

Recent Update of DBS

이 정 일

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DBS는 신경계 임상영역에서 가장 역동적으로 발전하고 있는 분야의 하나이다. 손떨림, 파킨슨병, 근이성 긴장증 등에서는 이미 공인된 치료기법이 되었지만, 이외의 새로운 적응증이나 target으로 영역이 넓어지고 있으며, DBS를 위한 hardware와 software의 개선이 지속적으로 이루어지고 있다.

새로운 적응증으로는 간질, OCD, Tourette syndrome 등에서 적지 않은 임상 결과가 축적되고 있고, depression, dementia에서는 pilot study 혹은 phase I trial의 결과가 보고되었으며, obesity, drug addiction 등이 앞으로의 새로운 clinical trial 대상으로 제안되고 있다. 기존의 적응증인 파킨슨병에서는 early stage에서의 DBS에 대한 전향적 무작위배정 연구 결과가 보고되었다.

파킨슨병은 이미 기존의 공인된 적응증이지만, PPN은 DBS의 새로운 target으로 시도되는 대표적인 예이다.

DBS를 위한 혁신적인 hardware와 software는 실험실 수준에서 다양한 방향으로 개발되고 있다. 임상에서 당장 이용 가능한 device는 기본적으로 기존의 DBS mechanism을 이용하지만, 개선된 design에 의하여 훨씬 향상된 기계적인 성능을 제공하며, 다양한 programming을 쉽게할 수 있는 모델이 도입되고 있다. 최근 보고된 interleaving programming에 의한 증례나, constant-current DBS에 대한 무작위배정 연구 결과는, DBS 영역에서 기술적인 개선이 임상적으로 유의한 치료 결과의 향상과 직결됨을 보여주는 사례이다.

Recent Update of DBS

- Expanding application
- New target
- New technology

Expanding application (Past)

1973	DBS for pain (Hosobuchi et al.)
1987	VIM DBS (Benabid; Siegfried)
1993	STN DBS (Benabid)
1997	FDA approval for thalamic DBS
2001	FDA approval for STN DBS
2003	FDA grants a Humanitarian Device Exemption for dystonia
2005	Designation by FDA as a Humanitarian Use Device for OCD

Expanding application (Recent)

- **Epilepsy**

1987 CM thalamus DBS (Velasco et al.)

2002 Amygdalohippocampal DBS (Boon)

2002 DBS of AN of thalamus (Lozano)

2010 SANTE trial

CE mark in Europe

2012 Health Canada License

More (Medtronic Registry for Epilepsy) Registry

- Secondary dystonia
- Gilles de la Tourette syndrome

Neurosurgery Publish Ahead of Print
DOI: 10.1227/NEU.0b013e3182535a00

What Patients with Gilles de la Tourette Syndrome Should be Treated with Deep Brain Stimulation and What is the Best Target?

99 cases reported since 1999

Significant functional impairment related to tic

Failure to respond to pharmacological and behavioral intervention

Target - GPi and medial thalamus

Expanding Application (Future)

- Depression
- Dementia
- Early stage Parkinson's disease
- Obesity
- Addiction management

ARCH GEN PSYCHIATRY/VOL 69 (NO. 2), FEB 2012

WWW.ARCHGENPSYCHIATRY.COM

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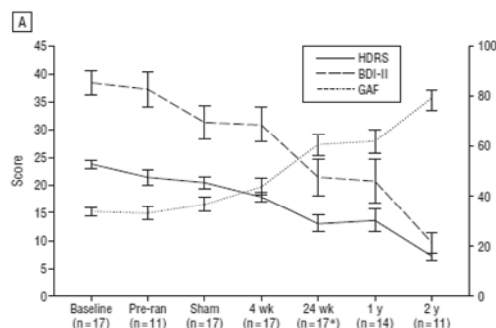
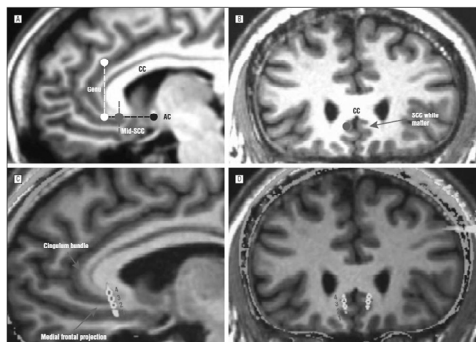
Downloaded from www.archgenpsychiatry.com at Samsung Medical Center, on March 20, 2012

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ONLINE FIRST

Subcallosal Cingulate Deep Brain Stimulation for Treatment-Resistant Unipolar and Bipolar Depression

Paul E. Holtzheimer, MD; Mary E. Kelley, PhD; Robert E. Gross, MD, PhD; Megan M. Filkowski, BA; Steven J. Garlow, MD, PhD; Andrea Barrocas, MA; Dylan Wint, MD; Margaret C. Craighead, BA; Julie Kozarsky, BA; Ronald Chismar, RN; Jared L. Moreines, BS; Klaus Mewes, PhD; Patricio Riva Posse, MD; David A. Gutman, MD, PhD; Helen S. Mayberg, MD



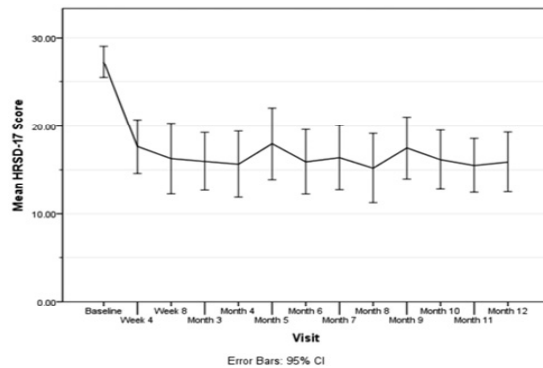
A multicenter pilot study of subcallosal cingulate area deep brain stimulation for treatment-resistant depression

J Neurosurg 116:315-322, 2012

Clinical article

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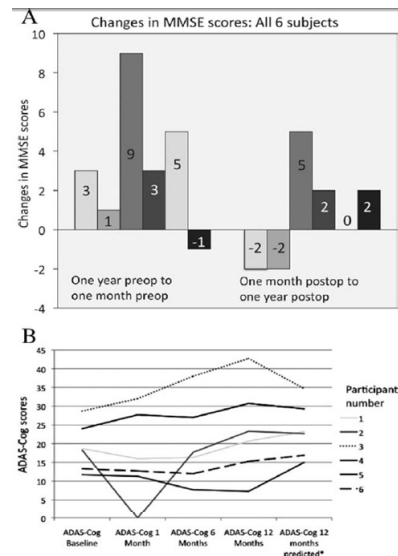
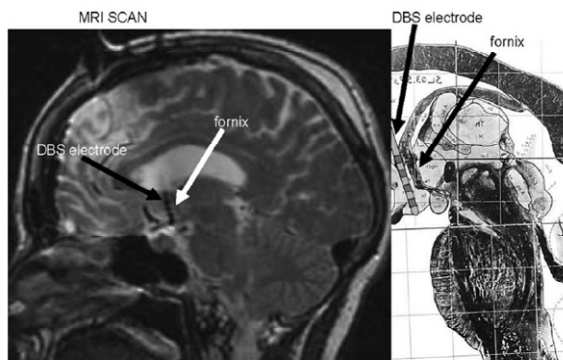
21 patents with bilat. SCG DBS

Reduction in HRS $\geq 40\%$
- 62% after 12 months

A Phase I Trial of Deep Brain Stimulation of Memory Circuits in Alzheimer's Disease

Annals of Neurology
Volume 68, Issue 4, Article first published online: 4 AUG 2010

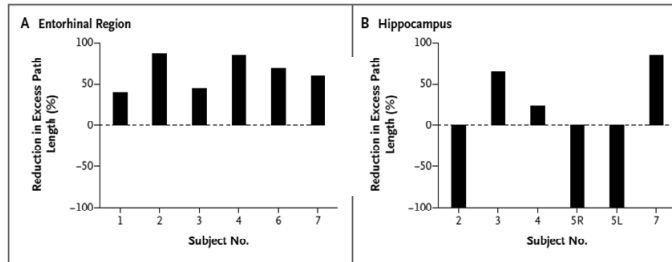
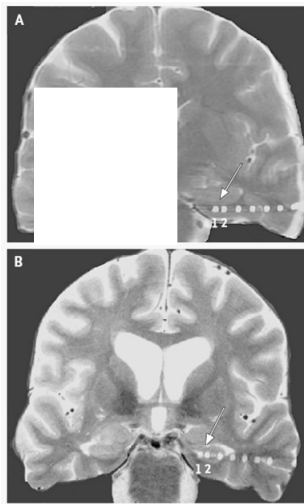
Adrian W. Laxton, MD,¹ David F. Tang-Wai, MDCM, FRCPC,^{2,5} Mary Pat McAndrews, PhD,³ Dominik Zumsteg, MD,⁴ Richard Wennberg, MD, FRCPC,⁵ Ron Keren, MD, FRCPC,² John Wherrett, MD, FRCPC,^{2,5} Gary Naglie, MD, FRCPC,² Clement Hamani, MD, PhD,² Gwenn S. Smith, PhD,⁶ and Andres M. Lozano, MD, PhD, FRCSC¹



Memory Enhancement and Deep-Brain Stimulation of the Entorhinal Area

N ENGL J MED 366;6 NEJM.ORG February 9, 2012

Nanthia Suthana, Ph.D., Zulfi Haneef, M.D., John Stern, M.D., Roy Mukamel, Ph.D., Eric Behnke, B.S., Barbara Knowlton, Ph.D., and Itzhak Fried, M.D., Ph.D.



CONCLUSIONS

Stimulation of the entorhinal region enhanced memory of spatial information when applied during learning.

New Target

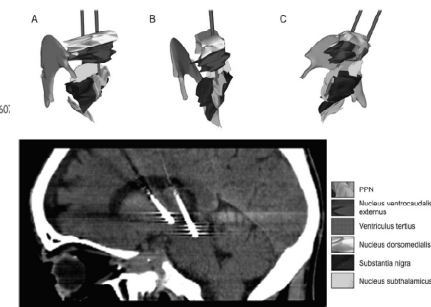
doi:10.1093/brain/awt346

Bilateral deep brain stimulation of the pedunculopontine and subthalamic nuclei in severe Parkinson's disease

Alessandro Stefani,^{1,2} Andres M. Lozano,³ Antonella Peppe,² Paolo Stanzione,^{1,2} Salvatore Galati,¹ Domenicantonio Tropea,¹ Mariangela Pierantozzi,¹ Livia Brusa,⁴ Eugenio Scarnati³ and Paolo Mazzone⁵

Brain (2007), 130, 1596–1607

A. Stefani et al.



Combined pedunculopontine-subthalamic stimulation in Parkinson disease

Neurology, 2012

S. Khan, MBChB, MRCS
S.S. Gill, MS
L. Mooney, BSc
P. White, PhD
A. Whone, PhD
D.J. Brooks, MD, DSc
N. Pavese, MD, PhD

ABSTRACT

Objective: To assess the effect of deep brain stimulation (DBS) in the pedunculopontine nucleus (PPN) and caudal zona incerta (cZi)—both separately and in combination—on motor symptoms and regional cerebral blood flow (rCBF) in patients with Parkinson disease (PD).

Methods: Four patients with bilateral cZi and PPN DBS electrodes were rated with the Unified Parkinson's Disease Rating Scale motor subscale (UPDRS-III) when taking and withdrawn from medication. A block of 16 [¹⁵O]-H₂O PET resting measurements of rCBF were performed in 4

concomitant low frequency stimulation of PPN and cZi regions induces additive brain activation changes and provides improved control of PD symptoms when medicated.

New Technology

Battery Predictability

Other System Improvements

Impedance Measurements

Programming enhancements

Patient programmer

Completing the Activa Portfolio

- **Activa PC**
 - Smallest dual channel primary cell
- **Activa RC**
 - World's first rechargeable INS for DBS
- **Activa SC**
 - Most advanced single channel primary cell INS

Advancing the DBS patient management experience



Programming Enhancements

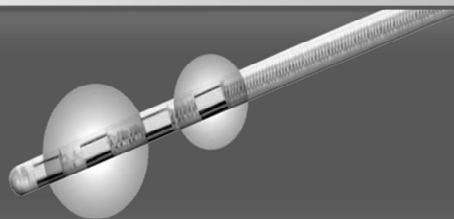
Activa SC, Activa PC and Activa RC offer a common programming platform with the following features:

- Up to Four Groups
- Information Stored in the INS
- **Voltage Mode and Current Mode**
- **Two Programs per Lead**

Most Advanced Programming Platform

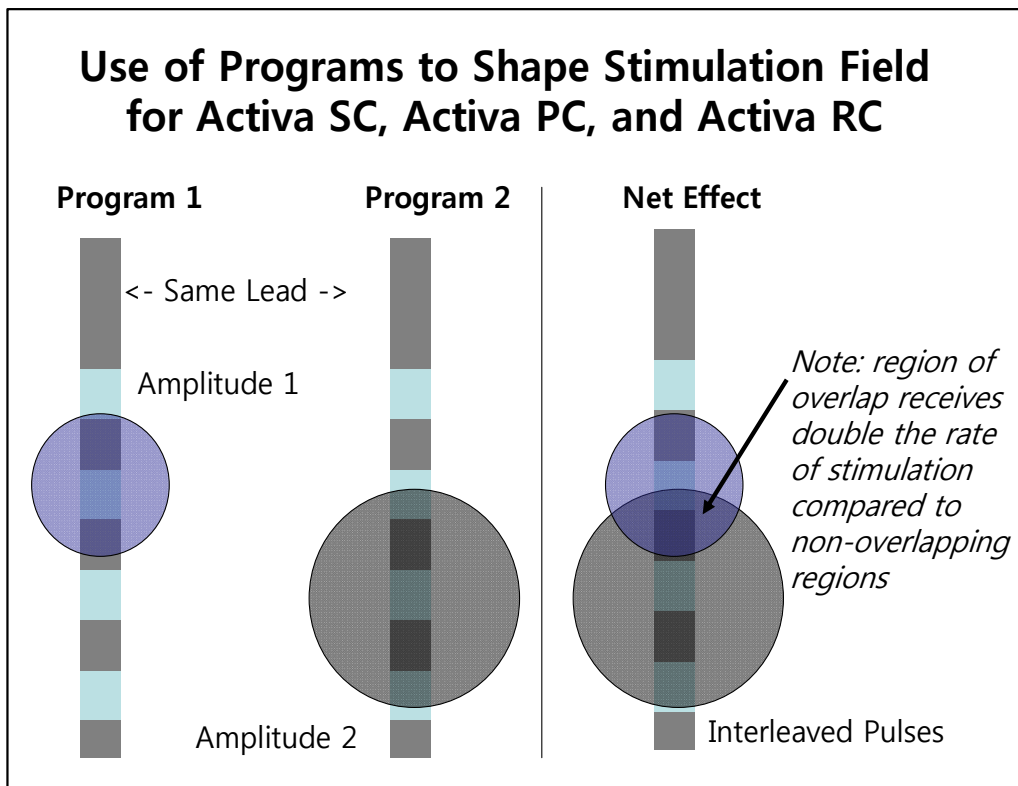
Interleaved Stimulation

Fine-tune the stimulation field when treating challenging patients

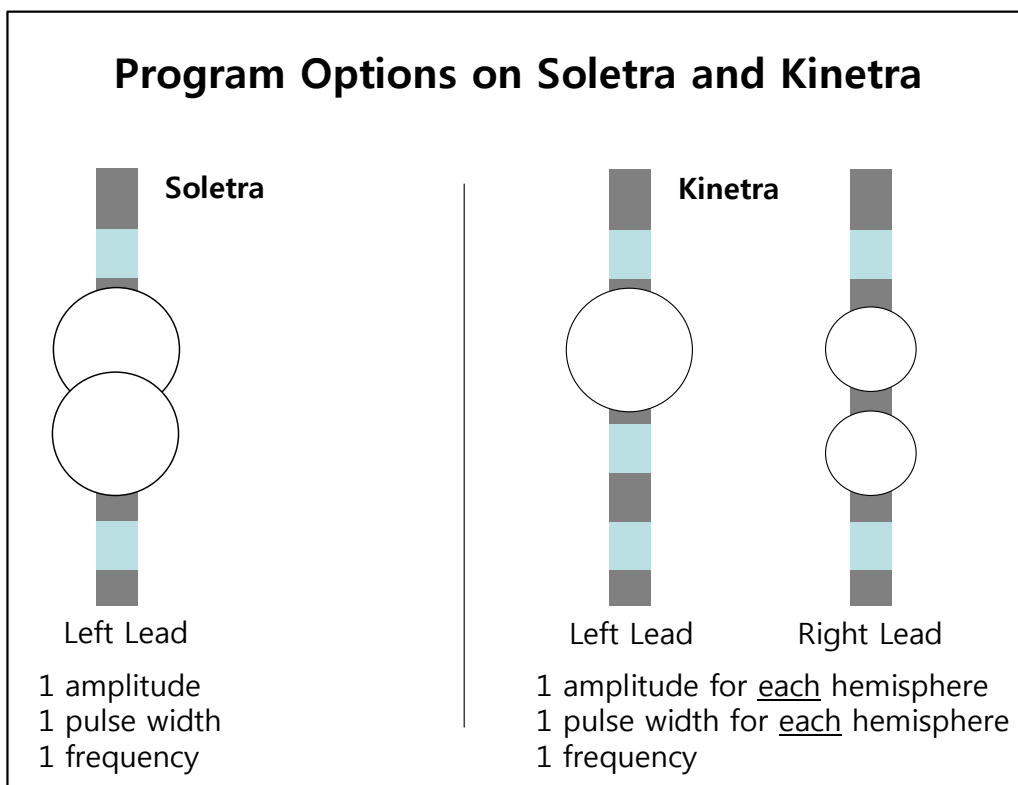


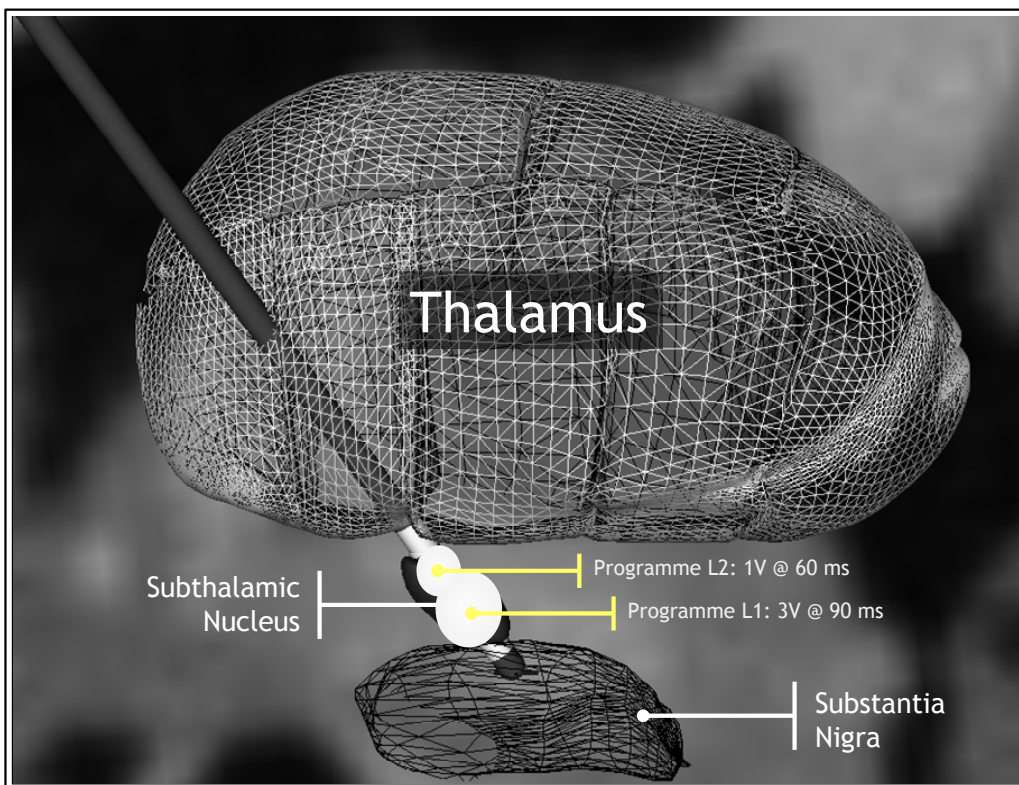
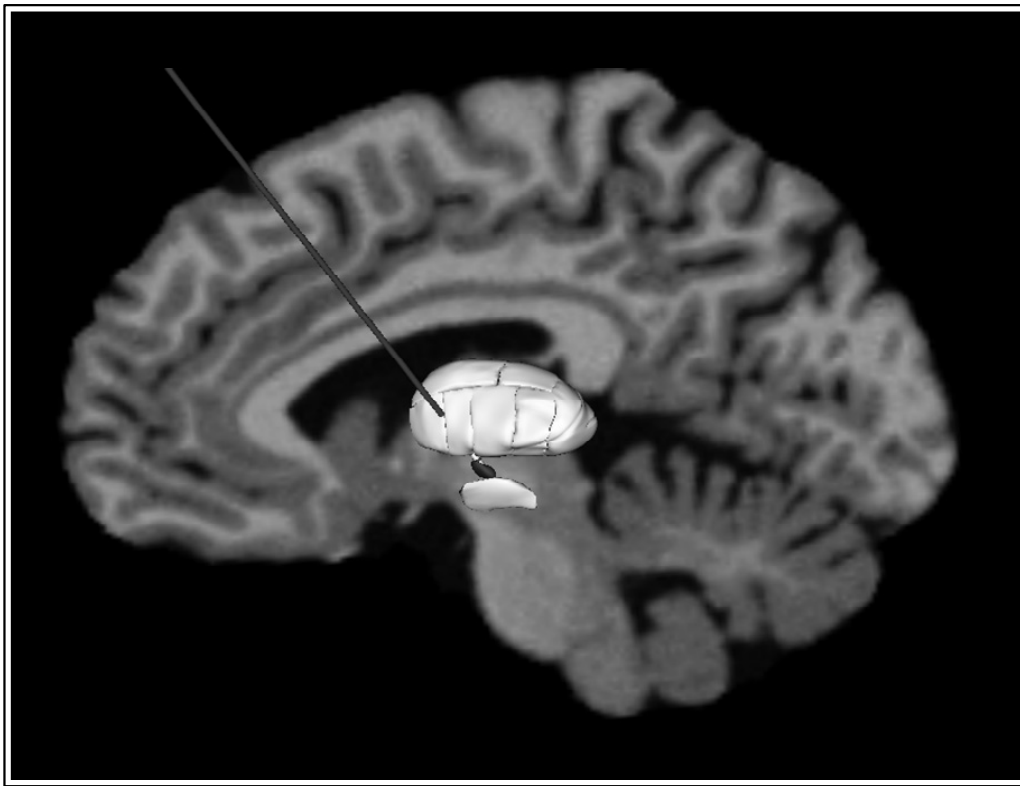
- In challenging situations with narrow therapy windows, Interleaving offers additional option

Use of Programs to Shape Stimulation Field for Activa SC, Activa PC, and Activa RC



Program Options on Soletra and Kinetra





Source: Wojtecki L, Interleaving programming of subthalamic deep brain stimulation to reduce side effects with good motor outcome in a patient with Parkinson's disease, *Parkinsonism and Related Disorders* (2010), doi:10.1016/j.parkreldis.2010.12.005

Contents lists available at ScienceDirect

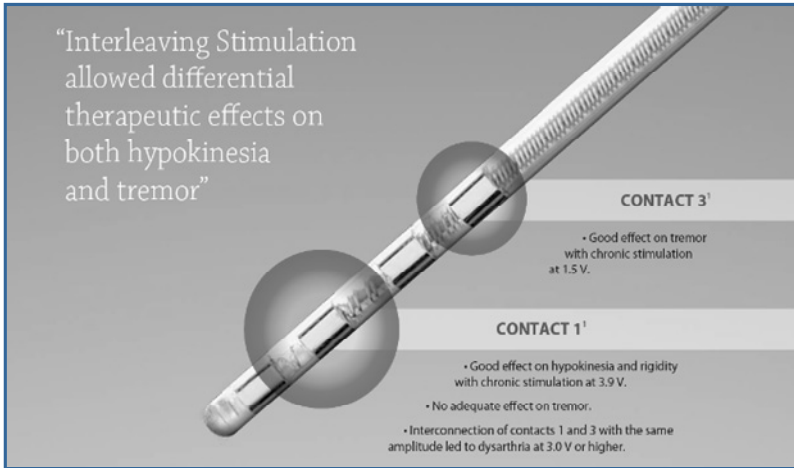
Parkinsonism and Related Disorders

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

ELSEVIER

Letter to the Editor

Interleaving programming of subthalamic deep brain stimulation to reduce side effects with good motor outcome in a patient with Parkinson's disease[☆]



"Interleaving Stimulation allowed differential therapeutic effects on both hypokinesia and tremor"

CONTACT 3¹

- Good effect on tremor with chronic stimulation at 1.5 V.

CONTACT 1¹

- Good effect on hypokinesia and rigidity with chronic stimulation at 3.9 V.
- No adequate effect on tremor.
- Interconnection of contacts 1 and 3 with the same amplitude led to dysarthria at 3.0 V or higher.

Case Report – JNeurology – Feb 2011

LETTER TO THE EDITORS

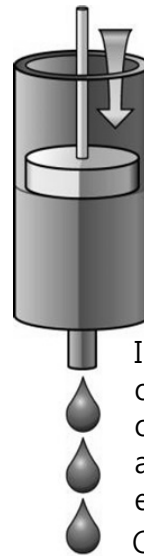
Combined stimulation of the substantia nigra pars reticulata and the subthalamic nucleus is effective in hypokinetic gait disturbance in Parkinson's disease

Daniel Weiss · Sorin Breit · Tobias Wächter ·
Christian Plewnia · Alireza Gharabaghi ·
Rejko Krüger

- Stimulation pulses can be delivered more selectively on distant contacts of a lead using a novel paradigm of the so called 'interleaved pulses', i.e., impulses are delivered simultaneously on two different contacts in alternating order (e.g., 125 Hz on each contact). Importantly, each of the contacts can be programmed with specific parameters (e.g., amplitude, pulse width).
- This novel paradigm might improve severe gait disturbances without worsening other parkinsonian symptoms as the conventional and primarily effective stimulation of the STN area can be maintained. Importantly, although isolated stimulation on SNr contacts ameliorated axial symptoms, it failed to improve segmental symptoms and was, therefore, not applied in our patient".

Current Mode and Voltage Mode

- Ohm's Law: $V = I \times R$
 - V = voltage, I = current, R = impedance
- Impedance is path-dependent and an attribute of the human body
 - As brain tissue changes, i.e., scar tissue heals, impedance can change so....
 - With voltage mode, voltage is set, and current varies automatically as impedance changes
 - With current mode, device holds current flow steady by dynamically adjusting voltage in response to changes in impedance

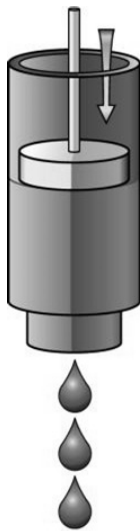


Voltage is the force on the piston

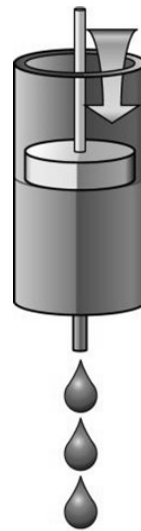
Impedance is the size of opening in the cylinder – resistance against the water/ electron flow
Current is the flow through the opening

Current Mode

- Current amplitude is set by programmer; device adjusts voltage dynamically



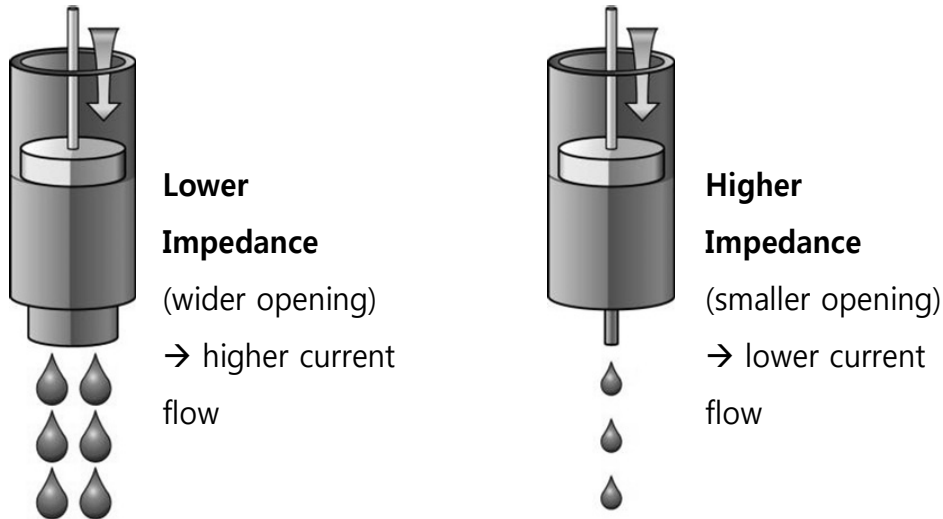
Lower Impedance
(wider opening) →
constant current
flow



Higher Impedance
(smaller opening) →
constant current flow

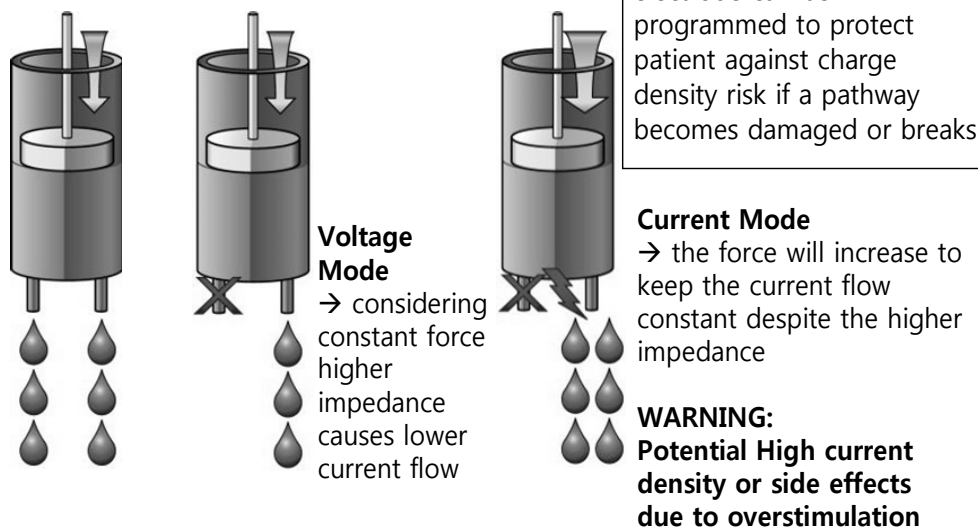
Voltage Mode

- Voltage amplitude is set by programmer; current adjusts dynamically



Two Current Pathways

- What Happens if One Pathway Breaks?



Lancet Neurol. 2012 Feb;11(2):140-9. Epub 2012 Jan 11.

Subthalamic deep brain stimulation with a constant-current device in Parkinson's disease: an open-label randomised controlled trial.

Okun MS, Gallo BV, Mandvybur G, Jajid J, Foote KD, Revilla FJ, Alterman R, Jankovic J, Simpson R, Junn F, Verhagen L, Arle JE, Ford B, Goodman RR, Stewart RM, Horn S, Baltuch GH, Kopell BH, Marshall F, Peichel D, Pahwa R, Lyons KE, Tröster AJ, Vitek JL, Tagliaati M; SJM DBS Study Group.

Prospective, randomized, multicentre trial

15 sites, 136 patients

Stimulation vs. control (implantation without activation for 3 months)

Constant-current DBS of the subthalamic nucleus produced significant improvements in good quality on time when compared with a control group without stimulation. Future trials should compare the effects of constant-current DBS with those of voltage-controlled stimulation.

Using Groups

- Clinicians can program up to 4 sets (A-D) of therapy parameters, selectable by the patient
 - Can be adjusted over time
 - Can be targeted at specific daily living activity

Reach optimized settings sooner with Programming Groups



Programming Groups

- **Kinetra and Soletra**

- a single therapy option, based on titration in clinic
 - Most patients return to clinic when adjustments are needed

- **Activa SC, Activa PC, Activa RC**

- more than one therapy option, for selection with patient programmer
 - Patient can try more than one therapy option between visits

Data Storage in INS

Record Effects

---Beneficial Effects---

Tremor
Location [dropdown]
Rating [dropdown]

Rigidity
Location [dropdown]
Rating [dropdown]

Motor Impairment
Location [dropdown]
Rating [dropdown]

Gait Impairment
Location [dropdown]
Rating [dropdown]

Other
Effect [dropdown]
Rating [dropdown]

Manage History





[X] [P]

Data stored in the INS for easy access to historical settings and other information

- Patient information is available in the device and travels with the patient
- Add new group from session history, avoiding potentially lengthy review of previous notes
- Screened settings can be viewed on a single screen, to facilitate selection of settings that maximize therapeutic benefit and longevity

Predictable Battery Life

Activa Portfolio

 ERI: Elective Replacement Indicator EOS: End of Service			
Therapy Screen Icon	Interpretation	Battery Voltage	Required Action
 OK	Battery is OK	2.9 V – 3.2 V	No Action Needed
		2.7 V – 2.8 V	Increase battery monitoring
 ERI	Battery is close to End of Service date	2.3 V – 2.6 V	Call your clinician: schedule replacement surgery
 EOS	Battery has depleted	2.2 V	Call your clinician immediately: replace neurostimulator

Different icons are displayed on the patient programmer as the battery voltage depletes.

Prediction of Implantable Pulse Generator Longevity in Deep Brain Stimulation: Limitations and Possible Solutions in Clinical Practice

Colin D.M. Stewart · Sam Eljamel

Centre of Neuroscience, Department of Neurosurgery, College of Medicine, Dentistry and Nursing, Ninewells Hospital and Medical School, Dundee, UK

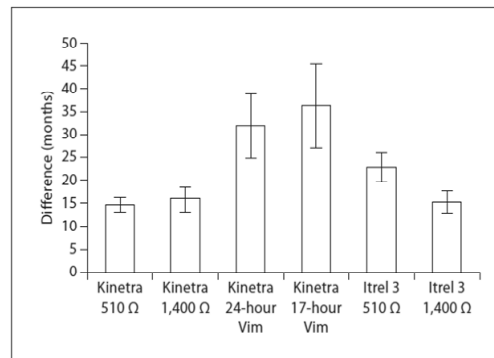
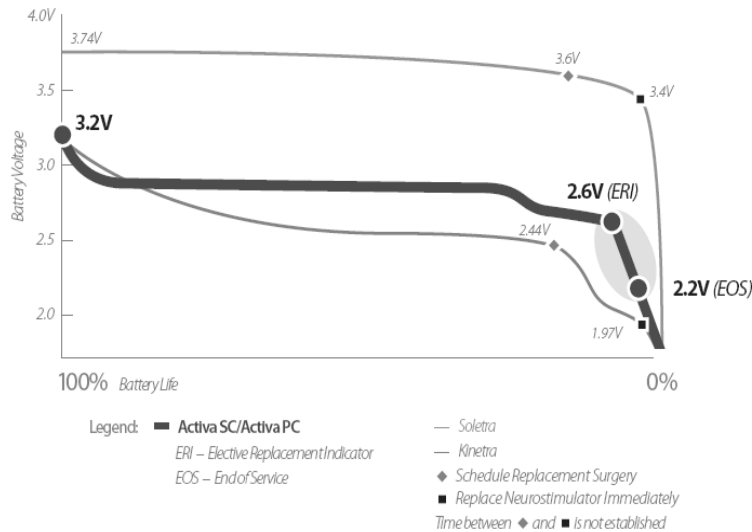


Fig. 1. Mean differences between actual and predicted IPG longevity. The smallest differences were observed in Itrel3 IPGs and the largest differences in Kinetra IPGs.

The longevity of IPGs could not be predicted accurately enough.... However, rechargeable IPGs may help avoid premature replacements and battery depletions.

Predictable Replacement Planning



Activa SC and Activa PC patients receive warning more than three months before EOS (End of Service)

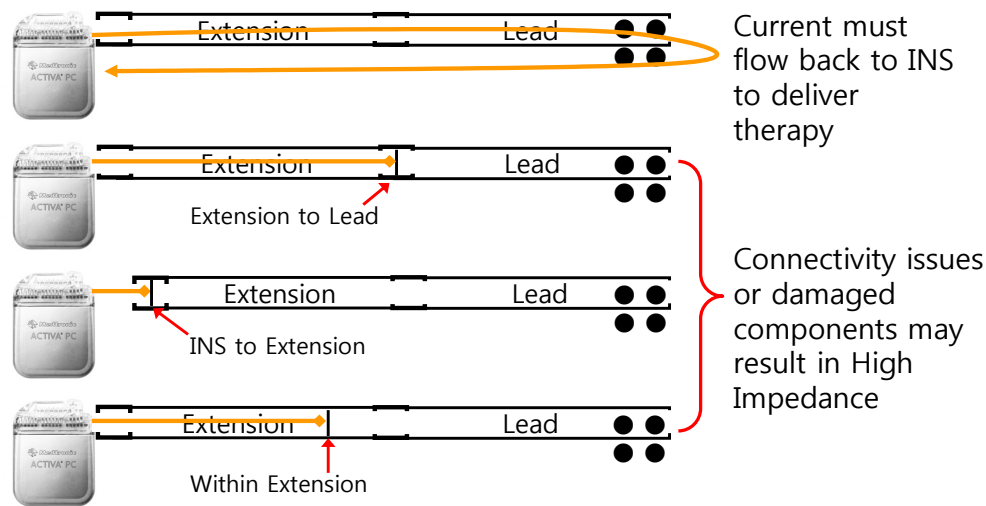
Patients with unusually high settings may receive their notification when less battery life remains

Other System Improvements

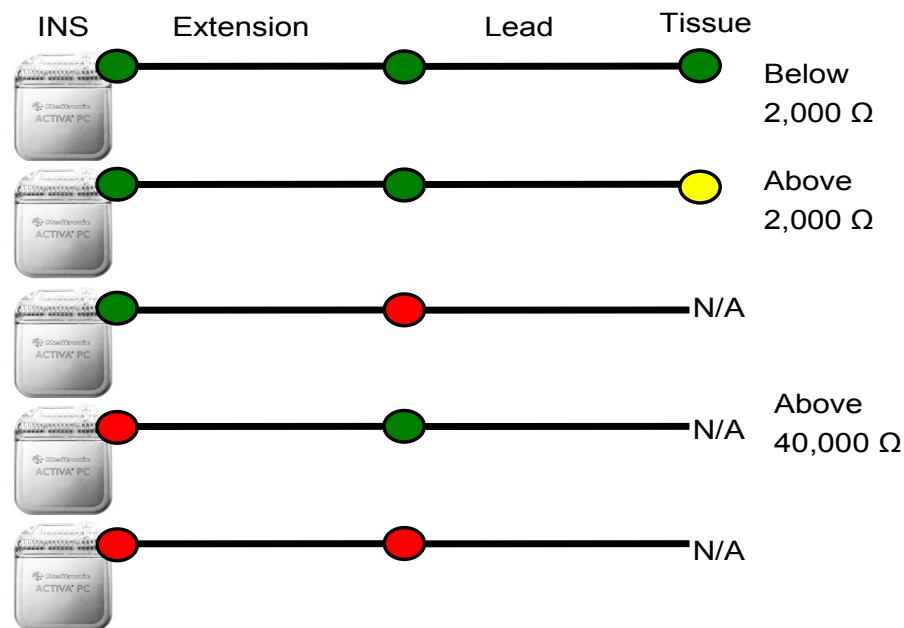
- **Improved output accuracy: Consistent therapy output as device nears End of Service (EOS)**
 - Therapy output is automatically monitored and maintained as battery voltage varies
 - As a result, therapy remains constant, even as EOS approaches
- **Programming flexibility and longevity improvements**
 - Eliminate significant battery drain as 3.6V threshold is exceeded (no more "doubler" effect)
 - Greater programming flexibility: Decisions regarding optimal parameters need not be constrained by discontinuities in longevity
 - As a result, higher settings patients will get improved longevity in Activa SC compared to Soletra
 - Pulse width step size
 - Smaller pulse width increments are available in Activa devices, versus Kinetra and Soletra
 - Adjust in 10 μ s increments using scroll wheel
 - As a result, don't have to jump from 60 to 90 μ s and risk significant longevity impact

Interpreting Impedance Results – Unipolar Impedance Path

Take Unipolar Impedance measurements to check connectivity of implanted system components



Interpreting Impedance Results: Unipolar Impedance Results and Connectivity



Improved Resistance to Environmental Interference Versus Kinetra and Soletra

- **Kinetra/Soletra: Stim ON/OFF with magnet**, INS has magnetic reed switch
 - Magnetic reed switch can be disabled in Kinetra
- **Activa Portfolio: Stim ON/OFF with telemetry-based patient programmer**, INS has no magnetic reed switch
 - Better protection against unintended therapy loss due to EMI than systems that turn stim ON/OFF with a magnet
 - No stim ON/OFF with a magnet

Patient Programmer

Patient Programmer




- Compatible with Activa SC, Activa PC and Activa RC neurostimulators
 - Model 37642 Patient Programmer has been updated to include Activa SC
- Patients can adjust parameters, and choose from up to 4 clinician defined stimulation groups
 - Designed to reach optimized settings sooner
- LCD screen provides patient with information about their therapy settings
- For dual implants: If in session with a neurostimulator, the patient programmer must be turned off before communicating with a 2nd neurostimulator
- Optional antenna (model 37092) available for patient programmer

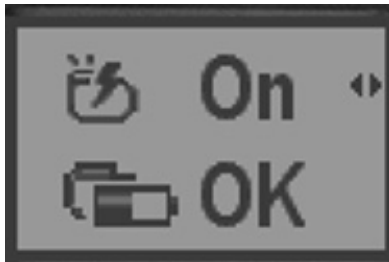
Patient Programmer Modes

- There are two modes available
 - Simple Mode
 - Advanced Mode
- Mode is determined by clinician based on patient needs

	Simple Mode	Advanced Mode
Turn therapy ON/OFF	●	●
Check INS Battery Status	●	●
Daily Battery Check Reminder	●	●
Additional Patient Programmer Features		
View and Adjust Therapy Parameters		●
Change Groups		●

Simple Mode Therapy Screen

- Always start by checking 
- Simple Mode Therapy Screen shows:
 - Therapy status: On/Off
 - INS battery status



Advanced Mode Therapy Screen

- Advanced mode shows:
 - Therapy on/off status
 - Battery status
 - Parameter settings and active group

Advanced Mode
Selection Box



Advanced Mode – Adjust Therapy

- Parameter Row

- Ability to adjust the parameter for each side based on clinician defined limits (rate must be the same for both sides)
- Icon indicates mirror image of patient, highlights side of body that is affected by therapy
 - Unlike 8840, which shows left/right brain



- Change Group



- Return to clinician settings

