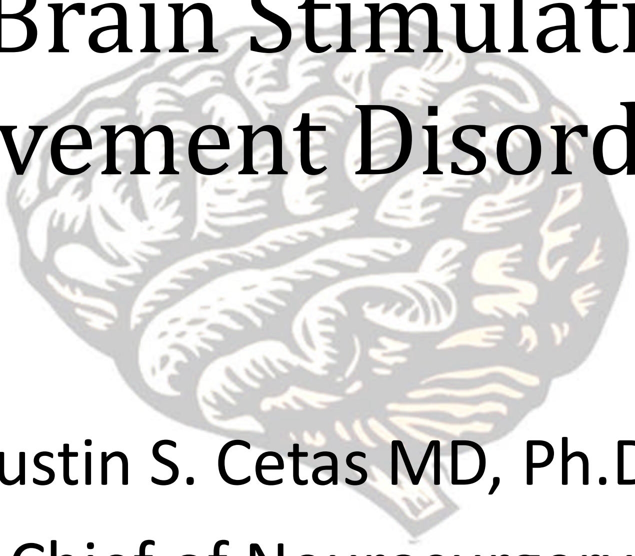
Deep Brain Stimulation for Movement Disorders



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Presentation Goals

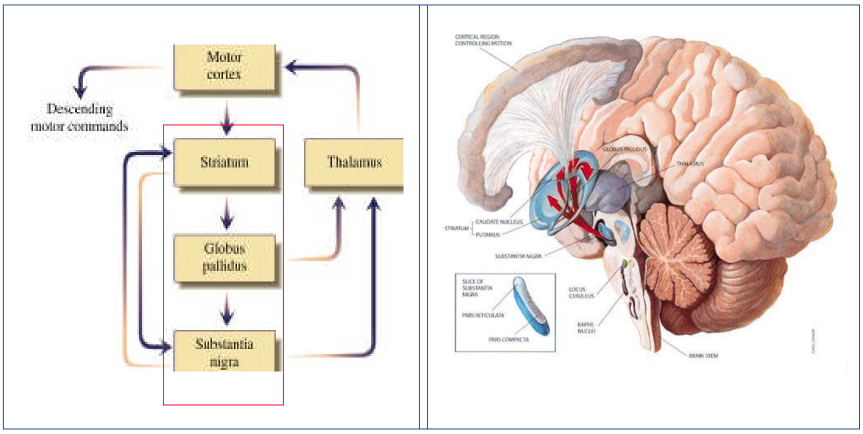
- A Brief History
- What is Deep Brain Stimulation?
- Who is surgery for?
- How will surgery help?
- What happens in surgery?
- How Does DBS work?

A Brief History of Surgery for Movement Disorders

- Earliest surgery probably in the 17th century with attempts to disable abnormal contracting muscle
- Late 1800s Removal of motor cortex
- 1930's and 40's many different targets for lesions, including motor cortex, cerebellum, spinal cord, and basal ganglia
- 1947 Stereotactic surgery introduced –allowed for select lesions to a wide range of targets but results variable
- DBS introduced 1977-marked reduction in speech deficits
- DBS for PD introduced in 1987
- MRI standardized target selection

SYNAPTIC CIRCUITRY OF THE BASAL GANGLIA

CORTICO-BASAL GANGLIA-THALAMO-CORTICAL PATHWAY



Essential Tremor

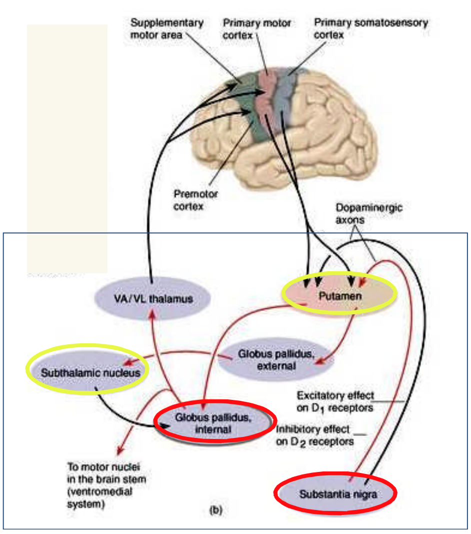
- First described in 1874 in Italian case report of an 18 year old man with an isolated action tremor
- More case reports followed and by mid 20th century was a well-recognized entity
- Most common form of tremor
- Often confused with Parkinson’s disease
- Two components to tremor: action and

Motor modulation of the basal ganglia

Focusing
- Inhibition of unintended movements
- Inhibitory output from GPi/SNr via indirect pathway
- Disinhibition of intended movements
- Reduction of inhibitory output via direct pathway

Scaling and termination of movement
- Facilitating the initiation of movement
- Inhibition of GPi/SNr via the direct pathway
- Stopping the ongoing movement
- Disinhibition of GPi/SNr via indirect pathway

SYNAPTIC CIRCUITRY OF THE BASAL GANGLIA



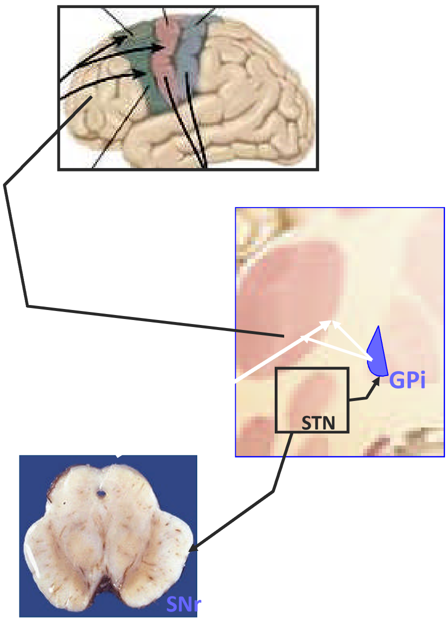
INPUT STRUCTURES
Striatum (Caudate + Putamen)
STN

Direct Indirect

OUTPUT STRUCTURES
Globus Pallidus internus (GPi)
Substantia Nigra pars reticulata

Current Indications for DBS

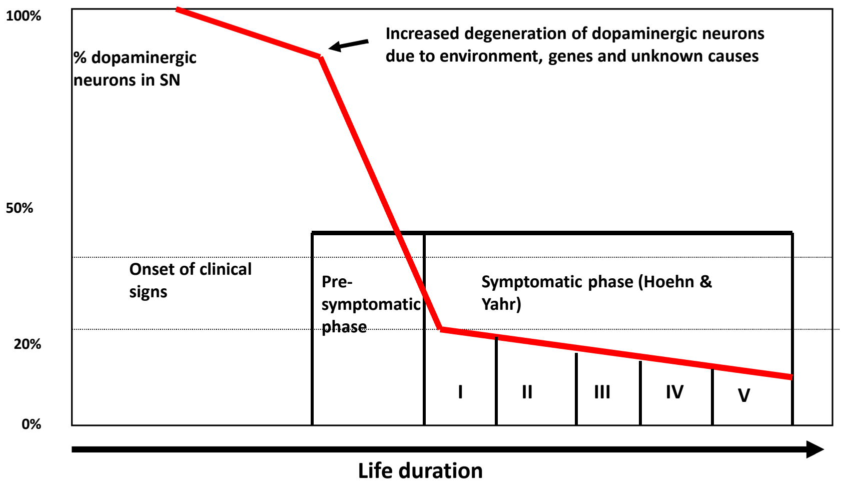
- Parkinson's Disease
- Dystonia
- Essential Tremor
- Other: Pain, OCD, Epilepsy, Obesity?



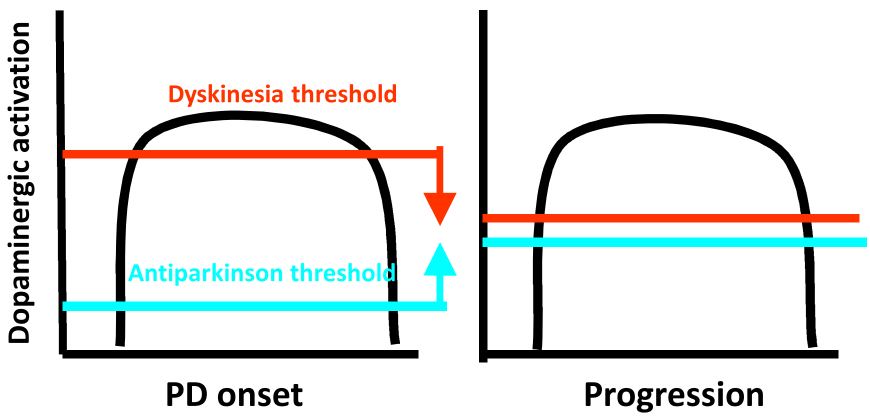
Pathophysiology of Parkinson's Disease

- Lack of striatal dopamine
  - Inactivation of the direct pathway
- **Activation of the indirect pathway**
  - Increased Gpi and SNr output
  - Increased inhibition of thalamus and brain stem neurons

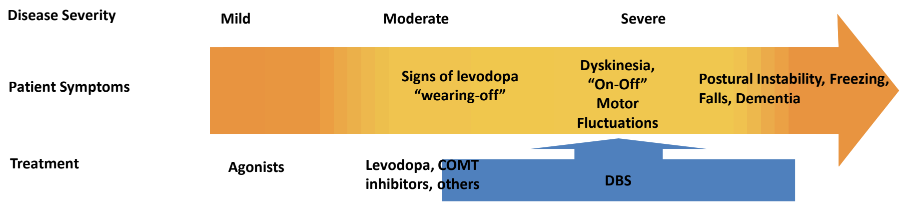
Natural history



Motor response to levodopa within the years: therapeutic window



Parkinson's Disease Treatment: Continuum of Interventions



Modified from Giroux, ML and Farris, SF. Cleveland Clinic Foundation 2005
Cleveland Clinic Foundation
Center for Neurological Restoration

DBS vs Best Medical Management

- Veterans Affairs Cooperative Studies Program (JAMA (2009) 301:63-70)
- Multicenter trial, 255 patients
- Compared time in "On" period between DBS and BMT at 6 months.
- Mean increase in 4.6h/d for DBS
- Increase in Quality of Life (PDQ-39)
- Higher incidence of falls and dystonia in DBS group at 6 mo.

DBS vs Best Medical Management

- UK Parkinsons trial (Lancet Neurology (2010) 9:581-91)
- 366 pts randomized to DBS vs BMT
- Mean improvement in PDQ-39 score of 5 points (mobility, activities of daily living, bodily discomfort)
- Increase in adverse effects on DBS patients

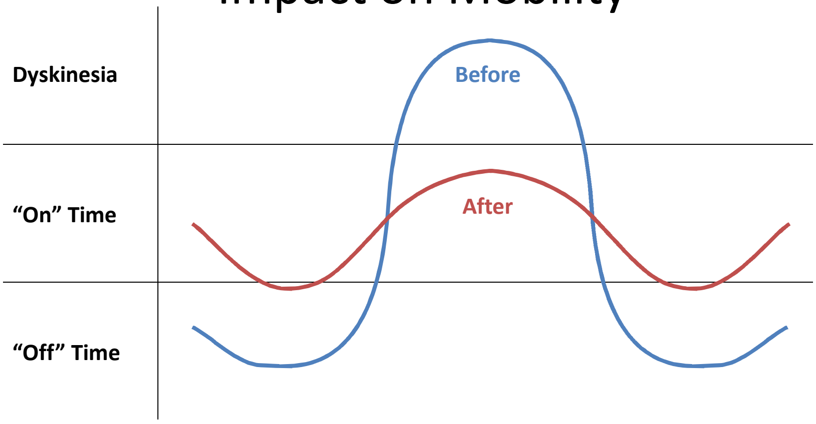
What Symptoms Does DBS Help?

- Off-time reduction (-2.5 hrs)
- On-time without Dyskinesia (+4.5 hrs)
- Tremor
- Medication Dosing
- Rigidity
- Bradykinesia (Slowness)
- Stooped Posture
- Shuffling Gait
- Activities of Daily Living

What is not often helped by surgery?

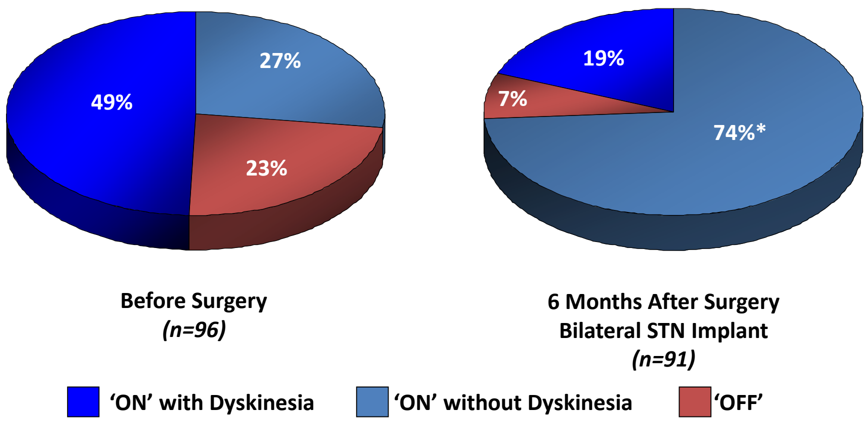
- Gait freezing
- Falling (if medications help falls then surgery will also help)
- Slurred speech (dysarthria)
- Swallowing difficulties
- Drooling
- Urinary and bowel dysfunction
- Cognitive deficits
- Obsessive and compulsive behavior
- Depression

Efficacy: Benefits of Therapy Impact on Mobility



This graph is only for illustrative purposes and does not represent actual "on" and "off" time.

"ON" Time Without Dyskinesias Improves from 27% to 74% of a Patient's Waking Day



N Eng J Med. 2001;345:956-63.

Dystonia Patient Selection

- Diagnosis of primary dystonia or carefully selected secondary dystonia
- Severe disability
- Difficult drug management
- Undergone a trial of L-dopa
- No dementia, no active psychiatric problems
- Normal brain imaging
- Good levodopa response
- Under 70 or in good physiological condition

DBS: mechanisms of action

- Neuroinhibition
  - Direct inhibition of axons/neurons
  - Indirect inhibition through GABAergic interneurons and axons
- Neuromodulation
  - Disruption of neural network by additional impulses generated by stimulation ("neural jamming")

DBS: Advantages

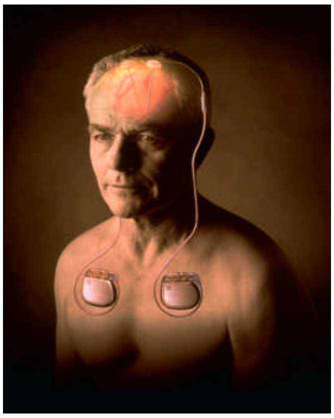
- Reversible
- Unilateral or bilateral
- No target lesion
- Low incidence of severe complications
- Allows new future therapies

DBS: Disadvantages

- Expensive
- Highly-specialized personnel
- Patient co-operation
- Generator related complications
- Periodic generator replacement

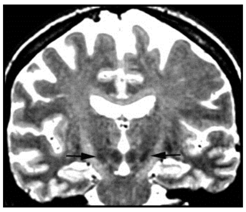
DBS: technique

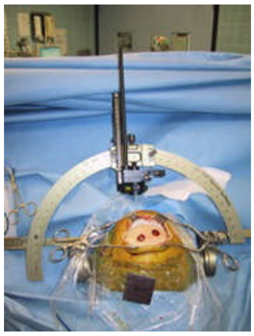
- Stereotactic neurosurgery
- Quadripolar electrode
-     (platinum/iridium)
- Rectangular stimulus
  of continuous or cyclic current
- 0-10,5 Volt
- 2-250 Hz
- 60-450 µsec
- Subcutaneous implantable
  pulse generator

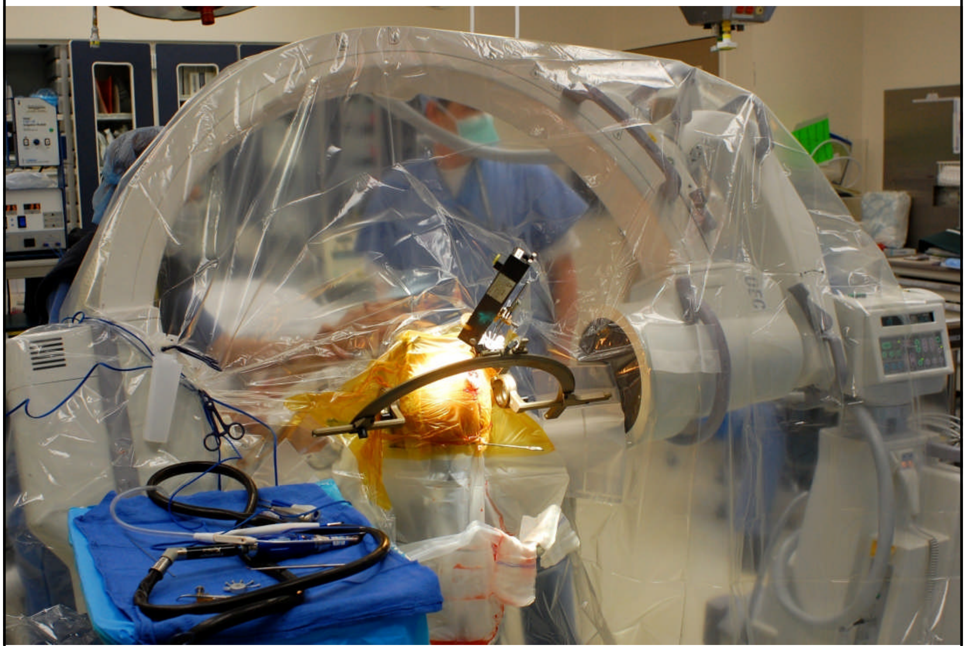


Surgical Technique

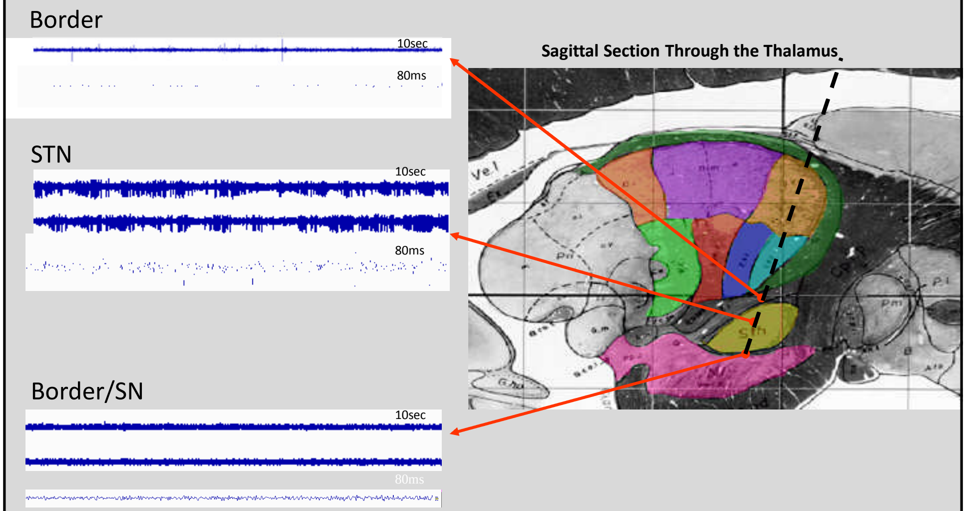
- Stereotactic frame placement or frameless stereotaxy
- Targeting
  - Imaging
  - Stereotactic targeting
  - Physiologic targeting (microelectrode recording and stimulation)
- Electrode placement
- Pulse generator implantation







Surgical Technique: Microelectrode Recording

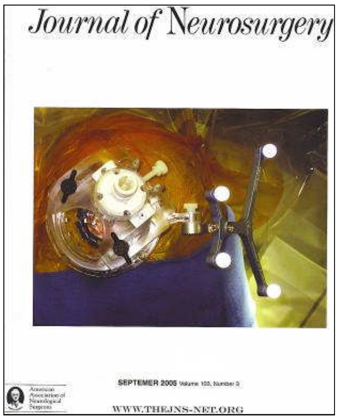


Frame vs. Frameless (Mini-Frame)

- Five small screws replace the head frame
- Passive Head Restraint
- Image-Guided Workstation

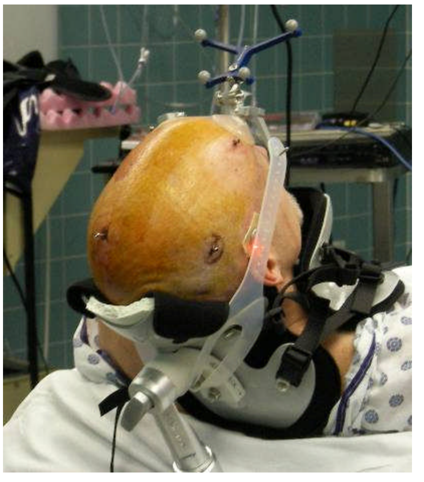

Proven Accuracy

A multi-center study found no significant difference between the accuracy of frameless navigation in which bone fiducial markers were used and the accuracy of a stereotactic frame, as reported in the literature.
Frameless stereotaxy using bone fiducial markers for deep brain stimulation. Journal of Neurosurgery 2005; 103: 404–413



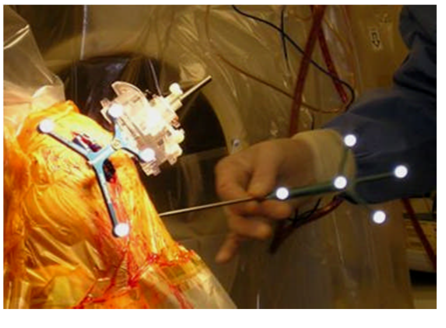
Non-Sterile Registration

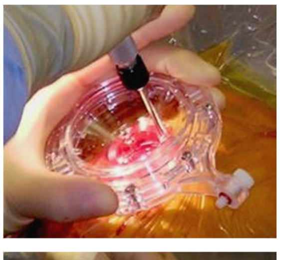
- Attach Medtronic Xomed™ FESS Frame
- Attach reference (Small Passive Frame)
- Register patient
- Navigate to find selected entry

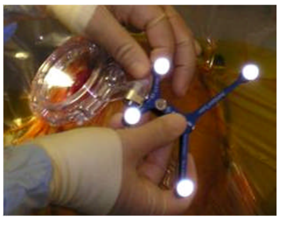


Sterile Registration

- Attach Nexframe® System
- Attach reference (Sm. Passive Frame)
- Register fiducial locations through drape

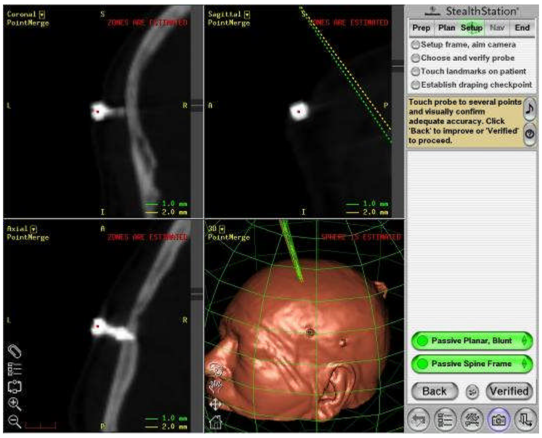






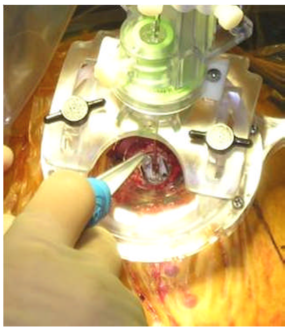
Verify Registration

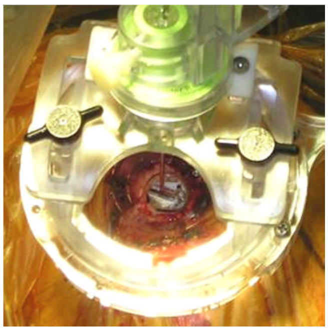
Point back to fiducials to verify accuracy



Retract Cannula, Install Stimloc™

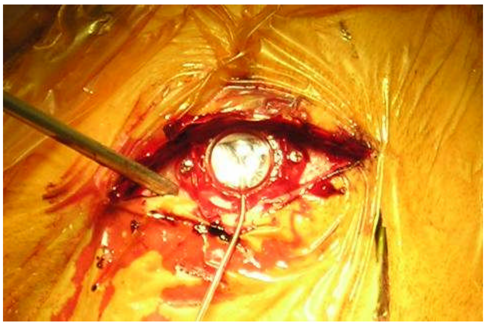
- Retract cannula until lead is visible
- Insert Stimloc cam; close around lead
- Mark lead above cam with marking pen





Lead Fixation

- Place DBS lead in Stimloc™ exit slot
- Place final Stimloc cap
- Complete procedure and remove fiducials



What Can Go Wrong?

No treatment in medicine is without risk, including medications

Temporary Side Effect	Permanent Side Effects
Confusion and Delirium (10%)	Brain hemorrhage (1%)
Hallucinations	weakness, paralysis
Weakness	Death (3/1000)
Hypophonia (8%)	Cardiac Event (3%)
Parasthesias (tingling)	
Infection (10 %)	
Lead migration or break (6%)	

DBS for PD: possible targets

- Thalamus (Vim, VL, CM)
- Globus pallidus (GPe and GPi)
- Subthalamic nucleus (STN)
- Others
  - Motor cortex
  - Peduncolopontine nucleus?
  - Substantia nigra compacta?

Vim DBS: Benefits

- Stable significant tremor control
- Bilateral procedure
- No neuropsychological deficits
- Reversible, mild, acceptable side-effects (31,6%)
- Transient paresthesias (9%)
- Foot dystonia (9%)
- Disarthria (15%)
- Balance impairment

Vim DBS: Limitations

- Four years after surgery 65% of patients have significant worsening in other PD signs
- Only 15% of PD patients have drug reduction at the last available follow-up

Vim DBS: Current indications

- ET
- MS tremor
- Post-traumatic tremor
- Midbrain tremor
- Some types of Dystonia?
- Tics?

DBS GPi: Benefits

- UPDRS-III improvement: 30-50%
- LID are the most improved
- Dorsal stimulation improves gait, akinesia and rigidity
- Posteroventral stim decreases LID and rigidity

DBS GPi: Limitations

- No anti-PD med reduction
- Some older reports suggest that the benefit is not stable over the years. Some patients have been operated later in the STN (Grenoble-Kiel) ➔ related to the position in the Gpi?
- Dorsal stimulation can induce dyskinesias
  Posteroventral stim can worse gait and akinesias with high voltages (interference with LD benefit)
- Neuropsychological evaluation: mild verbal fluence and visuoconstructive tests worsening

STN DBS : Benefits

- Good results for all the LD resposive symptoms
- Less energy consuming electrical parameters
- Less complex stimulation response compared to GPi
- Significant LEDD reduction
- Good target also for tremor
- LID reduction due to levodopa reduction (and perhaps because of a direct stim effect)
- Clinical benefit seems to be stable (some deterioration for axial signs)

STN DBS : Limitations

- Exclusion criteria for DBS
- Age?
- Unsolved neuropsychiatric issues
- Poor response to LD
- Complication after surgery
- Stimulation related
- Implanted devices related
- PD related
- Only symptomatic benefit (progression of akinesia, freezing and speech impairment)
- Intracerebral bleeding: 1-2%

DBS vs Best Medical Management

- Veterans Affairs Cooperative Studies Program (NEJM (2010) 362:2077-2091)
- Compared GPi vs STN DBS in 299 pts
- No difference in primary outcomes (UPDRS-III motor scores)
- Decreased dopaminergic medications in STN
- Decreased processing speed (visuomotor) and increased depression in STN
- Similar adverse events

Pre-operative patient program

- Neurological consultation
- Brain MRI
- Neuropsychological assessment
- Psychiatrist assessment
- Acute levodopa challenge
- Neurosurgical consultation
- Final decision

Patients Selection

- Severe disability
- Difficult drug management
- Good general health
- No dementia, no active psychiatric problems
- Normal brain imaging
- Good levodopa response
- Under 70 (?)

Predictive factors of adverse events

- Behavior instability
- Severe depression
- Cognitive impairment
- Levodopa-resistant signs
- Dysarthria
- Dysautonomia
- Balance impairment
- Poor general health
- Elderly

Treatment Plan

-2 month	Surgical Consultation
-2 week	Preoperative Evaluation
0	Surgery Halo Application MRI scan Surgical Implantation of Electrode and generator
1 to 3 days	Hospital stay
2 weeks	Postop visit with neurosurgeon
1 to 3 months	DBS programming and optimization
2 to 4 years	Generator Replacement

How Much Improvement Should I Expect in Parkinson's symptoms?

- Depends on your individual set of symptoms
- 40% improvement in UPDRS motor Off scores
- In general: the most you can expect is to be as good or slightly better than your best medicated state.
- Ex: If you are independent during the on-state, but wheel chair bound in the off-state, then you probably won't need the wheel chair

  Ex: If you have severe Parkinson's tremor, and don't tolerate dopaminergic medications, then the tremors can be blocked.

  Ex: If you have severe dyskinesia, then DBS will let you reduce the medications to prevent dyskinesia but remain in an on-state

  Ex: If you are completely wheel chair bound, and requiring full time care, then you will have some benefit. But it is unlikely to bring you back to independent living.

Weaver FM, Follett K, Stern M et al. Bilateral deep brain stimulation vs best medical therapy for patients with Advanced Parkinson disease. JAMA. 2009. 301:63-73.

How Much Improvement Should I Expect In Dystonia Symptoms?

- Depends on your individual set of symptoms
- Studies suggest an average 47% improvement in motor scores for generalized dystonia
- 60% improvement for focal or segmental dystonia
- Effects are sustained for at least 3 years
- Motor scores gradually improve over weeks to months
- Speech difficulties do not improve as readily

Tagliati et al 2011 Movement Disorders Vol 26 No. S1:S58-67

How Much Improvement Should I Expect In Essential Tremor Symptoms?

- Most series report 70-90% tremor control
- Head and voice tremor control rates lower and require bilateral DBS

Summary

- DBS Safe, effective and proven therapy for Parkinson’s, Essential tremor and dystonia
- Potential new indication
- Epilepsy, obesity, OCD, Pain to name a few