Contemporary Neurology

2025

The Changing Landscape of Deep Brain Stimulation

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January 18-21, 2025

CLEARWATER, FLORIDA

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Disclosures

I have received honoraria for consulting work with Medtronic, Inc. and Boston Scientific as well as serving on both of their advisory boards.

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Objectives

- Deep Brain Stimulation (DBS) Basics
- Indications for DBS
- Benefits and potential side effects of DBS surgery and therapy
- Who is a good candidate for DBS?
- Recent advances in DBS technology
- Updates in device platforms and capabilities
- Future Directions and Take Home Points

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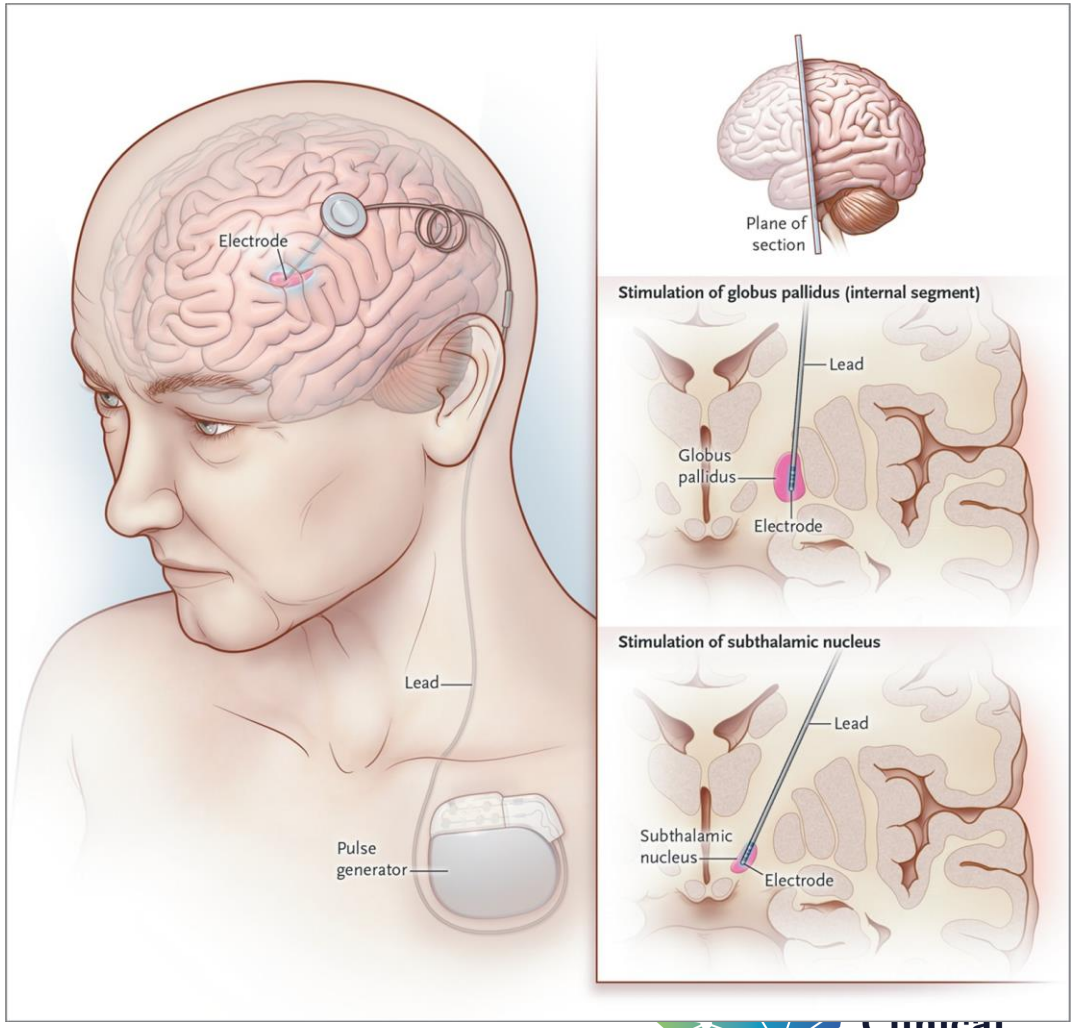
DBS Basics

- 1997 – FDA approval of DBS stimulation
  - VIM for tremor in ET and PD
- 2002 – FDA approved STN and GPI stimulation for Parkinson's
- 2003 – FDA approved GPI stimulation for dystonia
- Electrical stimulation of deep structures reversibly changes activity in those areas and mimics the effect of dopamine used in medications.
- Improves motor symptoms (bradykinesia, rigidity, tremor) and reduces fluctuations



Okun et al. 2019

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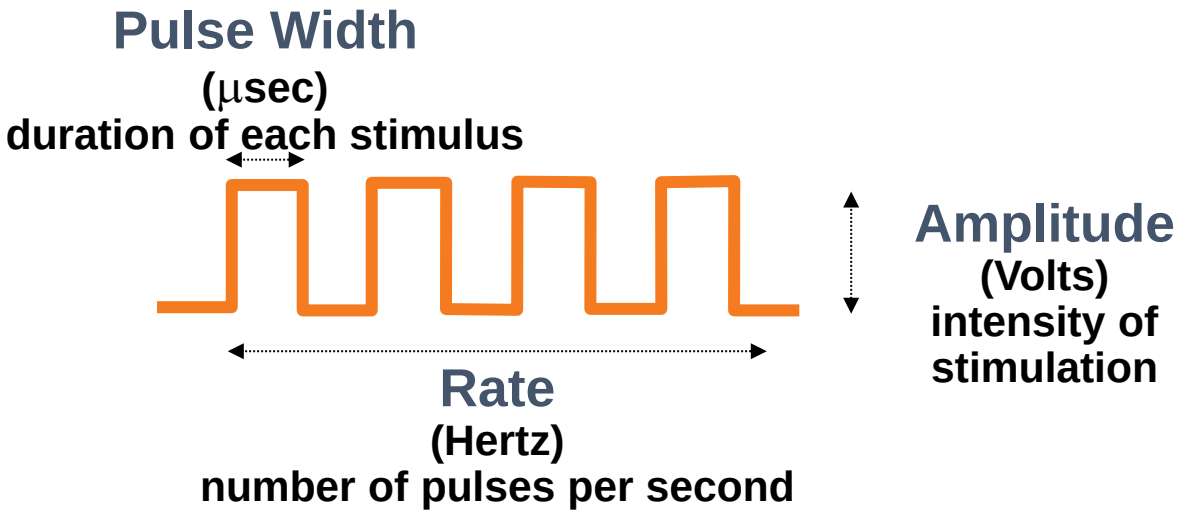
Basic Techniques and Stimulation Parameters

Monopolar Survey: Traditional initial programming approach (Volkmann et al 2006)

- Individual contact testing varying one parameter (usually amplitude) at a time while tracking clinical signs and symptoms.
- Clinical survey or road map of the therapeutic window for each contact (thresholds for clinical sign capture and side effect onset)
- Iterative trial-and-error approach is often time consuming and often requires multiple visits over to optimize patient outcome.
- Requires mental visualization of the anatomy and combining that with clinical exam.
- Passing this information to yourself or others for future visits is difficult



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DBS Indications and Potential Benefits

- **Benefits for Movement Disorders:**
  - Tremor (VIM for ET, any target for PD, GPI for dystonic tremor): Refractory tremor, multiple phenotypes
  - PD Motor symptoms (STN, GPI, or VIM): Tremor, Rigidity, Bradykinesia
  - Dystonia (GPI): Can improve dystonic posturing, blepharospasm
  - Chorea (GPI): Has been used for hemi-chorea, tardive dyskinesia

- **Possible Non-Motor Benefits:** Improvement in non-motor symptoms especially in PD such as anxiety, energy, sleep, urination. Some of these might be due to the stimulation and some is due to reduction in medications used to control motor symptoms.

- **Benefits for Non-Movement Disorders:** Treatment of refractory obsessive compulsive disorders (OCD), depression, epilepsy

- **Things DBS will not help:**
  - Balance
  - Memory
  - Disease Progression – **DBS Is NOT a CURE !**

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Potential DBS Related Side Effects

Potential Surgical Complications: DeLong et al 2014 found that 7.5% of 1757 patients had a side effect.

- Cerebral hemorrhage — 1.4%. Around 1-2% of hemorrhage may be symptomatic; permanent deficit (~1%)
- Infection — 3.6%. Most commonly at IPG implantation site (pectoral pocket), but can be intracerebral
  - Commonly around 1% to 2% at high volume centers.
- Cognitive/verbal fluency deficits — usually mild but occur in 5-15%, depending on study
- Confusion/delirium – 22% (Carlson et al 2014). Often transient.
- Seizure – 2-4% within 48 hours after surgery; chances of developing epilepsy <1%

Potential Stimulation Side Effects: Koeglsperger T et al 2019.

- Capsular side effects (Dysarthria, muscle contraction etc)
- Parasthesia, balance decline, mood/personality changes (impulsivity, mania, depression) which is more with STN stimulation.

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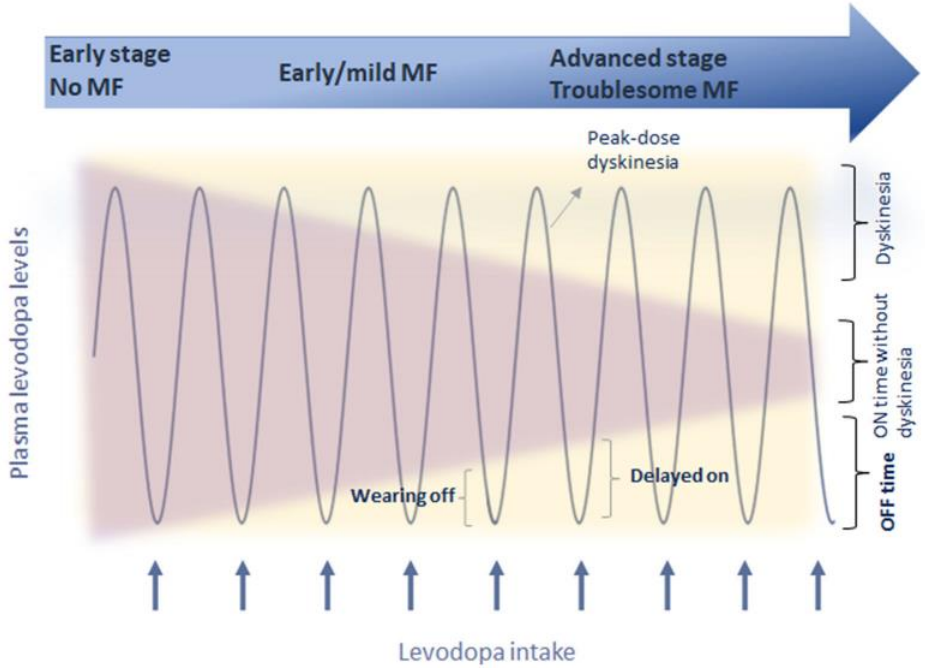
Who is a Good Candidate for DBS?

Parkinson's Disease: Fabbri et al. 2023

- Motor symptom improvement with dopaminergic replacement therapy
- Presence of motor fluctuations: alternating "ON" and "OFF" time with increasing "OFF" time > 3 hours/day
- Bothersome dyskinesia
- Medication side effects that limit escalation of oral medical therapy
- Medication refractory tremor

Essential Tremor: Moderate or Severe tremor affecting ADLs and refractory to more than one medication. No surgical contraindications

Dystonia: Blepharopasm, hemi-dystonia, cervical dystonia can all be treated, but dynamic dystonias with tremor or movement tend to respond best



Fabbri et al. 2023

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Contraindications for DBS

Parkinson's:

- Minimal response to dopaminergic replacement therapy
- Lack of motor fluctuations or bothersome dyskinesia
- Dementia
- Poor balance and frequent falling
- Atypical parkinsonism diagnosis
- Severe depression or unstable psychiatric disease

Essential Tremor: (contraindications for DBS might be a reason to consider FUS)

- Dementia
- Poor balance
- Medical Condition making surgery higher risk

Dystonia:

- Static dystonia fixed in position with contractures or limitations for improvement.
- DYT 1 responds best. Alternate mutations less responsive.

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Updates in DBS

- Advances in device technology
  - Hardware:
    - Smaller form factor rechargeable batteries now available with all 3 device companies
    - New leads: Directional leads, increased number of contacts for greater volume of tissue activation while maintaining precision. Can also help with stimulation of two nearby nuclei like STN and zona incerta (ZI) or VIM and ZI.
  - Software:
    - Real-time anatomy visualization, physiological biomarker tracking, AI driven programming help and algorithmic closed-loop changes, remote programming

- Advances in Surgical Targeting:
  - Tractography advances to fiber tracts of interest like DRT for tremor.
  - Intraoperative robotic guidance O-arm and other technology making asleep DBS more accurate and with similar outcomes to awake DBS

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Updates in DBS

- Anatomy based programming
  - Software based modeling that helps to find more optimal settings more quickly based on anatomy of the target structure and desired volume of tissue activation (VTA)
  - AI assisted programming complex VTA shapes
- Remote programming
  - Allows for remote access to patient programming to help span patients at great distances that require frequent programming optimization.
- Physiology driven programming
  - Can be used to reduce time spent programming
  - Often predicts contacts that would likely give best benefit
  - Used more in Parkinson's disease (PD) due to a more consistent LFP biomarker

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Anatomy-Based Programing

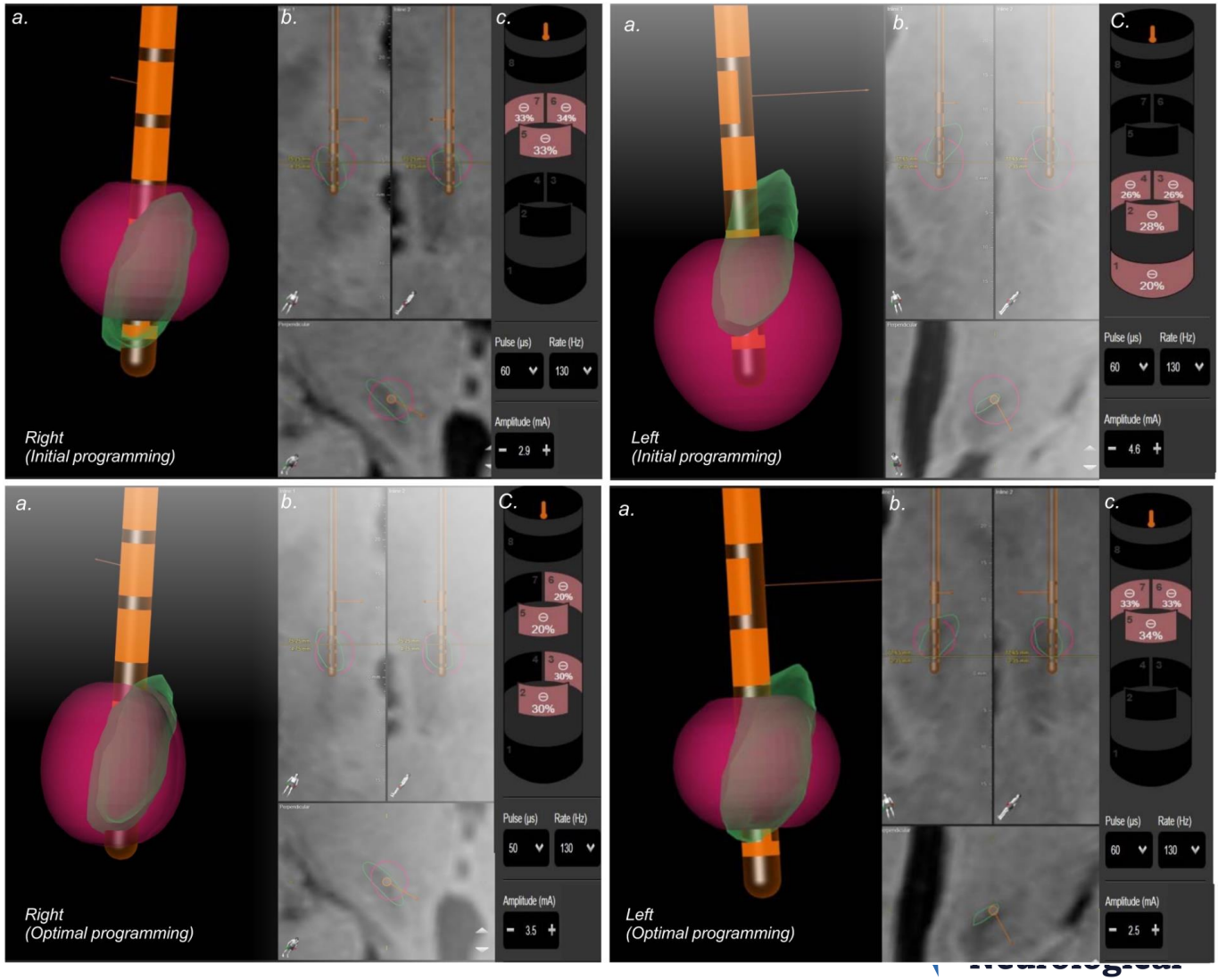
- Software based modeling using patient specific anatomy to find optimal stimulation settings for maximizing benefit and minimize side effects from unwanted stimulation of nearby structures

- Tractography advances have seen increased benefits for tremor and other symptoms with direct targeting of cerebellothalamic tracts (CBT), specifically the dentatorubrothalamic (DRT) tracts (Prent et al 2020).

- Closer proximity and more selective activation of DRTs showed improved tremor control and fewer side effects compared to pyramidal tracts (PTs) that caused dysarthria

The sequences used:

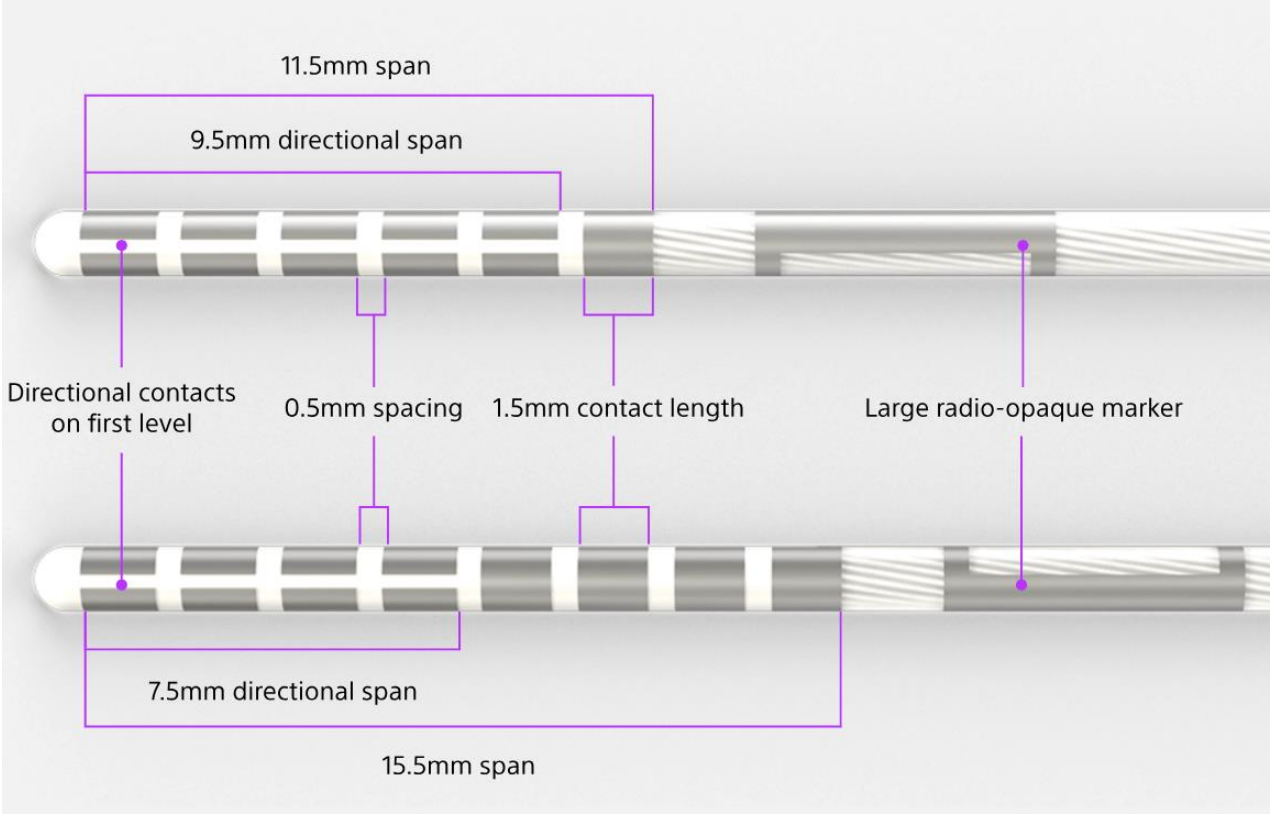
  - 3D sagittal T2 FLAIR, 3D T1 gadolinium, Post-op 3D helical CT.



Anatomy-Based Programing

- Programming more contacts can get complicated and time consuming.
- Artificial Intelligence (AI) Assisted Programming optimization now available.
- Uses anatomy and VTA modeling software with AI assisted programming using provider selected anatomy targets to stimulate and others to avoid.
- Decreased time of programming.
- Helps create unique solutions to complex cases to reduce side effects.

More contacts are better, right?



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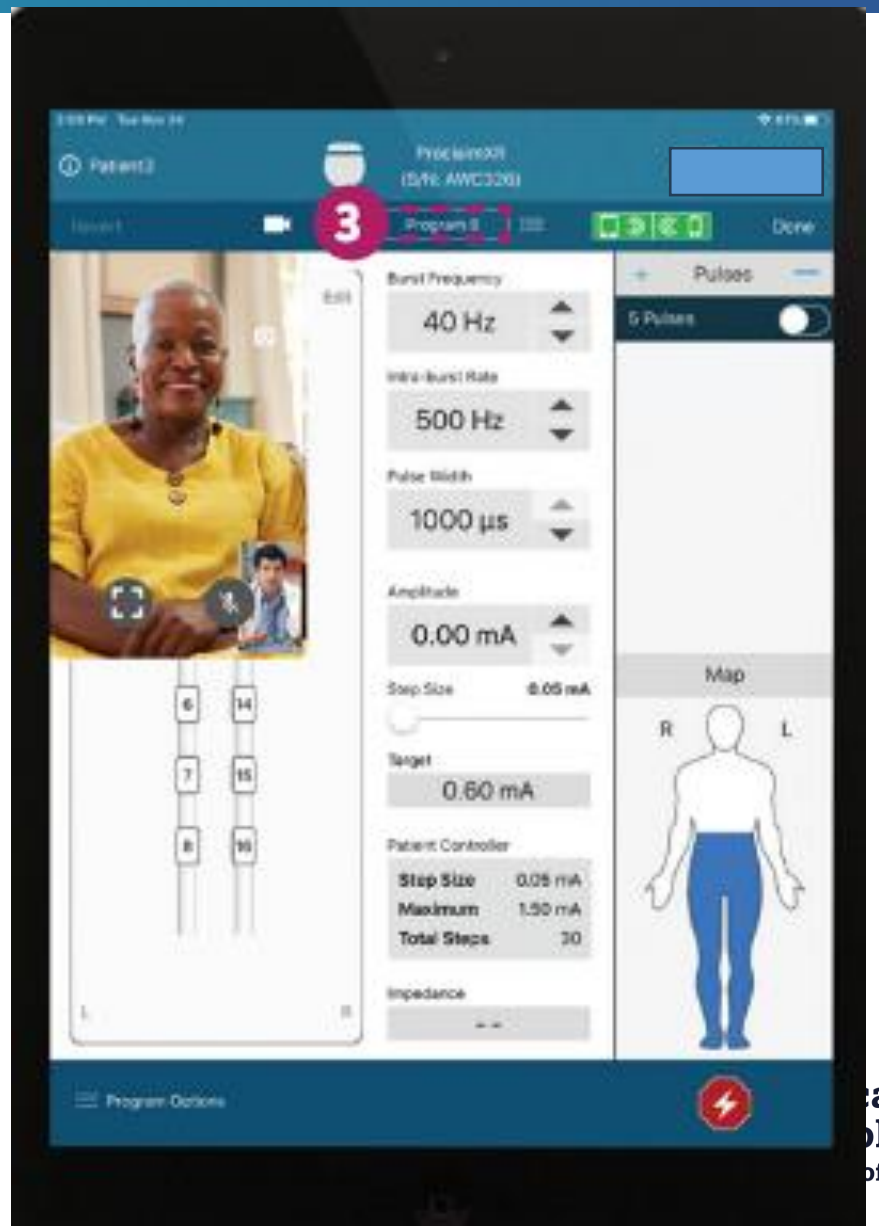
Remote Programming

Pros:

- Increased convenience for patients that have difficulty with travel to clinic
- Can help with urgent programming issues such as side effects or troubleshooting.
- Allows for more frequent visits for adjustments which prevents some people from choosing DBS therapy.

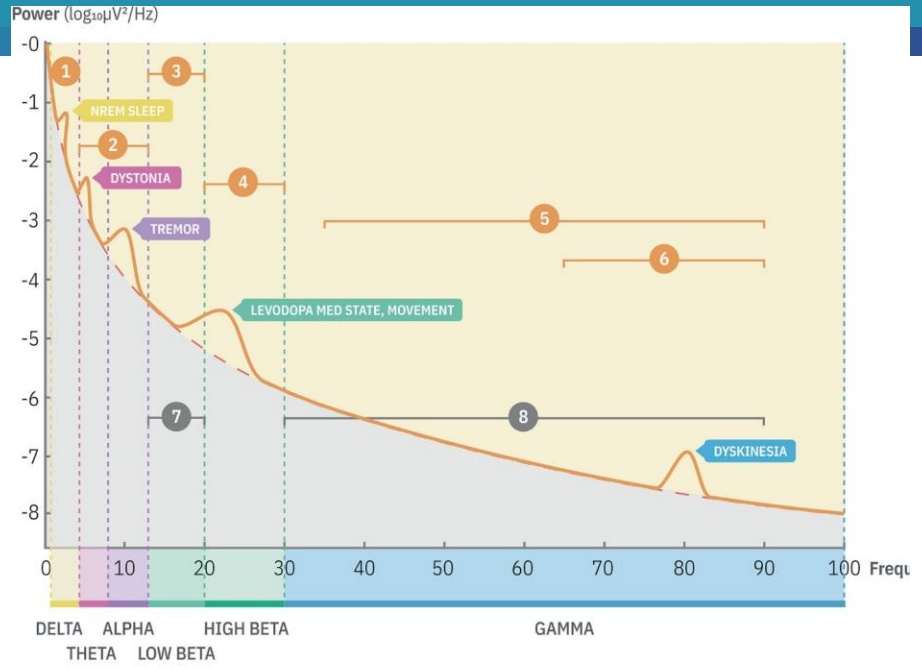
Cons:

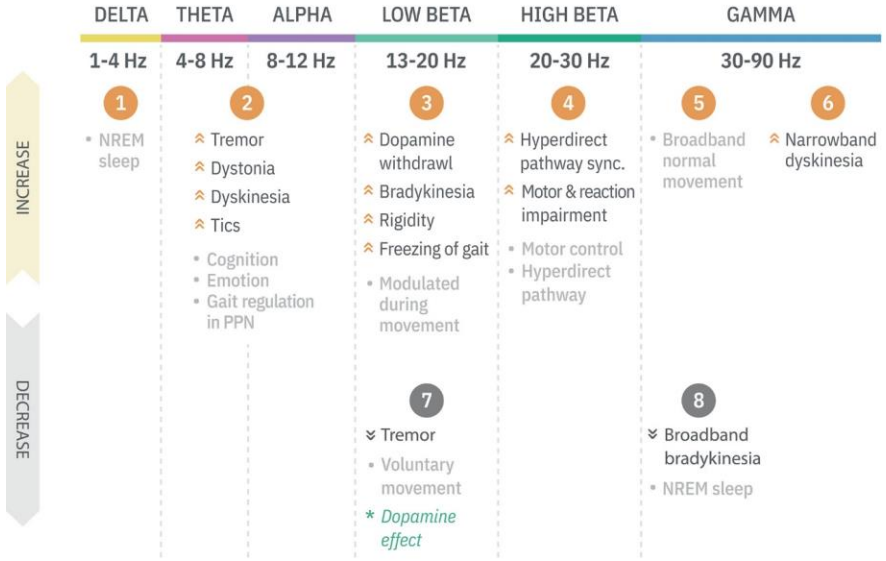
- Limited to areas with good Internet coverage
- Patient evaluation and stimulation adjustments are limited compared to in person.
- May require multi-state licensing



Physiology-Based Programming

- Requires an identified biomarker with consistent local field potential (LFP) range for the system to track (Sirica et al 2021, Neumann et al 2023).
- Attention paid to signal amplitude (power) and frequency rather than morphology because it is displayed in a power spectral density plotted created by a fourier transform multiple signal of differing frequencies.
- Used to track disease state based on activity in certain frequency bands
- Higher activity means less symptom control.
- Lowering activity relates to better symptom control from stimulation or medication.
- Can be used in programming to select electrodes with the best signal to improve efficacy and reduce side effects.
- Helpful for patients with dynamic and complex patterns of symptoms and side effects like frequent wearing off and biphasic dyskinesias.





Physiology-Based Programming

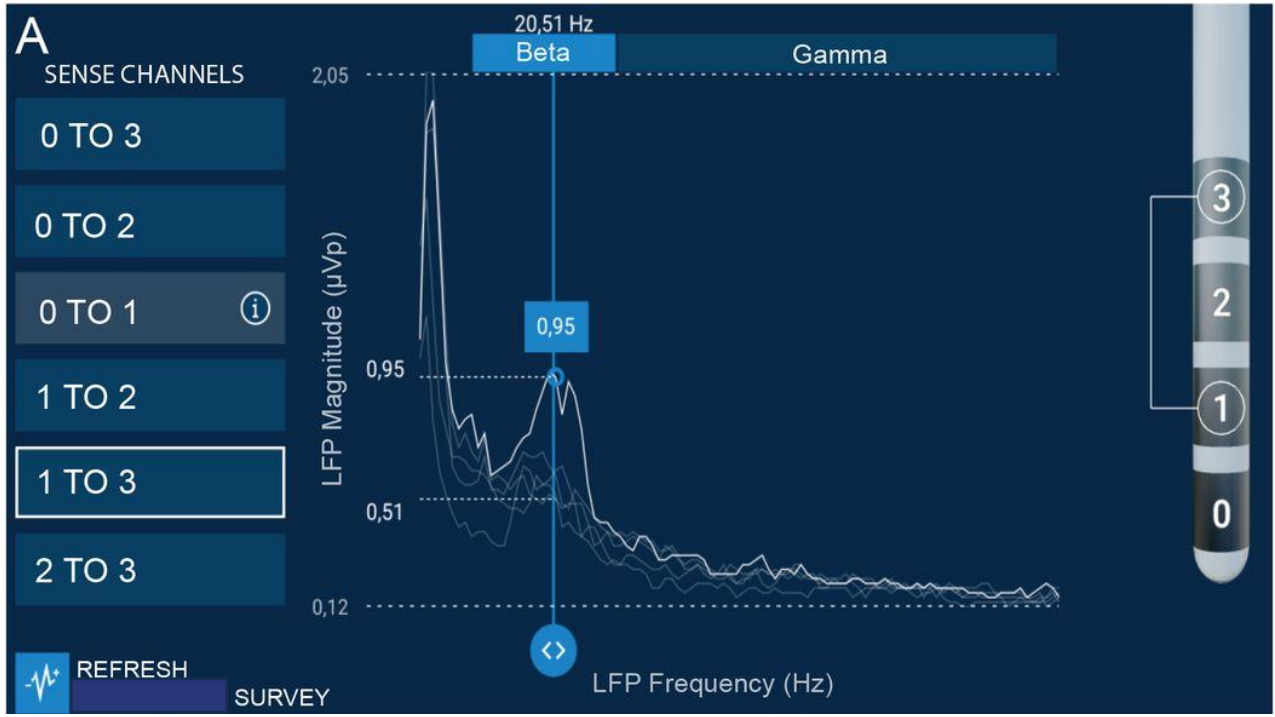
LFPs of Interest Based on Disease

Parkinson's disease:

- Alpha frequency (8 to 12 Hz) : tremor
- Beta frequency (15 to 30 Hz) : rigidity, bradykinesia
- Gamma (30 to 90 Hz) : dyskinesia

- **Dystonia:** LFPs synchronized in the theta/alpha (4–13 Hz), beta (13–35 Hz) and gamma (60–90 Hz)

- **Essential tremor:** LFP synchronization in the theta/alpha (4–13 Hz) and beta (13–35 Hz)



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Adaptive Therapy

- Closed-loop therapy with real-time adjustments in stimulation **amplitude** in response to changes in reference or control local field potential (LFP) signal. This can have several advantages.
  - Improvements in battery life
  - Improved efficacy
  - Reduced side effects (dyskinesia)
  - Potentially treating other features of disease like FOG, sleep

- Little and colleagues showed a 27% improvement in motor symptoms and 56% reducing in power use with adaptive programming in a small 8 patient study that was the first trial comparing adaptive and continuous DBS in the STN (Little et al 2013)

- Oehrn and colleagues at UCSF published an article this year detailing their experience with their own version of closed-loop stimulation using motor cortext feedback in a subgroup of patients with pre-existing DBS systems (Oehrn et al, 2024)

nature medicine

Article

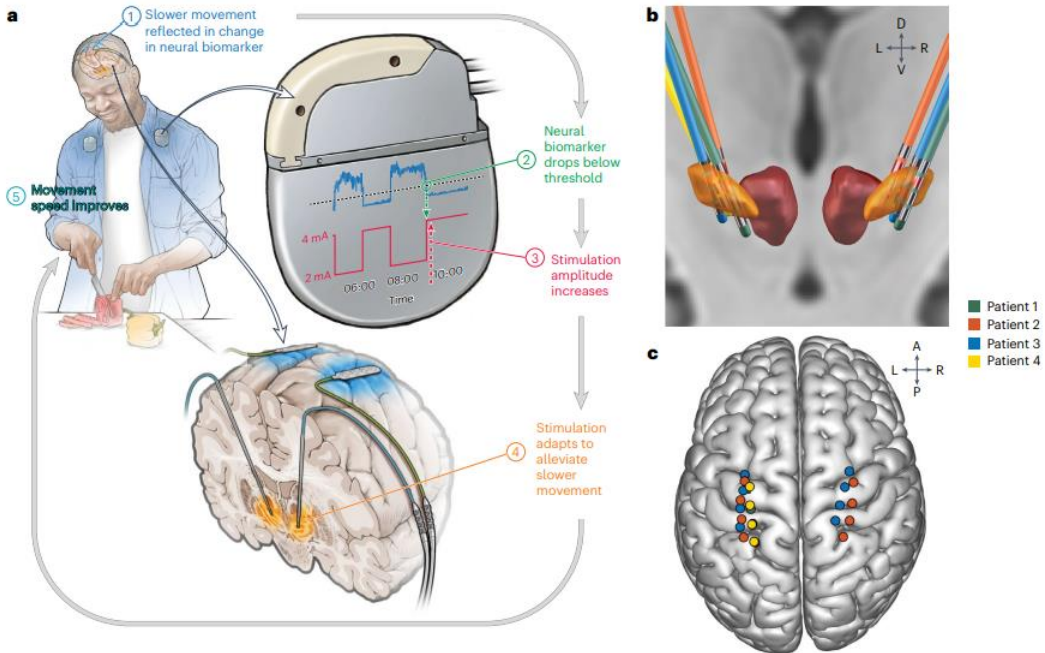
https://doi.org/10.1038/s41591-024-03196-z

Chronic adaptive deep brain stimulation versus conventional stimulation in Parkinson's disease: a blinded randomized feasibility trial

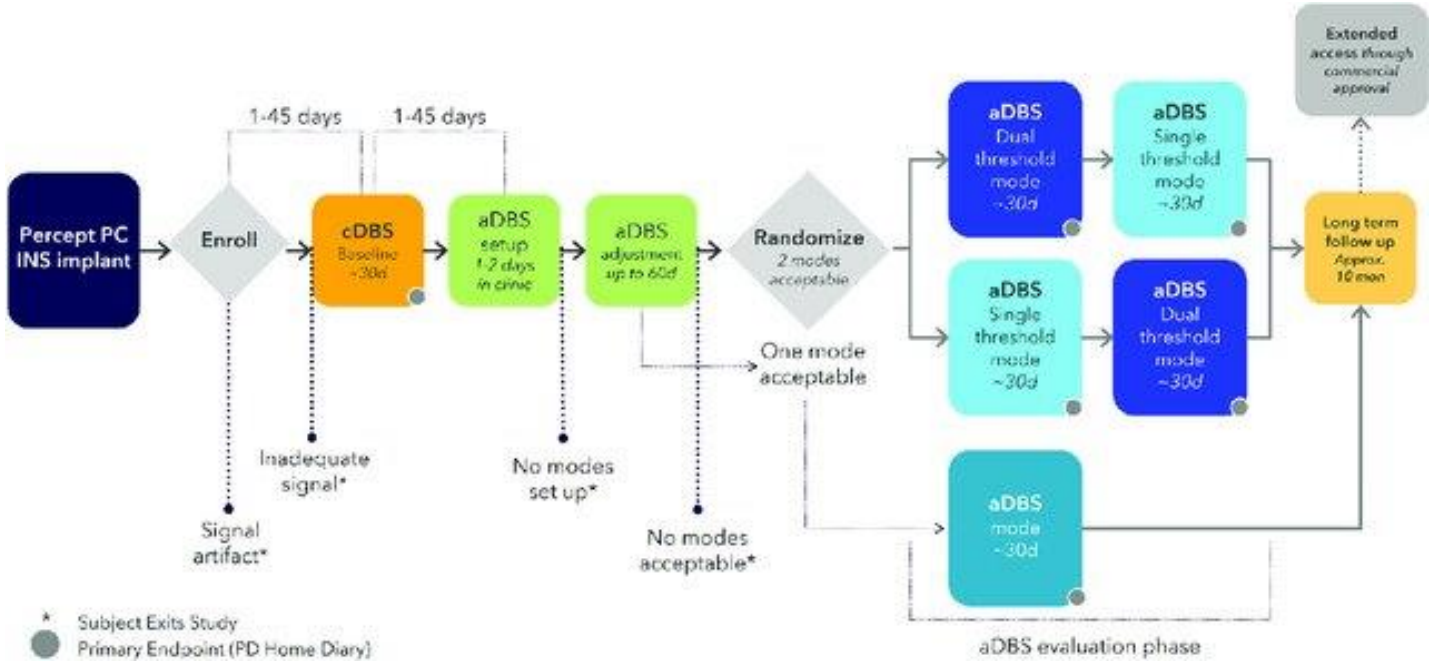
Received: 4 January 2024

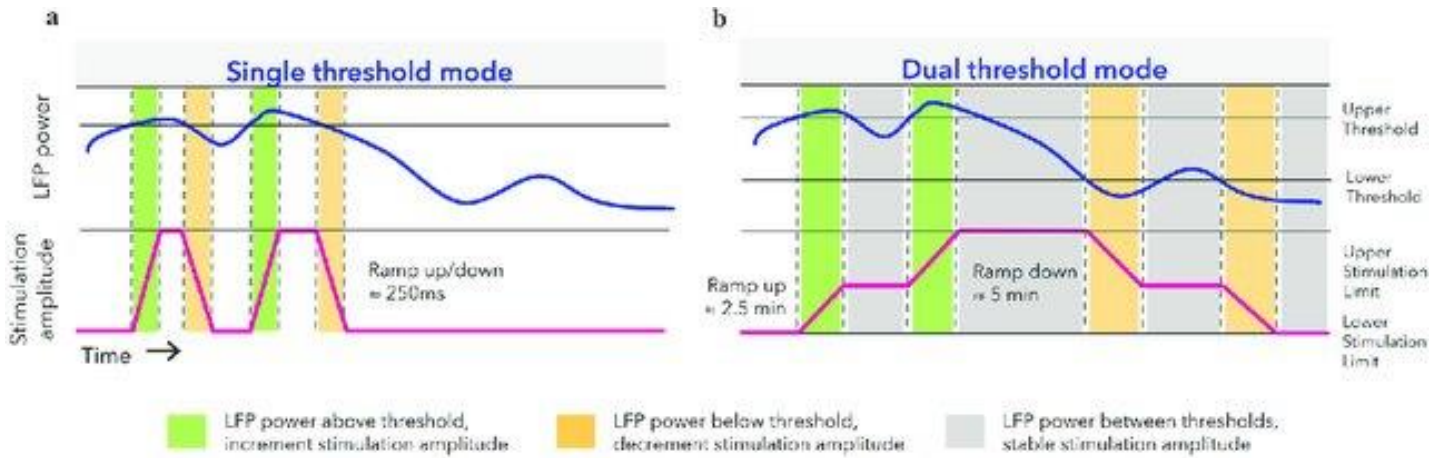
Accepted: 15 July 2024

Carina R. Oehrn, Stephanie Cernera, Lauren H. Hammer, Maria Shcherbakova, Jiaang Yao, Amelia Hahn, Sarah Wang,



Adaptive Therapy





npj | parkinson's disease

Article

Published in partnership with the Parkinson's Foundation

https://doi.org/10.1038/s41531-024-00772-5

Sensing data and methodology from the Adaptive DBS Algorithm for Personalized Therapy in Parkinson's Disease (ADAPT-PD) clinical trial

Check for updates

Scott Stanslaski[1], Rebekah L. S. Summers[1], Lisa Tonder[1], Ye Tan[1], Michelle Case[1], Robert S. Raike[1], Nathan Morelli[1], Todd M. Herrington[2], Martijn Beudel[3], Jill L. Ostrem[4], Simon Little[4], Leonardo Almeida[5], Adolfo Ramirez-Zamora[6], Alfonso Fasano[7,8], Travis Hassell[9], Kyle T. Mitchell[10], Elena Moro[11], Michal Gostkowski[12], Nagaraja Sarangmat[13] & Helen Bronte-Stewart[14] On behalf of the ADAPT-PD Investigators

Adaptive deep brain stimulation (aDBS) is an emerging advancement in DBS technology; however, local field potential (LFP) signal rate detection sufficient for aDBS algorithms and the methods to set-up aDBS have yet to be defined. Here we summarize sensing data and aDBS programming steps associated with the ongoing Adaptive DBS Algorithm for Personalized Therapy in Parkinson's Disease (ADAPT-PD) pivotal trial (NCT04547712). Sixty-eight patients were enrolled with either subthalamic nucleus or globus pallidus internus DBS leads connected to a Medtronic Percept™ PC neurostimulator. During the enrollment and screening procedures, a LFP (8–30 Hz, ≥1.2 μVp) control signal was identified by clinicians in 84.8% of patients on medication (65% bilateral signal), and in 92% of patients off medication (78% bilateral signal). The ADAPT-PD trial sensing data indicate a high LFP signal presence in both on and off medication states of these patients, with bilateral signal in the majority, regardless of PD phenotype.

LFP detected in 84.8% of patients on medication and in 92% of patients off medication

>90% of patients chose to stay on adaptive therapy

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Adaptive Therapy

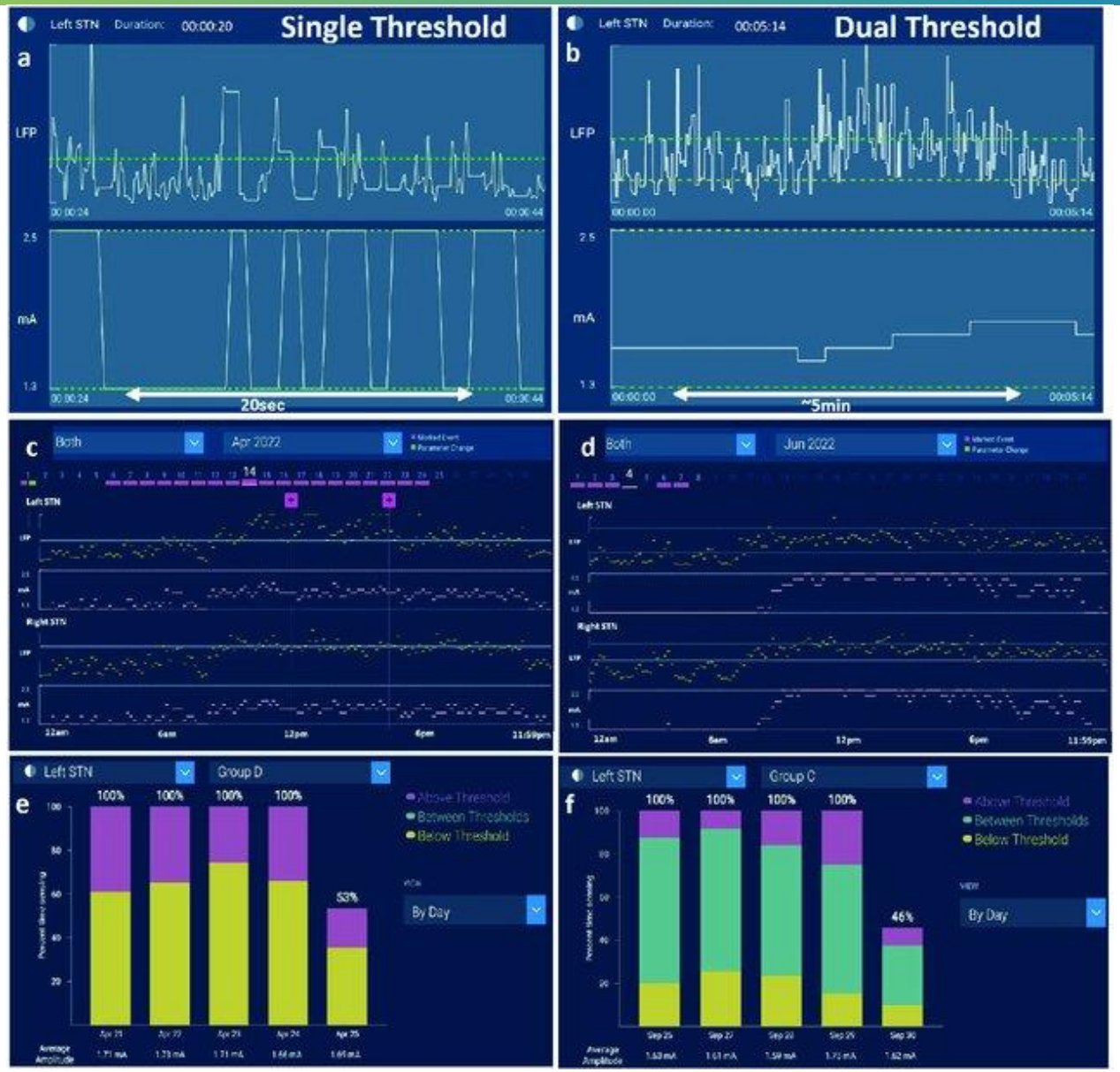

Fig. 3. from above methodology paper by Stanslowski et al 2024. It shows an example of LFP signal visualization during aDBS programming and enables visualization of stimulation amplitude adjustment during LFP signal fluctuation above or below LFP thresholds:
(a) single threshold (t = 20 s)
(a) and dual threshold (t = 5 min)
(b) mode aDBS; Timeline feature demonstrating a 24-h interval of LFP signal fluctuation (yellow)
(c) aDBS stimulation amplitude (pink) for single threshold
(d) dual threshold mode. Note the LFP suppression during night hours.
(e) Chronic LFP chart illustrating time within threshold for single threshold (e) and dual threshold (f) mode aDBS

Data extracted from a single participant in the ADAPT-PD trial.

Adaptive Therapy Just Received CE Mark Approval in the EU on Jan 13, 2025!

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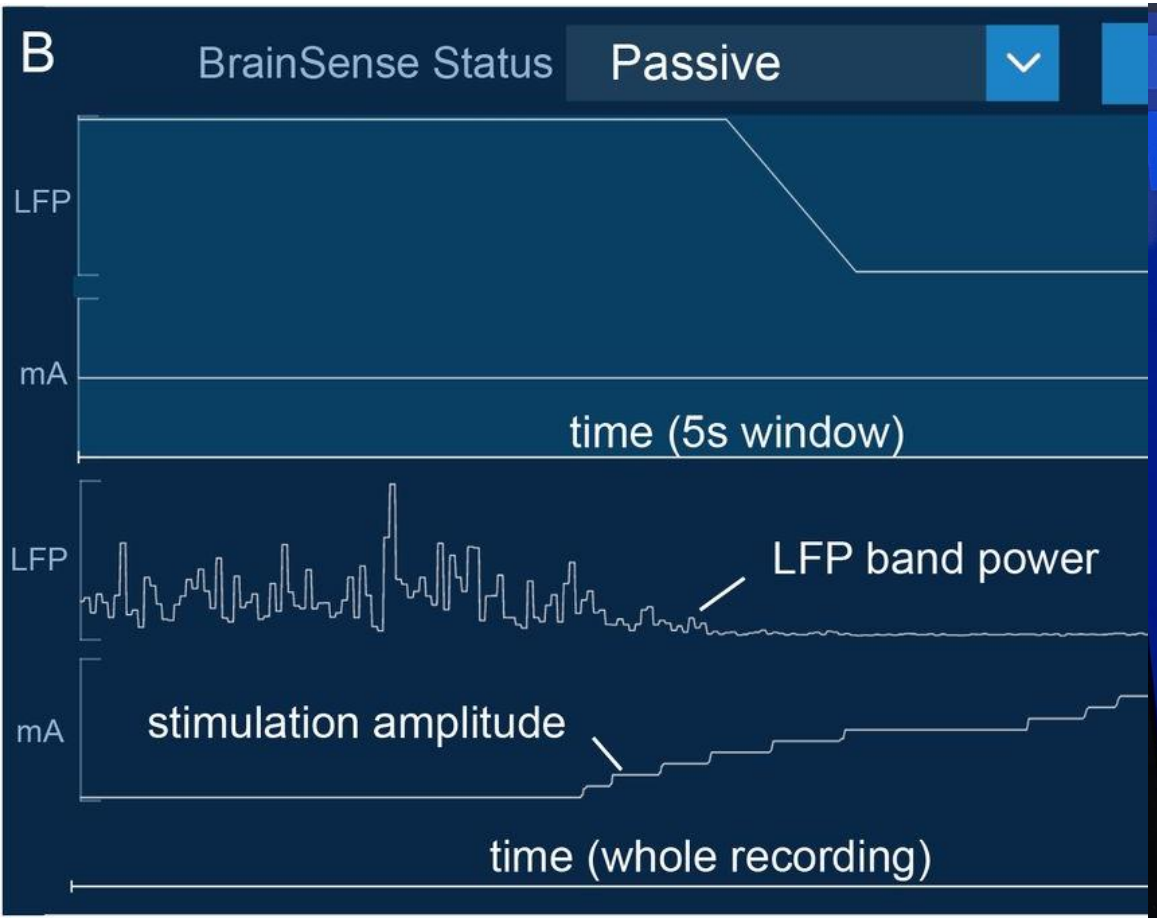
Adaptive Therapy

High amplitude signal with variability is “suppressed” by higher amplitude stimulation



Combining Technologies – Patient Case

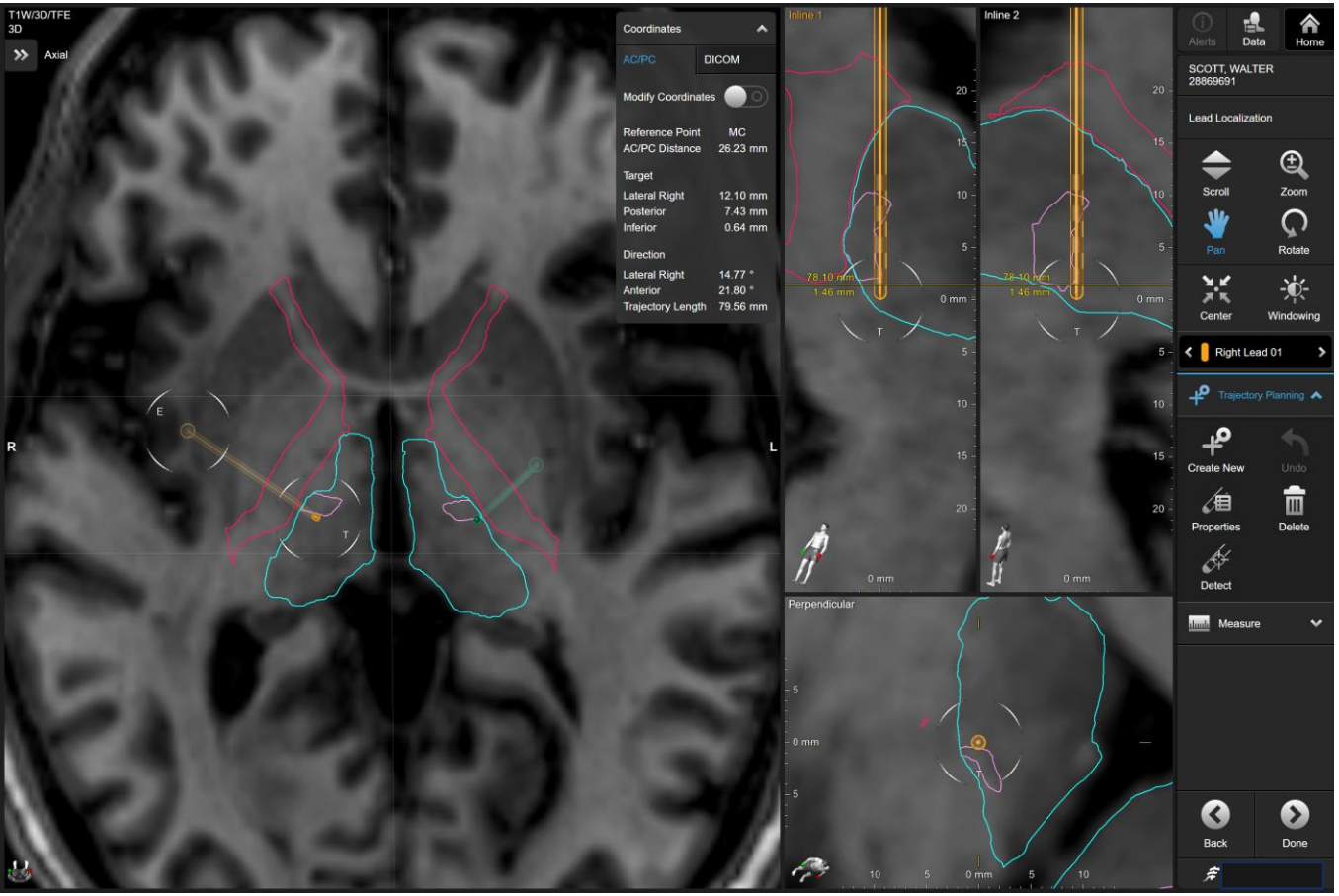
High amplitude signal with variability is “suppressed” by higher amplitude stimulation

- **The Case:** Medically refractory essential tremor (ET) with hx of severe neuropathy. DBS implanted 8 years ago with leads in bilateral VIM. Good tremor control initially, but control has waned over time with tremor progression. Now when he tries to increase stimulation amplitude his speech slurs and his left hand becomes “clumsy”.
- **Problem Assessment:** Bothersome Tremor more on the left hand
- **Current Limitations:** Slurred speech and “clumsy movements”
- **The Goal:** Improve tremor control w/ fewer side effects

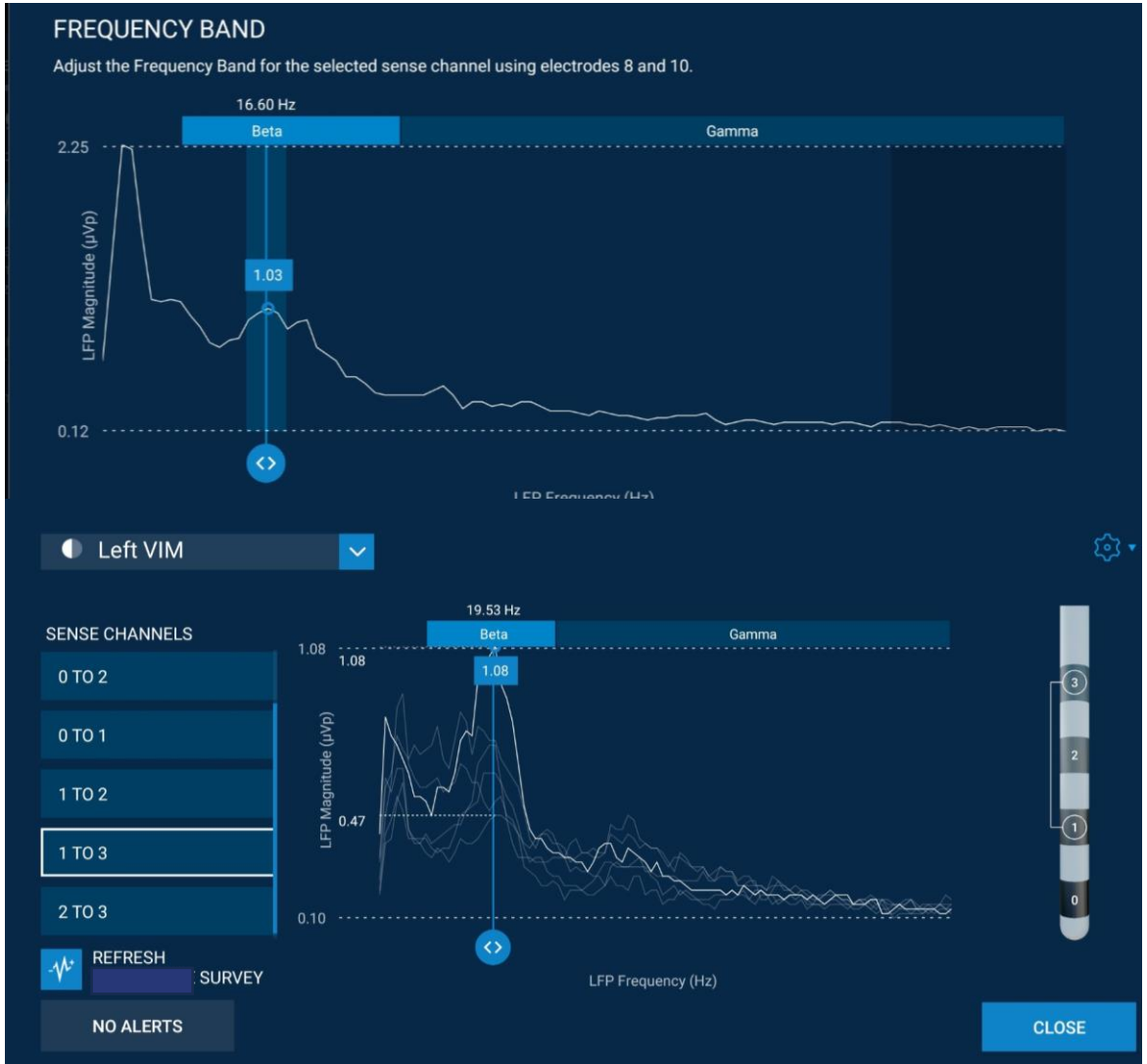
Video of original stimulation settings before changes. →

Combining Technologies – Patient Case

Anatomy Visualization



Physiological marker tracking



Combining Technologies – Patient Case

Outcome: Optimization of DBS settings using a combination of anatomy visualization and physiological marker suppression. Adaptive therapy would potentially help reduce habituation

Off Stimulation

Existing Settings

Final Settings

Future Directions and Take Home Points

Things happening now and in the near future:

- Advancements in device and software technology
- AI Driven solutions for more complex programming shapes
  - AI programming assist
  - Adaptive stimulation

Take Home Points:

- Think of DBS for refractory tremor, when there is increasing motor fluctuations, dynamic dystonia.
- DBS isn't likely to help memory or balance, but it can make it worse.
- New devices capabilities of anatomy visualization, remote programming, and adaptive stimulation can further optimize therapy and improve patient QOL.
- Adaptive therapy might also allow for optimization of things that seem in direct conflict like tremor and dyskinesia or hallucinations and sleep.

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Questions