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Deep Brain Stimulation

Surgical Treatment for Parkinson's Disease

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National Capital Neurosurgery

Director of Neurosurgery and Neurosciences, Holy Cross Hospital

Clinical Professor Neurosurgery, GWU

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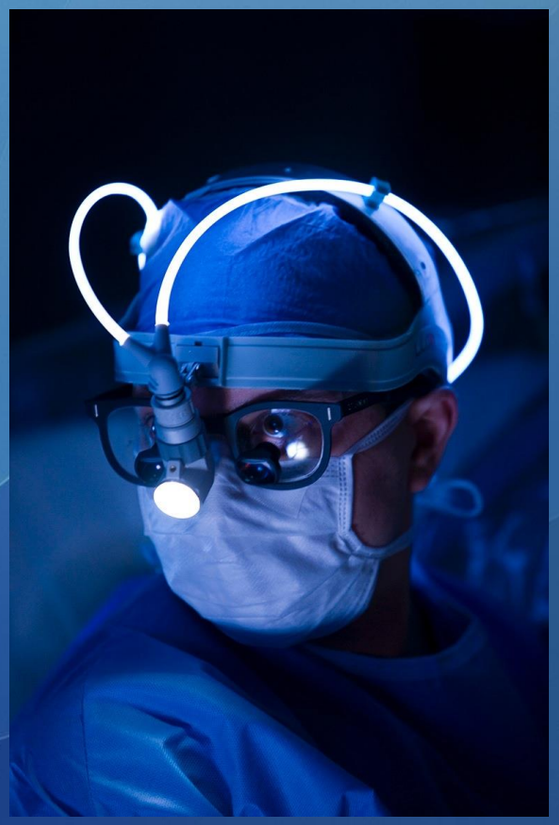
Background and Disclosures

- Board Certified Neurosurgeon
  - FAANS, in practice >17 years
- Director of Neurosurgery and Neurosciences: Holy Cross Health
- Clinical Professor of Neurosurgery, GWU
- Research in PD, Brain electrophysiology, Patent: Cell transplantation into the brain
- Medical Advisory Board Member: PFNCA
- Previous Board Member: Parkinson's Action Network



- Served on the Technical Advisory Board to Medtronic for DBS
- Instructor of Abbott Medical

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History of Movement Disorder Surgery

- 1930-1940 “Tractotomy”
  - Severing connections in the brain
- 1940’s Stereotactic Pallidotomy and Thalamotomy: Spiegel and Wicis
  - Burning holes in the brain
- 1950’s Choroidal Artery Ligation: Cooper
  - Surgical strokes: 10-15% complication rate
- 1970’s - 90’s Resurgence of Pallidotomy: Laitenen
- 1980’s to present Neural Transplantation: Madrazo
- Chronic Stimulation
  - 1975- treatment for chronic pain
  - 1987’s to present for Movement Disorders Benibid

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Neural Prosthetic

- Electrical stimulation to modulate output from target
- Based on “lesioning” studies
- Mimic lesioning with fewer adverse events
- Symptomatic treatment
  - Tremor
  - Bradykinesia
  - Rigidity
  - Freezing
  - Dystonia
  - Dyskinesia

“That’s amazing—I was just thinking the same thing.”

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FDA Approved

- DBS for Tremor
  - 1997 - FDA approval - thalamic stimulation
- DBS for PD
  - Late 2001 - FDA approval - bilateral
- DBS for Dystonia
  - 2003- FDA approval

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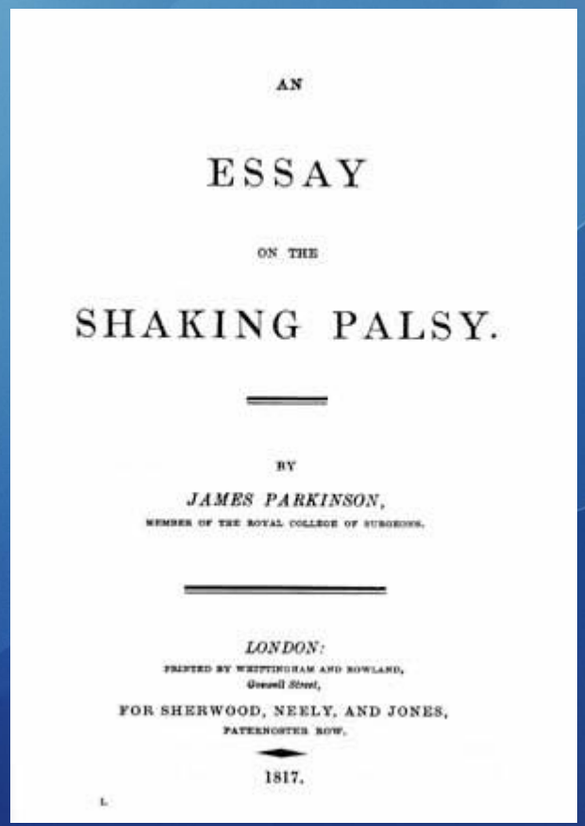
Parkinson's Disease

- Death of Dopaminergic Cells in the brain - not just the SN
- Suicide? - apoptosis
- Murder? - toxic exposure
- Both
  - genetic predisposition
  - toxin exposure



AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,

MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:

PRINTED BY WHITTINGHAM AND ROWLAND,
Goswell Street,

FOR SHERWOOD, NEELY, AND JONES,
PATERNOSTER ROW.

1817.

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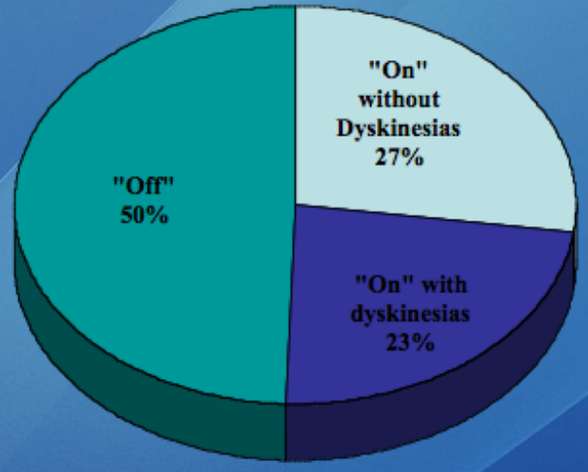
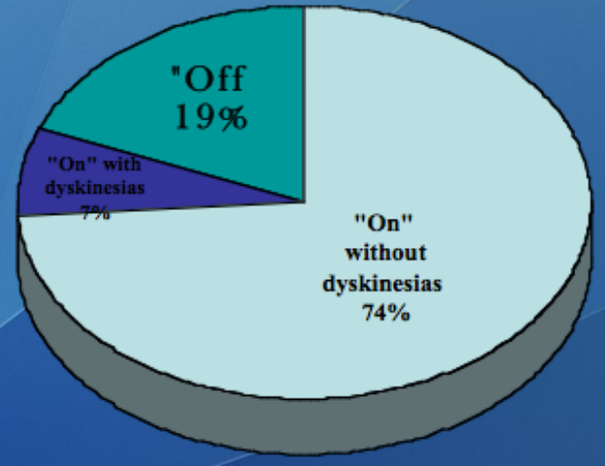
Deep Brain Stimulation for PD

- Current prosthetic paradigm
  - FDA approved
  - Proven track record
  - NEJM September 2001
- Not experimental

NEJM Vol 345 No 13 9/27/2001



Baseline Assessment



6 Months After Bilateral STN Stimulation

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DBS v. Best Medical Therapy

A Randomized Trial of Deep-Brain Stimulation for Parkinson's Disease

NEJM 2006; 355 896-908

- 156 patients randomized to DBS and medical therapy vs. Medical therapy alone
- Endpoints: measured at baseline and at 6 months
  - Quality life measurements by questionnaire (PDQ-39)
    - DBS show greater improvement p = 0.02, mean improvement by 9.5 points
  - Severity of Symptoms by UPDRS- III
    - DBS shows greater improvement p <0.0001, mean improvement 19.6 points
- Adverse Events
  - DBS had more serious side effects 13% vs 4% P<0.04 (including cerebral hemorrhage)
  - Medication group had more frequent adverse events (64% vs. 50% p = 0.08)
- Improvements were in motor scores, ADLs, well-being, stigma, bodily discomfort
- Conclusion: "...patients under 75 years of age with severe motor complications of Parkinson's disease, neurostimulation of the subthalamic nucleus was more effective than medical management alone."

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DBS vs. Medical Treatment in PD

Bilateral Deep Brain Stimulation vs Best Medical Therapy for People with Advanced Parkinson's Disease

JAMA 2009; 301(1) 63-73

- 255 Randomized Patients 121 - DBS, 134 - Best Medical Therapy - compared "on time." motor function, QOL, Cognitive function and adverse events
- DBS patients gained an average of 4.6h/d of "on time" vs. 0h/d $p<0.001$
- 71% of DBS patients motor function improvement vs. 32% $p<0.001$
- 7/8 QOL scores significantly improved with DBS as did the summary of QOL vs. No significant improvement $p<0.001$
- Cognitive function slightly decreased at the 6month mark with DBS
- More adverse events with DBS $p<0.001$ (49 adverse events with DBS vs 15)
- Conclusion: Deep Brain stimulation is superior to best medical therapy for people with Parkinson's Disease, in regard to increased "on time", UPDRS scores and Quality of Life self assessment.

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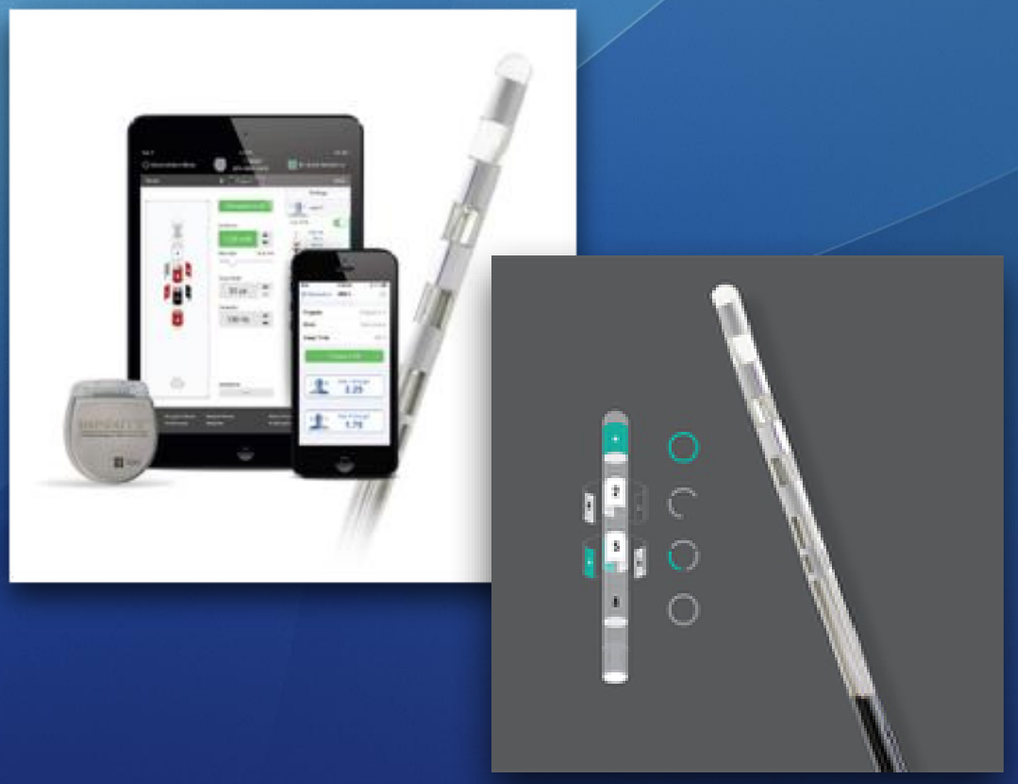
DBS Devices

- Implants
  - Lead to target in brain
  - Pulse generator and extension cable
- Programable
  - Externally by Neurologist and Patient
  - Battery will require replacement
  - even with re-chargeables



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DBS Patient Selection

- Idiopathic Parkinson's Disease
  - Significant "motor fluctuations"
  - Poor on time not amenable to medication alterations
  - Responsiveness to Carbidopa/Levodopa
    - "On/Off" Evaluation
      - Intolerance to medication
- Intact cognitively
  - MMSE >23, Mattis >125
- If depression - treated
- Expectations
  - Best "on time" increased three fold

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"Damn it, I'm a brain surgeon, not a rocket scientist!"

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Two Stage Surgery

- Two stage process
  - 1st Implant Lead - stereotactic surgery
    - usually done awake

- 2nd Implant IPG (Implantable Pulse Generator)
  - Done under general anesthesia

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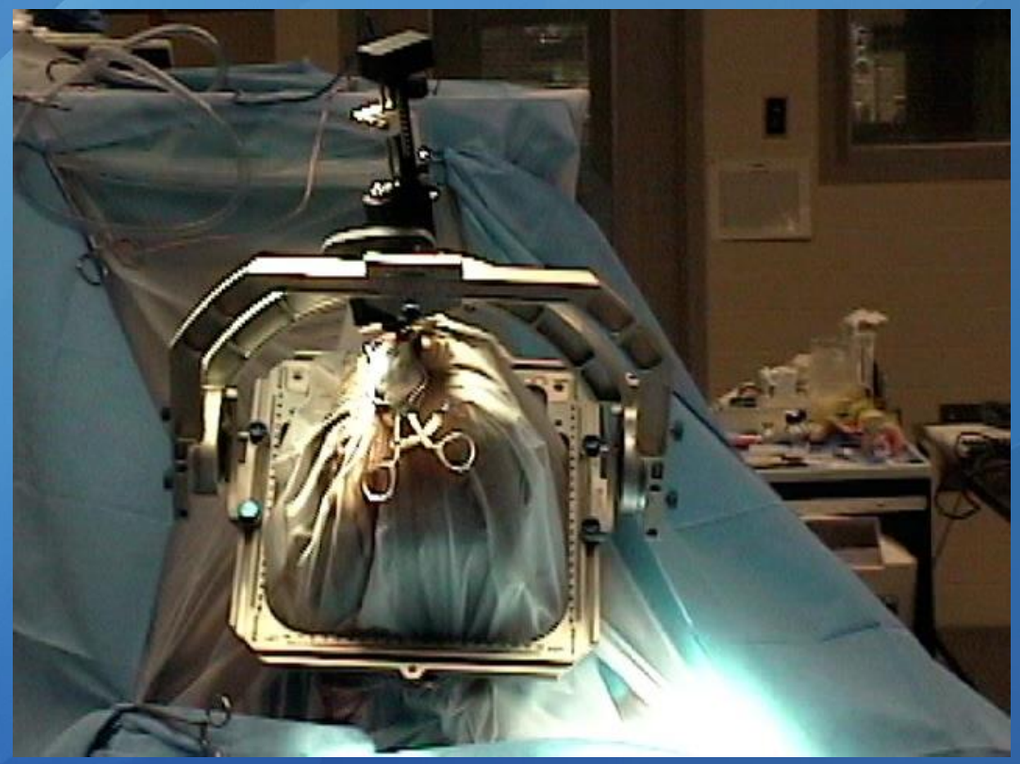
First Stage

- Lead Placement
  - precise implantation of the lead into the brain
  - Stereotactic procedure
    - Frame Based
    - Frameless
  - Microelectrode recording
  - Test stimulation

Frame-based DBS

- Uses titanium cage applied to skull
- Requires all imaging the day of surgery
  - Lengthens surgery
- Dependent on placement of frame
  - the more accurately it is placed the more accurate the placement
- Fixes patient to bed throughout operation
- Fatigue factor - wearing the frame



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Frameless DBS

Uses bone screws for accuracy

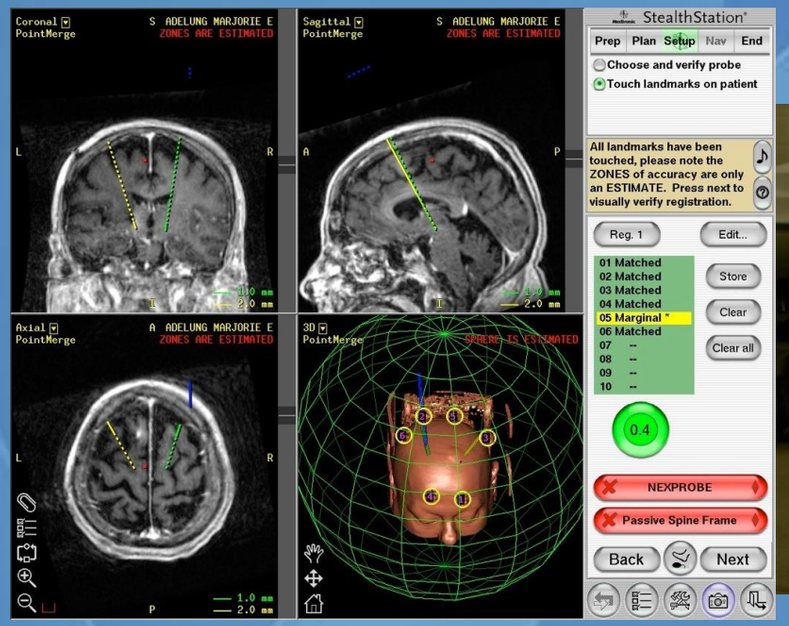
Imaging can be done 1 week or more before surgery

Patient is NOT immobilized for surgery

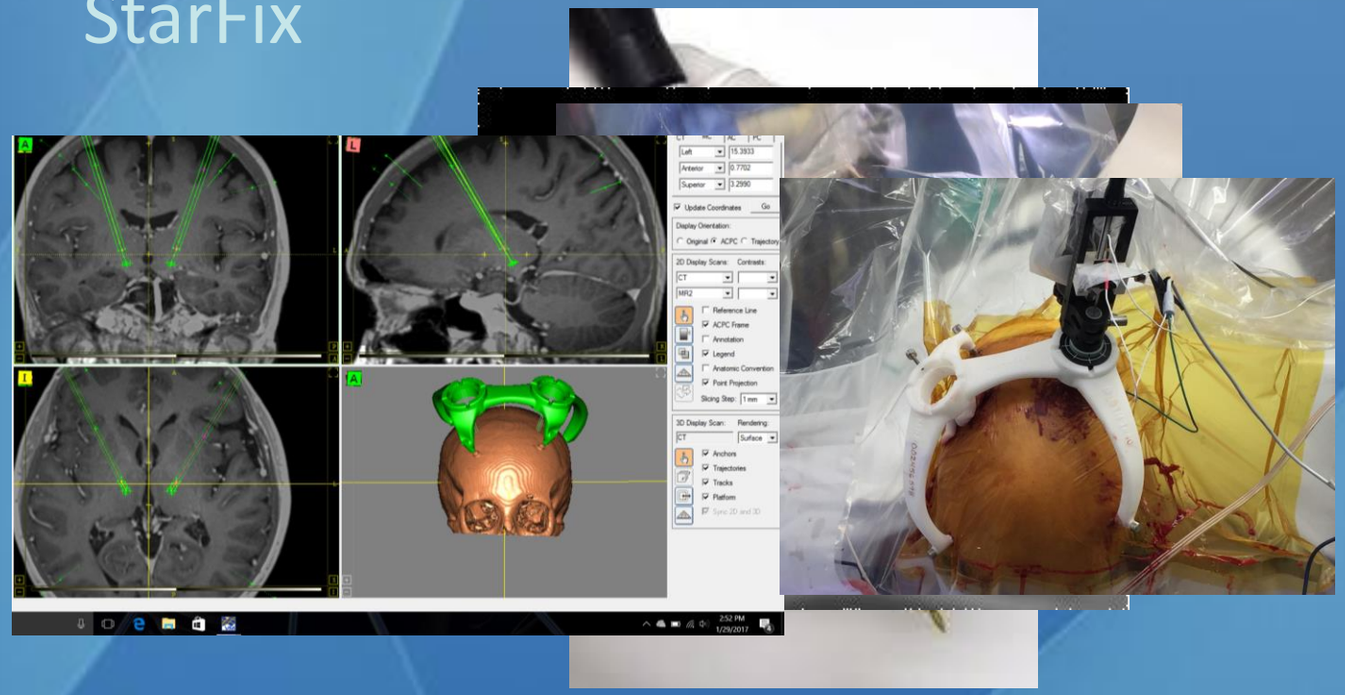
Generally a faster operation

NO SACRIFICE in accuracy

NexFrame



StarFix



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Surgical Overview

- Stop all Movement Disorder medication 6pm prior to surgery
- Surgery in AM the following day
  - Awake but sedated
  - Microelectrode recordings
    - listen to the brain to localize target
  - Test stimulation
    - look for benefit
    - screen for side effect
    - Secure electrode and close
- Admitted to ICU
  - Imaged the next day and discharged

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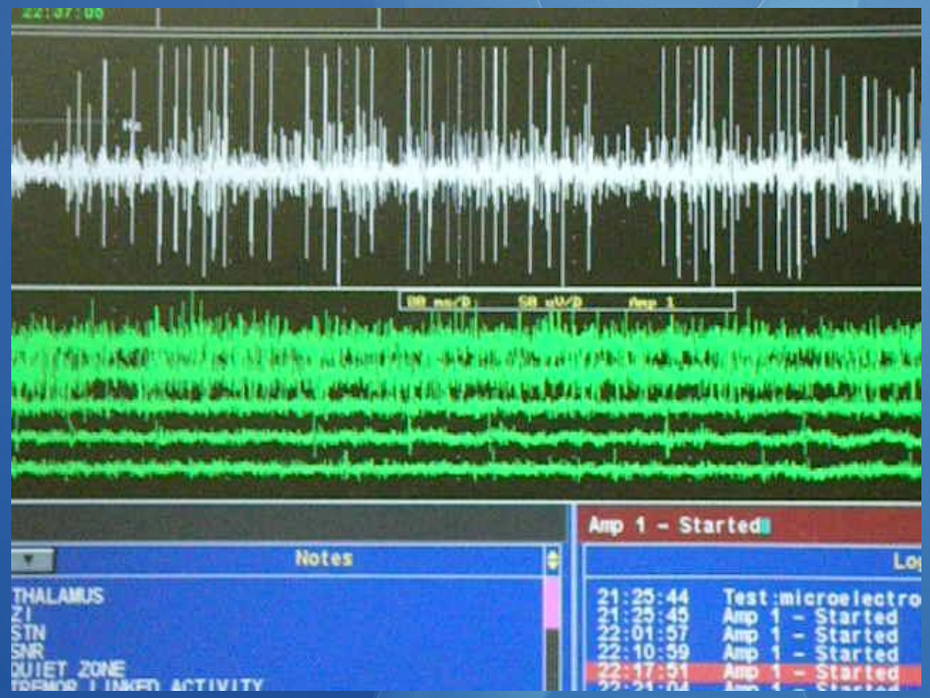
Microelectrode Recording and Test Stimulation



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Target Selection

Vim: Ventral intermediate nucleus of the Thalamus

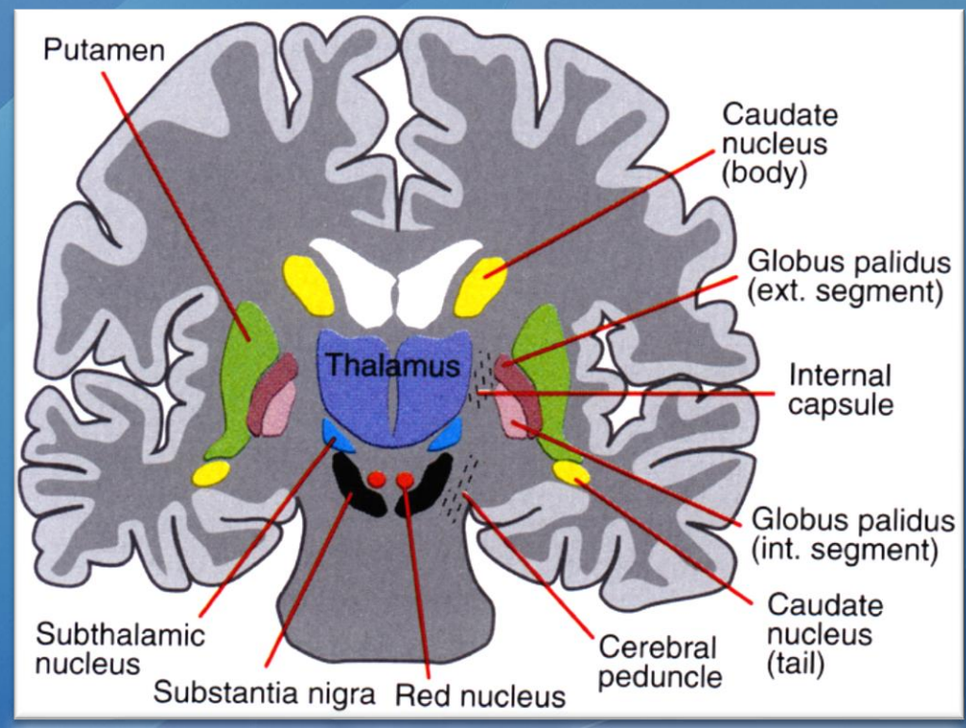
Tremor control, little to no reduction in freezing, bradykinesia, rigidity, dyskinesia

GPi: Globus Pallidus (internal segment)

Reduction in dyskinesia, rigidity, freezing and tremor. No significant reduction in medication

STN: Subthalamic nucleus

Reduction in tremor, bradykinesia, freezing, rigidity, reduction in medication with many patients which reduces dyskinesias.



There may be more cognitive decline in STN DBS than GPi PLoS One. 2016; 11(6): e0156721
STN had better results in motor function vs. GPi Lancet Neurol 2013 Jan;12(1):37-44

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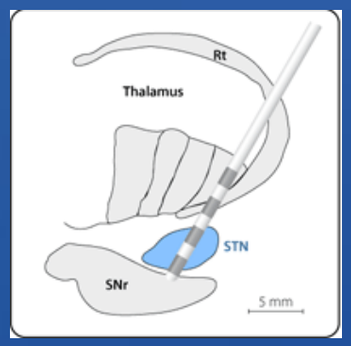
Outcomes: STN DBS

- Bilateral STN
  - Tremor 82% improvement
  - Bradykinesia 79% improvement
  - Rigidity 81% improvement
  - Dyskinesia 71% improvement
  - Medication reduction 40-50%



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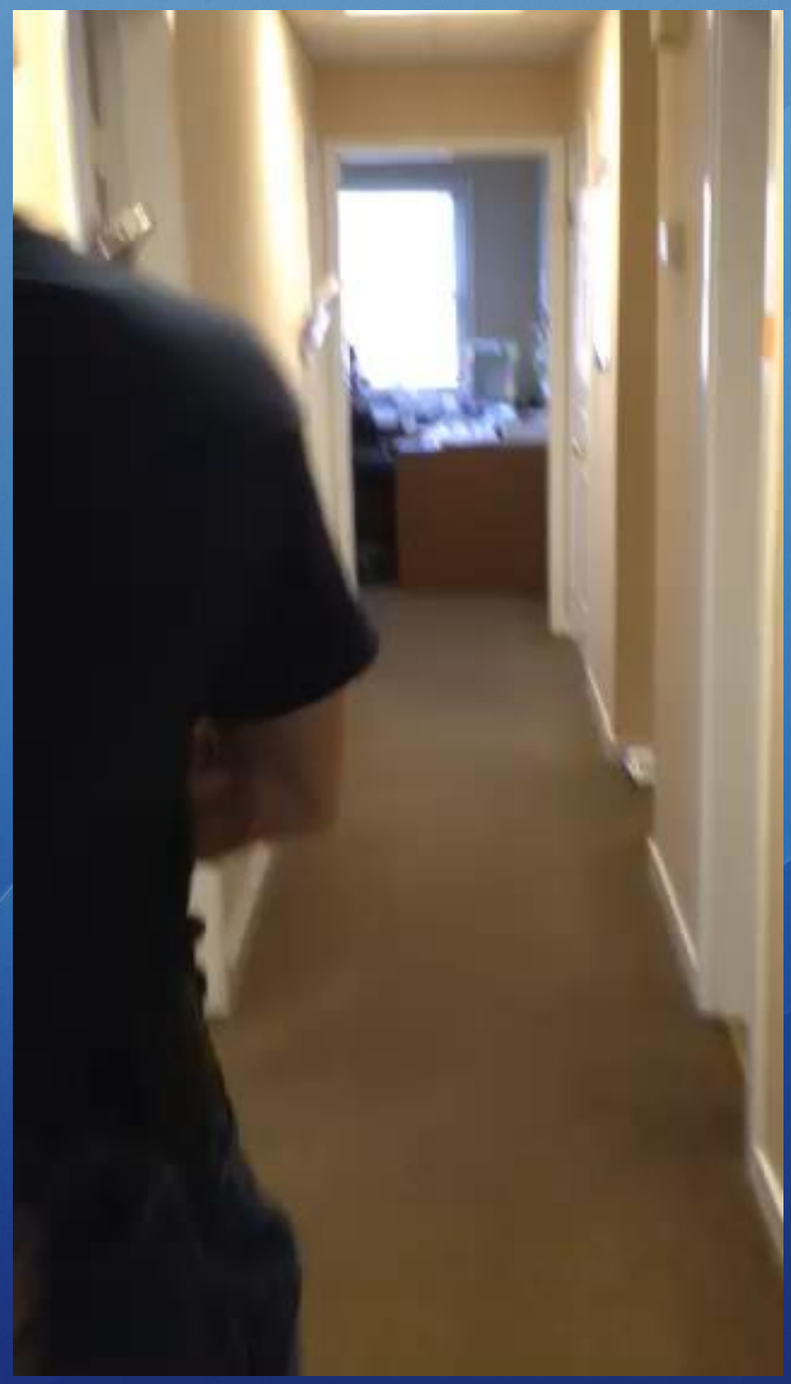
Outcomes: GPi DBS

- Bilateral GPi
  - Tremor 70% improvement
  - Bradykinesia 80% improvement
  - Rigidity 83% improvement
  - Dyskinesia 85% improvement
  - Medication reduction <20%

*Fewer Cases: Cannot compare to STN



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Expectations

- Deep Brain Stimulation is NOT a cure
- Tremor Control does not mean tremor arrest in every case
- Parkinson's Disease symptoms that are improved are not completely arrested
  - tremor, bradykinesia, dyskinesia, rigidity
  - expect your best "on" time to be the majority of your day
  - DBS does not replace the use of medication
- Dystonia improvement is better in large muscle groups

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Complications

"Listen up, my fine people, and I'll sing you a song 'bout a brave neurosurgeon who done something wrong."

Complications

Lead Migration/Breakage (1-3%) <1%

Usually due severe trauma or twisting of the cables

Infection (3-23%) 2%

Pulse generator is more common than "brain lead"

Hemorrhage - Blood clot (2%) <1%

Most are insignificant found on postop imaging

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NCN Experience

- Longest Experience DBS in Washington Metro Area
  - Collaboration with NIH
  - First Case 2001
  - >1000 DBS cases
  - First and only to do frameless DBS in DC and Maryland
  - >65% Parkinson's Disease
  - ~25% Essential Tremor
  - OCD, Tourette's syndrome, pain, MS related tremor

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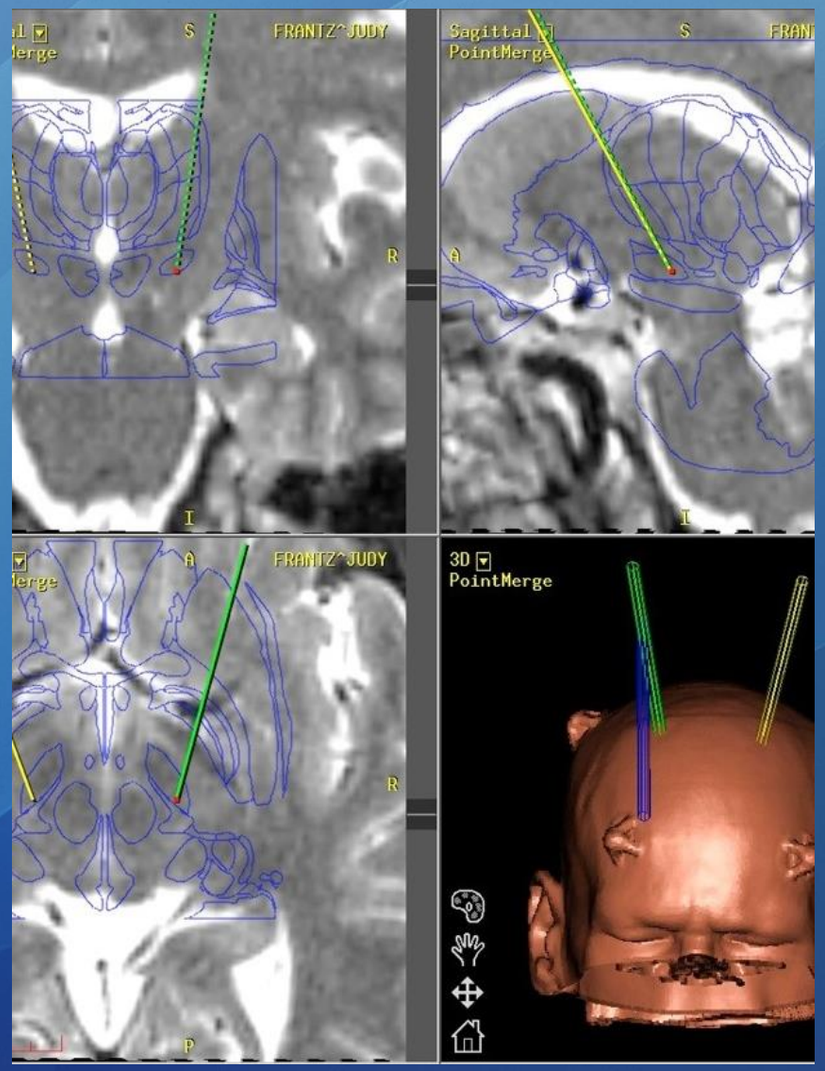
NCN Research

- ***Frameless Accuracy in DBS***
- Compared postop image to predicted implant site from planning and recording
- Looked at 109 implants
- No difference in accuracy with frame as compared to literature
- Presented Neuromodulaiton and Pain Conference, Napa California 2008



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NCN Research

- ***Brain Impedance Recovery after DBS***
- How does the brain recover from DBS surgery
- Does this effect how we stimulate the brain?

- J of Neurol Neurosurg Psychiatry 2013;0:1-4 doi:1136/

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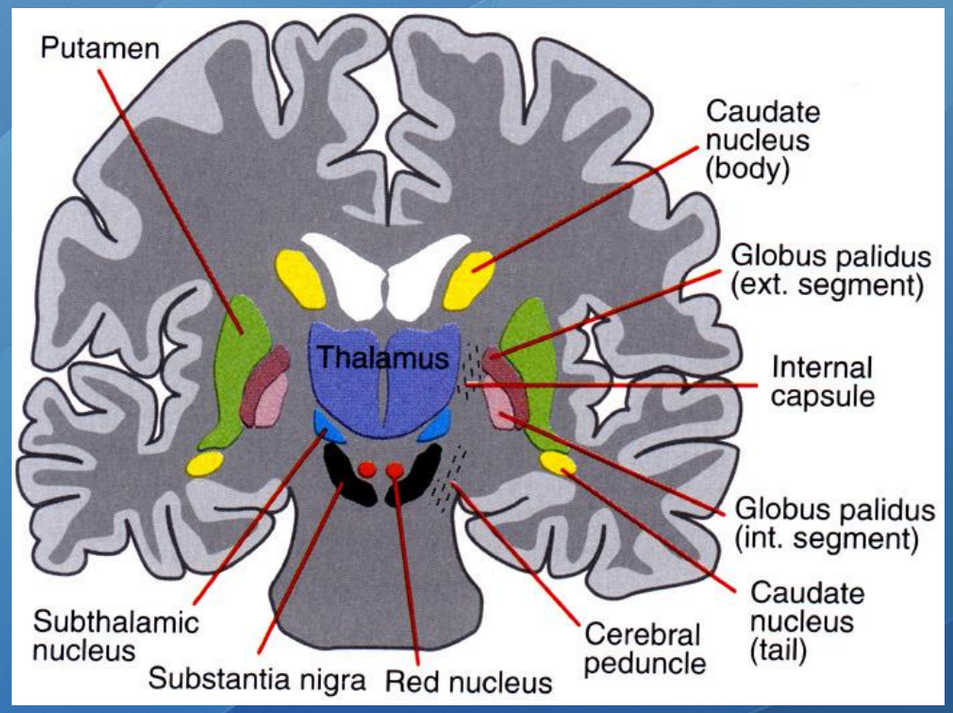
NCN Research

- ***Target selection***
- How do we pick which target is best for which patient
- Devise an algorithm to help with target selection



- ***Alteration of Final Target based on MER or Macrostimulation – a functional approach to DBS***
- Looking at anatomic verses physiologic targeting in DBS