MedStar Georgetown University Hospital

Knowledge and Compassion
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April 17, 2018

Deep Brain Stimulation

Christopher G. Kalhorn, MD, FACS, FAANS
Associate Professor of Neurosurgery
Director of Movement Disorder Surgical Program
MedStar Georgetown University Hospital
National Parkinson's Foundation Center of Excellence

Christopher G. Kalhorn MD FACS FAANS

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Stryker
Visum Surgical Light
Stryker
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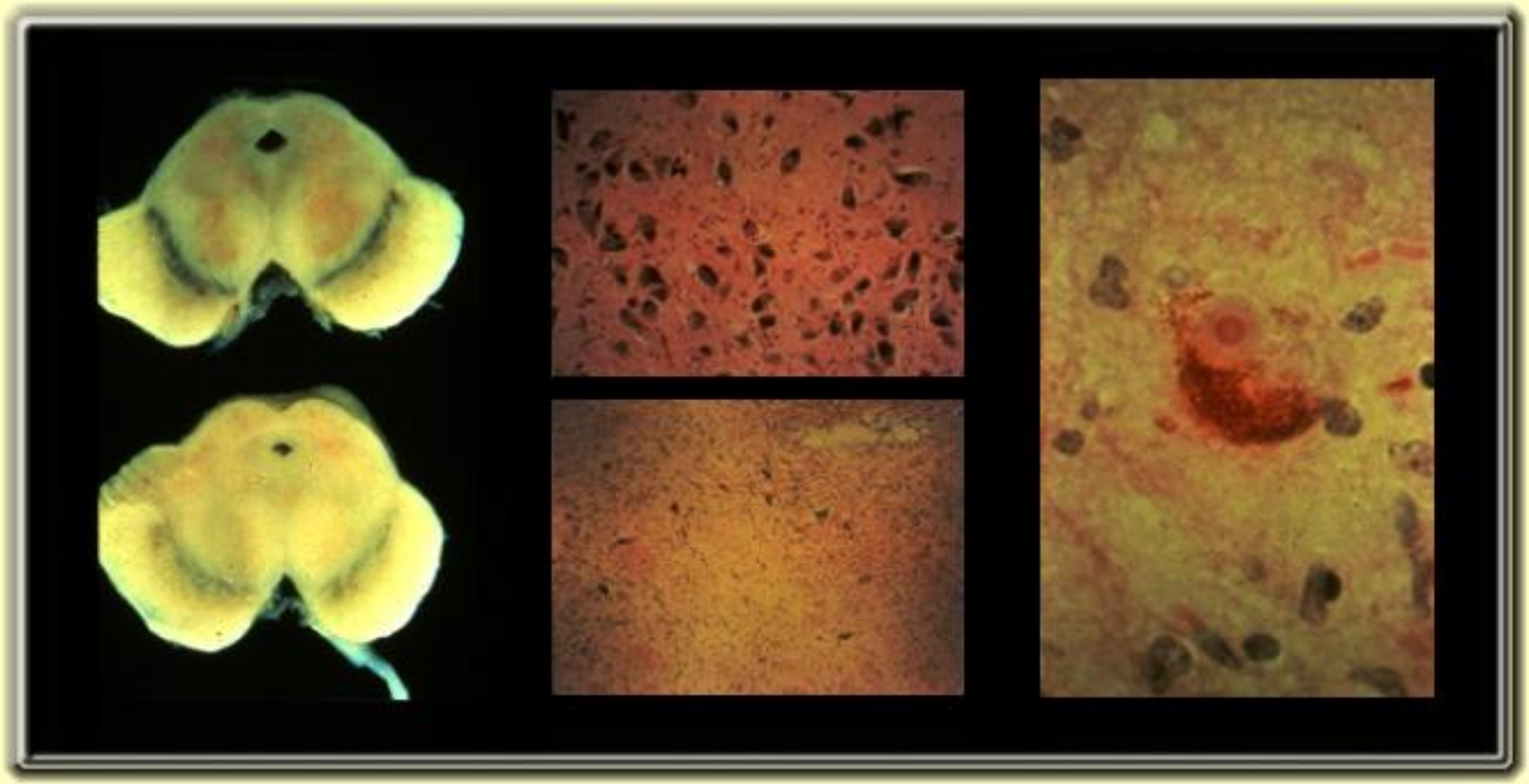
SANDELL

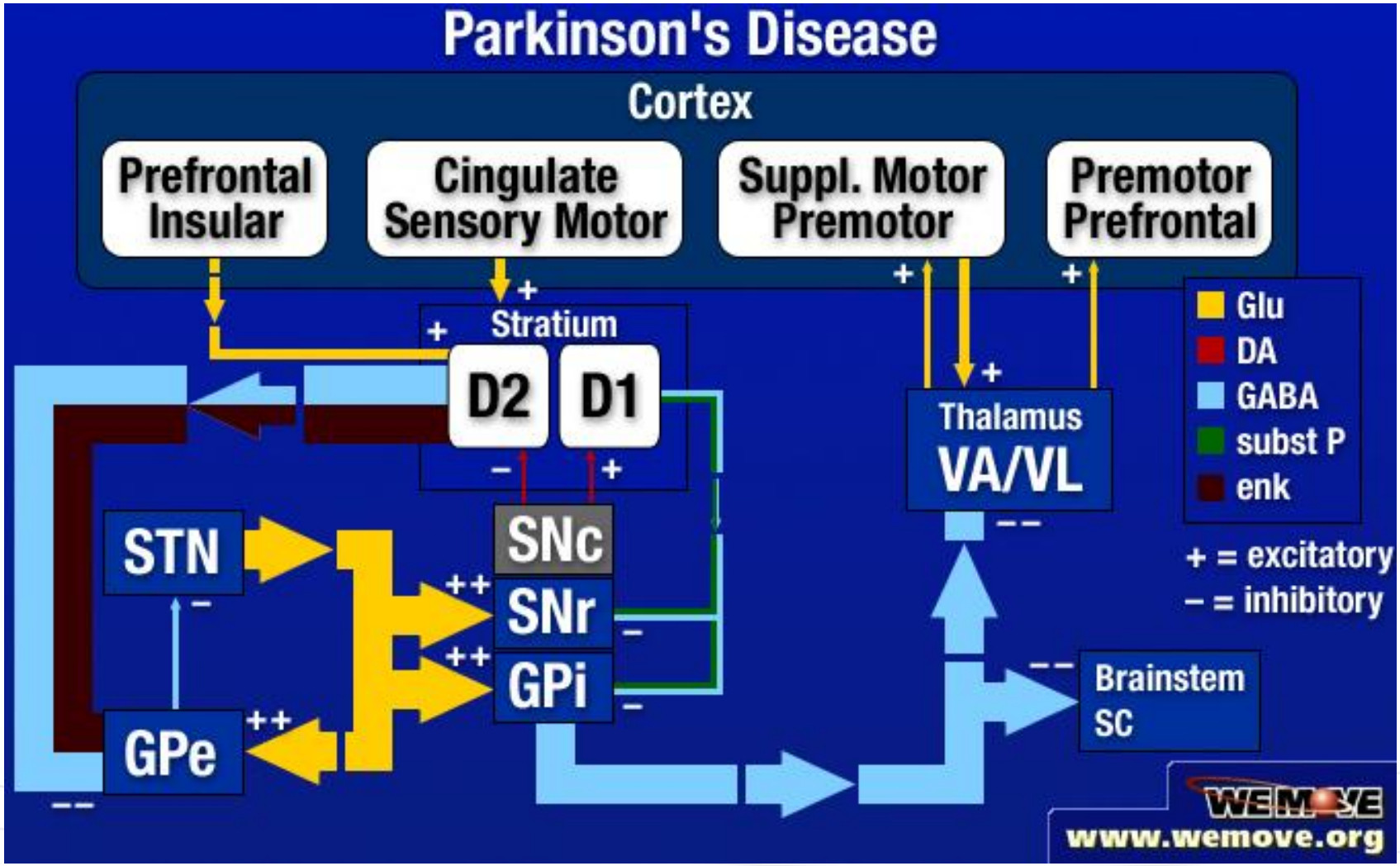
Pathology of Parkinson's Disease



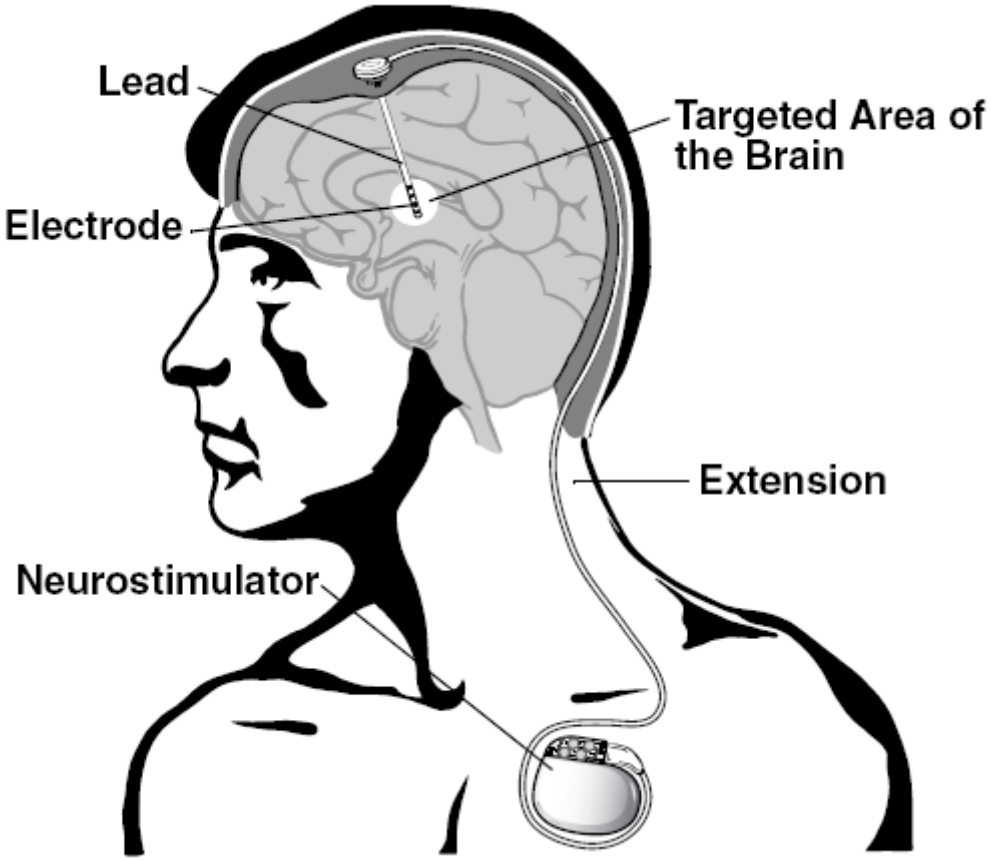
Deep Brain Stimulation (DBS)

- High frequency, pulsatile, bipolar electrical stimulation
- Stereotactically placed into target nucleus
- Can be activated and deactivated with an remote control
- Exact physiology unknown, but higher frequencies mimic cellular ablation
- May mediate imbalance in beta/gamma activity

Function Anatomy of Parkinson's Disease



Deep Brain Stimulation



Deep Brain Stimulation

- Mimics the effect of a lesion without destroying brain tissue
- FDA approved for Parkinson's disease and Essential Tremor
- Stimulation of the STN and the GP can improve the full constellation of parkinsonian motor features

The Deep Brain Stimulation for Parkinson's Disease Study Group

- Prospective, double-blind, crossover study in patients with advanced PD
- Electrodes were implanted in the STN or pars interna of the globus pallidus
- Patients then underwent bilateral high frequency deep brain stimulation

Results

- Demonstrated an improvement in the motor score of 49 percent in the STN and 37 percent in the GP

Results

- Percentage of time during the day that patients had GOOD MOBILITY without involuntary movements increased from 27 percent to 74 percent with STN stim and 28 percent to 64 percent with GP stimulation

Movement & Control

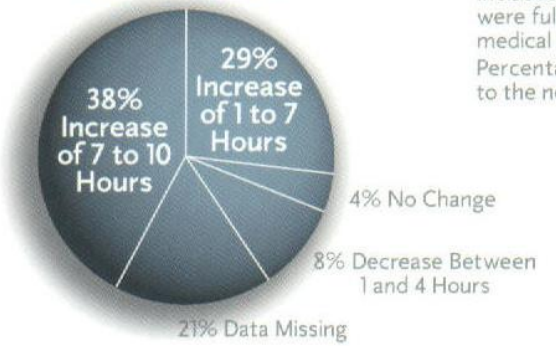
Activa Therapy Increases "On" Time By Over 6 Hours

In Medtronic multicenter clinical studies, Activa neurostimulation leads were implanted in the subthalamic nucleus (STN) or the globus pallidus interna (GPi). Activa Therapy increased "on" time – periods of good motor function and symptom relief – by an average of more than 6 hours per day at 12 months.[1]

STN Patients
Average Improvement
6.1 Hours*

Absolute Change in Daily "On" Time at 12 Months (n=40*)

GPi Patients
Average Improvement
6.7 Hours*



Absolute Change in Daily "On" Time at 12 Months (n=24*)

* Includes only patient data that were fully verified against medical records.
Percentages have been rounded to the nearest whole percent.

Results

- Stimulation and medication act together
- Stimulation improves tremor, rigidity, bradykinesia, gait, and ADLs

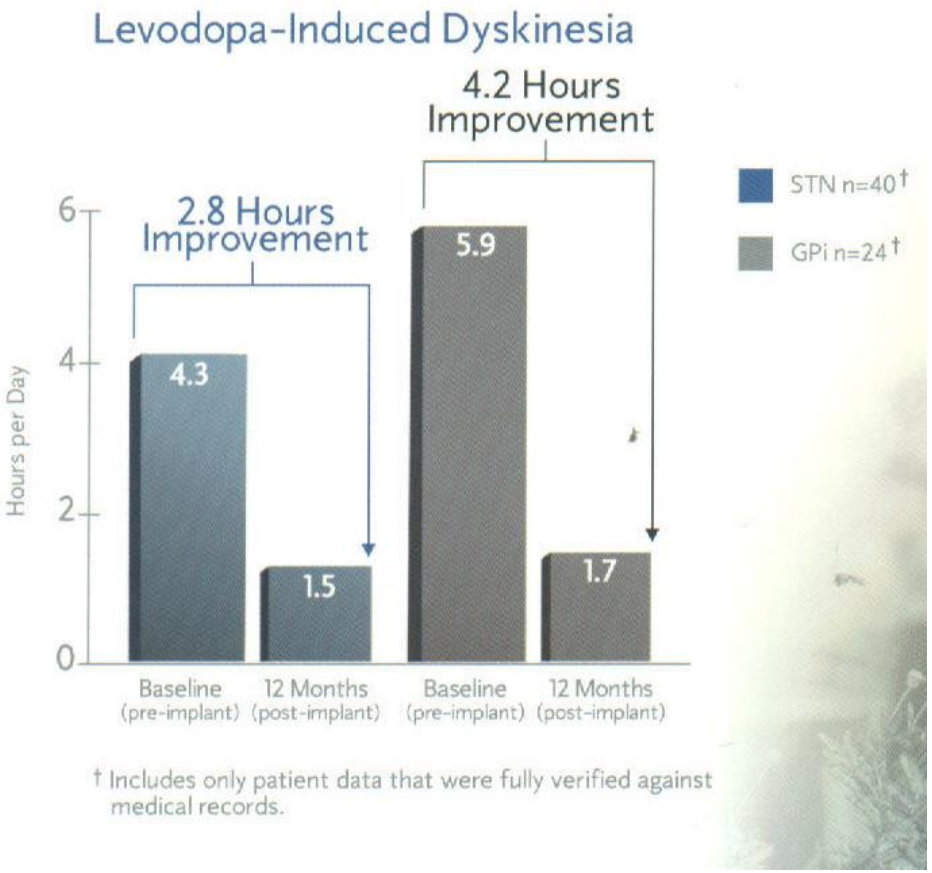
Medication Reduction

- Daily levodopa dose was reduced from 1218.8 mg at base line to 764 mg with STN stimulation

While Decreasing Levodopa-Induced Dyskinesia

Activa Therapy patients benefit from dramatic improvement in movement and mobility while experiencing fewer hours of levodopa-induced dyskinesia – which can be as disabling as Parkinson's disease itself. [9]

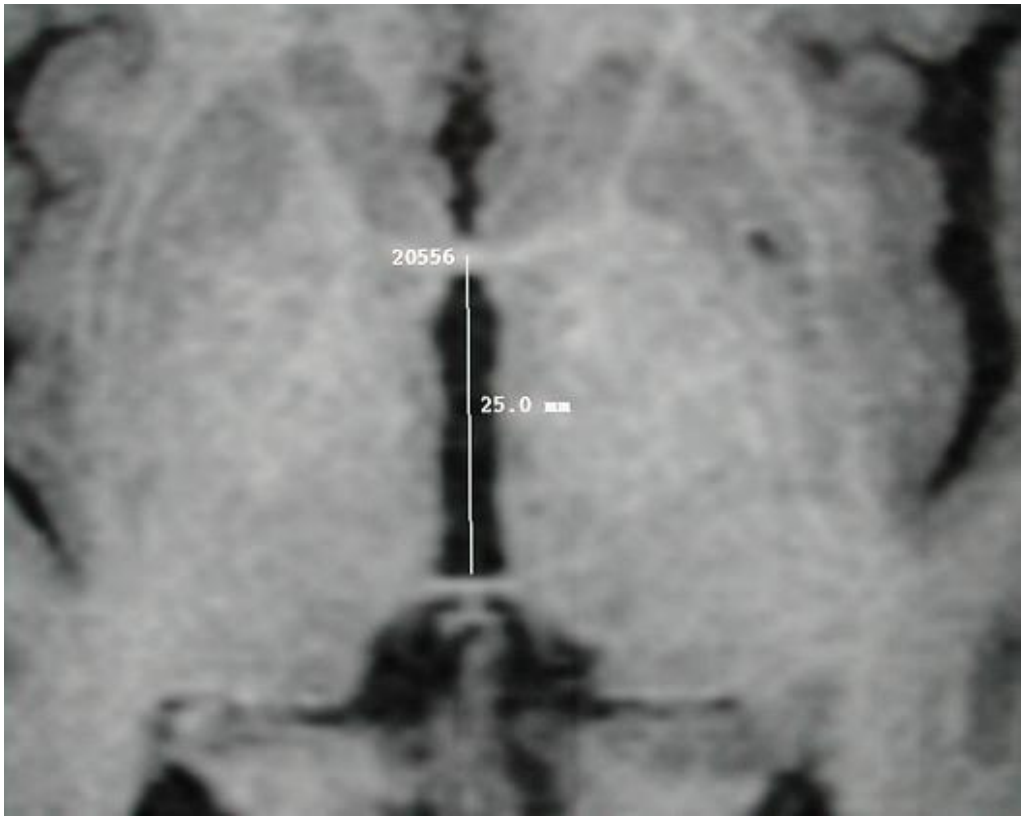
In the clinical studies, Activa Therapy reduced dyskinetic "on" time by an average of 2.8 hours in STN patients and 4.2 hours in GPi patients. [1]

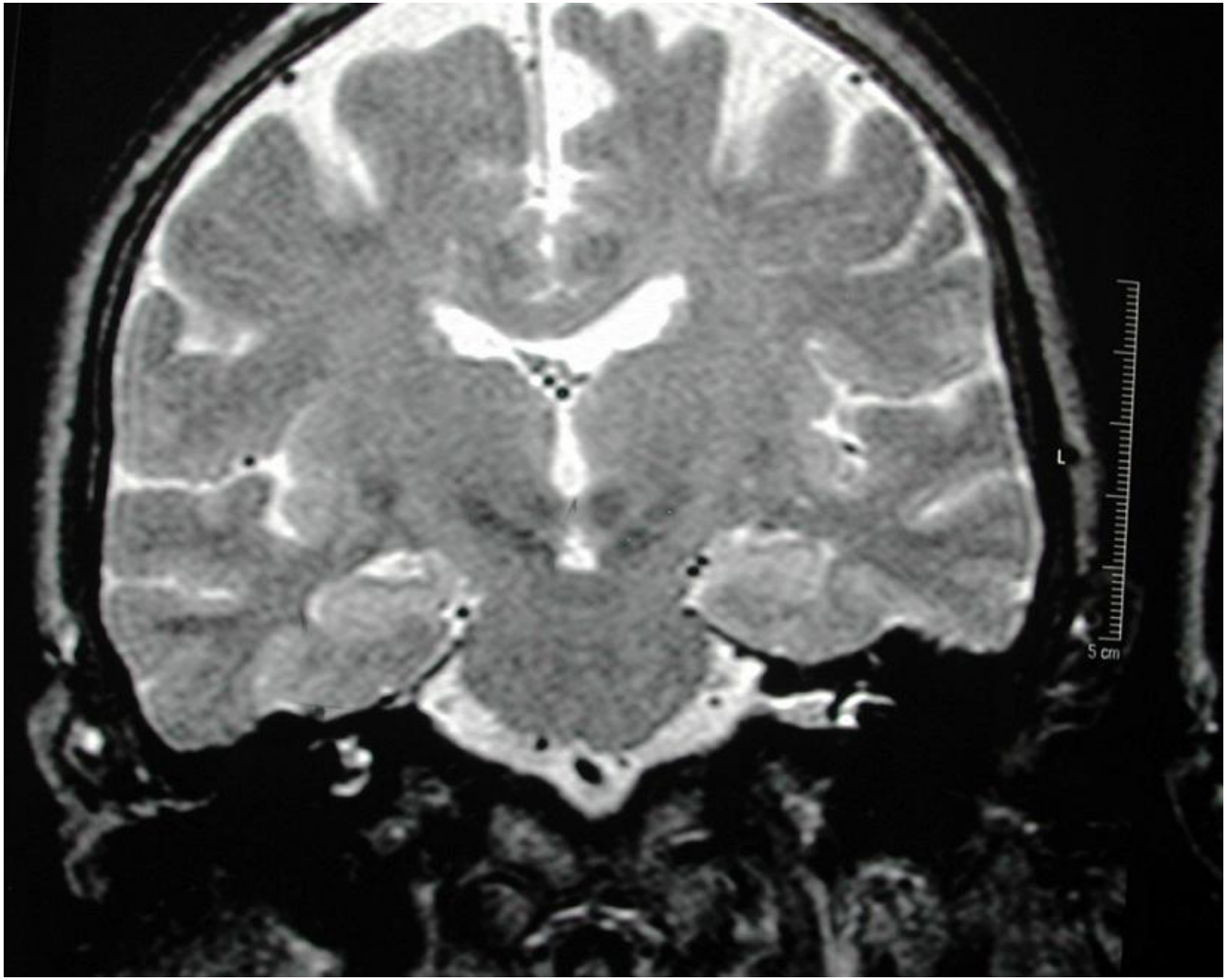


Intended Target Location

- STN-center of motor territory
- Gpi-anterolateral part of the motor territory internal pallidium

- Indirect
  - AC -PC / MCP
  - Formulas available
  - Easily see AC-PC
  - Spatial position of basal ganglia varies
- Direct
  - See structures
  - Refine indirect target
  - Requires excellent T2 images
  - Inconsistent between centers
  - Borders are not always perfectly visualized

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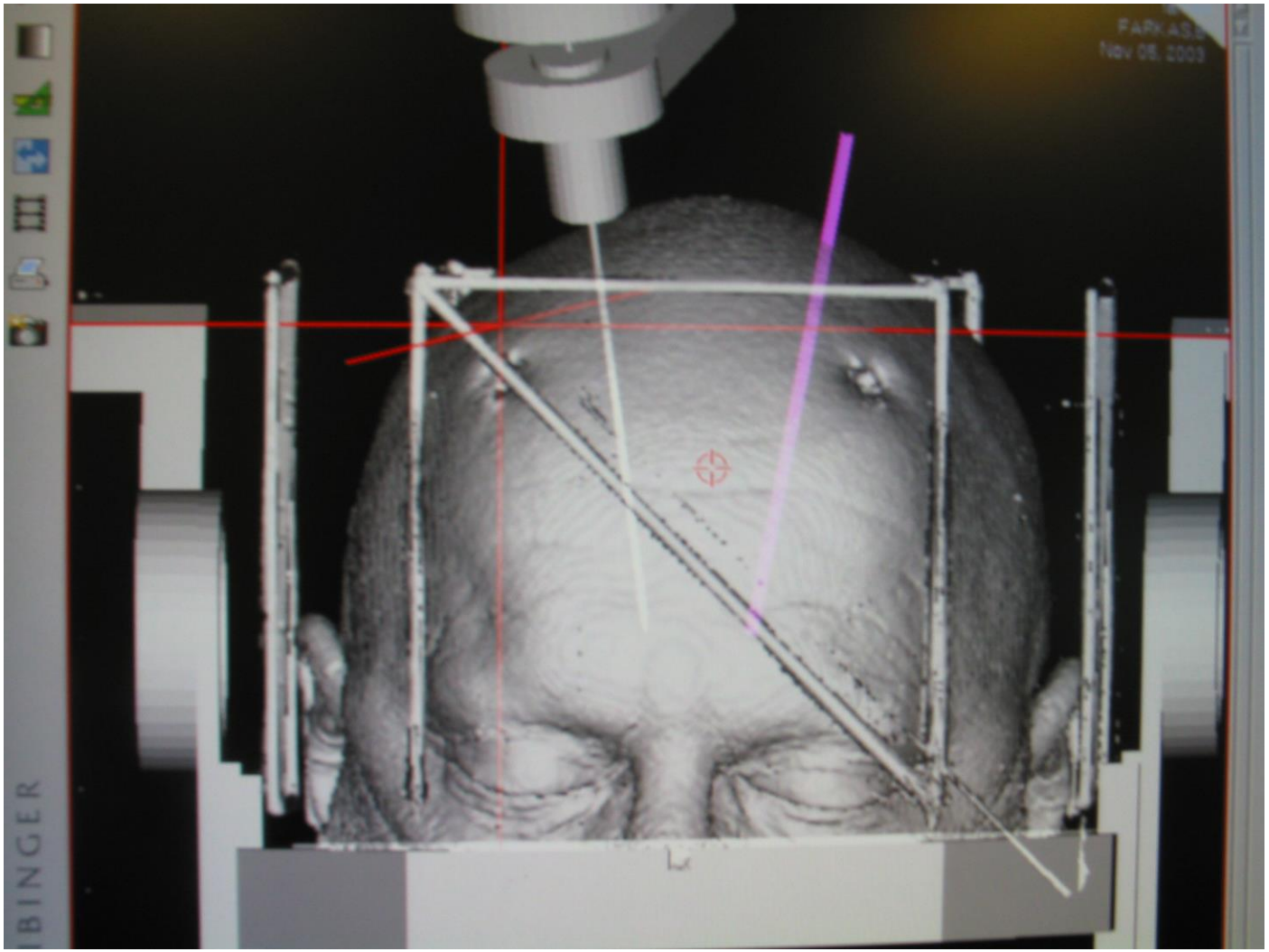
5 cm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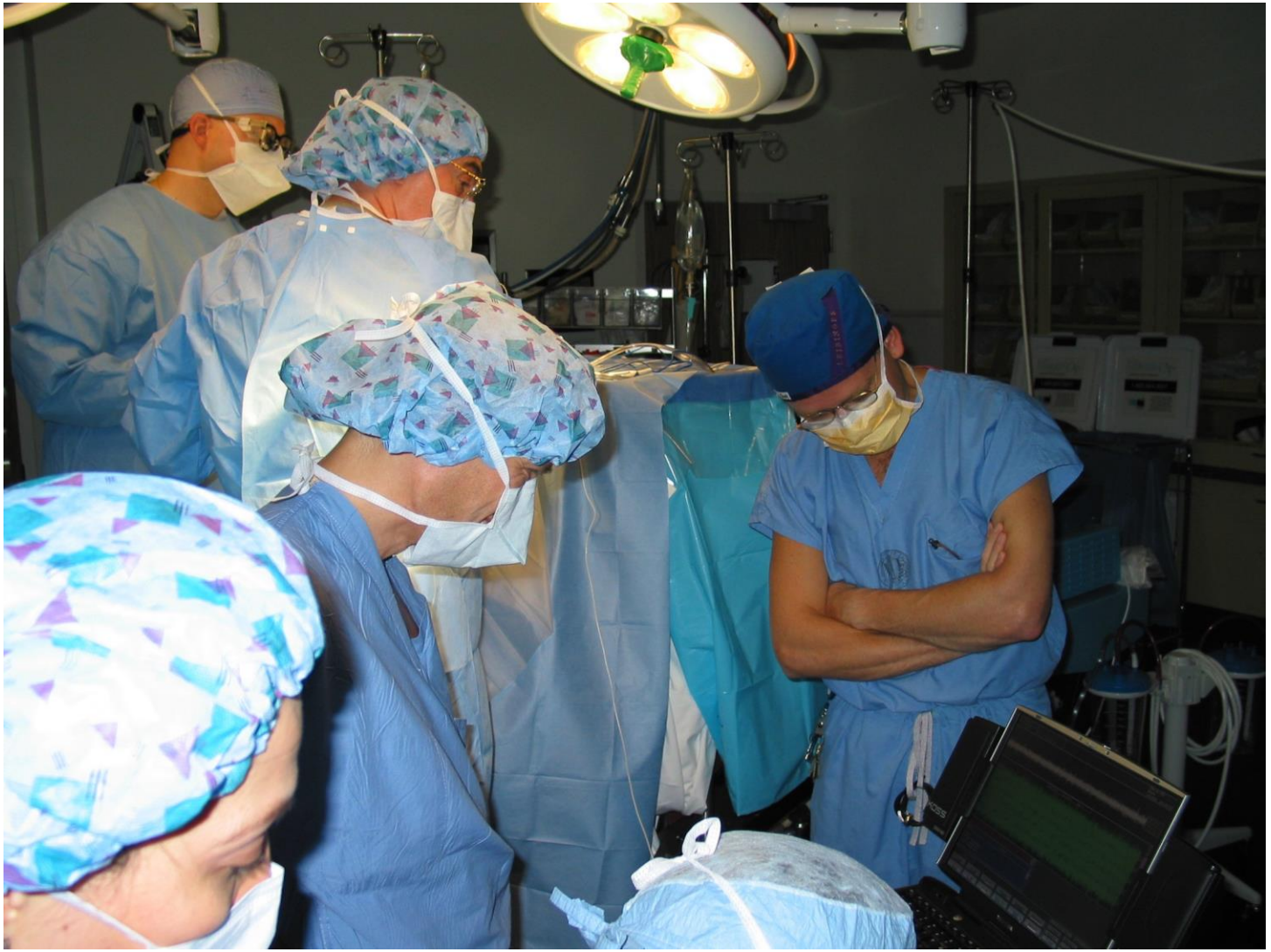
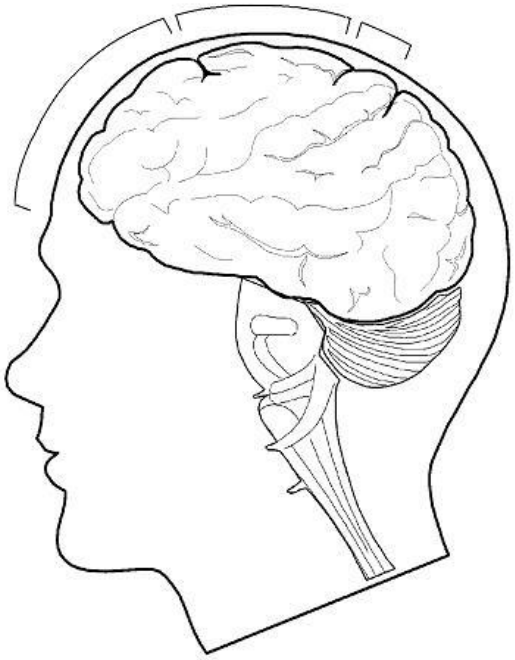
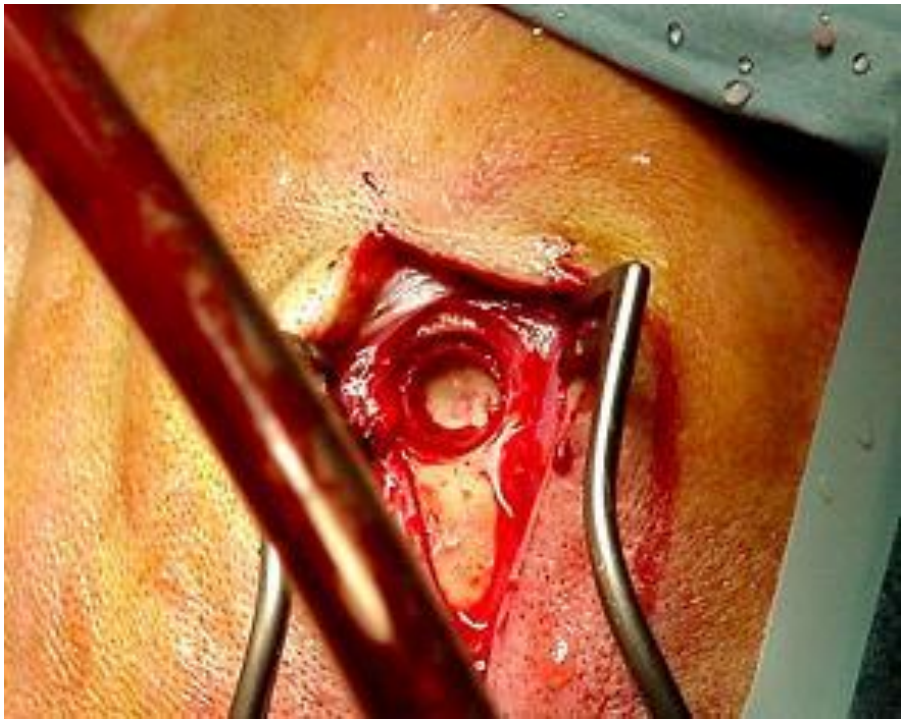


Entry Point and Trajectory Determination

How is the entry point determined?

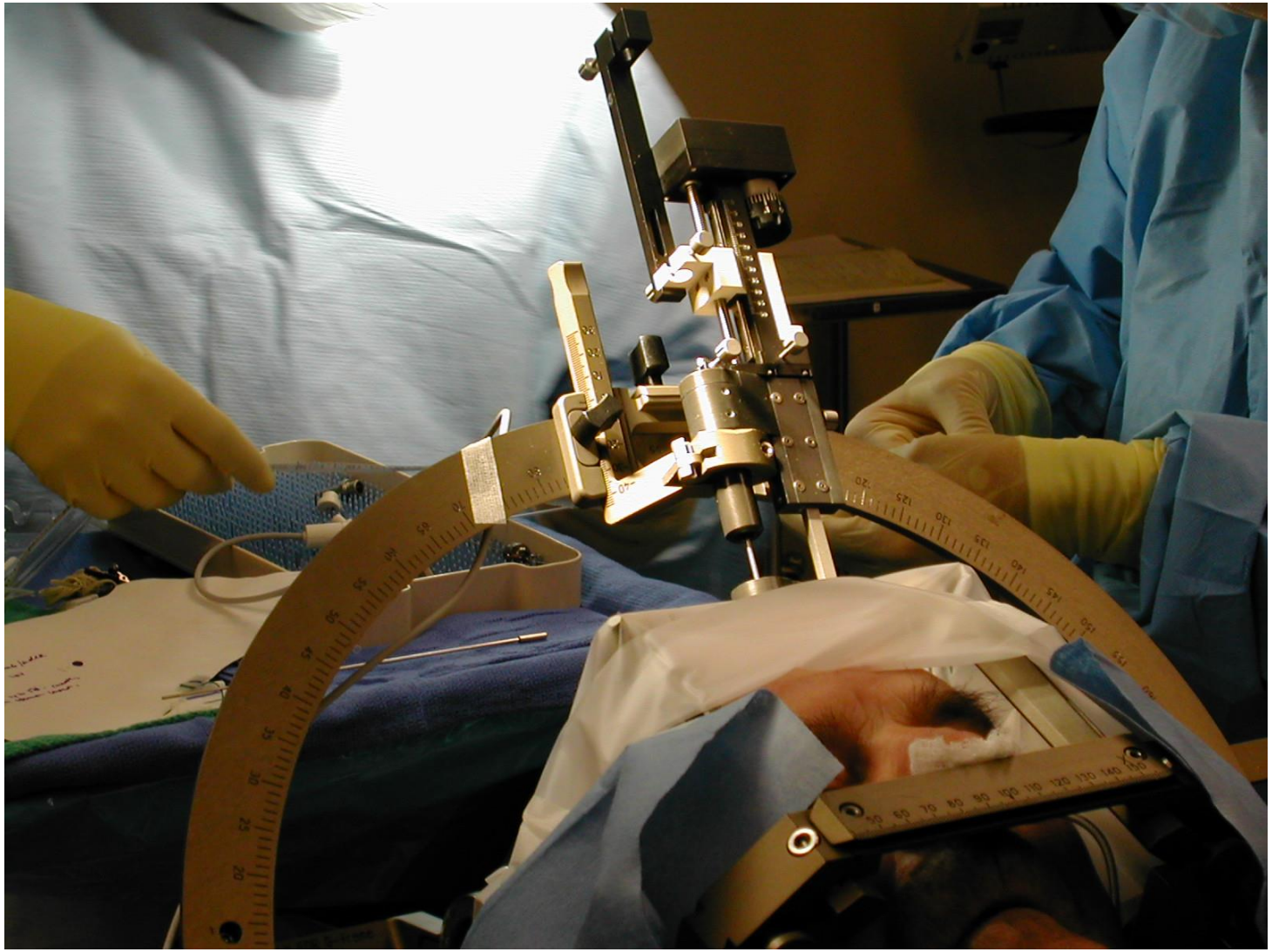


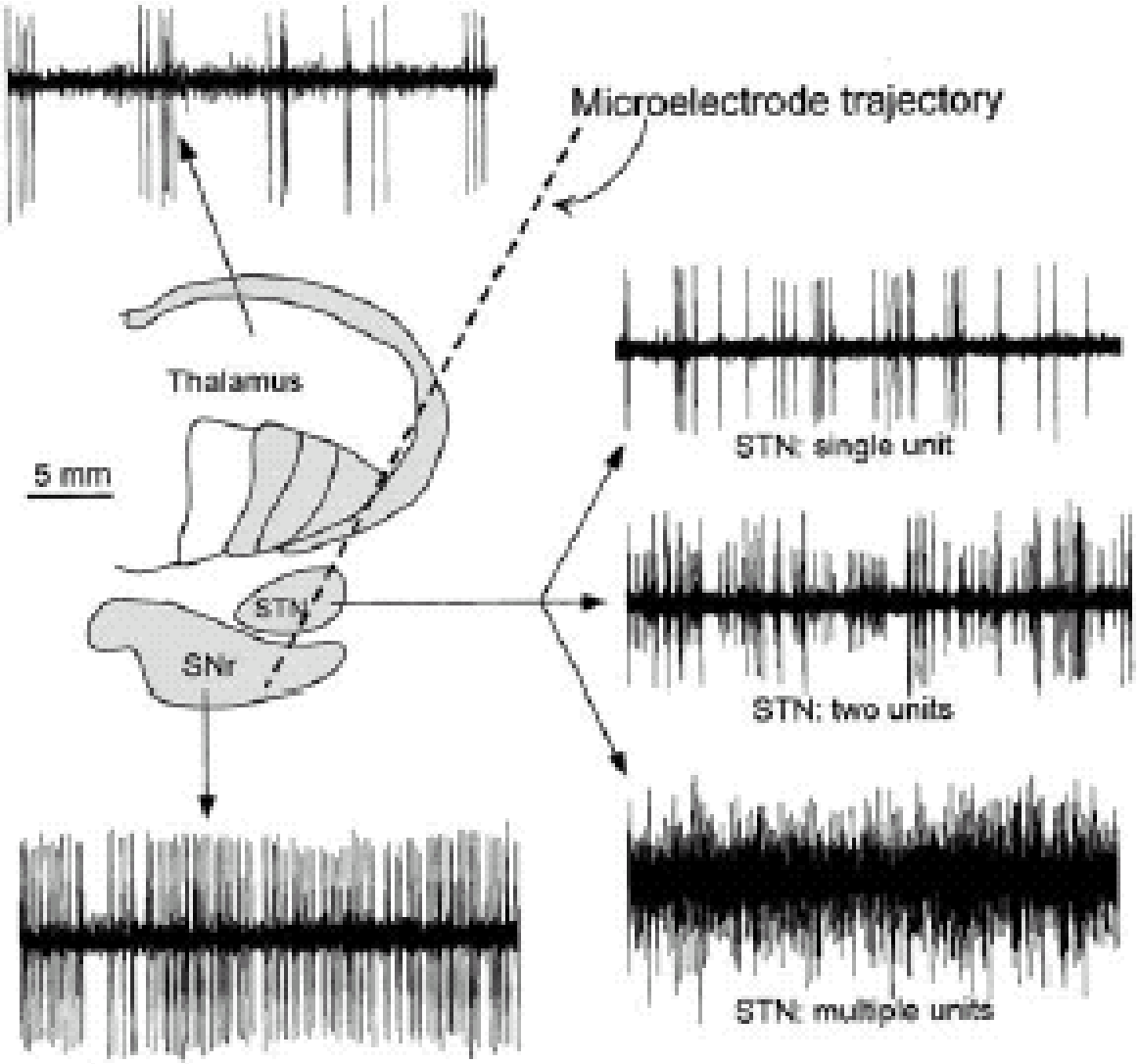


Why is physiological confirmation needed?

- Application accuracy of frames
- Image distortion.
- Imperfect visualization of target.
- Brain shift.
- Physiological function and anatomic location are not always the same.

A number of studies suggest that MER mandates a significant move of (2mm or greater) in 25% to 50% of the cases.



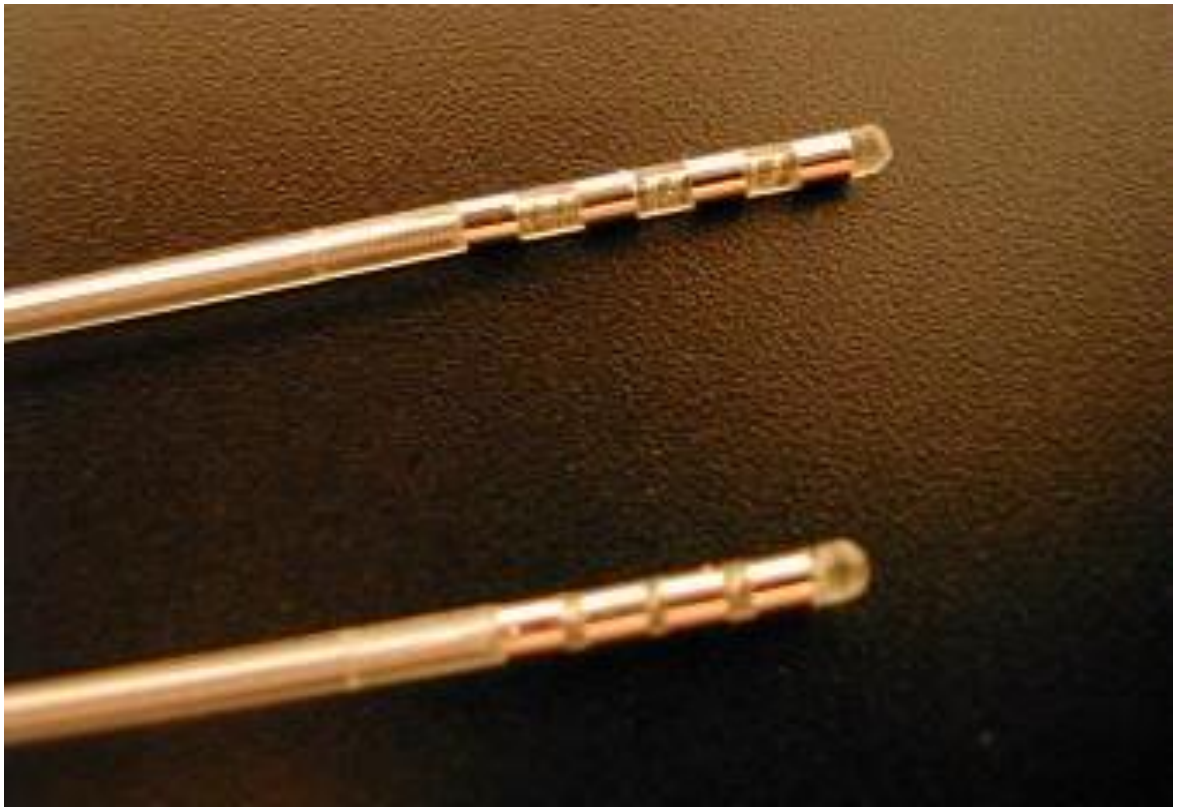

Microelectrode trajectory
Thalamus
5 mm
STN
SNr
STN: single unit
STN: two units
STN: multiple units

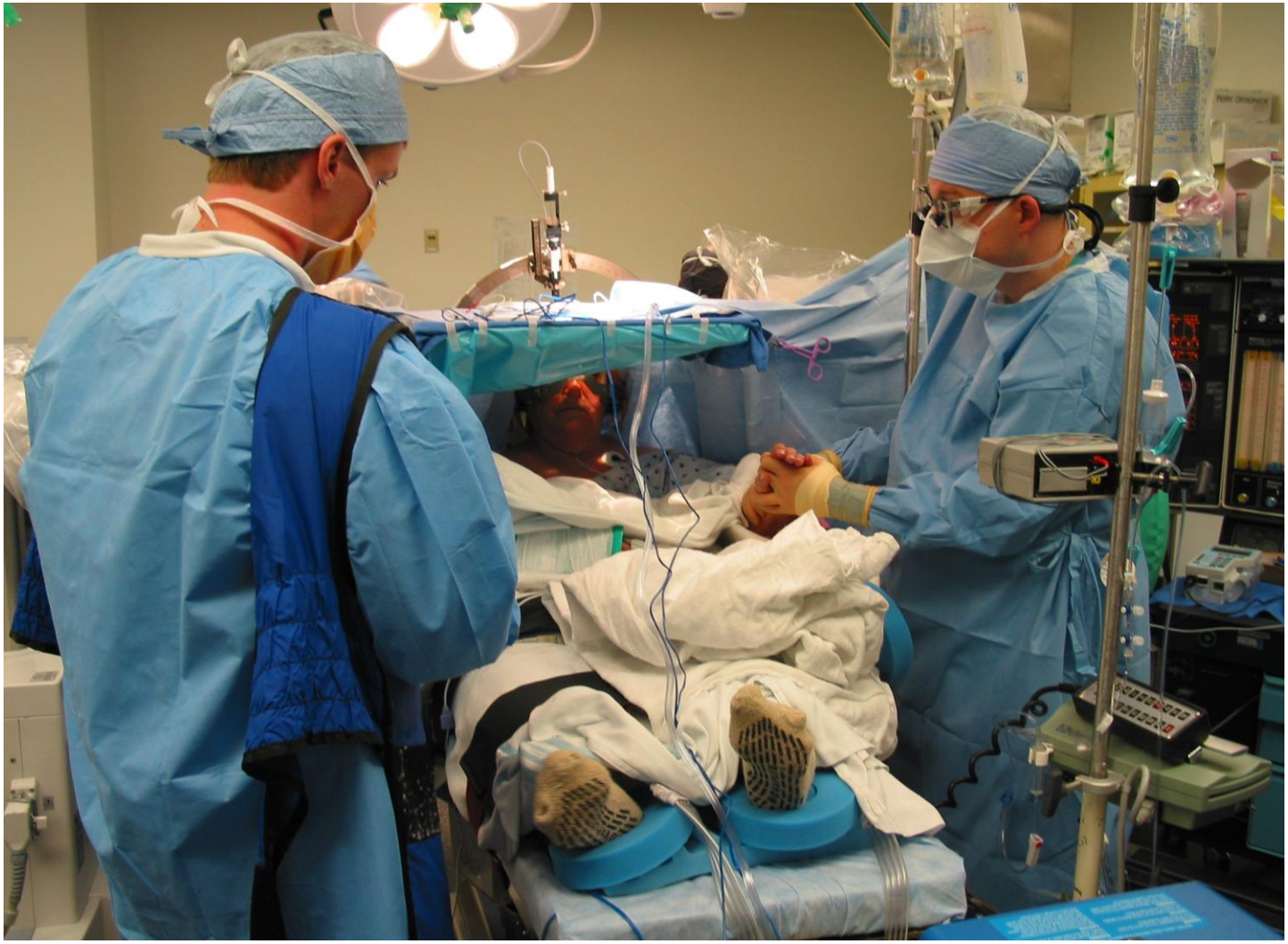
STN MER Acceptance

- Minimum 4 mm of STN cells with motor activity

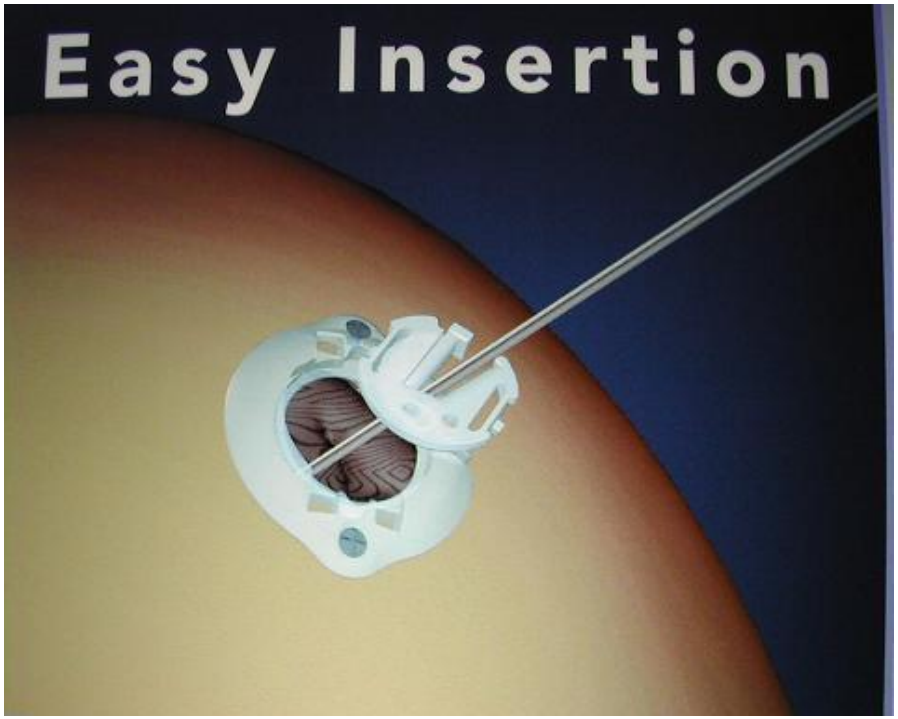
Lead Placement

- 3387 or 3389





IGN Navigus



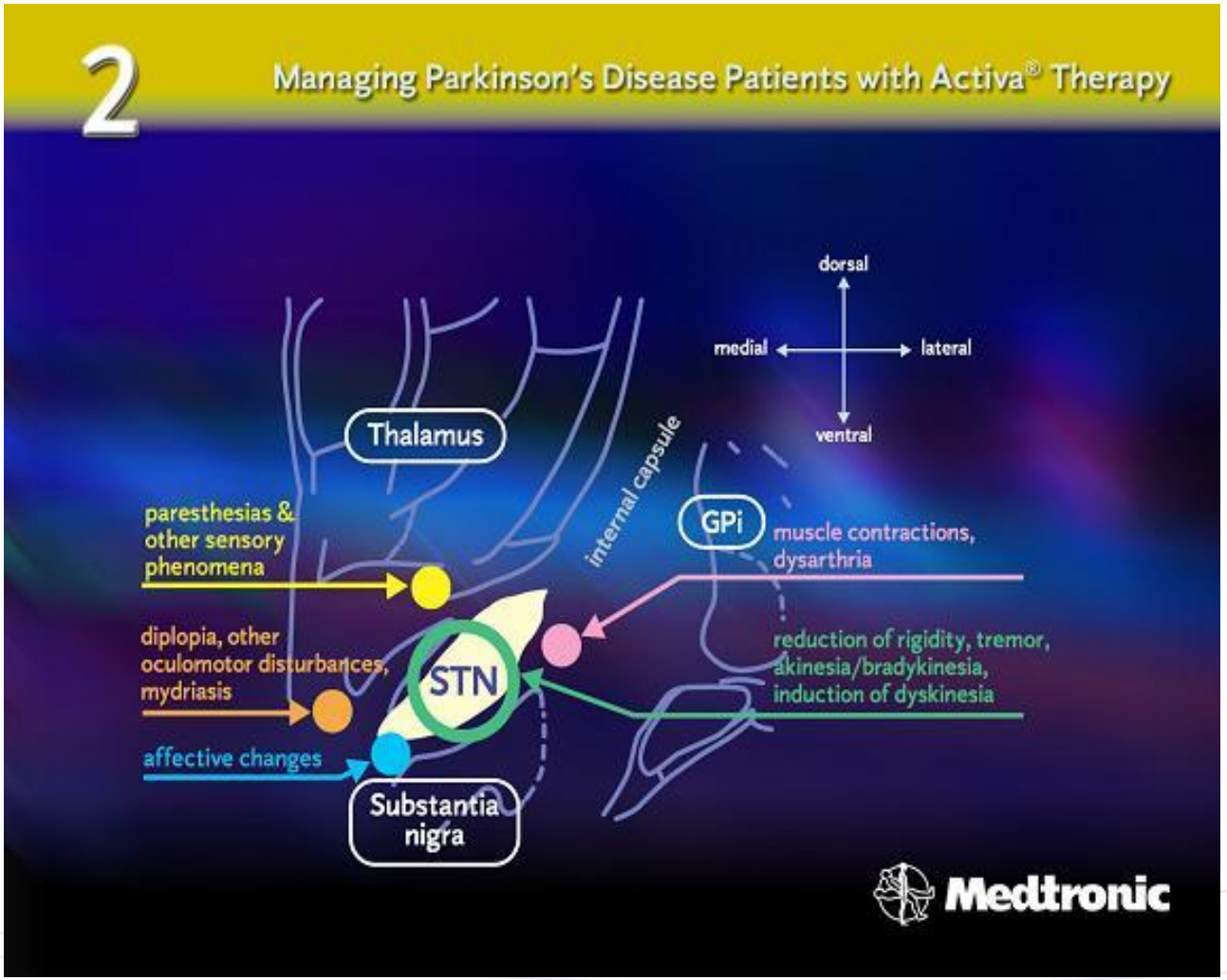
Test Stimulation

STN

- Side effects are more predictive of proper lead placement than efficacy of motor symptoms.
- If no reproducible adverse effect is elicited, it is likely that there is an electrical malfunction or the lead is too superior

Test Stimulation Side Effects

- STN



Deep Brain Stimulation – Candidates for Surgery

- Safe and effective
- Moderate to Severe Parkinson's (medically intractable)
- Young and otherwise in good health
- No significant cognitive impairment
- Not for newly diagnosed Parkinson's disease

Subthalamic DBS

- All cardinal features of PD noted to improve in open label trials
- “Off” UPDRS improved 60%
- “On” UPDRS improved 10%
- Increased “on” time
- Reduced dyskinesia
- Reduced medication requirements

Bilateral Subthalamic DBS

- Bilateral placement appears to be superior to unilateral placement
- Theorized neuroprotective mechanism, but no clinical evidence supporting this
- AE: confusion and hallucinations, increased dyskinesia before medication adjustments, eyelid opening apraxia, weight gain, surgical complications

Neurostimulation for Parkinson's Disease With Early Motor Complications EARLYSTIM

- *New England Journal of Medicine* February 14, 2013
- 2 year trial 251 patients randomly assigned to DBS plus medical therapy versus medical therapy alone
- Patients implanted earlier in course of disease 7.5 years vs 11-13
- Endpoints QOL, motor disability, ADL's, motor complications UPDRS III, II, IV
- Good on time

Results

- STN stimulation was superior to medical therapy in patients with PD
- QOL improved by 7.8 points P=0.0002
- DBS superior with respect to motor disability P<0.0001
- ADL's superior P<0.0001
- Levodopa induced motor complications P<0.0001
- Good on time without dyskinesia P=0.01

EARLYSTIM

- Neurostimulation in combination with medical therapy can improve motor symptoms
- This is better than medical therapy alone Levodopa response predicts the extent of the effect of DBS on motor signs
- Adverse events slightly higher in the neurostim group Slightly higher incidence of depression
- NEUROSTIMULATION may be a therapeutic option for patients At an earlier stage than current recommendations suggest