LFP frequency bands associated with symptoms in specific disease states.

	Delta (0-4 Hz)	Theta/Alpha (4-13 Hz)	Low Beta (13-20 Hz)	High Beta (20-35 Hz)	Gamma (35-250 Hz)
PD: Akinetic-Rigid symptoms			●	○	○
PD: Tremor symptoms		●			●
Essential Tremor		●	○	○	
Dystonia‡(tonic)	●		○		○ (60-90 Hz)
Dystonia‡(phasic)		●	○		○ (60-90 Hz)

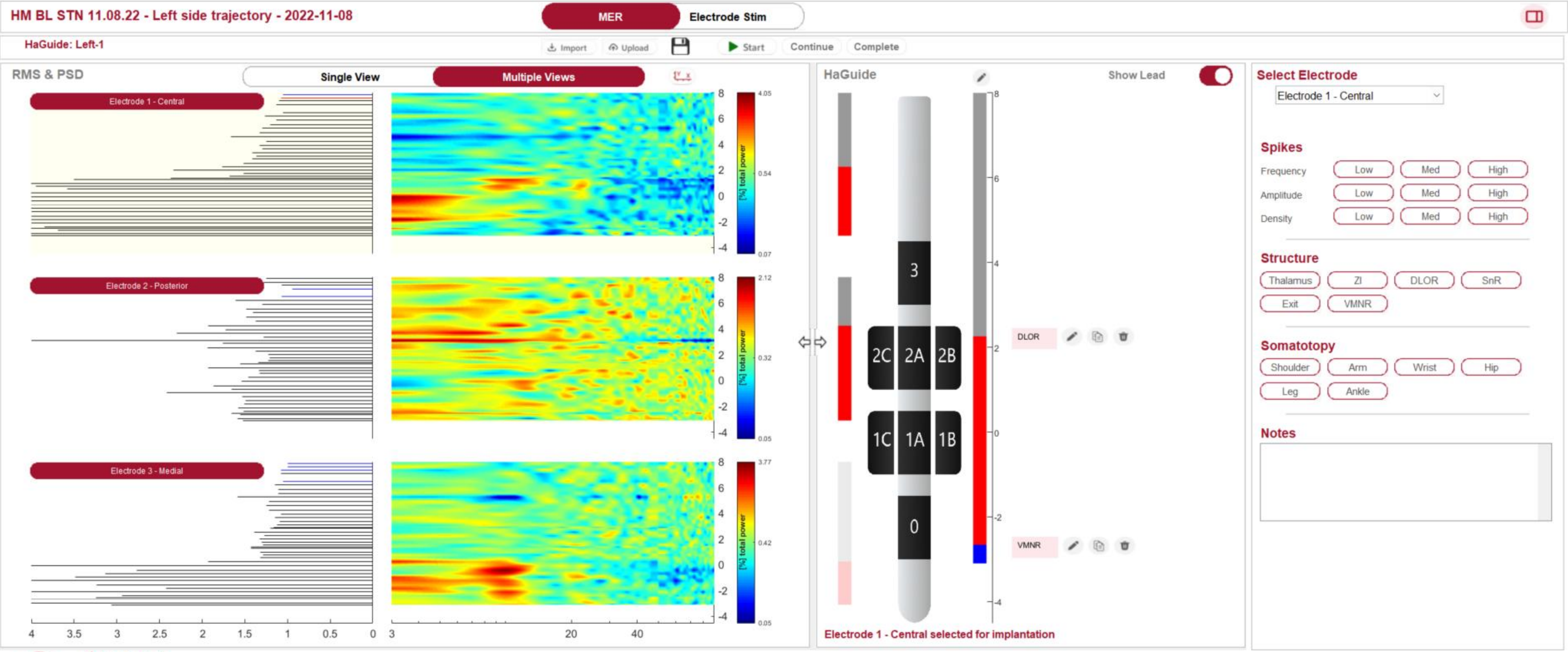
● likely association of LFP band to disease state (large body of literature supports findings)

○ potential association of LFP band to disease state



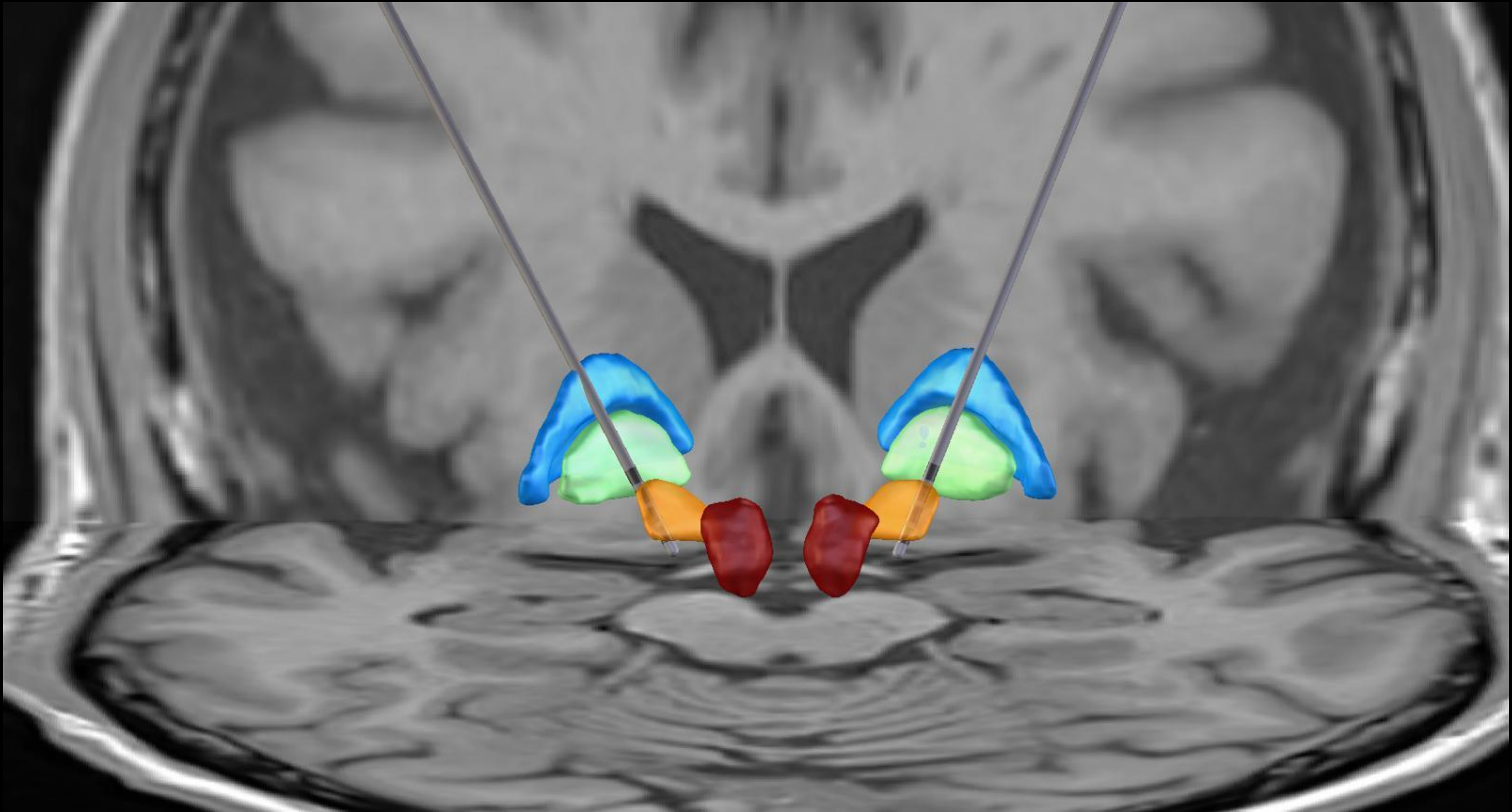
We now use intraoperative biomarkers to increase DBS implant confidence, simplify MER, and adjust lead implant depth, such that the segmented contacts sit around LFP hotspots of interest.

Incorporating MER and LFPs During DBS Surgery



ALPHA omega
Defining Neuroscience Technology

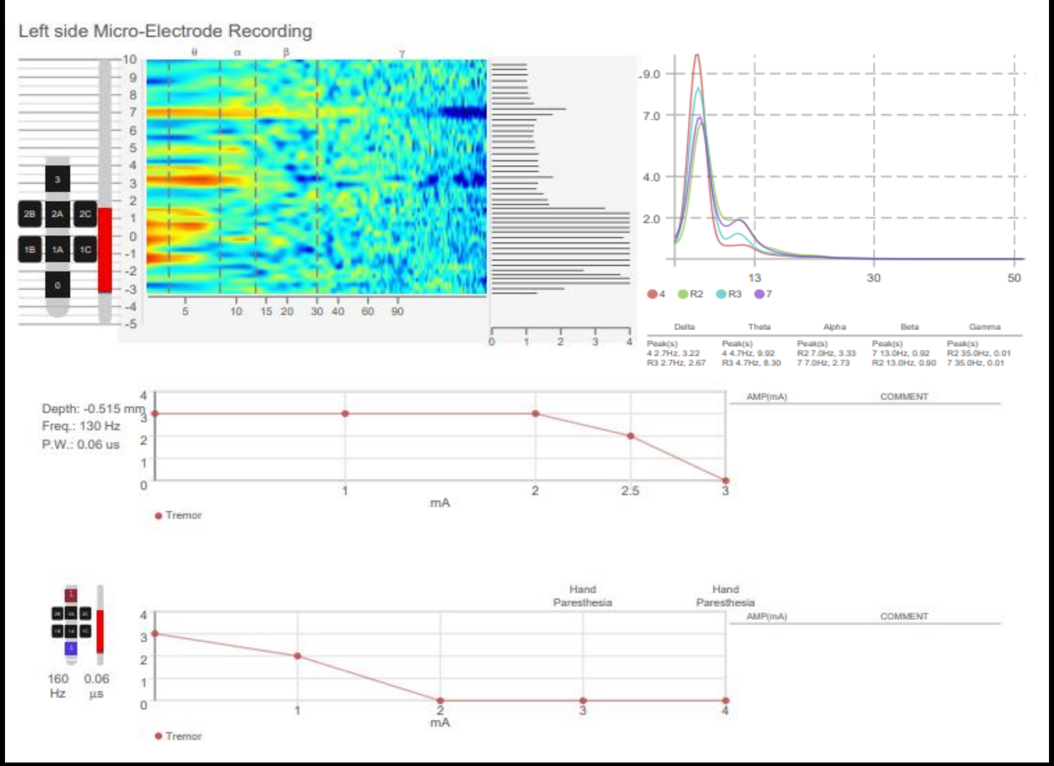
Advanced Imaging to Verify Electrode Placement

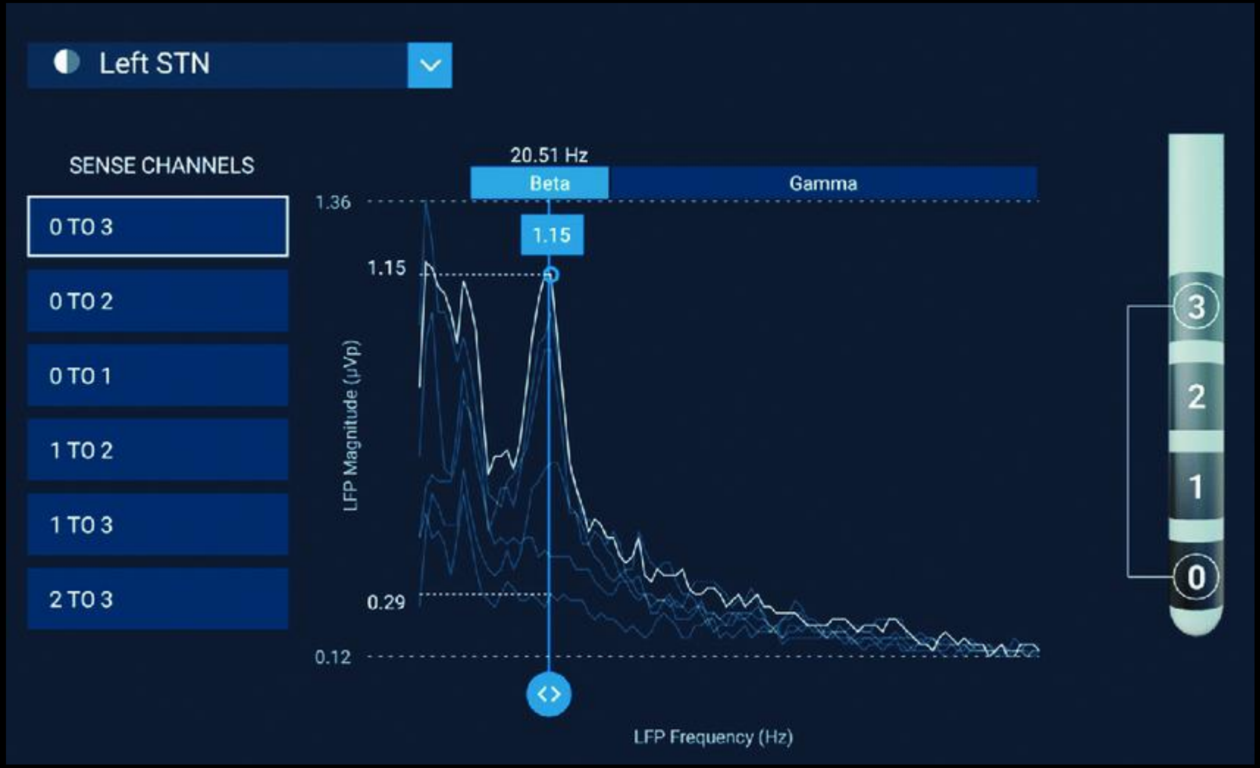


Customized Reports To Facilitate Programming

Transmit an Objective Summary of Intraoperative Recordings, Imaging, and Findings:

1. Microelectrode Recording and Macrostimulation Summary with HaGuide Plot
2. Intraoperative Stimulation Parameters, Efficacy Confirmation, Potential Side Effects
3. Local Field Potential Recordings from DBS Lead(s)
4. Confirmatory Imaging of DBS Lead(s) with Anatomical Atlas-Based Target





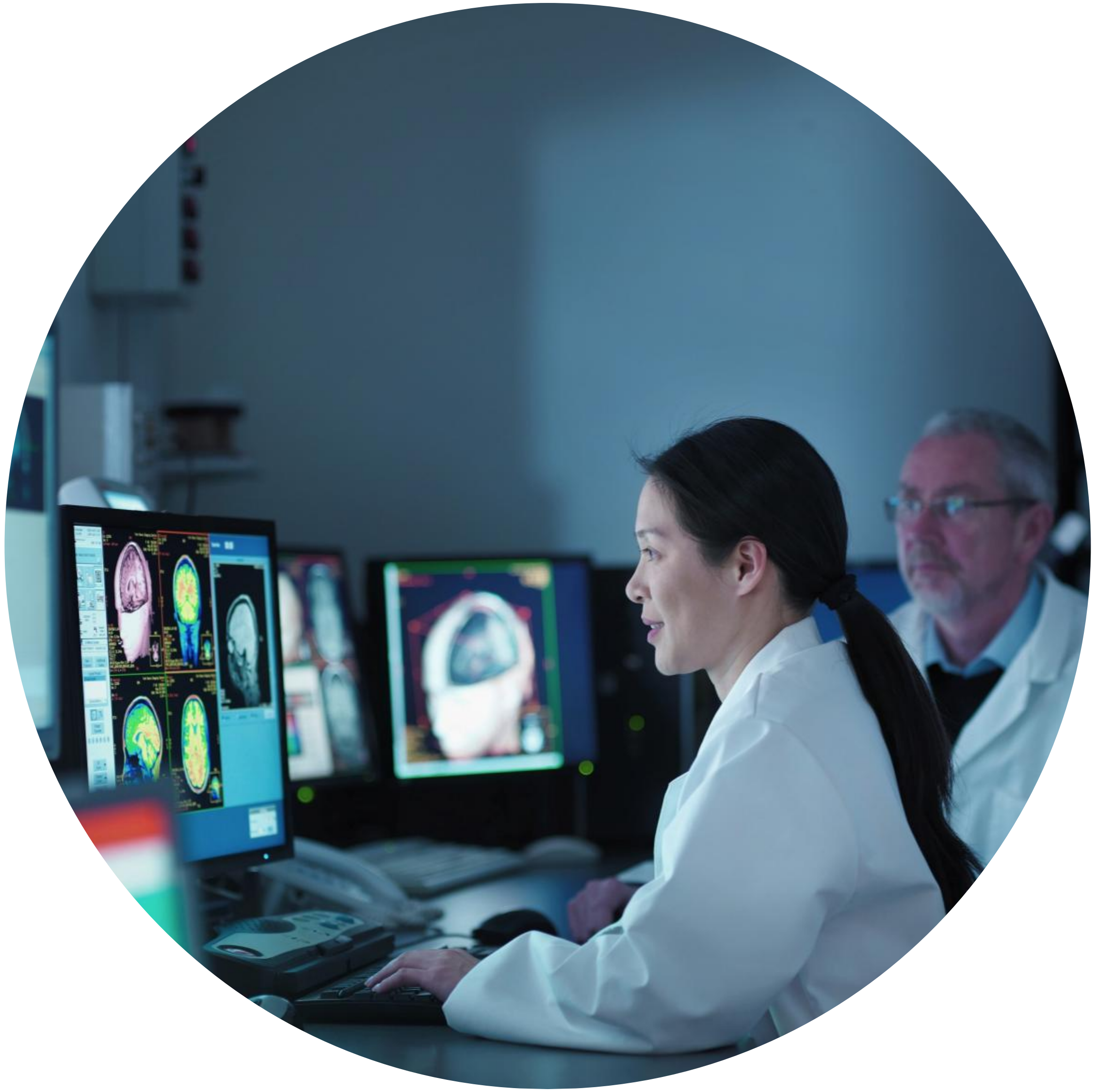
Clinical Uses of LFPs in Parkinson's Disease

LFPs are stable over time

LFPs can correlate with clinical symptoms

LFPs can correlate with therapy (medication and stimulation)

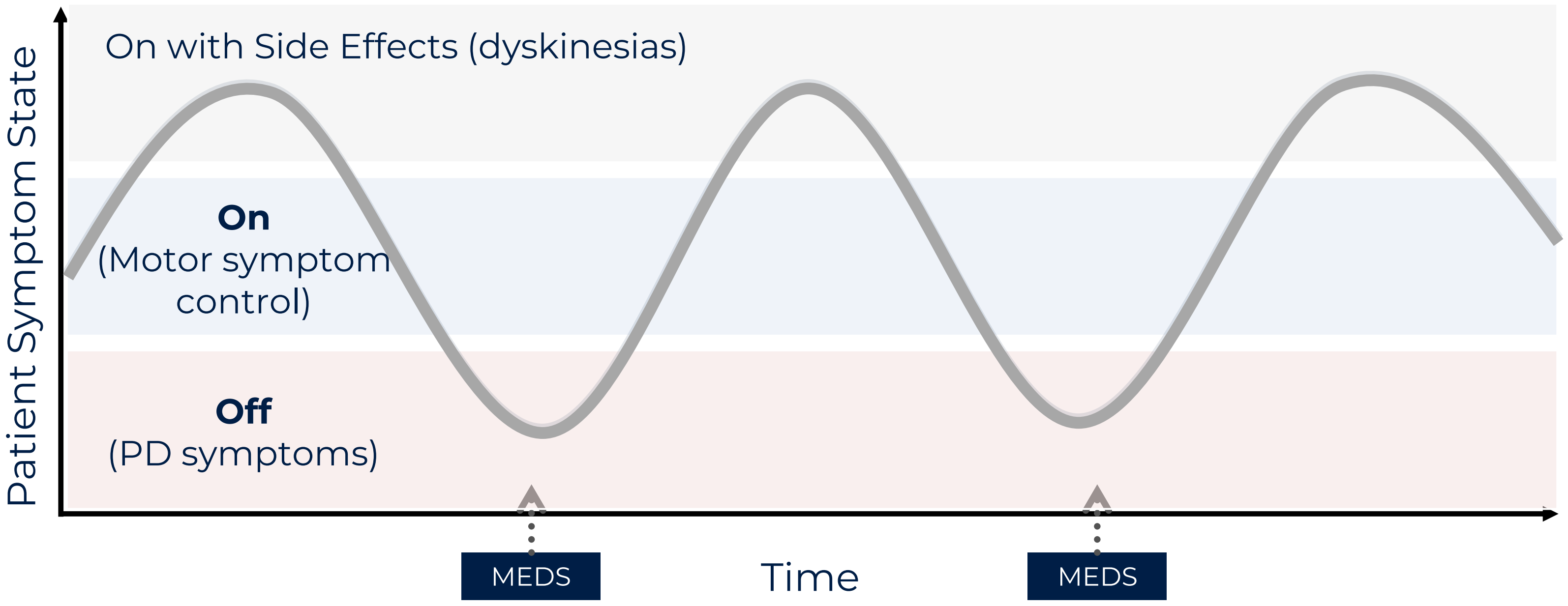
LFPs can be used to inform clinical management

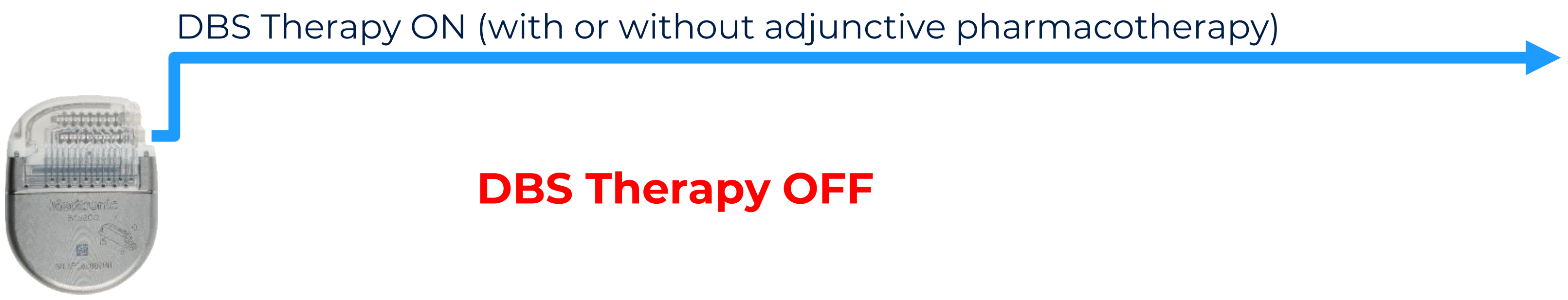


Why Have LFP Technology in Neurostimulators?

- LFP brain signals may contain information about fluctuations that are experienced by the patient

- Understanding these fluctuations may be useful in adjusting therapies to better manage patients





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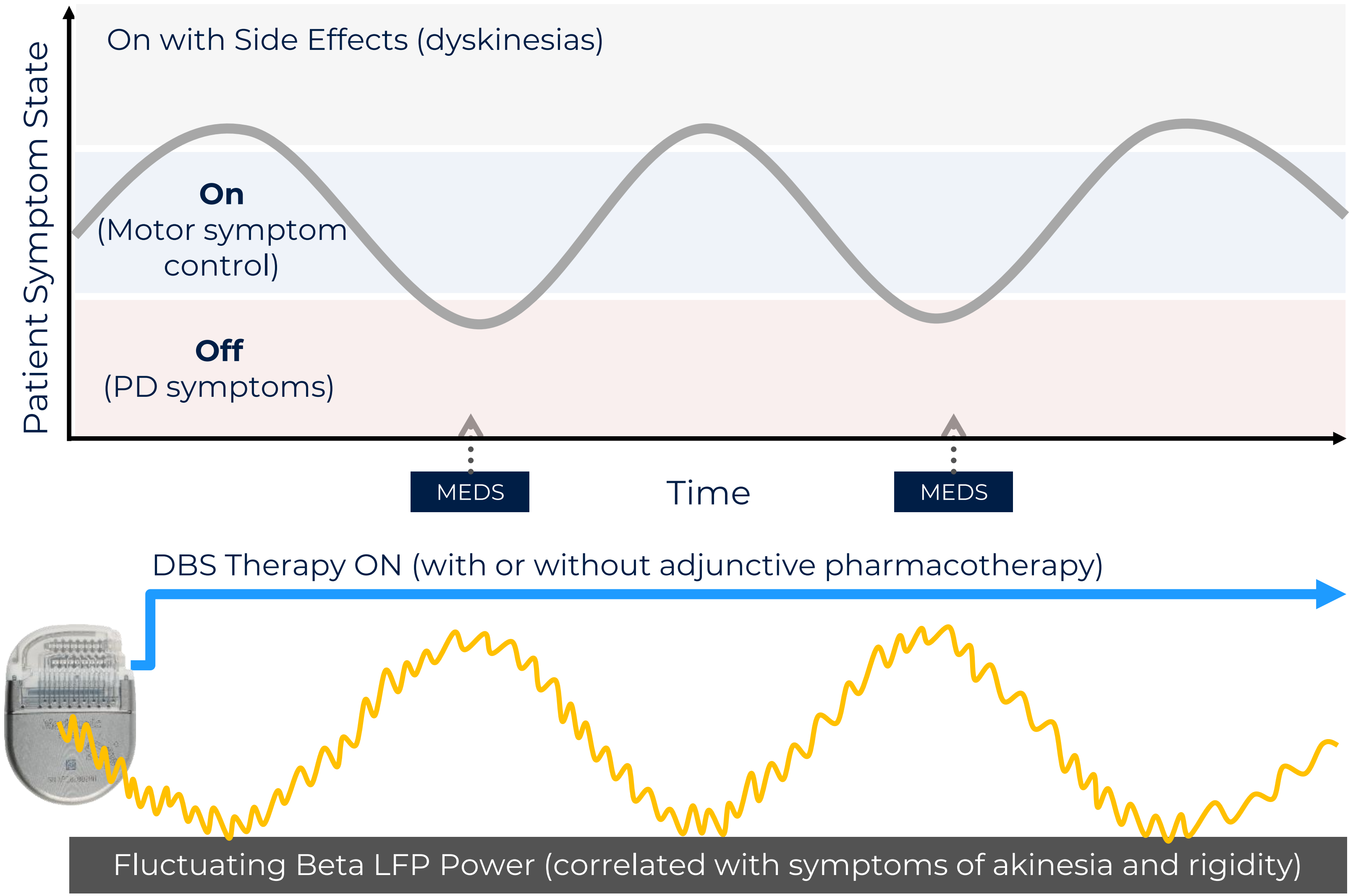
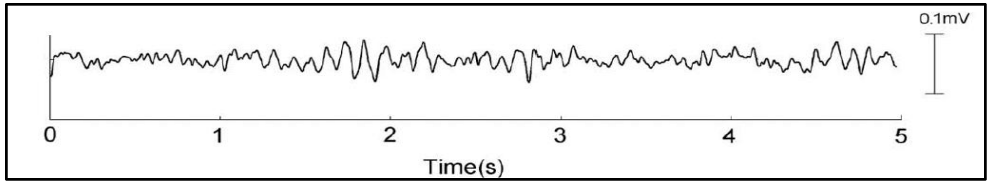
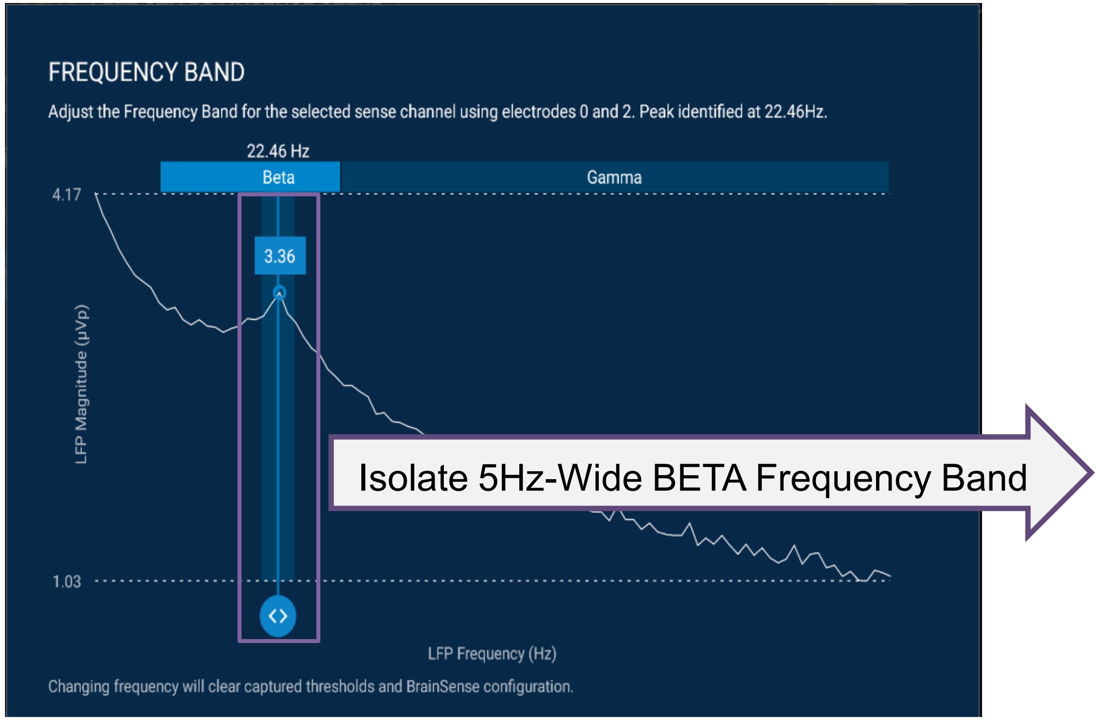


LFP Signal Analysis with DBS Software



FFT



Raw brain LFP signal collected

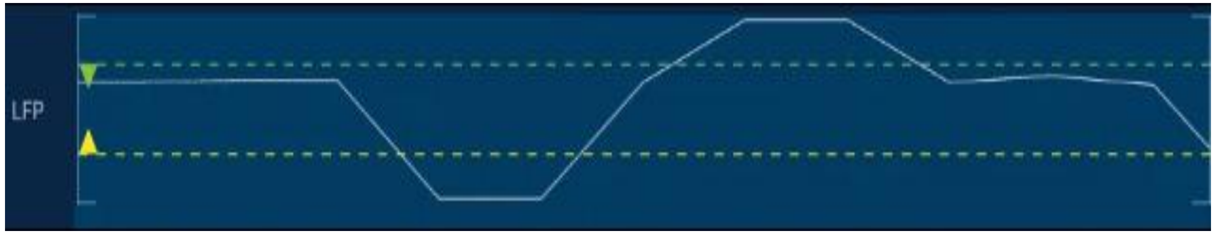
Raw data not visualized directly in tablet
(Saved as an exportable file)

Frequency breakdown

Identify atypical peaks at any LFP frequency up to 100 Hz

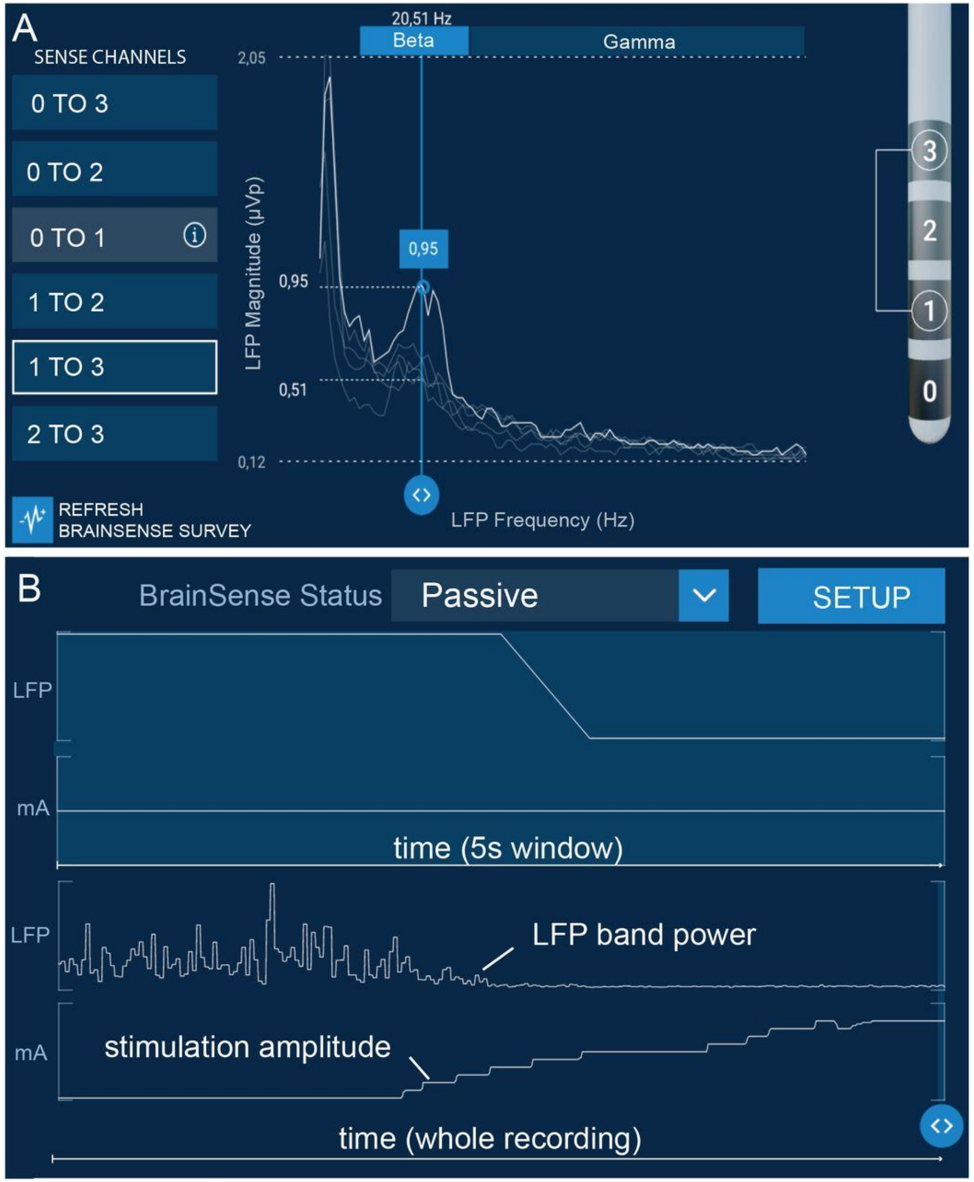
Record Isolated Frequencies in real-time

Track beta as it responds to stimulation changes



LFPs Provide Additional Data to Neurologists

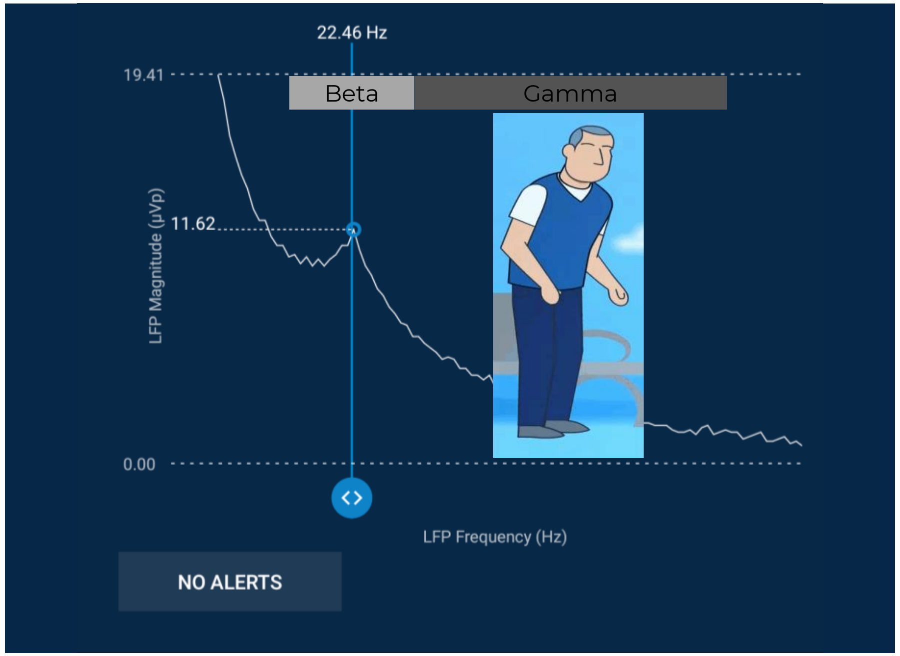
- Insight into the brain when the patient is not in the clinic
- Electronic patient diary stored on the device
- Objective monitoring of LFP changes over time – correlate with patient symptoms, medication usage, and/or sleep cycles
- Ability to sense and record frequency bands from 0 to 100 Hz (delta, theta, alpha, and gamma frequencies)
- “At-a-glance” summary of objective data that reflects patient experience outside the office



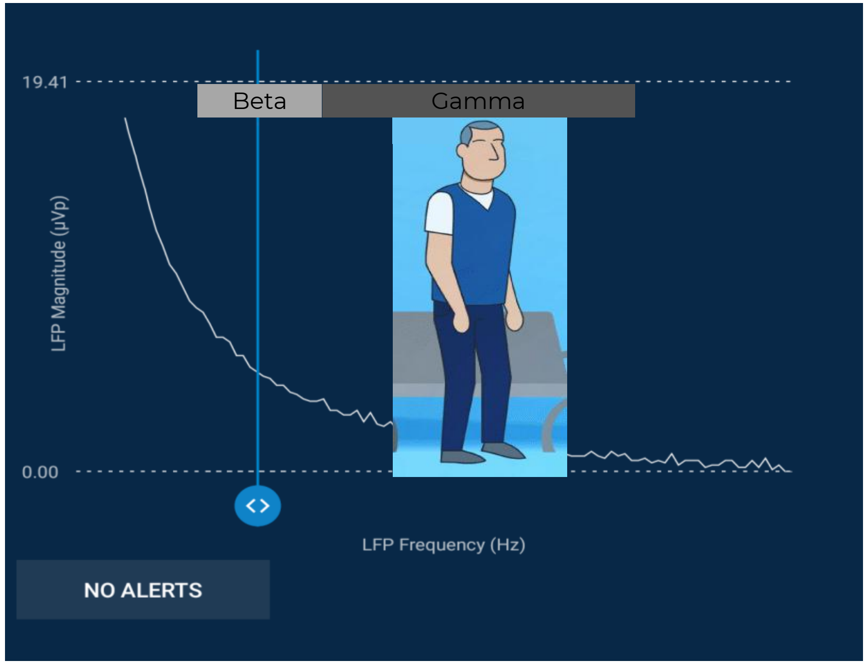
Incorporating LFP Neurostimulators to Clinical Practice

Snapshot in time

Patient with Akinesia and/or rigidity

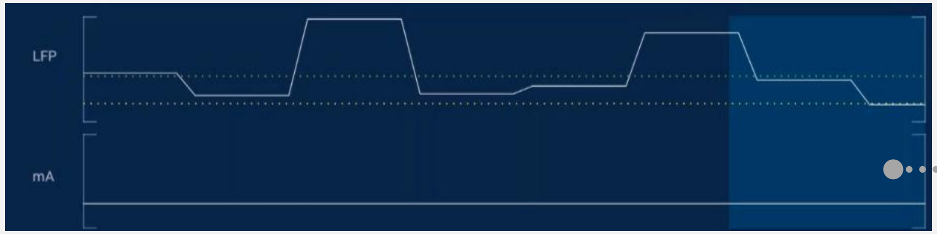


Asymptomatic patient



LFP power (Beta)

Stimulation amplitude



Stimulation ramping up

Summary

- Deep brain stimulation is a safe technology to address Parkinson’s disease symptoms with a low side-effect profile.

- Deep brain stimulation is not a therapy of last resort and may be initiated earlier in the disease course.

- Deep brain stimulation surgery can be personalized to patient preferences.

- Local field potentials and biomarkers of Parkinson’s disease can be recorded in the OR and used to facilitate deep brain stimulation programming.

- Local field potentials form the basis of adaptive deep brain stimulation.

- Adaptive deep brain stimulation can improve on-time in patients beyond what standard deep brain stimulation alone can.

This is the Moment to **END** Parkinson's Disease

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