6 May 2026

Options of Device-Aided Therapy in Advanced Parkinson's Disease

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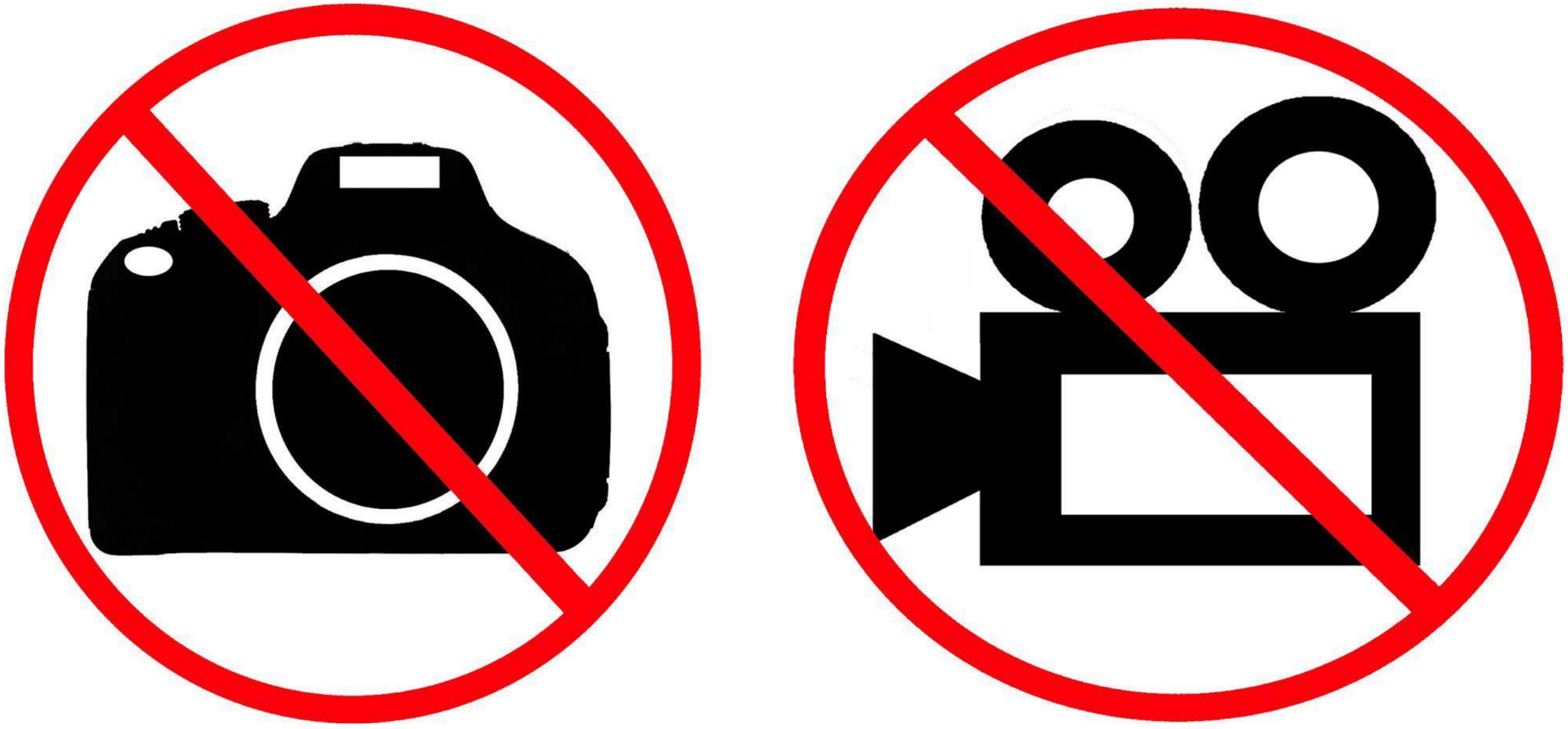


Disclosure

- Associate Professor Phokaewvarangkul had received consultancy fees from Medtronic, Boston Scientific, Britannia Pharmaceuticals, and Eisai Asia.
- She received a speaking honorarium from Medtronic, Boston Scientific, Boehringer Ingelheim, Roche (Thailand), BL HUA, GlaxoSmithKline, Ipsen Pharma, Novartis, Servier, Berlin Pharmaceutical, Abbott, Sandoz, Pfizer, Eisai (Thailand), TEVA, Abbvie, STADA, Mitsubishi Tanabe Pharma, and Bgrimm pharma.
- She is affiliated with research supported by Insightec.

Outline of Talk

- Introduction to Device-Aided Therapy (DAT) for Parkinson’s Disease
- Understanding in infusion therapy
- Understanding in DBS therapy
- Understanding in MRgFUS therapy
- Understanding in Upcoming Advanced therapy

Introduction to Device-Aided Therapy (DAT) for Parkinson's Disease

Device-aided treatment for Parkinson's disease

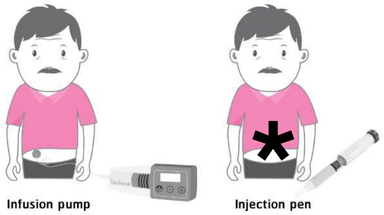
Infusion therapies

PEG-J tube

LCIG

LECIG

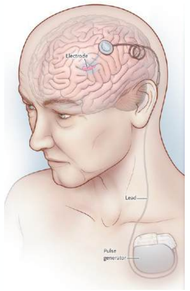
Subcutaneous infusion



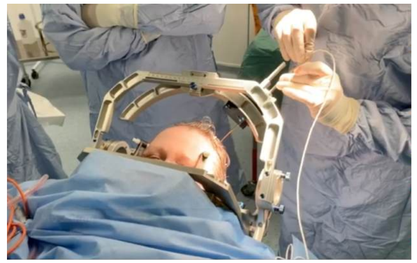
CSAI

Foslevodopa/
foscarbidopa

Functional neurosurgery

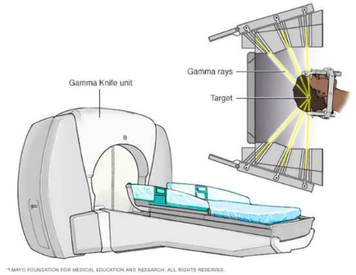


DBS



RF lesioning

MRgFUS



Gamma Knife
Radio Surgery

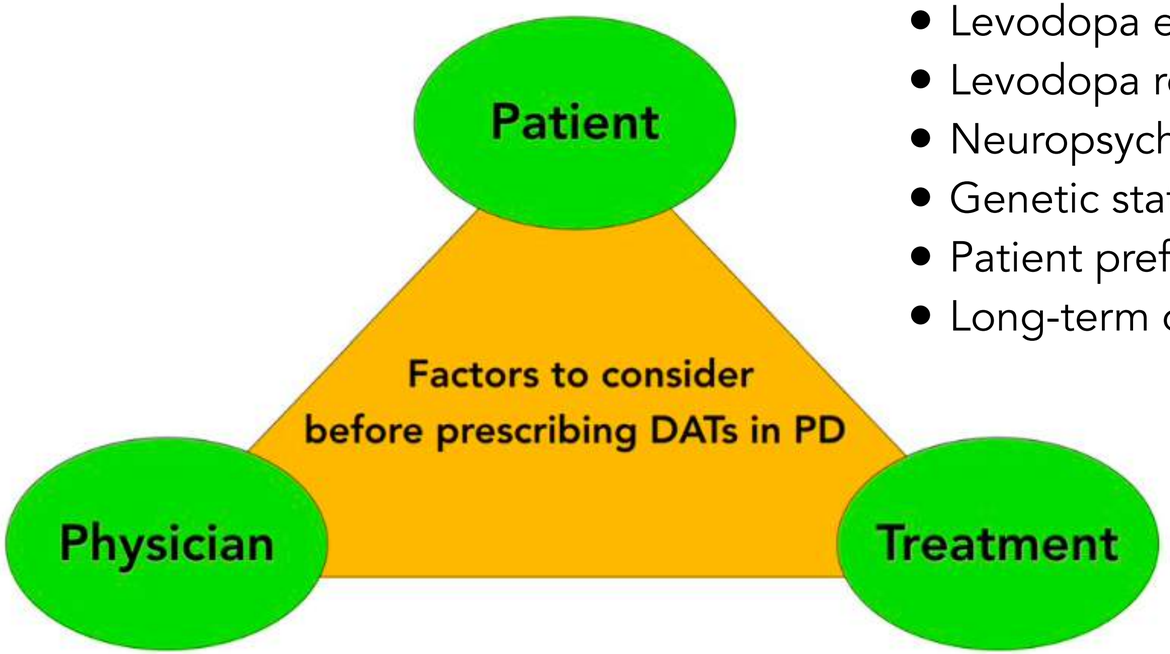
Upcoming Advanced Therapy!

Stem Cell Therapy
iPSCs & hESCs

Granted conditional approval in Japan

Gene Therapy

Factors for consideration



- Diagnosis
- General medical conditions
- Levodopa equivalent dosage
- Levodopa responsiveness
- Neuropsychiatric status
- Genetic status
- Patient preference
- Long-term device care plan

- Physician expertise and experience
- Availability of experienced nurses or PD nurse specialists
- Hospital facilities

- Availability
- Treatment invasiveness
- Risks and benefits compared to other treatments
- One-time or longitudinal treatment
- Reimbursement methods
- Prognosis after each treatment

Phokaewvarangkul O, et al. J Neural Trans 2024; doi:10.1007/s00702-024-02782-2.

Problems	CSAI	LCIG	LECIG	DBS
General information				
Old age > 75 years				
Treatment invasiveness				
No family supports				
Independent needs				
History of abdominal surgery				
Motor symptoms				
Severe motor fluctuations				
Refractory tremor				
Severe dyskinesia				
Non motor symptoms				
Mild cognitive impairment				
Dementia				
Uncontrolled psychiatric issues				
Suicidal thought				
Orthostatic hypotension				
Levodopa responsive poor balance and falls				
Levodopa unresponsive poor balance and falls				

Phokaewvarangkul O, et al. J Neural Trans 2024; doi:10.1007/s00702-024-02782-2.

Understanding in infusion therapy

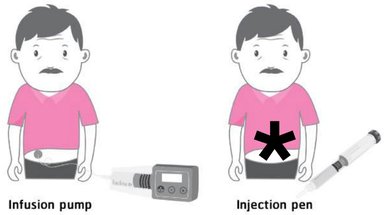
Why Use Infusion Therapies?

Enteral Feeding Tube/PEG-J tube

LCIG

LECIG

Subcutaneous infusion



CSAI

Foslevodopa/ foscarbidopa

- Infusion therapy delivers medication more continuously and provides more consistent and reliable symptom relief.
- Infusion therapy also reduces the need to take oral medication so many times throughout the day.
- Infusion therapies are usually more effective than long-acting PD pills and patches.

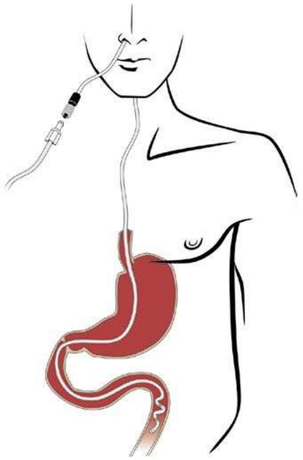
Senek M, et al. Sci Rep 2020; 10: 18057
Antonini A, et al. J Neurl Trans 2023;130:1349–1358
Auffret M, et al. J Neural Trans 2023;130:1411-32.
Phokaewvarangkul O, et al. J Neural Trans 2024; doi:10.1007/s00702-024-02782-2.

Understanding Levodopa-Carbidopa Intestinal Gel treatment

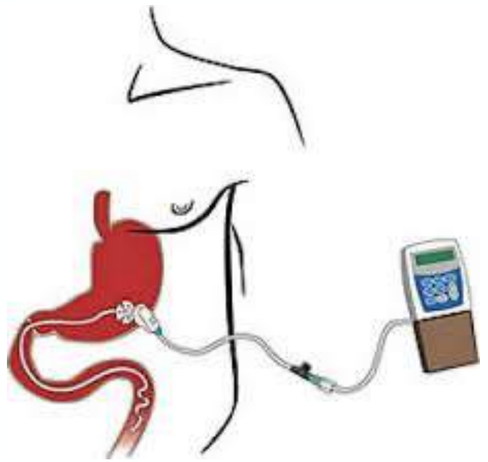
LCIG specifications and contents

Types of injection	Continuous infusion pump
Indications	Motor complications despite optimized oral medications
Contraindication	Dementia, a poor response to levodopa, difficulties handling the infusion device, previous abdominal surgery
Contents	A 100 ml cassette contains 2000 mg of levodopa and 500 mg of carbidopa (Levodopa 20 mg/ml & carbidopa 5 mg/ml)
Doses	From calculated daily consumption (Usage hour 16-24 hr per day)
Equipments	Percutaneous endoscopic gastrostomy-Jejunostomy (PEG-J)

Naso-jejunal tube
(Test treatment)



PEG-J tube
(Permanent treatment)



Timpka J, et al. Inter Rev Neurol 2017;132:453-74.

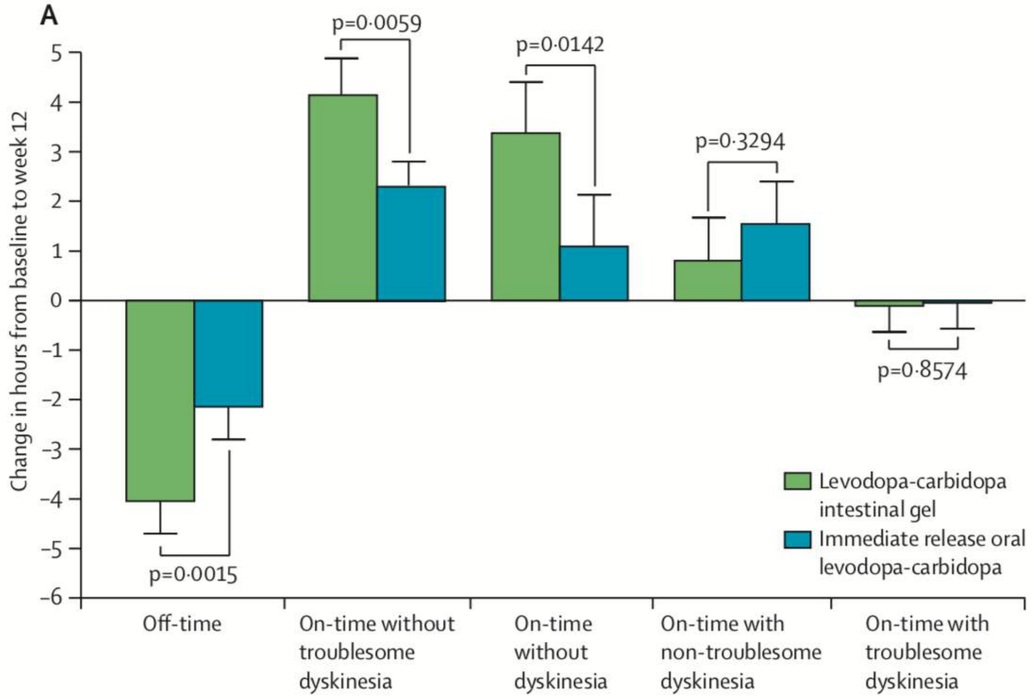
Continuous intrajejunal infusion of levodopa-carbidopa intestinal gel for patients with advanced Parkinson's disease: a randomised, controlled, double-blind, double-dummy study

C Warren Olanow, Karl Kieburtz, Per Odin, Alberto J Espay, David G Standaert, Hubert H Fernandez, Arvydas Vanagunas, Ahmed A Othman, Katherine L Widnell, Weining Z Robieson, Yili Pritchett, Krai Chatamra, Janet Benesh, Robert A Lenz, Angelo Antonini, for the LCIG Horizon Study Group

12-week double-blind study (Oral LD +LCIG vs. Oral LD + Placebo gel)

Significant improvement

- Reduced off time (hour per day)
- Increased on time (hour per day)
- Improved PDQ-39 (QOLs)
- Improved clinical global impression-improvement (CGI-I)



69 (88.7%) of patients had device-related complications

Olanow C, et al. Lancet Neurol 2014;13:141-9.

LCIG adverse events

Naso-jejunal tube

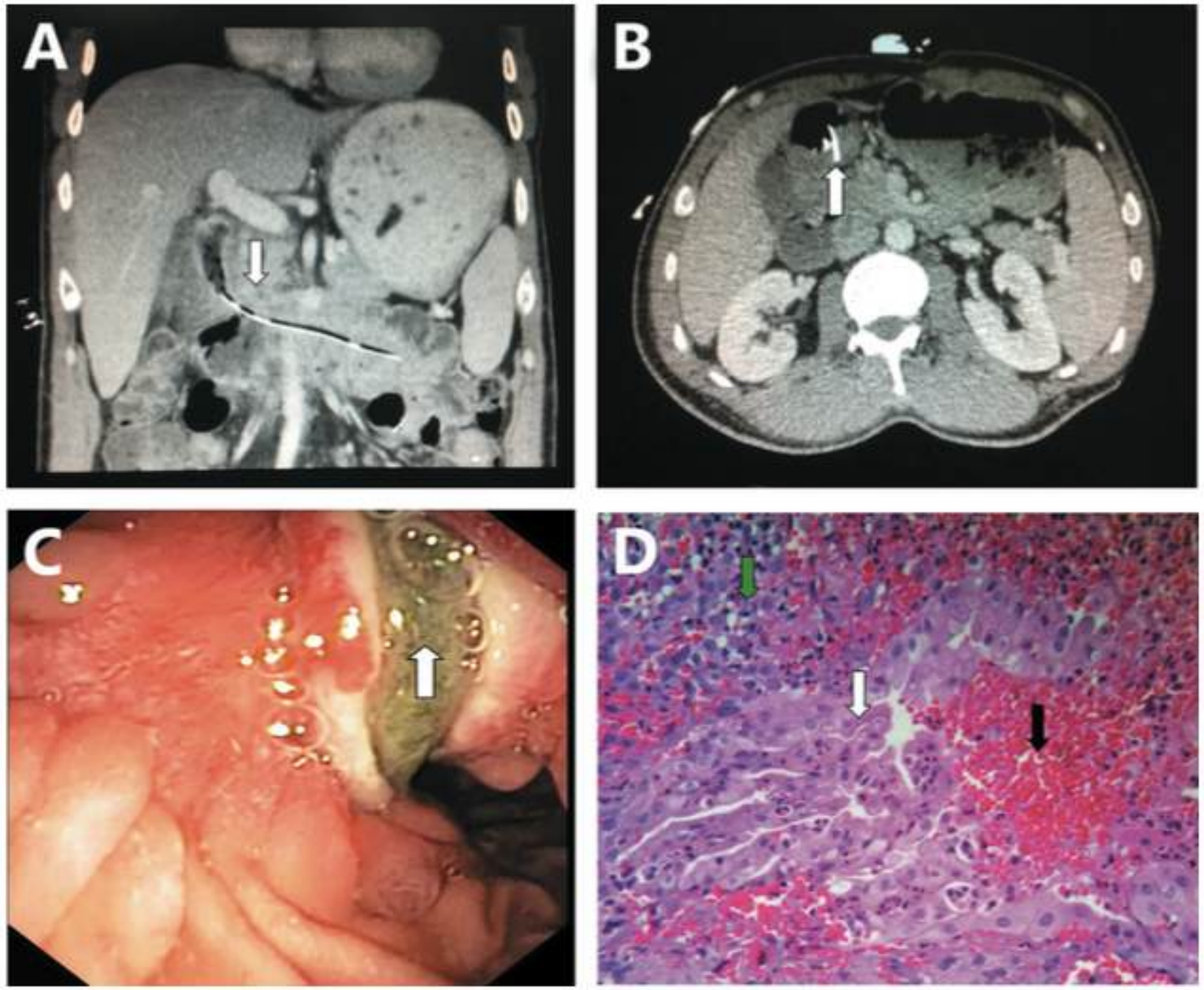
- Oropharyngeal pain
- Abdominal distension
- Abdominal pain
- Abdominal discomfort
- Gastrointestinal injury
- Esophageal hemorrhage
- Anxiety, dysphagia, vomiting

PEG-J tube

- Abdominal distension
- Abdominal pain
- Abdominal discomfort
- Flatulance
- Pneumoperitonium
- Dislocation or obstruction of the intestinal tube

Olanow C, et al. Lancet Neurol 2015;13:141-9
Slevin j, et al. J Parkinson Dis 2015; 5:165-74
Abbvie Product characteristics 2016

PEG-J tube related complication



Recurrent Pancreatitis as a Rare Complication of Duodenal Levodopa Infusion Treatment

Onanong Jitkritsadakul, MD,[1] Priya Jagota, MD[1]
Sitthi Petchrutchatachart, MD,[1] Lalana Sansopha, MD[2]
Rungsun Rerknimitr, MD,[3] Roongroj Bhidayasiri, MD, FRCP, FRCPI[1,4,*]

[1]Chulalongkorn Center of Excellence on Parkinson's Disease and Related Disorders Chulalongkorn University and King Chulalongkorn Memorial Hospital Bangkok, Thailand; [2]Department of Pathology, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand; [3]Division of Gastroenterology, Department of Medicine, Faculty of Medicine Chulalongkorn University and King Chulalongkorn Memorial Hospital Thai Red Cross Society, Bangkok, Thailand; [4]Department of Neurology, Geffen School of Medicine at UCLA Los Angeles, California, USA

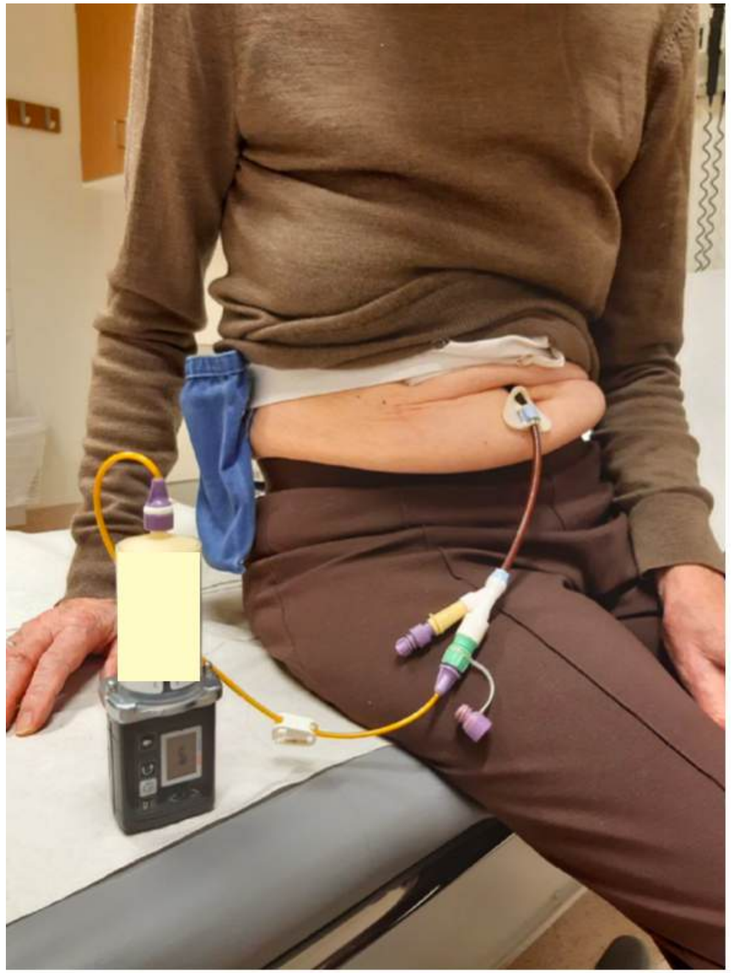
Phokaewvarangkul (Jitkritsadakul) O, et al. Mov Disord 2013;28:1308-10.

Understanding Levodopa-Entacapone-Carbidopa Intestinal Gel treatment

LECIG specifications and contents

LECIG infusion was first approved for use in Sweden in 2018 and has now received marketing authorisation in several other European countries and Australia.

Types of injection	Continuous infusion pump
Indications	The treatment of advanced PD with severe motor fluctuations and/or dyskinesia
Contraindication	Dementia, a poor response to levodopa, difficulties handling the infusion device, previous abdominal surgery
Contents	A 47 ml cartridge contains 940 mg levodopa (20 mg/ml), 235 mg carbidopa (5 mg/ml), and 940 mg entacapone (20 mg/ml).
Doses	From calculated daily consumption (Usage hour 24 hr per day)
Equipments	Percutaneous endoscopic gastrostomy-Jejunostomy (PEG-J) — Same as LCIG



Senek M, et al. Mov Disord 2017; 32:283–286.
Nyholm D, Jose W. Ther Advance Neurol Disord 2022;15:1-15.

LECIG: Real-World Experiences

LECIG vs. LCIG

- The LECIG infusion pump is smaller and lighter than the LCIG infusion pump.
- The dose of LECIG decreased by 35%
- Equal in treatment response scale
- Compatibility with an existing PEG-J tube

LECIG vs. BMT

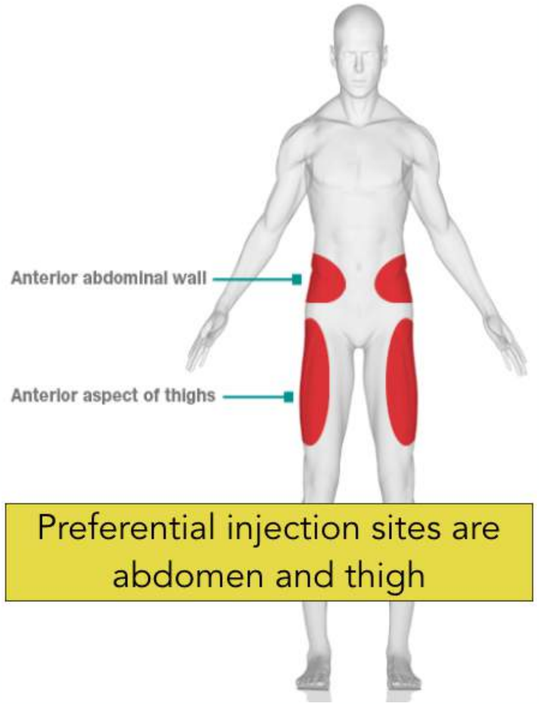
- The significant daily off hours reduction
- Significant reduction in the duration and severity of peak-dose dyskinesia
- Improvement of freezing
- Significant improvements can be observed in H&Y scale scores in both the on and off states

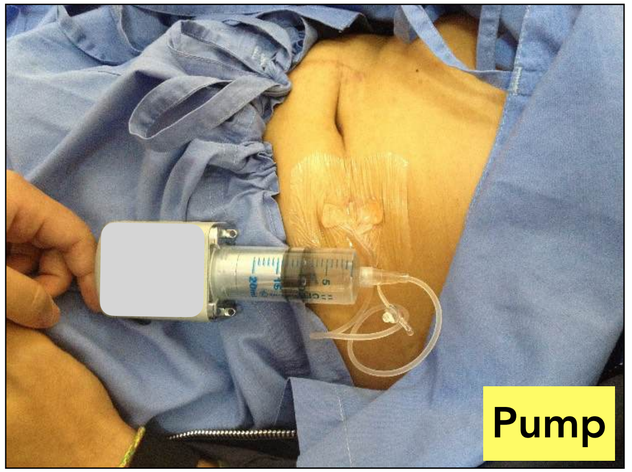
Szatmari S, et al. Pharmaceutics 2024,16,453.
Jose W. J Neural Transmission 2023;130:1379-82.
Nyholm D, et al. Ther Advance Neurol Disord 2022;15:1-15.
Senek M, et al. Mov Disord 2017; 32:283–286.
Senek M, et al. Sci Rep 2020; 10: 18057

Understanding subcutaneous injection of Apomorphine

Apomorphine specifications and contents

Types of injection	Continuous infusion pump
Indications	Motor complications despite optimized oral medications
Contraindication	Dementia, a poor response to levodopa, difficulties handling the infusion device (** drug-related dyskinesia, hallucination, and ICDs)
Contents	10 mg/ml solution 5 ml per ampule 1:1 NSS Dilution 1mg = 0.2 ml (1 mg of apomorphine equal to 10 mg LED)
Doses	Usually 4-8 mg/h Maximum 16 -24 h per day
Equipments	Needle and a continuous pump





Bhidayasiri R, et al. Clin Neuropharm 2015;38:89-103.
Bhidayasiri R, et al. Parkinsonism Relat Disord 2016;33:S42-S48.
Timpka J, et al. Inter Rev Neurol 2017;132:453-74.

Continuous subcutaneous Infusion of Apomorphine provides both short-term and long-term benefits for PD-related symptoms

Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial

Regina Katzenschlager, Werner Poewe, Olivier Rascol, Claudia Trenkwalder, Günther Deuschl, K Ray Chaudhuri, Tove Henriksen, Teus van Laar, Kevin Spivey, Senthil Vel, Harry Staines, Andrew Lees

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Long-term safety and efficacy of apomorphine infusion in Parkinson's disease patients with persistent motor fluctuations: Results of the open-label phase of the TOLEDO study

Regina Katzenschlager [a,*], Werner Poewe [b], Olivier Rascol [c], Claudia Trenkwalder [d], Günther Deuschl [e], K Ray Chaudhuri [f], Tove Henriksen [g], Teus van Laar [h], Donna Lockhart [i], Harry Staines [j], Andrew Lees [k]

12-week double-blind phase and the 52-week open-label phase (Apomorphine vs. Placebo)

Significant improvement in the following parameters

- Reduced off time (hour per day)
- Increased on-time (hour per day)
- Reduced levodopa equivalent dose (mg)
- Improved Patient Global Impression
- No any unexpected safety signals

Significant improvements in the following parameters were sustained for up to 64 weeks.

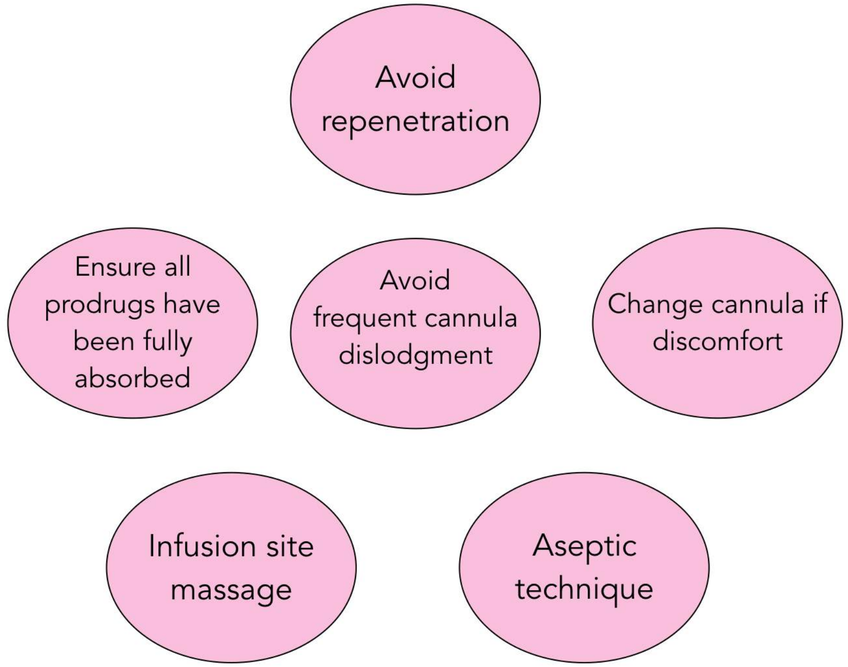
- Daily OFF time reduction of 3.66 hr (2.72) hours
- Daily ON time without troublesome dyskinesia increment of 3.31 hr (3.12)
- Daily LED dosage reduction by 543 mg (±674)
- Daily levodopa dosage reduction by 273 mg (±515)

Katzenschlager R, et al. Lancet Neurol 2018;17:749-59.
Katzenschlager R, et al. Parkinsonism Relat Disord 2021;83:79-85.

Understanding continuous subcutaneous injection of foslevodopa/foscarbodopa

Foslevodopa-foscarbidopa specifications and contents

Types of injection	Continuous infusion pump
Indications	Motor complications in PD patients
Contraindication	Hypersensitivity, narrow-angle glaucoma, severe heart failure, acute stroke, severe cardiac arrhythmia, history of melanoma
Contents (Prodrugs)	• 1 ml contains 240 mg foslevodopa and 12 mg foscarbidopa. • 1 ml of prodrugs equivalent to approximately 170 mg levodopa and 9 mg carbidopa per 1 ml. • Solution for injection 10 ml
Doses	0.6 ml = 100 mg LED Usually 24 hours per day (The maximum recommended daily dose of foslevodopa is 3,525 mg per day equivalent to approximately 2,500 mg levodopa daily).
Equipments	Needle and a continuous pump



Recommended Practices to Reduce the Risk of Infusion-Site Adverse Events

Rosebraugh M, et al. *Ann Neurol* 2021; 90: 52–61.

Fung V, et al. PRDOA 2024;10:100239.

https://docetp.mpa.se/LMF/Produodopa.pdf

Continuous subcutaneous injection of foslevodopa/foscarbodopa provide short-term and long-term benefits for PD-related symptoms

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

A 12-week RCT

Compared to levodopa-carbidopa, there is significant improvement in the following parameters

- Greater reduction in daily OFF time
- Greater increase in daily ON time without troublesome dyskinesia
- The most frequent adverse events are infections and infestations

Neurol Ther (2023) 12:1937–1958
https://doi.org/10.1007/s40120-023-00533-1

ORIGINAL RESEARCH

Continuous Subcutaneous Foslevodopa/Foscarbidopa in Parkinson's Disease: Safety and Efficacy Results From a 12-Month, Single-Arm, Open-Label, Phase 3 Study

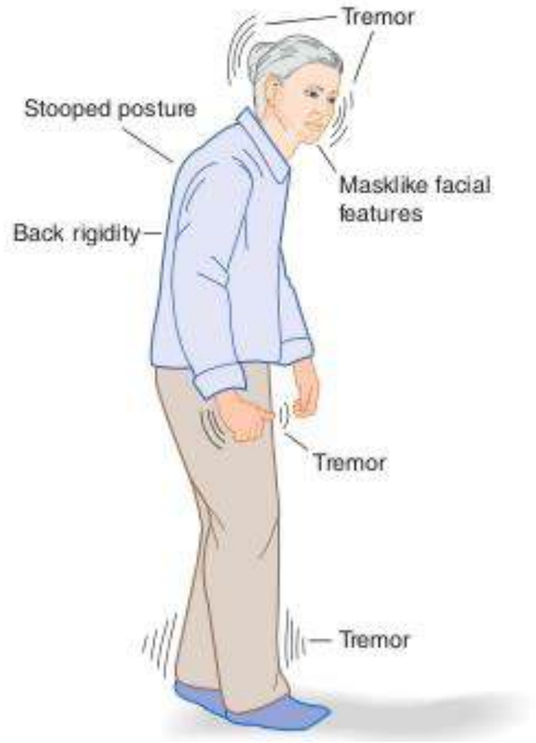
54-week open-label study

Significant improvements in the following parameters compared to baseline

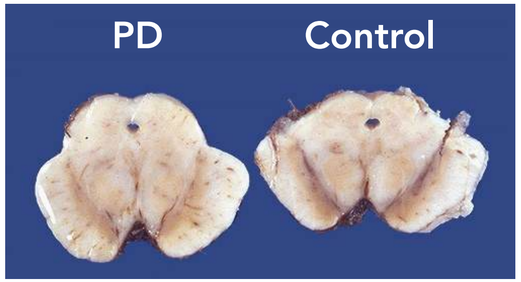
- Daily OFF time reduction of 3.5 hr (±3.1) hours
- Daily ON time without troublesome dyskinesia increment of 3.8 hr (±3.3) hours
- 50% of patients reported improved morning akinesia
- Improvement in sleep and QOLs

Soileau M, et al. Lancet Neurol 2022;21:1099-109.
Aldred J, et al. Neurol Ther 2023;12:1937-58.

Understanding in DBS therapy

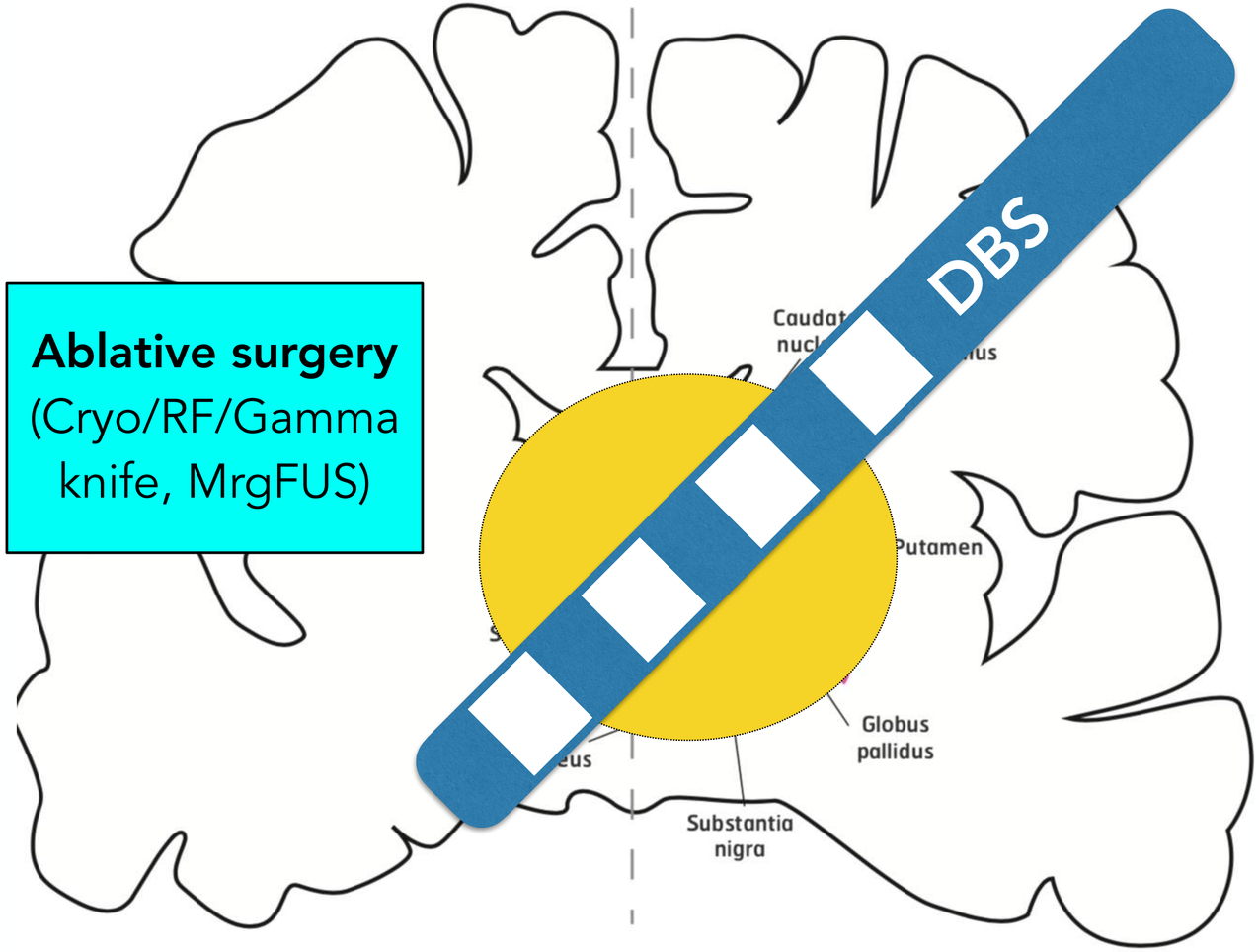


Loss of dopaminergic neurons in SNc



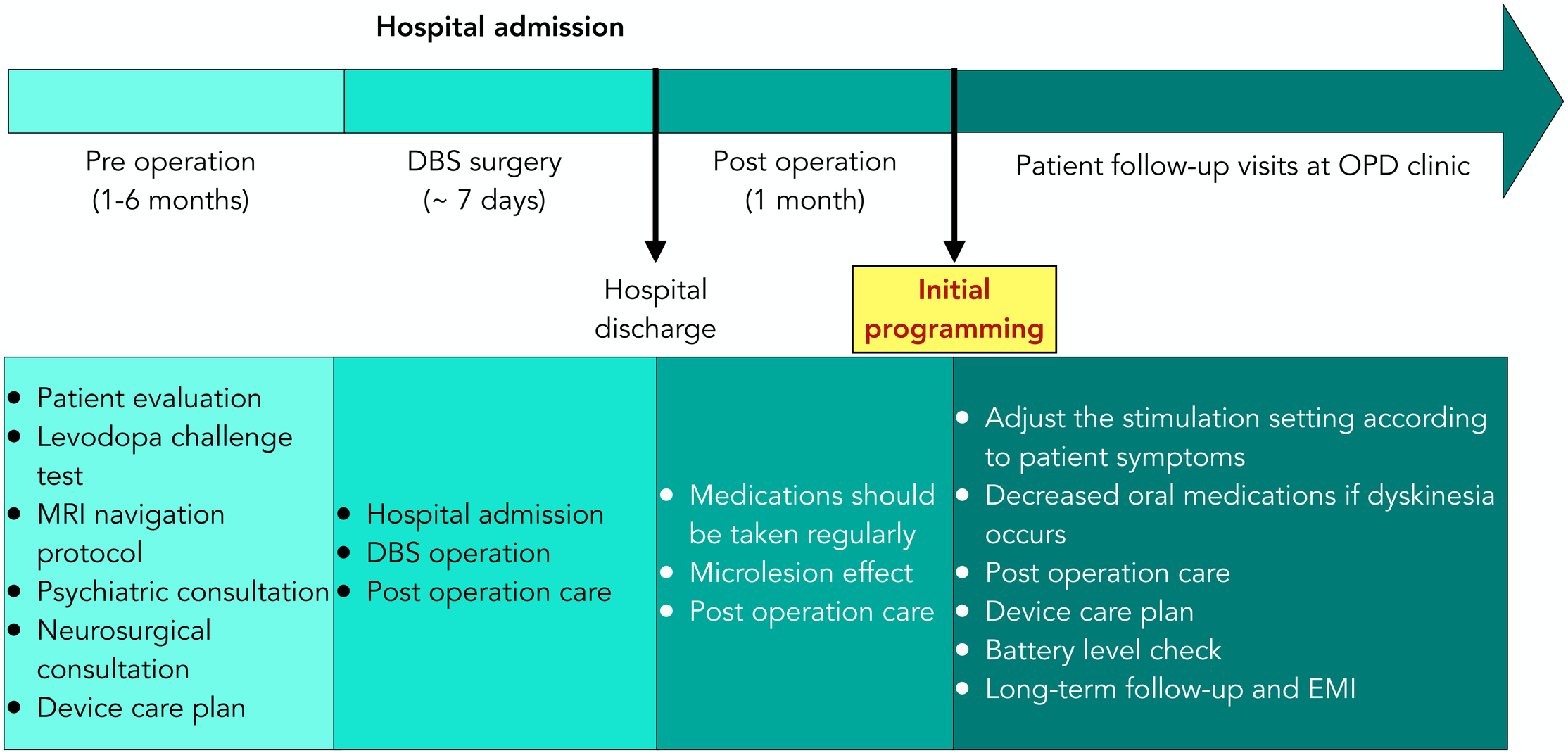
How does the DBS work?

Ablative surgery (Cryo/RF/Gamma knife, MrgFUS)

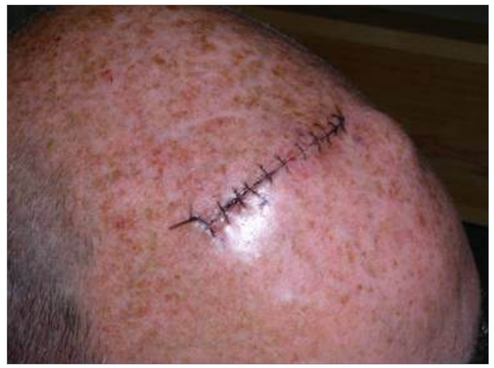


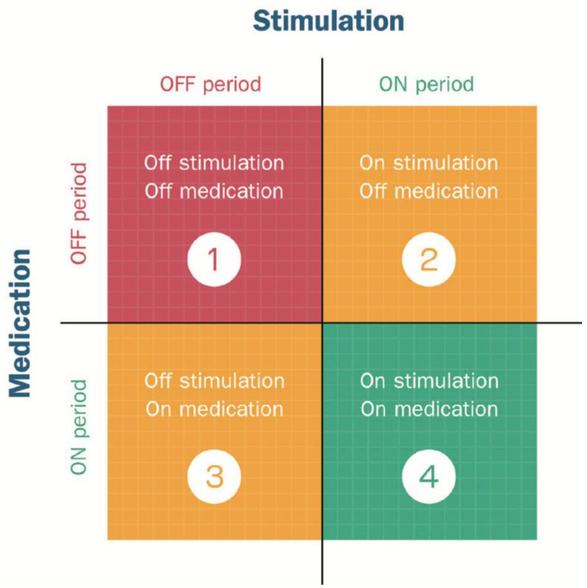
High-frequency stimulation(>100 Hz) = therapeutic effects of ablative surgery

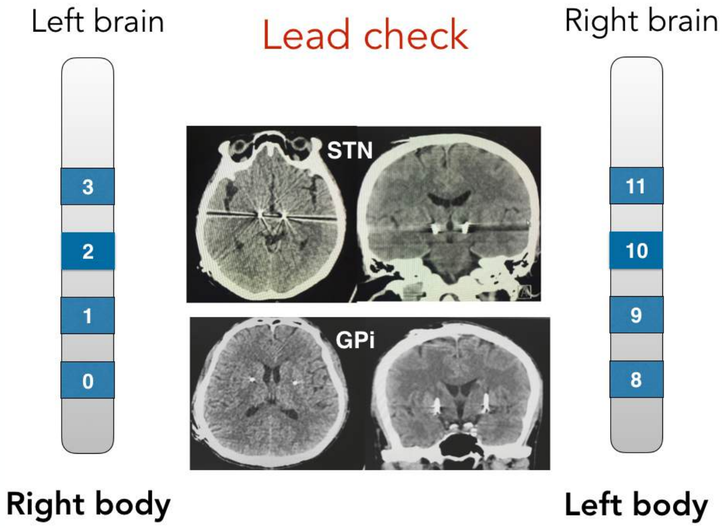
Timelines of DBS procedures



Initial programming with the standard monopolar review technique







Time-consuming procedures!

Volkmann J, et al. Mov Disord 2006;21:S284-9.
Picillo M, et al. Brain Stimulation 2016;9:425-37.

Refine Parameters at Follow-Up Programming Visits

Frequent visits in the first 6 months for slow stimulation titration with medication reduction

If basic programming fails due to adverse effects, try different stimulation contacts.

All these tasks are time-consuming!!!

Are there any ways to finalize DBS settings that seem better and faster?

Here is how we can integrate advanced technologies into our conventional DBS programming

Standard clinical care programming

Physiology

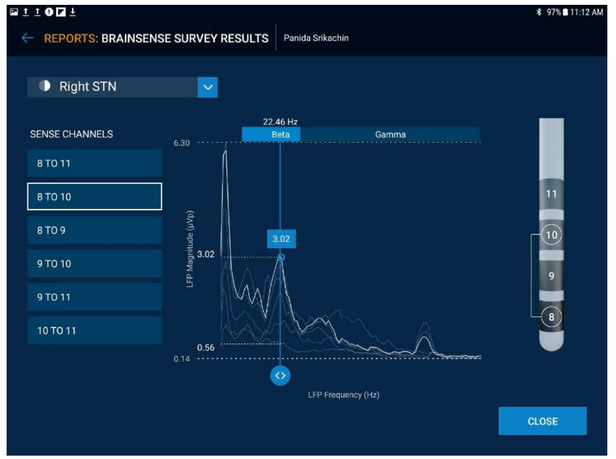
Sensing-based DBS programming

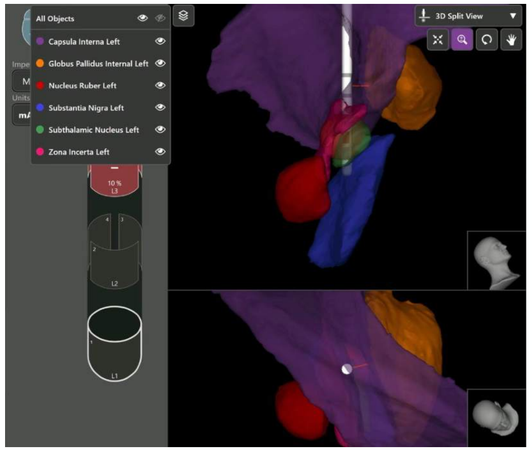
Anatomy

Image-guided programming

Monopolar Review
Conventional DBS

Electrophysiology biomarkers



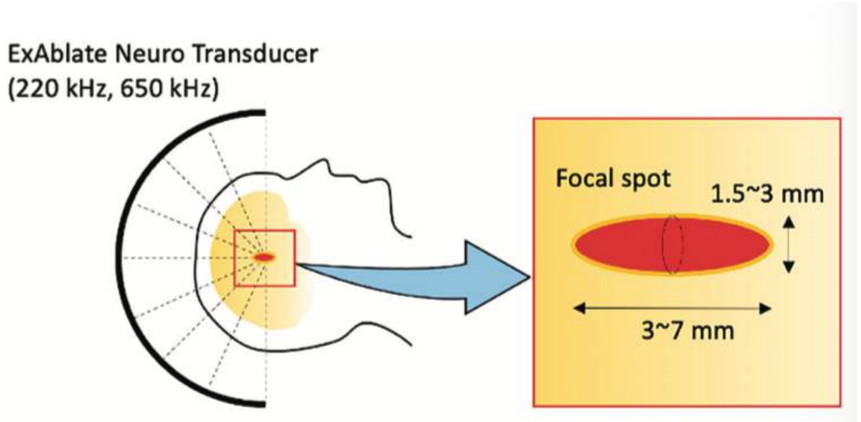


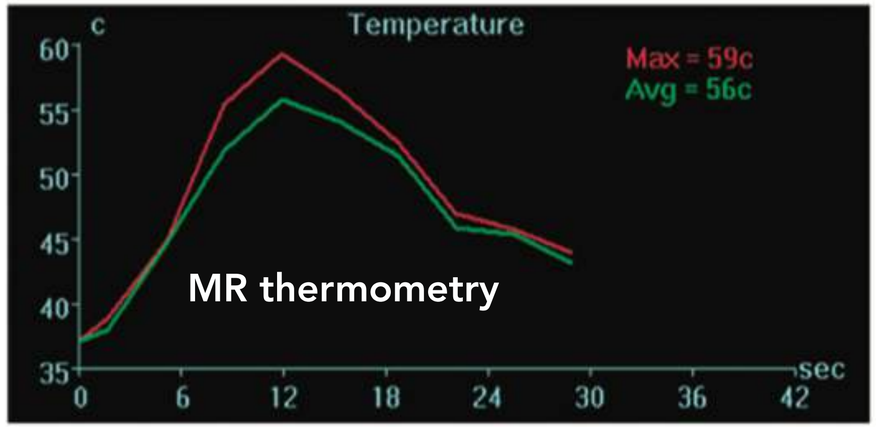
Swinnen B, et al. Neuromodulation 2025;28:501-10.
Rolland A, et al. Journal of Parkinson's Disease 2024;14:111-9.

Understanding in MRgFUS therapy

Transcranial MRgFUS

Features	Low-intensity (LIFU)	High-intensity (HIFU)
Frequency transducers	220 KHz	**650 KHz**
Functions	• Neuromodulation • BBB disruption • Acoustic activation of drug agents	**Precise thermal ablation of brain tissue**
Need of MR thermometry	LIFU can be used with or without MRT	**Need**
Final ablative sonications raise focal temperatures	< 0.1°C	**> 55 °C**
Tissue damage and micro bleeding	No	**Yes**





Mattay R, et al. Am. J Neuriradiol 2024 ; doi 10.3174.

Timelines of MRgFUS in theTreatment of Movement Disorders

Jung N, et al. J Korean Med Sci 2018;33: e279.
Food and drug administration, USA

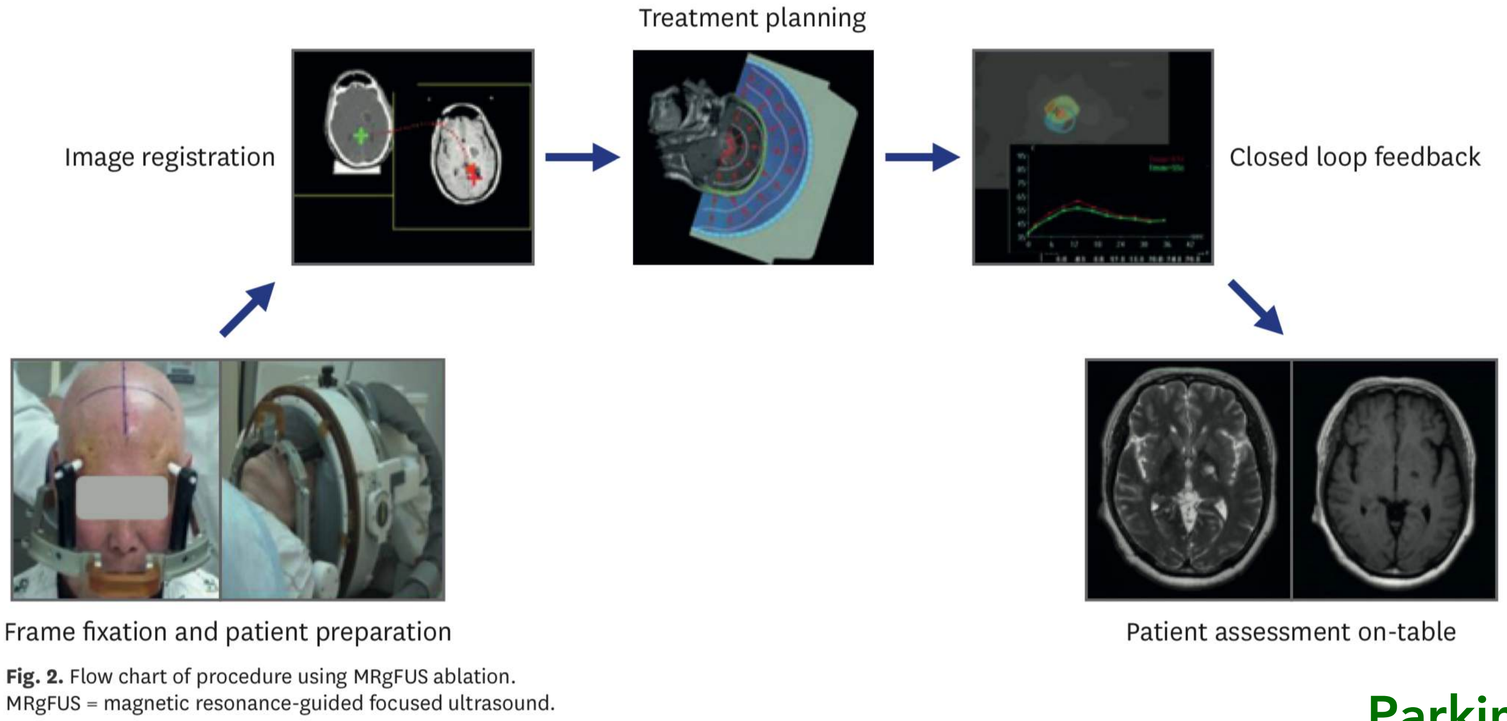


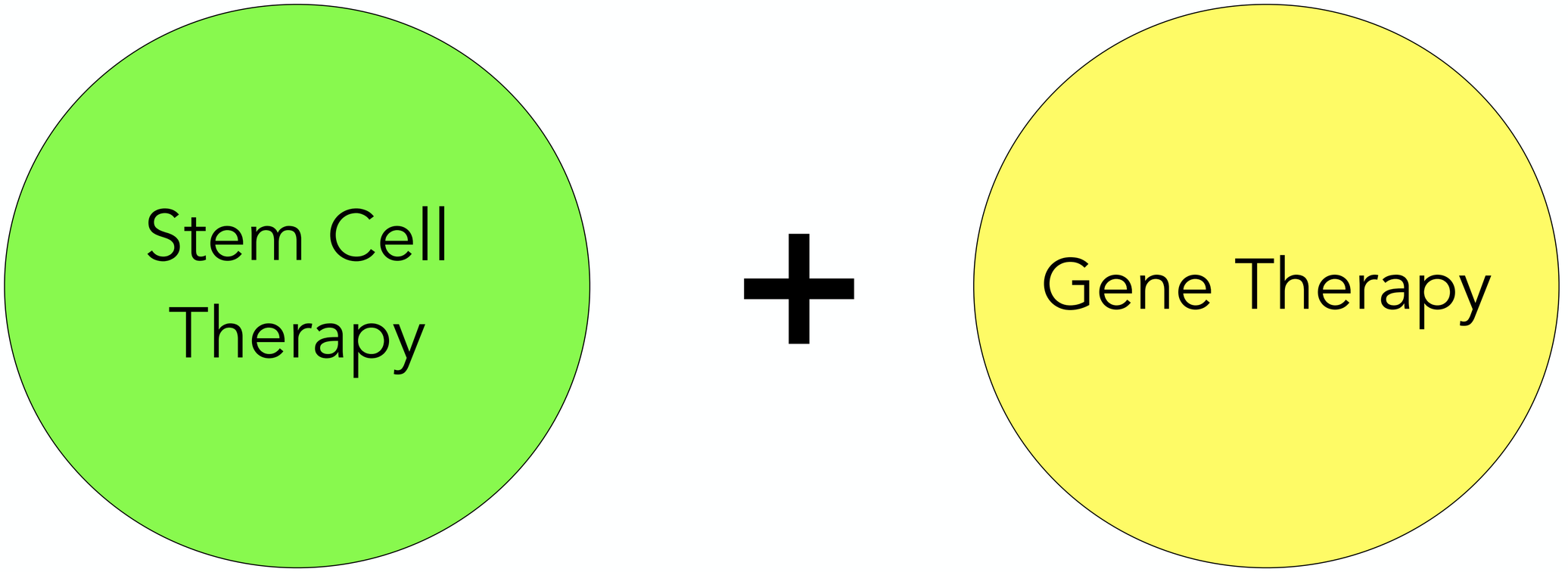
Fig. 2. Flow chart of procedure using MRgFUS ablation.
MRgFUS = magnetic resonance-guided focused ultrasound.

Essential tremor (FDA 2016) → **Tremor's dominant Parkinson's disease (FDA 2018)** → **Parkinsonian symptoms in Parkinson's disease (FDA 2021)**

Approved Stage Bilateral (both sides) FDA 2025

Understanding in Upcoming Advanced therapy

Upcoming Advanced Therapy for PD



Granted conditional approval in Japan

Phase I/II Clinical trial GT0003X

Stem Cell Therapy in Parkinson's Disease

- Stem cell therapy for PD aims to replace dopamine-producing neurons lost to the disease, using induced pluripotent stem cells (iPSCs) and human embryonic stem cells (hESCs).
- Two new clinical trials (Phase I and II), both published in Nature, evaluated the safety and potential benefits of transplanting early-stage dopamine-producing cells derived from specific stem cell types.
- Japan has granted conditional approval for the first stem-cell therapy (iPS), but it is not FDA-approved in the US.

Suwamoto N, et al. Nature 2025;641: 971-977.
Tabar V, et al. Nature 2025;641:978-983.

Article

Phase I trial of hES cell-derived dopaminergic neurons for Parkinson's disease

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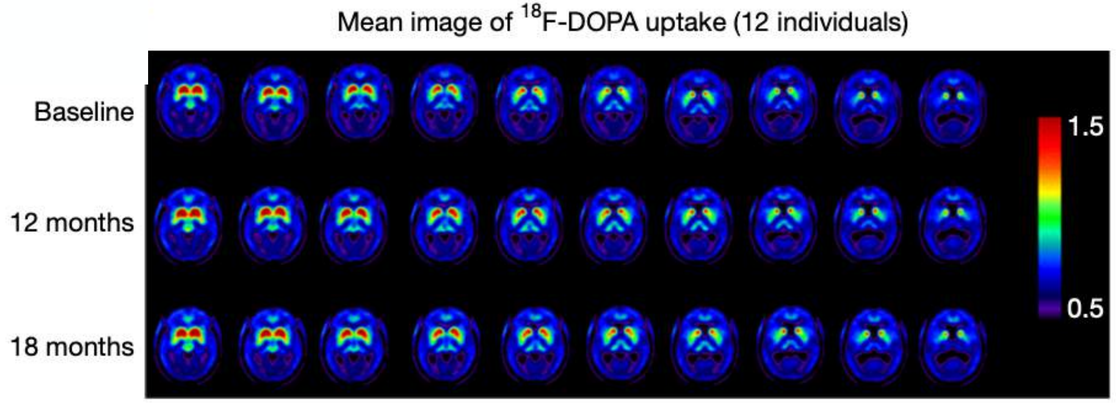
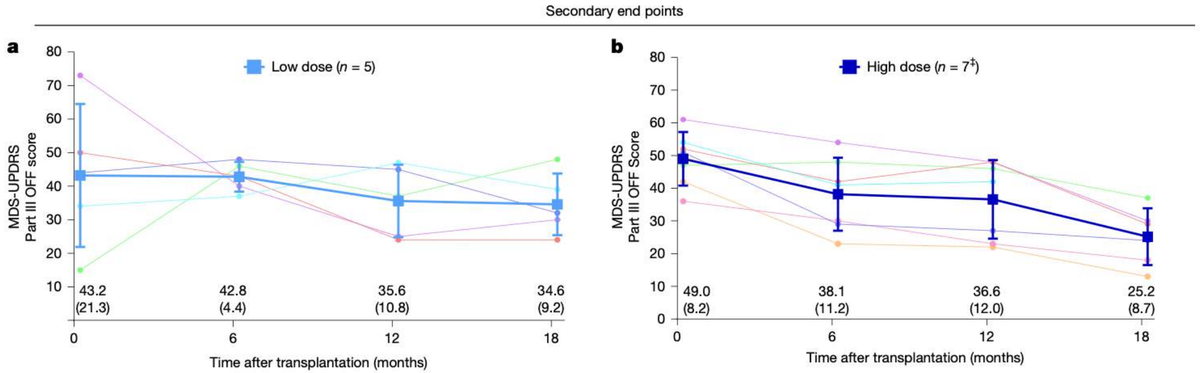
- Phase I trial tested bemdaneprocel (hESCs)
- 12 patients: low-dose (n=5) and high-dose (n=7)
- Cells implanted bilaterally into the putamen + 1 year immunosuppression
- Results: Safe and well-tolerated
  - Evidence of graft survival (↑18F-DOPA PET uptake at 18 months)
  - High-dose group: improvement in MDS-UPDRS III (OFF) and on time
  - No graft-induced dyskinesia
- Conclusion: therapy appears safe and promising and needs larger future trials

Table 1 | Summary of treatment-emergent SAEs at 12 months post transplantation

	Low dose (*n*=5)			High dose (*n*=7)		
Participants reporting, *n* (%) (total number of events)						
	0 events	1 event	≥2 events	0 events	1 event	≥2 events
TESAE	4 (80.0)	1 (20.0) (1)	0	6 (85.7)	1 (14.3) (1)	0
Related to surgery	5 (100)	0	0	6 (85.7)	1 (14.3) (1)	0
Related to transplanted cells	5 (100)	0	0	7 (100)	0	0
Related to immunosuppressive drugs	5 (100)	0	0	7 (100)	0	0
Tumour or abnormal tissue overgrowth related to presence of transplanted cells	5 (100)	0	0	7 (100)	0	0
Intracerebral haemorrhage that is deemed life threatening	5 (100)	0	0	7 (100)	0	0
Deaths	0			0		

Summary of treatment-emergent SAE (TESAE) for all patients, according to dose group.





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Article

Phase I/II trial of iPS-cell-derived dopaminergic cells for Parkinson's disease

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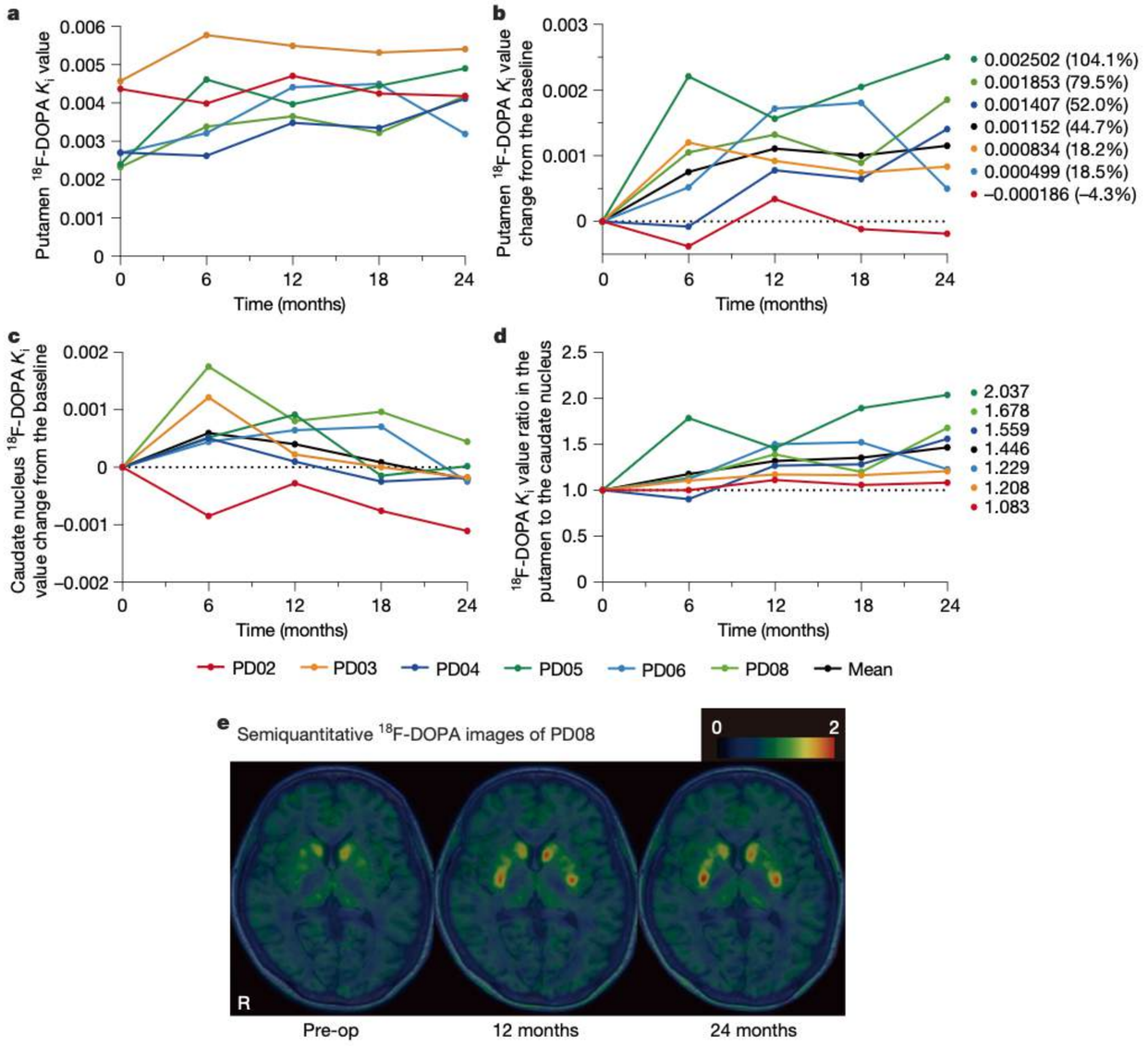
Nobukatsu Sawamoto[1,8], Daisuke Doi[2,8], Etsuro Nakanishi[1,8], Masanori Sawamura[1,8], Takayuki Kikuchi[3], Hodaka Yamakado[1], Yosuke Taruno[1], Atsushi Shima[1], Yasutaka Fushimi[4], Tomohisa Okada[4], Tetsuhiro Kikuchi[2], Asuka Morizane[2], Satoe Hiramatsu[2], Takayuki Anazawa[5], Takero Shindo[6], Kentaro Ueno[7], Satoshi Morita[7], Yoshiki Arakawa[3], Yuji Nakamoto[4], Susumu Miyamoto[3], Ryosuke Takahashi[1]✉ & Jun Takahashi[2]✉

- A Phase I/II trial tested induced pluripotent stem cells
- 7 patients (ages 50–69) received bilateral transplants (low dose = 3, high dose = 4)
- Follow-up: 24 months with primary safety focus; secondary: motor function & dopamine production
- Results: No serious, no tumour formation, mild dyskinesia
- Motor improvement: OFF scores, ON scores, and HY
- Dopamine activity increased (higher in the high-dose group)
- Conclusion: iPS-derived cells survived, produced dopamine, and appeared safe.



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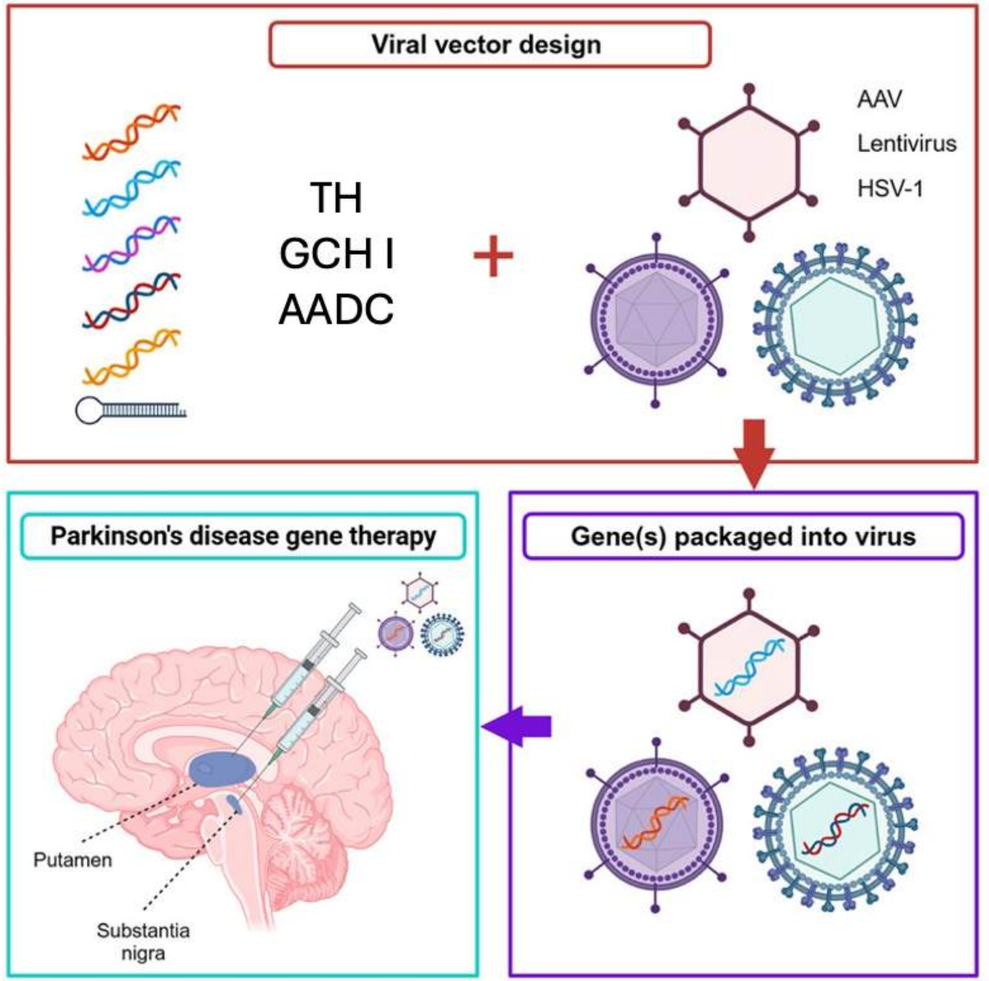
Gene Therapy in Parkinson's Disease

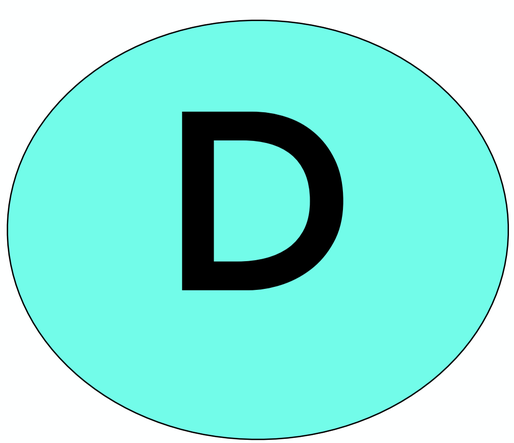
- This therapy delivers three key enzymes required for dopamine synthesis: tyrosine hydroxylase (TH), aromatic L-amino acid decarboxylase (AADC), and GTP cyclohydrolase I (GTPCH1) to restore physiological dopamine levels.
- Using an adeno-associated virus (AAV) as a viral vector containing 3 enzyme genes (AAV2-AADC/-GCH/-TH), these genes are introduced into striatal cells via stereotactic surgery.
- This gene therapy offers several advantages, including continuous dopamine synthesis, reduced medication use, and improved motor function.



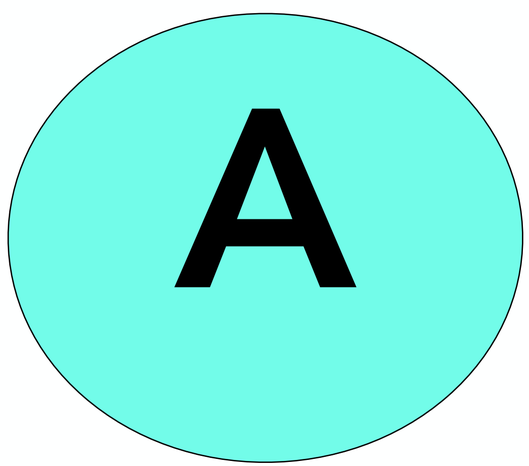
Muramatsu K, et al. Pediatrics and Neonatology 2023;23:53-59.
Muramatsu S, et al. Molecular Therapy 2010;18:1731-5.

Key Takeaways

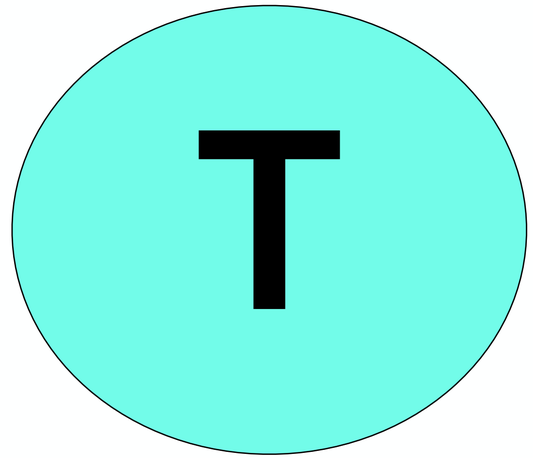
3 Patient-Focused Mottos for Device-Aided Therapy in Parkinson's Disease



Delivering Precision



Advancing Care



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6 May 2026

Options of Device-Aided Therapy in Advanced Parkinson's Disease

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