

WHAT IS NEW IN PARKINSON'S DISEASE TREATMENT?

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**AMERICAN
PARKINSON DISEASE
ASSOCIATION**

Strength in optimism. Hope in progress.

WHAT IS NEW IN PARKINSON'S DISEASE TREATMENT?

- 5 new medications in the past 5 years
 - Inbrija
 - Kynmobi
 - Ongentys
 - Nourianz
 - Dhivy
- On the horizon
 - Subcutaneous levodopa
- New DBS advances
- Focused ultrasound
- Some other hot topics:
 - The vibro-tactile glove
 - Biomarkers for PD
- Advances in our understanding of exercise and diet
 - SPARX2 and SPARX3 trials
 - adherence to MIND or Mediterranean diet delayed disease onset

INBRIJA™ - LEVODOPA INHALATION POWDER

What is it?

- Levodopa inhalation powder to be used as needed in between regular carbidopa/levodopa dosages if Parkinson's symptoms start to return. There is absorption of the medication through the lungs.

What doses are available?

- One dose is two 42 mg capsules, with no more than one dose per OFF period, up to 5 times a day



<https://www.acorda.com/products/products/inbrija>

INBRIJA™ - LEVODOPA INHALATION POWDER

When should I ask my doctor about it?

- If your regular dose of carbidopa/levodopa is not lasting until the next scheduled dose or you're experiencing a return of PD symptoms

Extra notes:

- Device can't be preloaded. Levodopa capsules should only be used with the INBRIJA inhaler and must stay in their blister package until immediately before use. Pulmonary absorption bypasses the GI tract.



<https://www.acorda.com/products/products/inbrija>

KYNMOBI – APOMORPHINE SUBLINGUAL

What is it?

- A sublingual film containing the dopamine agonist apomorphine, that dissolves under the tongue. It is used when needed if there is wearing OFF between doses of Levodopa

What doses are available?

- 10 mg, 15 mg, 20 mg, 25 mg, 30 mg

When should I ask my doctor about it?

- If you are experiencing OFF time between doses



ONGENTYS® - OPICAPONE

What is it?

- A once daily Catechol-O-methyltransferase (COMT) inhibitor to be used in those taking carbidopa/levodopa and experiencing OFF periods

What dose is available?

- 50 mg

When should I ask my doctor about it?

- If you are experiencing OFF time between doses

NOURIANZ® - ISTRADEFYLLINE

What is it?

- A medication with a new mechanism of action, adenosine inhibition, to be used as an add-on treatment to carbidopa/levodopa for those experiencing OFF periods

What doses are available?

- 20 mg and 40 mg tablets
- Recommended dose is 20 mg (up to a maximum of 40 mg)

When should I ask my doctor about it?

- If you are experiencing OFF time between doses

DHIVY – CARBIDOPA/LEVODOPA

What is it?

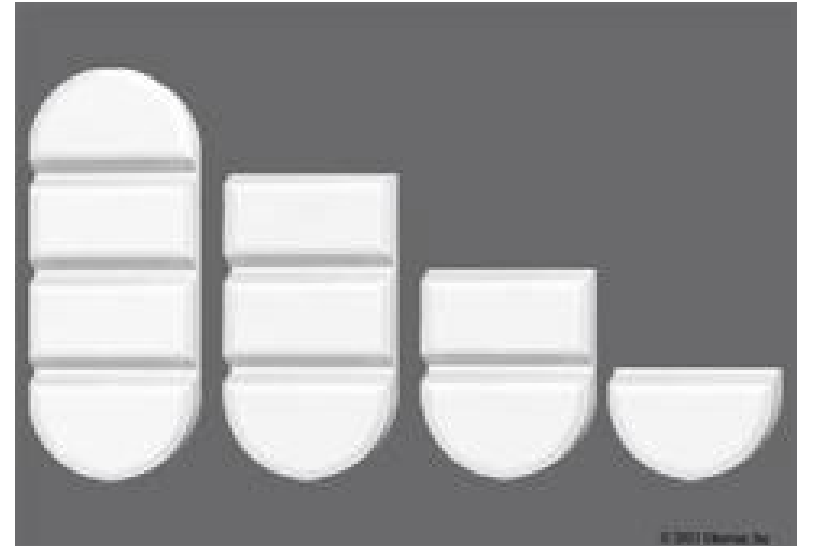
- A carbidopa/levodopa in a scored tablet that can be split into 4 precise segments

What dose is available?

- 25/100, in 6.25/25 segments

When should I ask my doctor about it?

- If you find that you need more precise dosing than you are taking



SUBCUTANEOUS LEVODOPA

Foslevodopa/foscarbidopa, developed by Abbvie, is a formulation of levodopa/carbidopa that allows for subcutaneous (SC) infusion

A similar product is being developed by Neuroderm



Phase 3 study compared subcutaneous Levodopa + placebo tablets with subcutaneous placebo + Levodopa tablets. SQ Levodopa resulted in significantly more ON time without troublesome dyskinesias and less OFF time than the control. Infusion site reactions were very common, but most were mild.

THE LANCET
Neurology

Sub

ARTICLES | [VOLUME 21, ISSUE 12, P1099-1109, DECEMBER 2022](#)

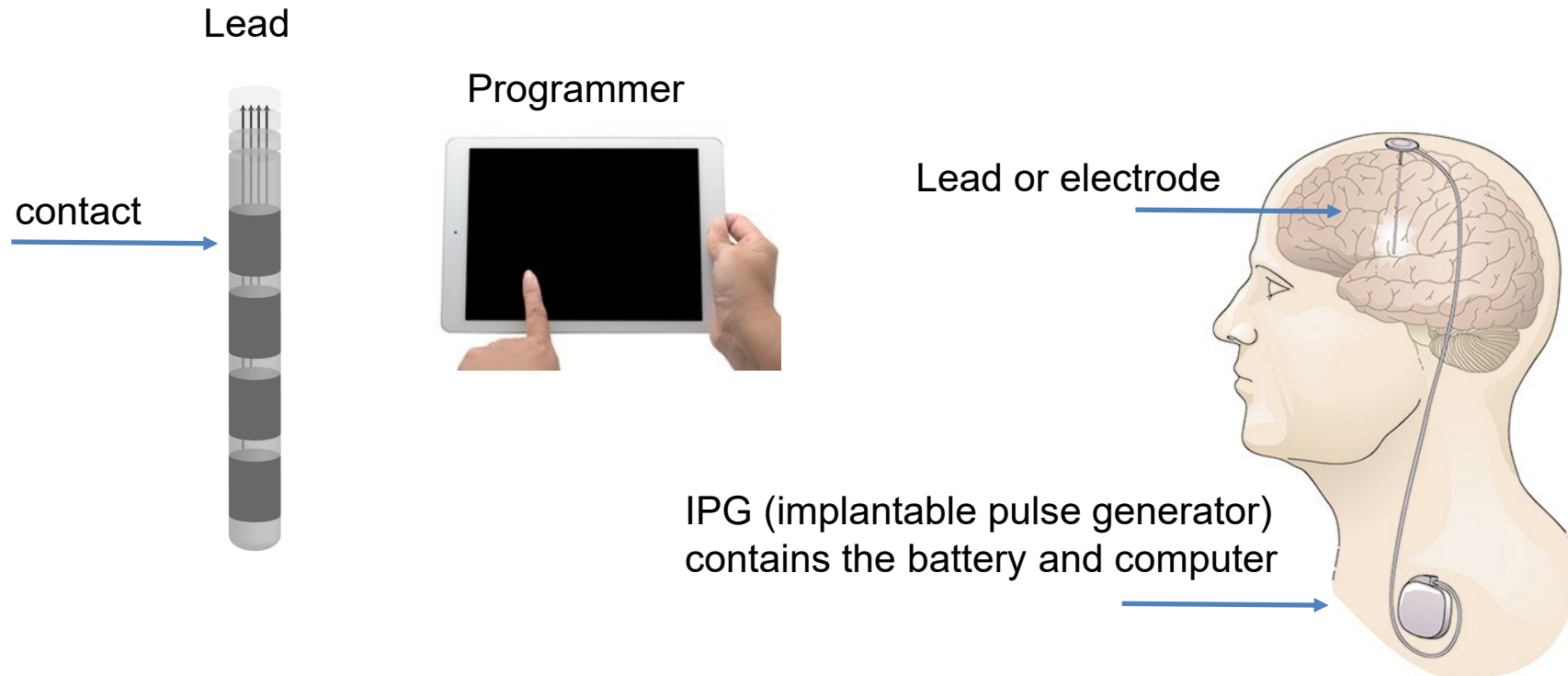
Safety and efficacy of continuous subcutaneous foslevodopa-foscarbidopa in patients with advanced Parkinson's disease: a randomised, double-blind, active-controlled, phase 3 trial

[Michael J Soileau, MD](#)   • [Jason Aldred, MD](#) • [Kumar Budur, MD](#) • [Nahome Fisseha, PharmD](#) • [Victor SC Fung, FRACP](#) • [Anna Jeong, MD](#) • et al. [Show all authors](#)

Published: December, 2022 • DOI: [https://doi.org/10.1016/S1474-4422\(22\)00400-8](https://doi.org/10.1016/S1474-4422(22)00400-8) •



DEEP BRAIN STIMULATION



<https://www.ninds.nih.gov/About-NINDS/Impact/NINDS-Contributions-Approved-Therapies/DBS>

NEW DEVELOPMENTS IN DEEP BRAIN STIMULATION

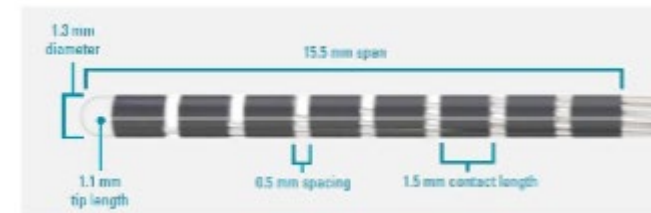
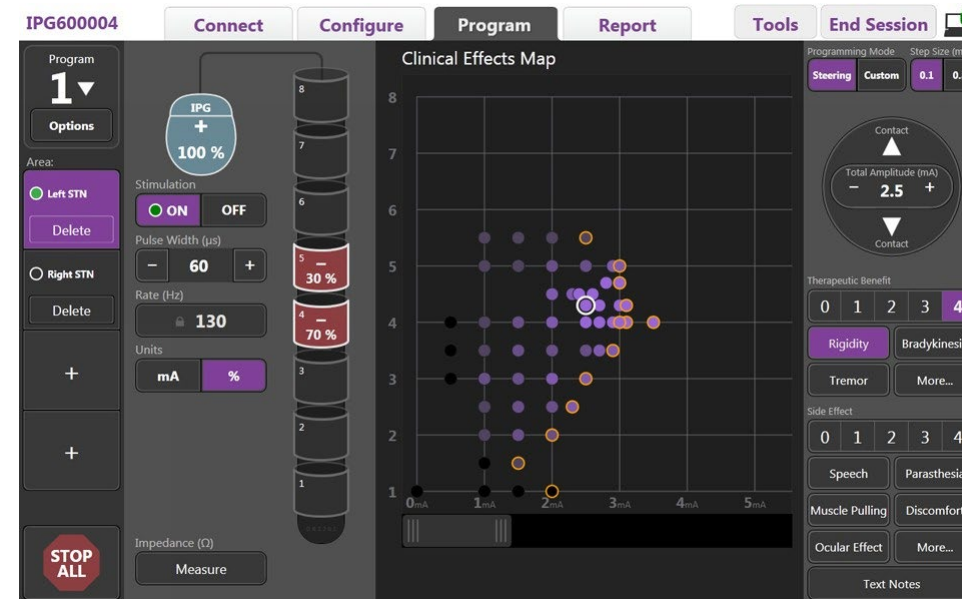
Three companies offer DBS for PD:

- Medtronic
- Abbott
- Boston Scientific
- In 2016, FDA approved DBS for **earlier stage Parkinson's disease**
- All newly-implanted systems are now **MRI-conditional**
- Medtronic and Boston Scientific have a choice of a **rechargeable battery**
- One **dual channel IPG** can control electrodes on both sides of the brain
- Surgery can be performed in the bore of a CT scanner or MRI machine
 - Allows for visualization of the advancing electrode
 - Allows for the patient to be **asleep during the procedure**

NEW DEVELOPMENTS IN DEEP BRAIN STIMULATION

Boston Scientific

- Vercise™ system approved in 2017
- Electrode has more contacts (8 instead of 4)
- MICC – multiple independent current control
 - Each electrode has its own energy source
 - Much more customizable field of stimulation

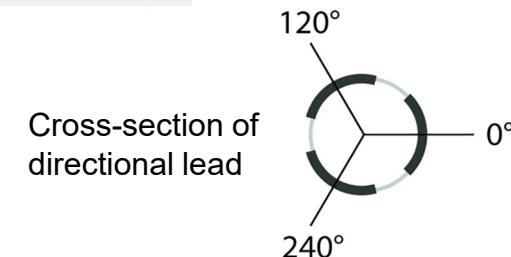
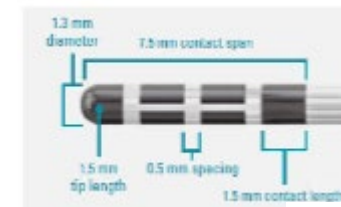


<https://www.bostonscientific.com/en-EU/products/deep-brain-stimulation-systems/Vercise-PC-DBS.html>

NEW DEVELOPMENTS IN DEEP BRAIN STIMULATION

Boston Scientific

- The Cartesia™ lead was approved in 2019
- Uses directional leads
 - The two middle contacts are divided into three sections around the circumference of the electrode
 - Stimulation can be applied to one, two or three of the sections
 - Allows for the field of stimulation to be steered in a particular direction, thereby reducing side effects of stimulation



NEW DEVELOPMENTS IN DEEP BRAIN STIMULATION

Abbott

- Infinity™ system approved in 2016
- First to introduce directional leads
- Wireless communication system between the programmer and the patient
 - Allows patient to move around during programming
- Patient can make some changes on their own



<https://www.neuromodulation.abbott/us/en/hcp/products/dbs-movement-disorders/st-jude-medical-infinity-dbs-system>

NEW DEVELOPMENTS IN DEEP BRAIN STIMULATION

Medtronic:

- Percept™ PC Neurostimulator with Brainsense™ Technology approved in 2020
- The system captures local field potentials (LFPs) from the neurons that are in contact with the DBS electrode
- DBS adjustments could be made based on LFP patterns as they correlate with reported symptoms and medication ingestion



[Medtronic.com/percept](https://www.Medtronic.com/percept)

FOCUSED ULTRASOUND

- Focused beams of ultrasound energy converge within the brain tissue to form a small lesion that interferes with the brain circuitry
- Approved for tremor control in PD in 2018
- In 2021, approved for bradykinesia, rigidity and dyskinesias



VIBROTACTILE GLOVE



VIBROTACTILE GLOVE

Two feasibility studies were conducted (Pfeiffer KJ et al [Front Physiol.](#) 2021; 12: 624317. doi: [10.3389/fphys.2021.624317](#))

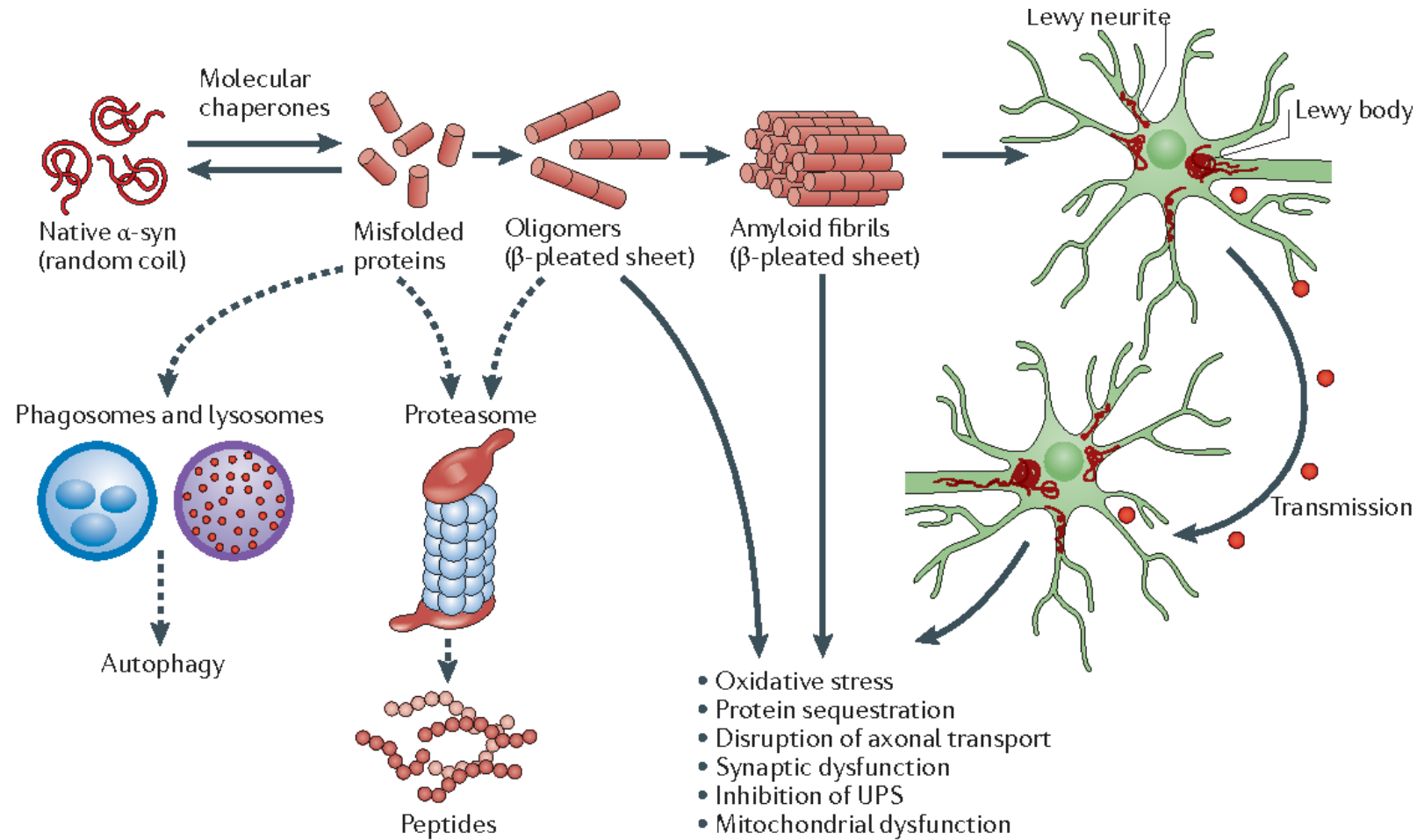
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- 8 PWP were studied
- Motor ability improved in both studies
- No side effects were noted

Three additional studies are being planned, but recruitment is not yet open

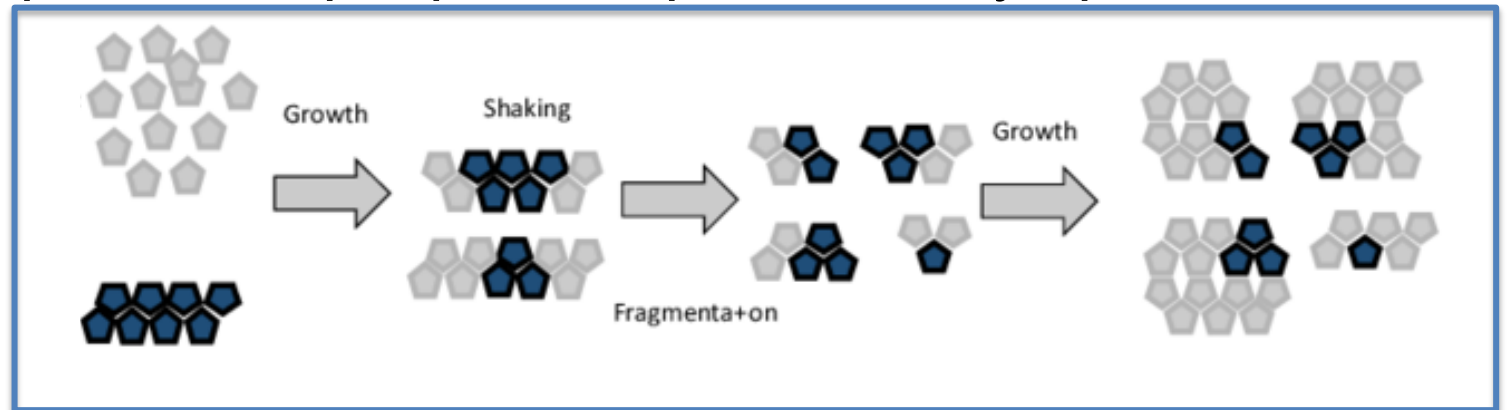
- Vibrotactile coordinated reset for the treatment of Advanced PD (NCT05504902)
- VCR: A treatment for early stage PD (NCT05545826)
- VCR for the treatment of post surgery refractory PD patients (NCT05558189)

ALPHA-SYNUCLEIN AGGREGATION



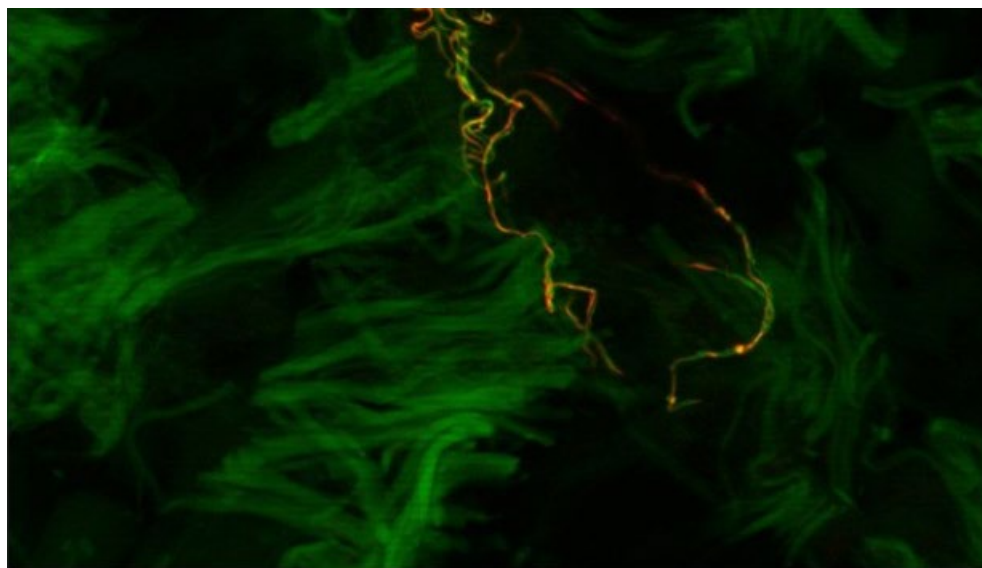
SYN-TAP

- Misfolded alpha-synuclein can be present in blood and cerebrospinal fluid (CSF)
 - levels are very low and difficult to detect
 - Blood levels are lower than CSF levels
- Seed amplification assay (SAA)
 - Sample of patient's CSF is mixed with normal proteins
 - If there is misfolded alpha-synuclein in the sample, it triggers aggregation (clumping) which can be detected using a fluorescent probe
 - New study shows that it is positive in people with pre-motor symptoms



SYN-ONE TEST

- Detection of phosphorylated alpha-synuclein in dermal nerves found in skin biopsy
- Three 3-mm biopsies from near the shoulder, the knee, and the ankle



Phosphorylated alpha
synuclein in a skin biopsy

EXERCISE: MOVE IT OR LOSE IT!



- Exercise and movement are vital to maintain quality of life
- Many non-motor features of PD such as constipation, fatigue and depression, improve with exercise and fitness

SPARX2 STUDY

128 early PD patients, not on dopamine medications, were enrolled in either:

- High-intensity treadmill exercise (4 days per week, 80%-85% maximum heart rate)
- moderate-intensity treadmill exercise (4 days per week, 60%-65% maximum heart rate)
- wait-list control

After 6 months, high intensity group had a 0.3 point change in their United Parkinson's Disease Rating Scale. Control group had a 3 point change ([JAMA Neurol](#). 2018 Feb; 75(2): 219–226)



[JAMA Neurol. 2018 Feb; 75\(2\): 219–226.](#)

Published online 2017 Dec 11. doi: [10.1001/jamaneurol.2017.3517](https://doi.org/10.1001/jamaneurol.2017.3517)

PMCID: PMC5838616

PMID: [29228079](https://pubmed.ncbi.nlm.nih.gov/29228079/)

Effect of High-Intensity Treadmill Exercise on Motor Symptoms in Patients With De Novo Parkinson Disease
A Phase 2 Randomized Clinical Trial

SPARX3 TRIAL

Washington University St. Louis

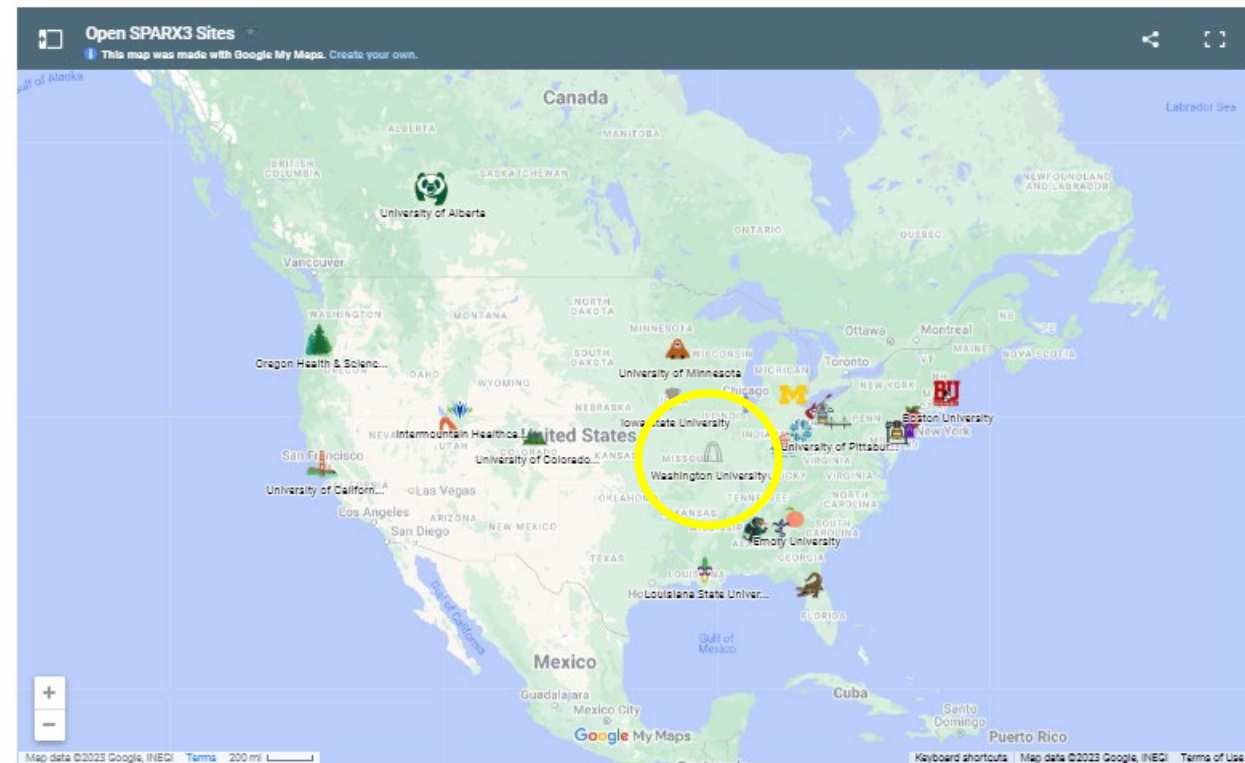
Contact: Martha Hessler 314-286-1478
mjhessler@wustl.edu

PI: Gammon Earhart, PhD



Study in Parkinson's Disease of Exercise Phase 3 Clinical Trial

We are pleased to announce 25 sites are open for enrollment for SPARX3.



SPARX3 STUDY

Looking for people with:

- PD diagnosis within the last 3 years
- Aged 40-80
- Positive DaTscan
- Not currently on any PD medication and not expected to require medication for the next 6 months
- But – can have taken PD medication in the past – but none within the 60 days prior to starting the study



DIET

Mediterranean diet

- Vegetables
- Fruits
- Whole grains
- Legumes such as beans, peas and lentil
- Nuts
- Low-fat proteins, such as fish and poultry
- Olive oil

MIND diet

- Green, leafy vegetables
- All other vegetables
- Berries
- Whole grains
- Beans
- Nuts
- Poultry
- Fish
- Olive oil
- Wine



RESEARCH ARTICLE | [Open Access](#) | [CC](#) [i](#)

MIND and Mediterranean Diets Associated with Later Onset of Parkinson's Disease

Avril Metcalfe-Roach BSc, Adam C. Yu MSc, Ella Golz BA, Mihai Cirstea MS, BSc, Kristen Sundvick BSc, Daniel Kliger BA, Liam H. Foulger, Melissa Mackenzie MD, B. Brett Finlay PhD ... [See all authors](#) ▾

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AMERICAN PARKINSON DISEASE ASSOCIATION

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