Brain Control
or
What To Do When Your Circuits Don't Work

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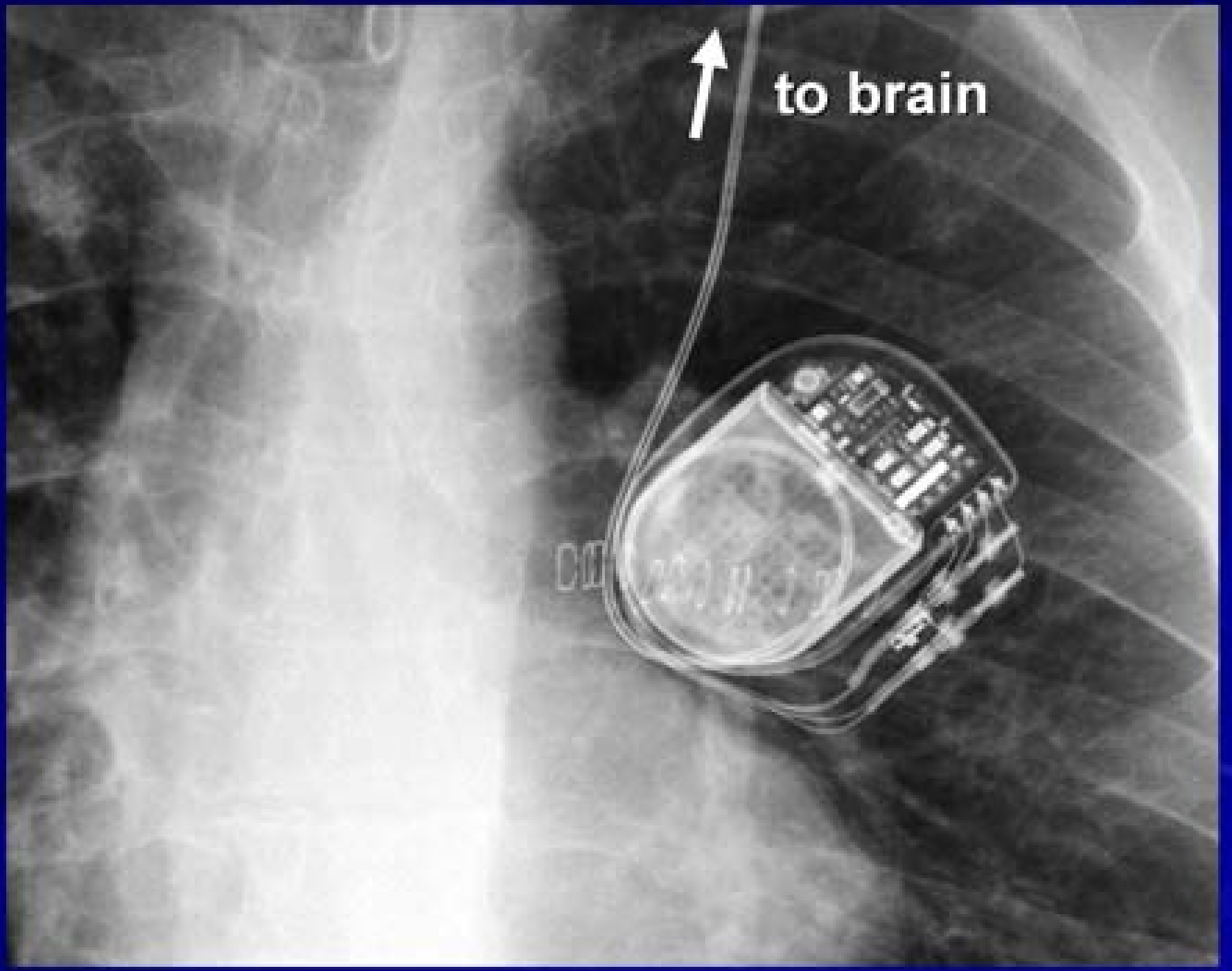
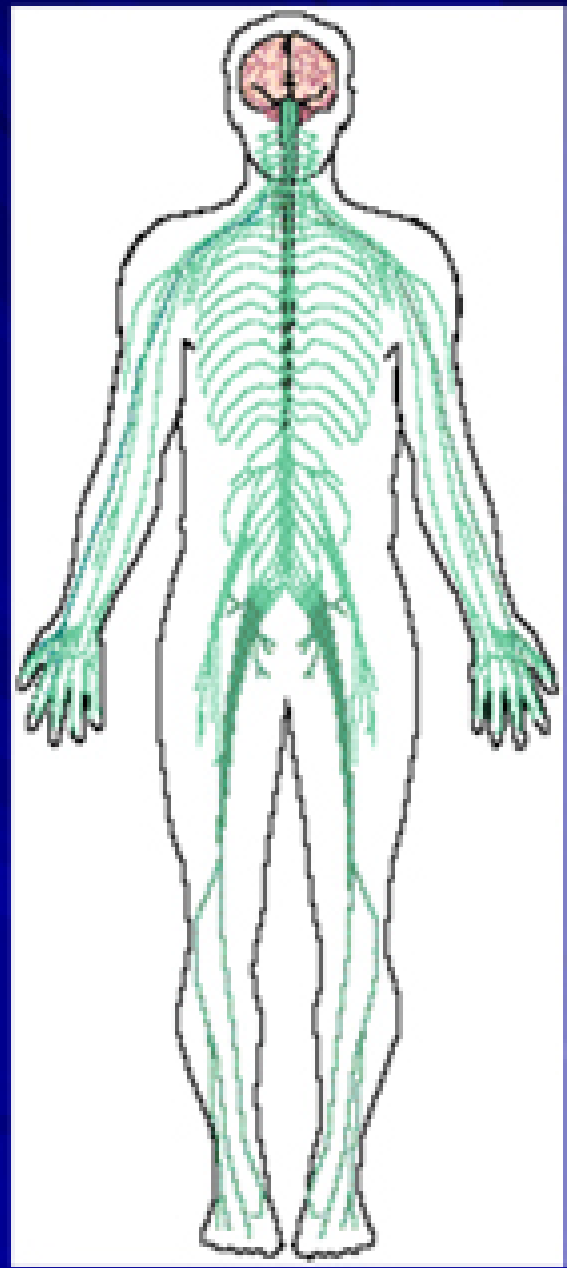
Functional Neurosurgery Bioengineer

KAISER PERMANENTE®

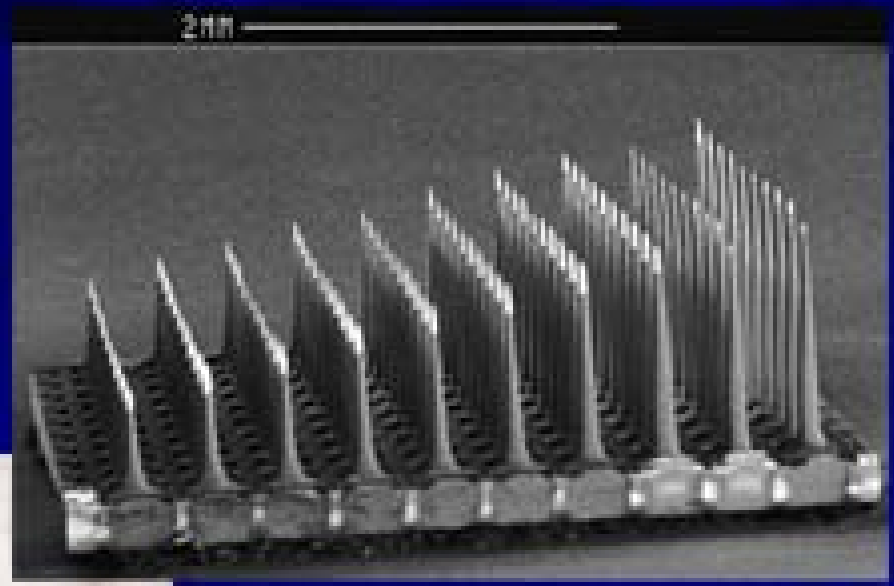

to brain

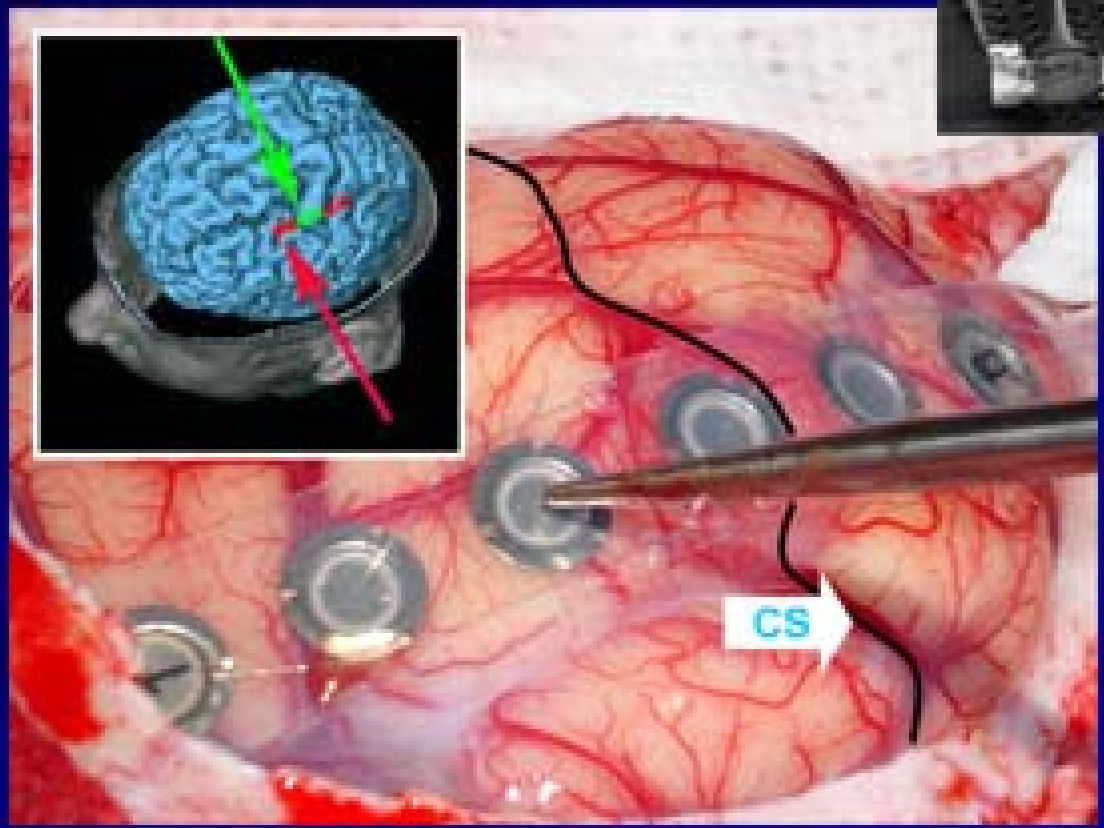
Input/Output to/from the Brain

- Outputs:
  - Control one's own muscles
  - Synthetic speech
  - Control one's environment
- Inputs:
  - Sensory (vision, hearing)
  - Reduce pain
  - Damp epileptic feedback loops
  - Replace lost neuron linkages
  - Regulate behavioral pattern generators



Output from motor cortex





(above) Permanent electrode array

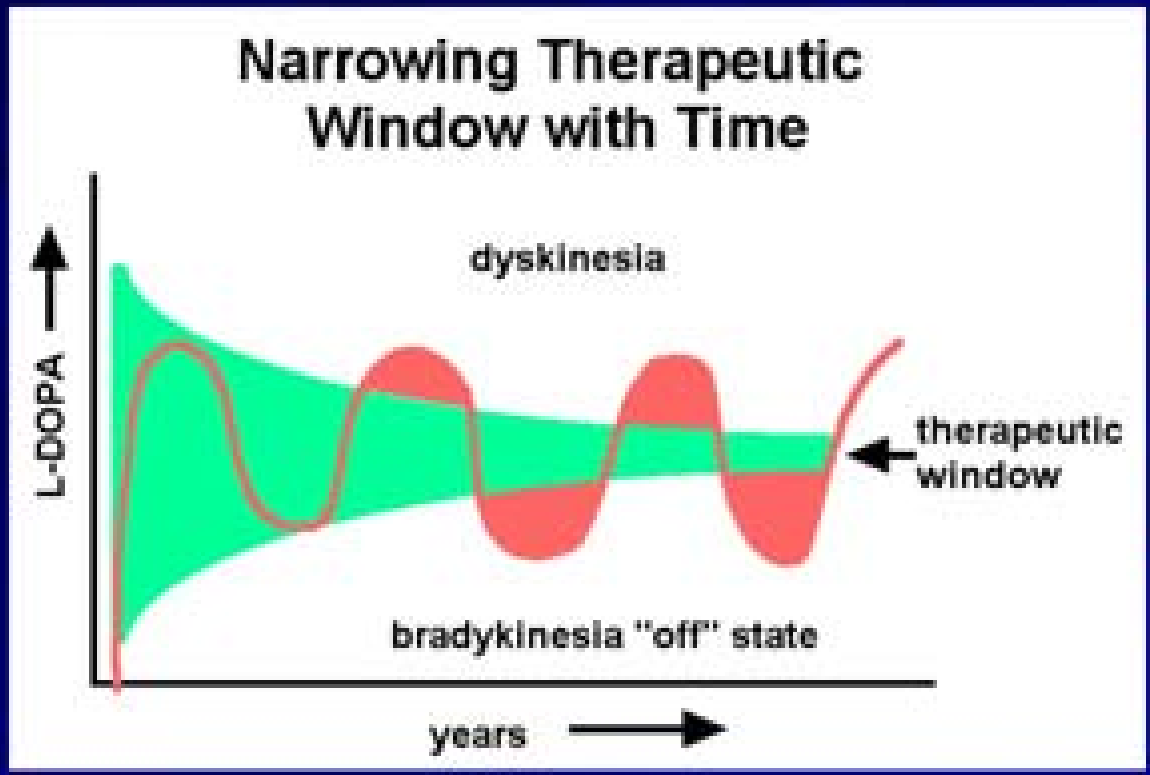
(left) Intraoperative mapping of motor & sensory cortex

electrodes = 5 mm dia

How to treat mis-wiring of the brain?

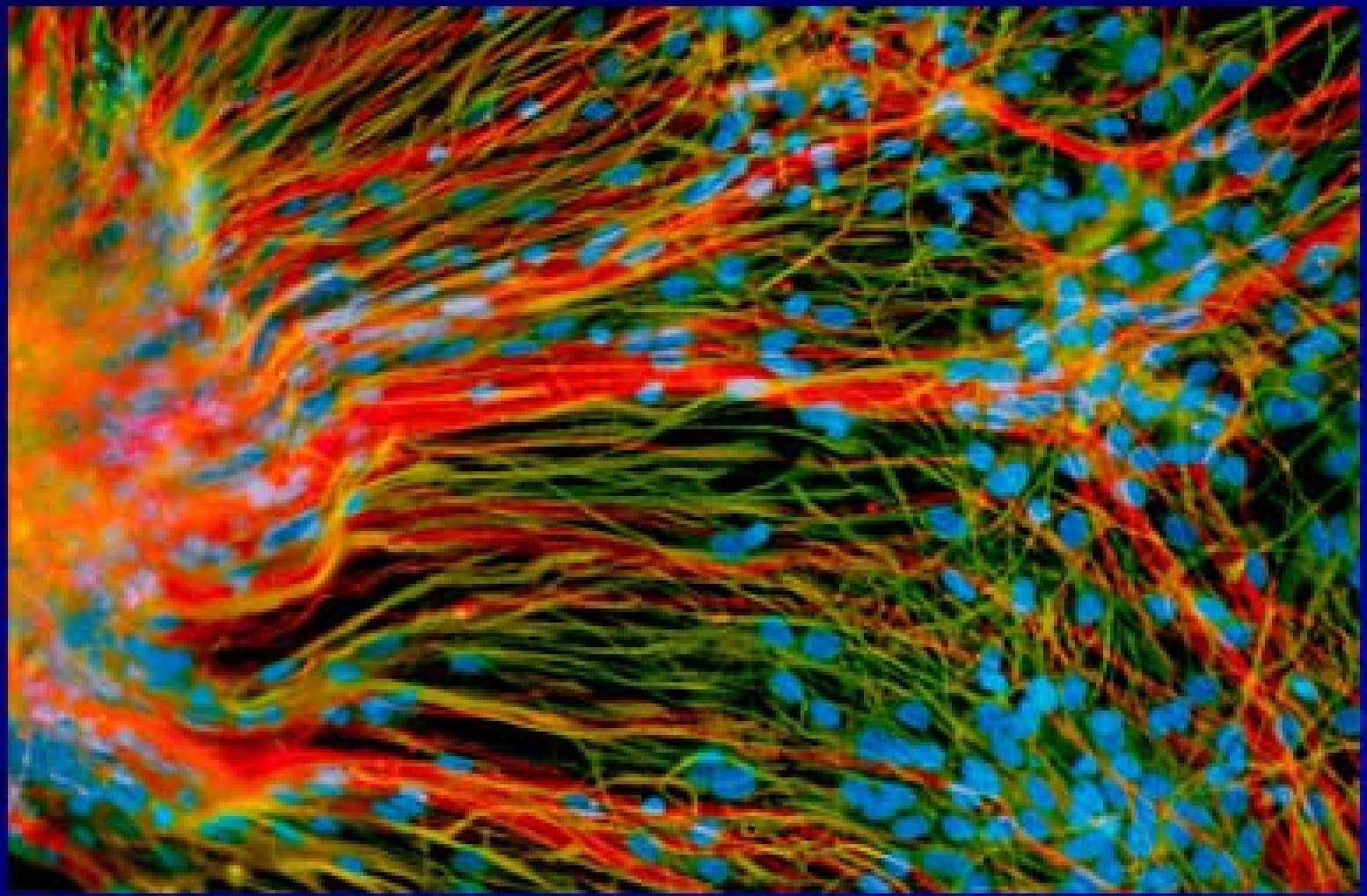
- Drug replacement
  - Injections, pills
  - Infusion pumps
- Surgically implanted prosthesis (electrodes)
  - Cortical (shallow)
  - Deep (basal ganglia)
  - Peripheral
- Regeneration
  - Stem cell implantation
  - Nerve guides

Limits of Drug Therapies

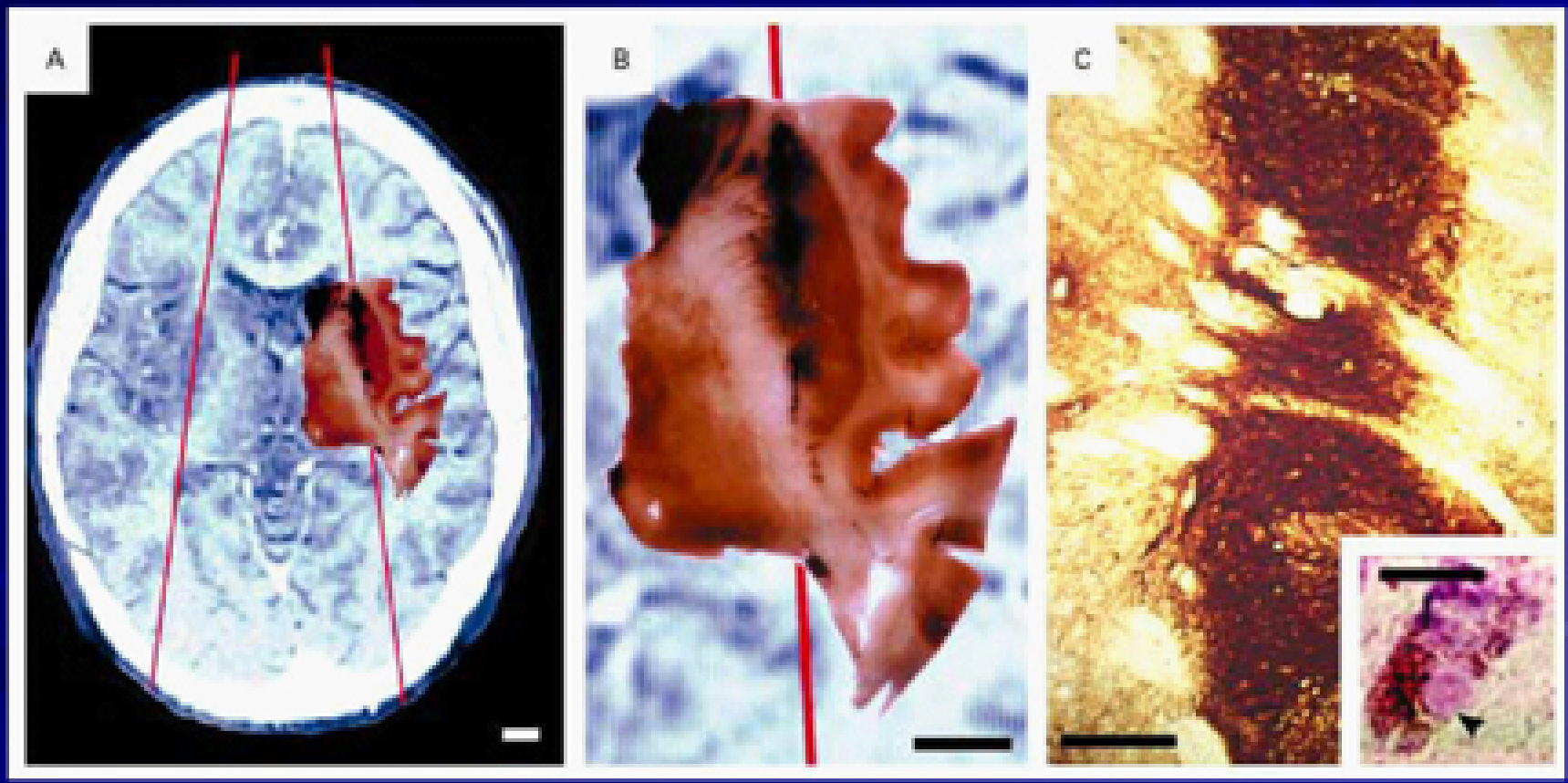


- Effective dose decreases
- Duration of effect decreases
- Side-effects increase

Stem cell implants



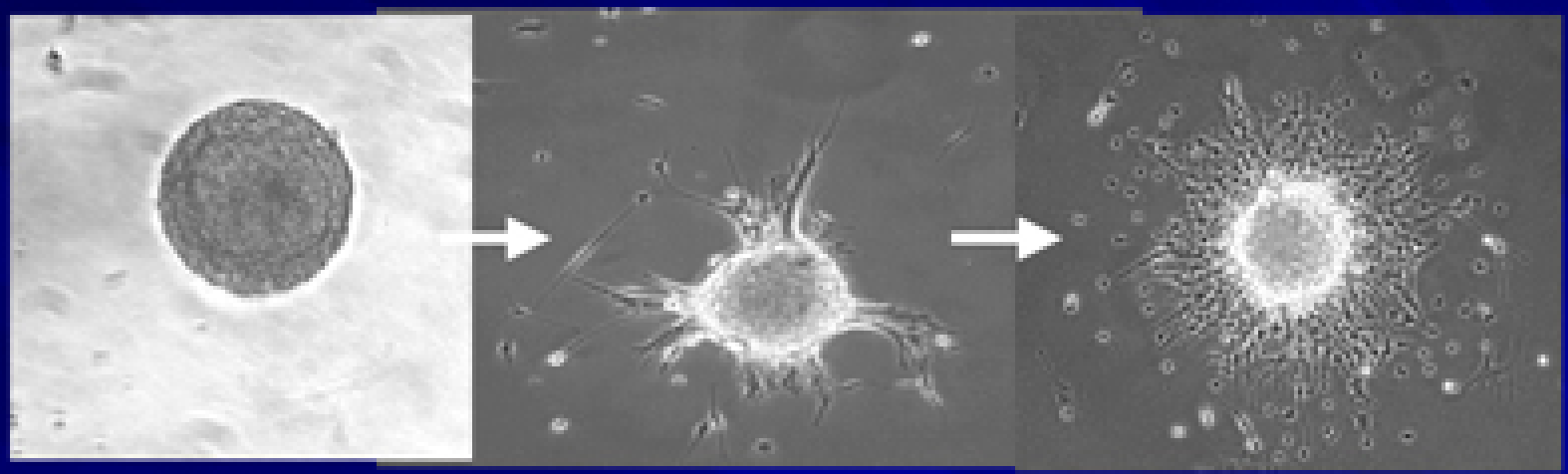
Results of clinical trial of Parkinsons cell therapy

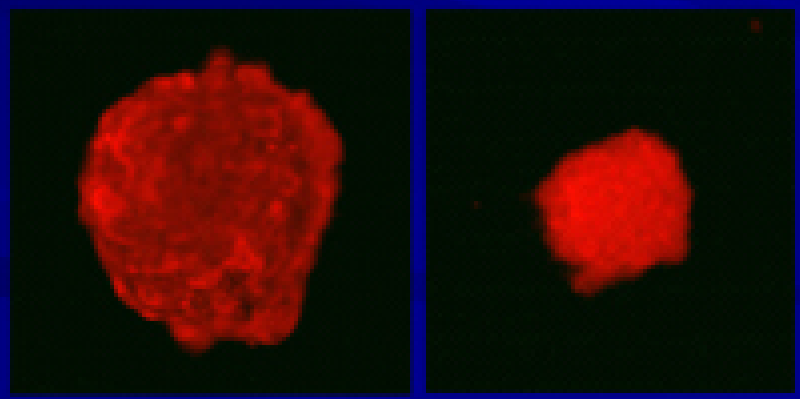


Freed, et al., NEJM, 3/01

Adult Stem Cells

"Neurosphere" from rat brain

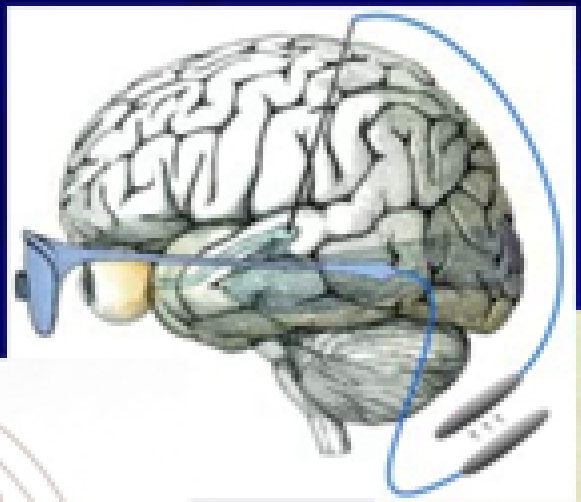


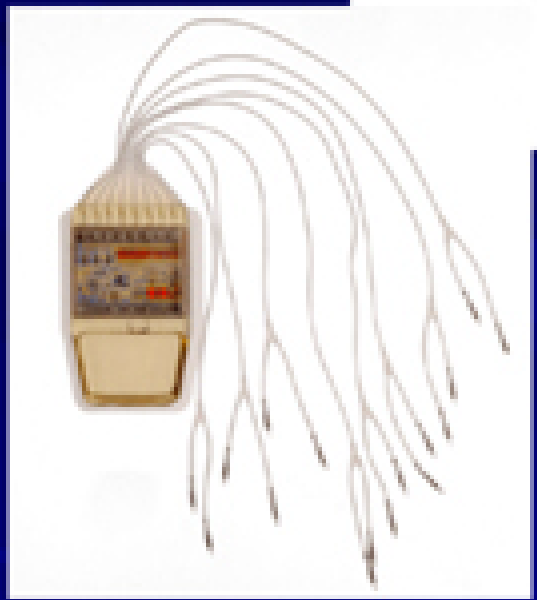


Nestin stain BRDU stain

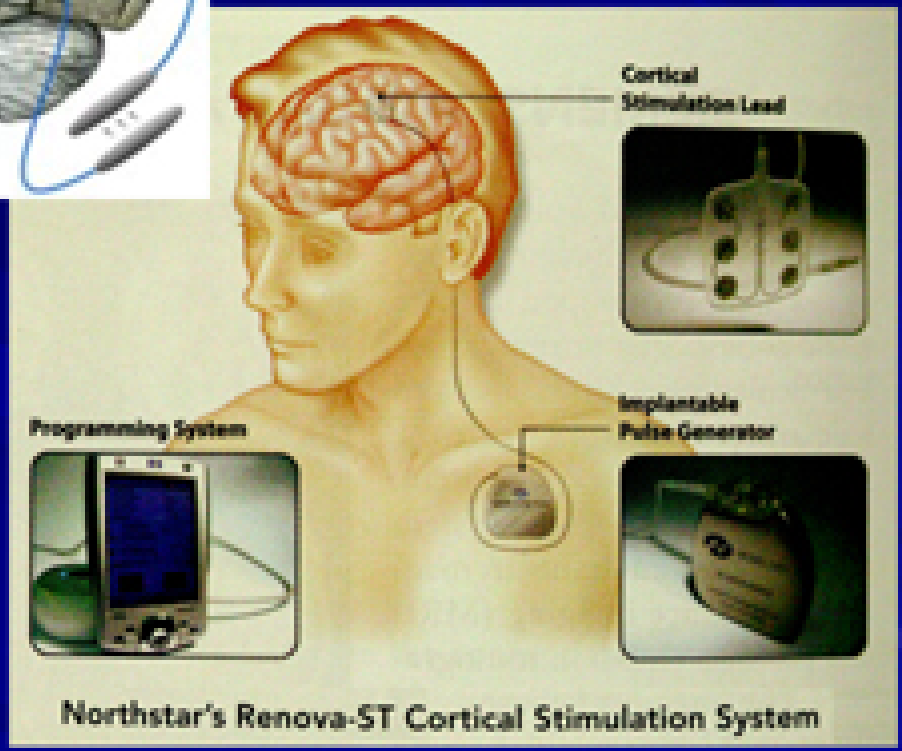
Uses of brain stimulators

Harvard optic tract vision restoration





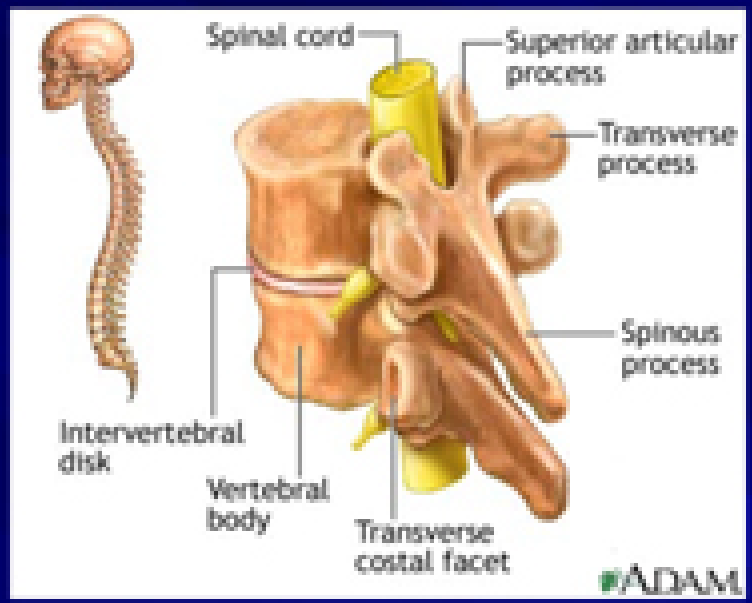
Cleveland "BrainChip" upper limb motor restoration

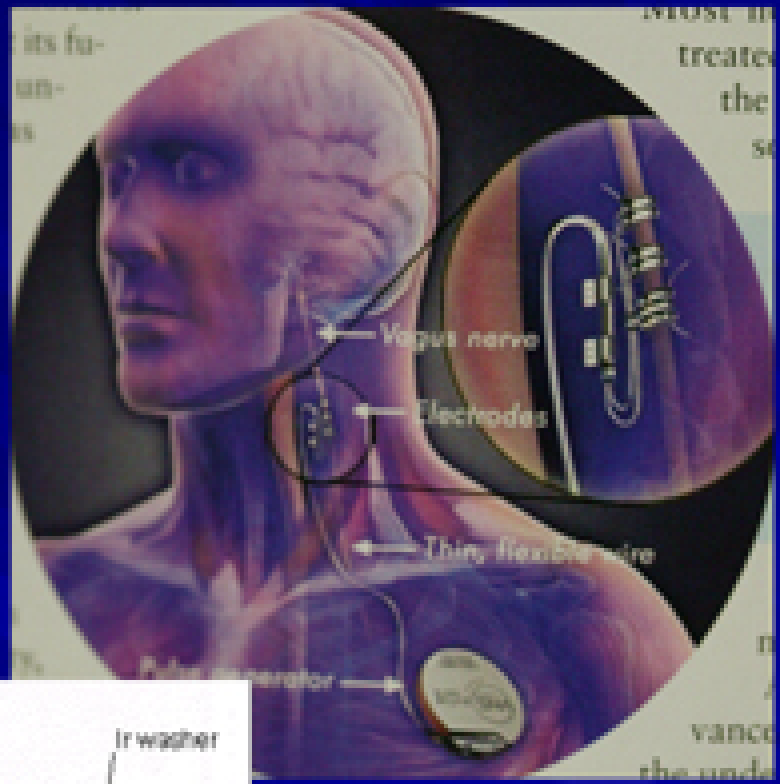


Epileptic seizure prevention

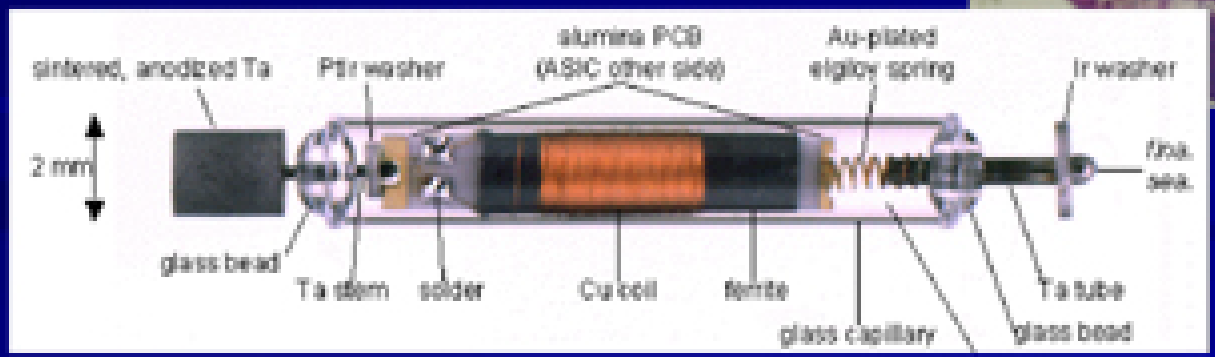
Stimulation distal to the brain

Spinal cord - pain



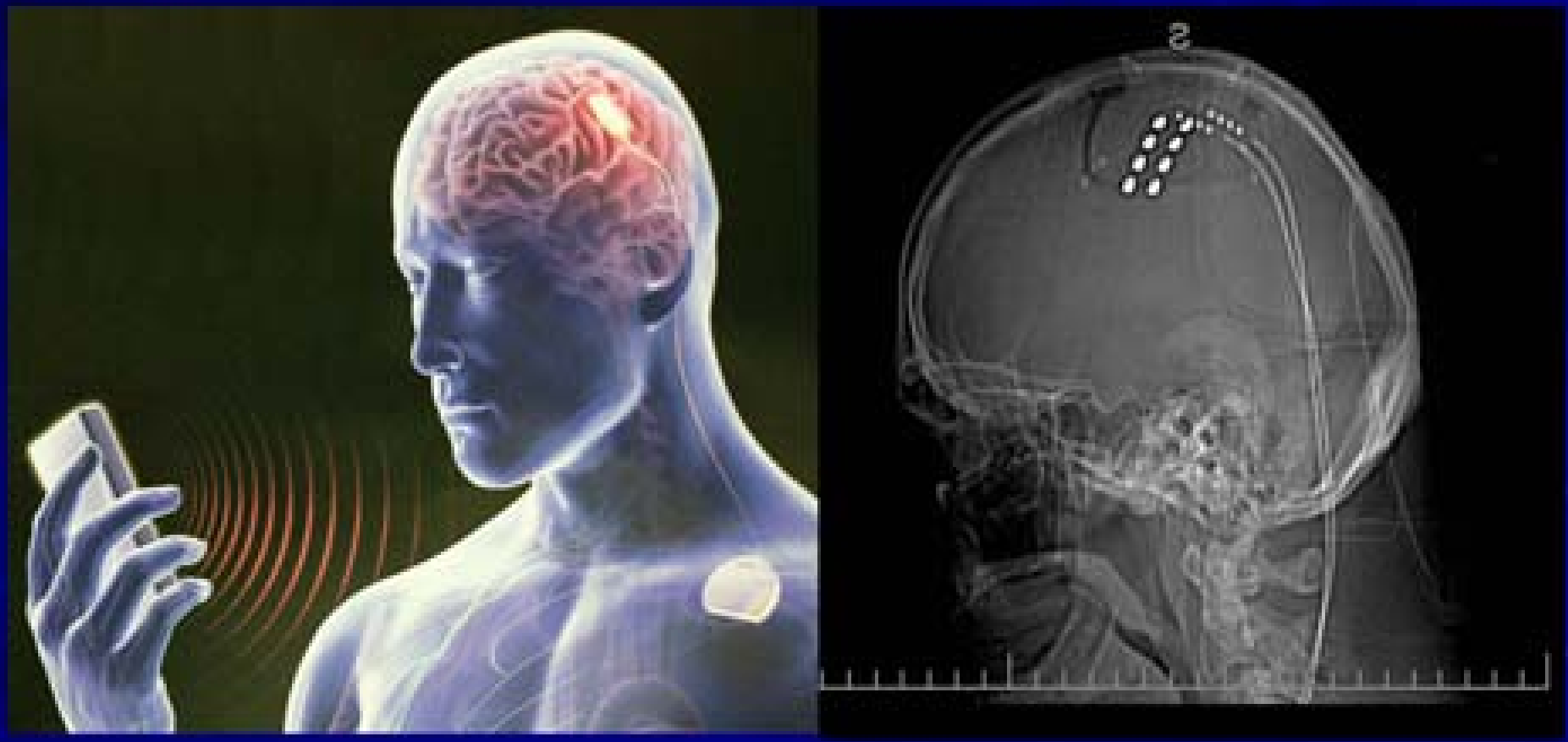


Vagus nerve - pain

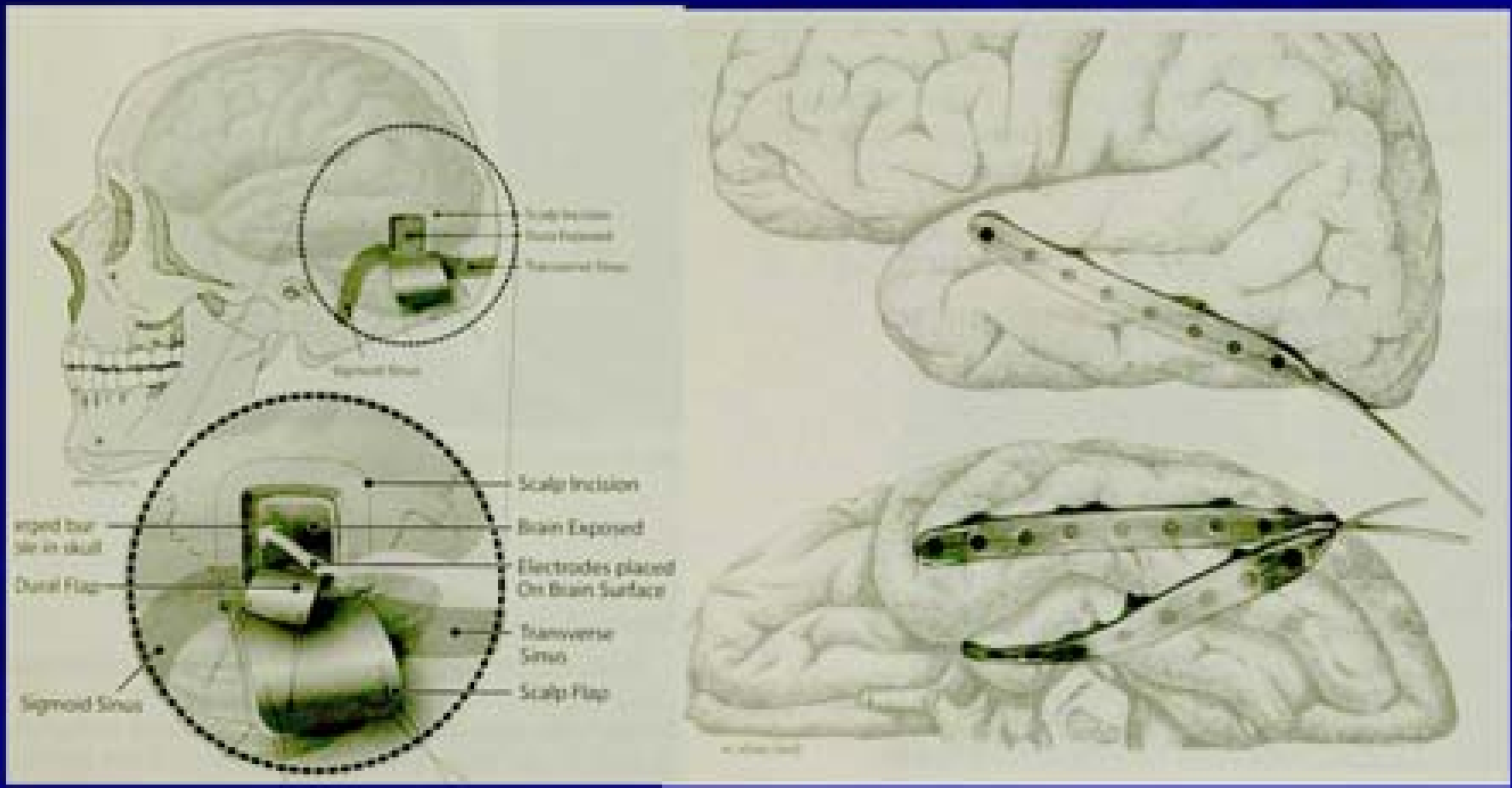


< "BION" – muscle force

Cortical (surface) electrodes

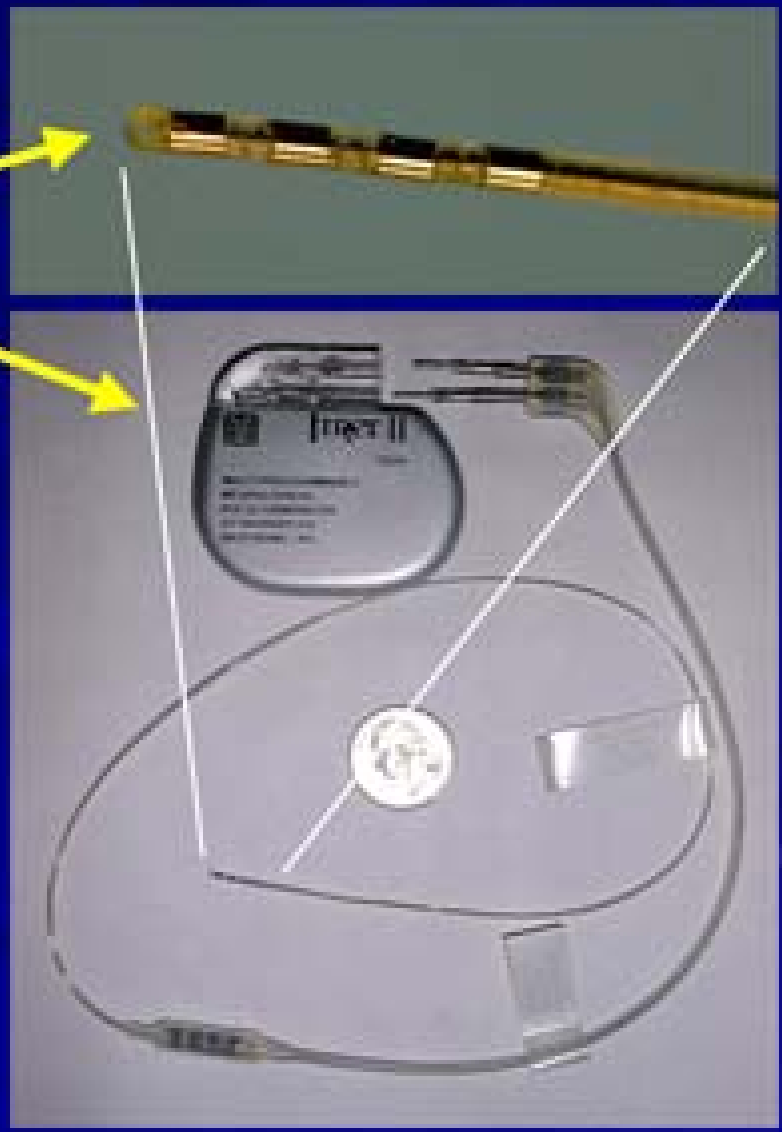


Simple surgery for cortical electrodes

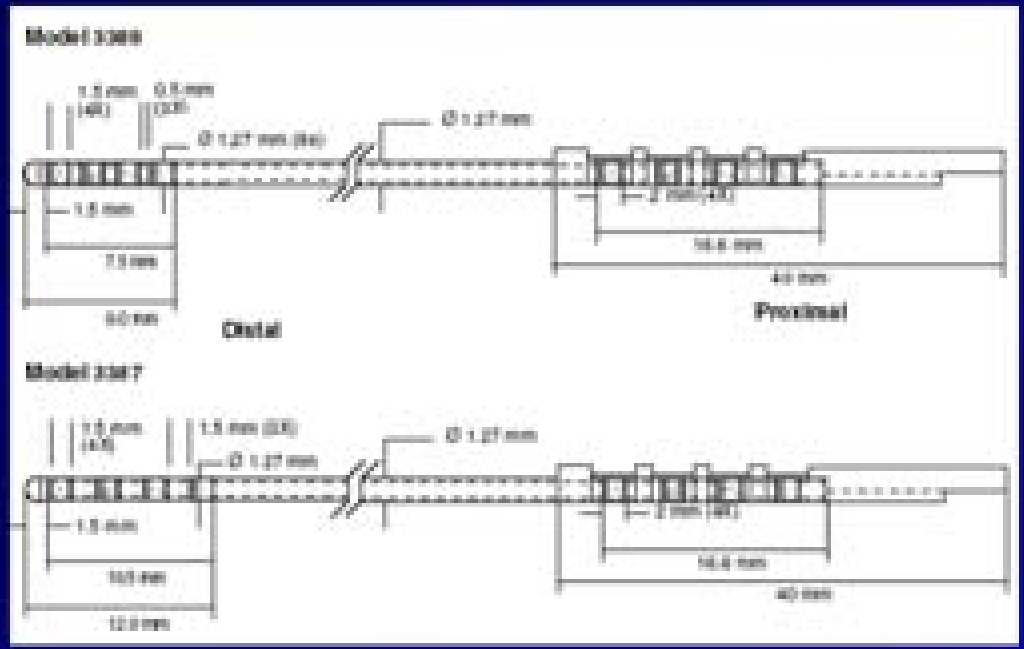


What is Deep Brain Stimulation?

- DBS is chronic stimulation by electrodes connected to a programmable stimulator (like a pacemaker) in the chest wall.
- 4 electrodes (contacts) per site, spaced 0.5 to 1.5 mm apart
- Uni- or bilateral sites
- Implantation by stereotactic surgery (unlike cortical surface electrodes)



DBS electrode details



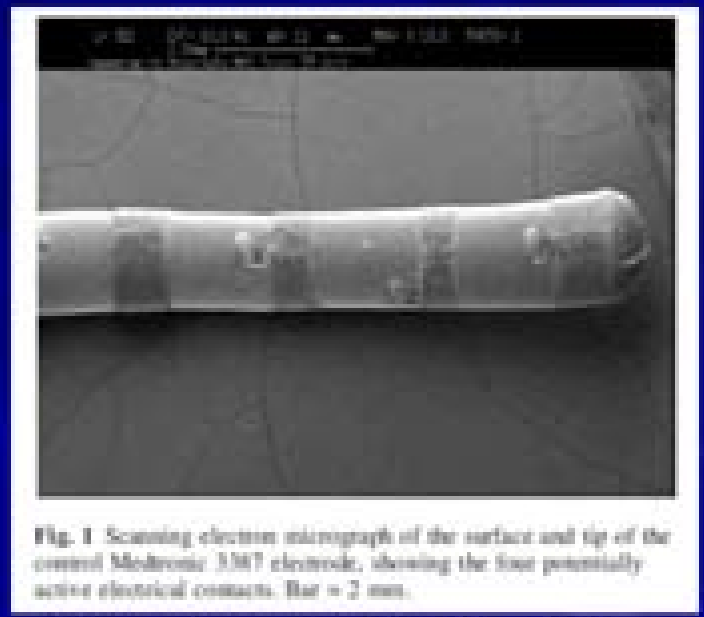
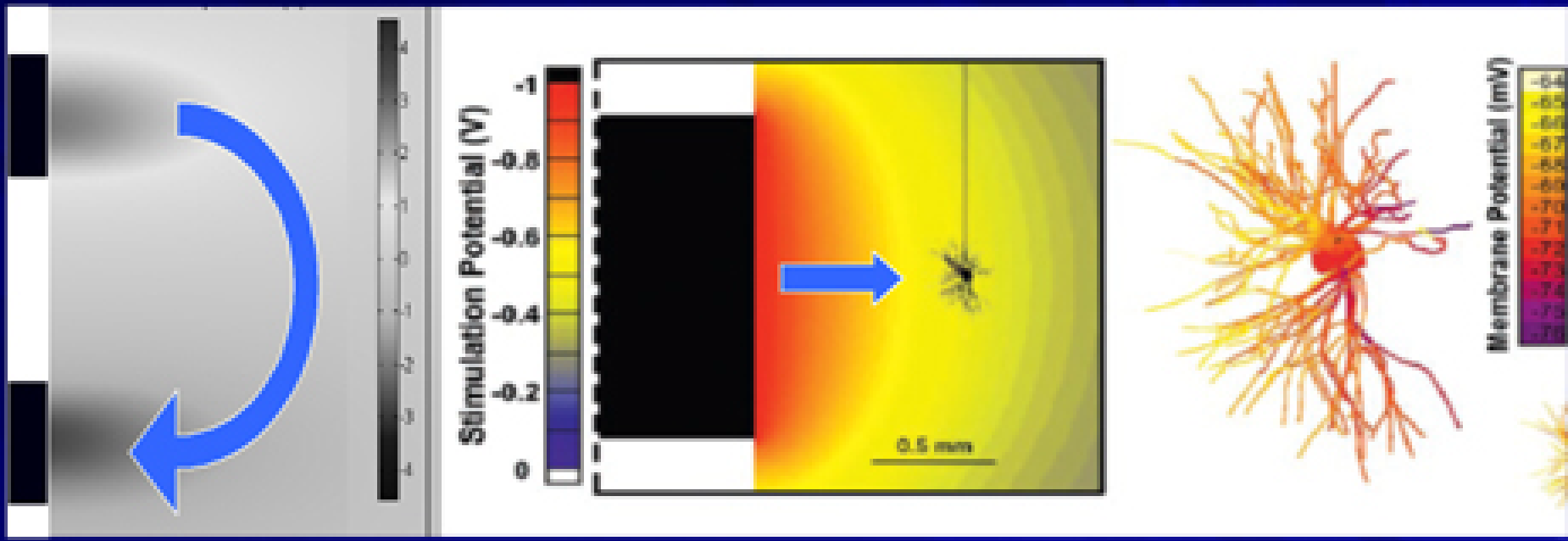


Fig. 1 Scanning electron micrograph of the surface and tip of the central Medtronic 3387 electrode, showing the four potentially active electrical contacts. Bar = 2 mm.

From Moss, et al, *Brain*, 2004 Dec;127(Pt 12):2755-63

Effect of stimulation on neurons



Potential field generated by positive (top) and negative (bottom) electrodes (black)

Neuron drawn to scale superimposed on potential field

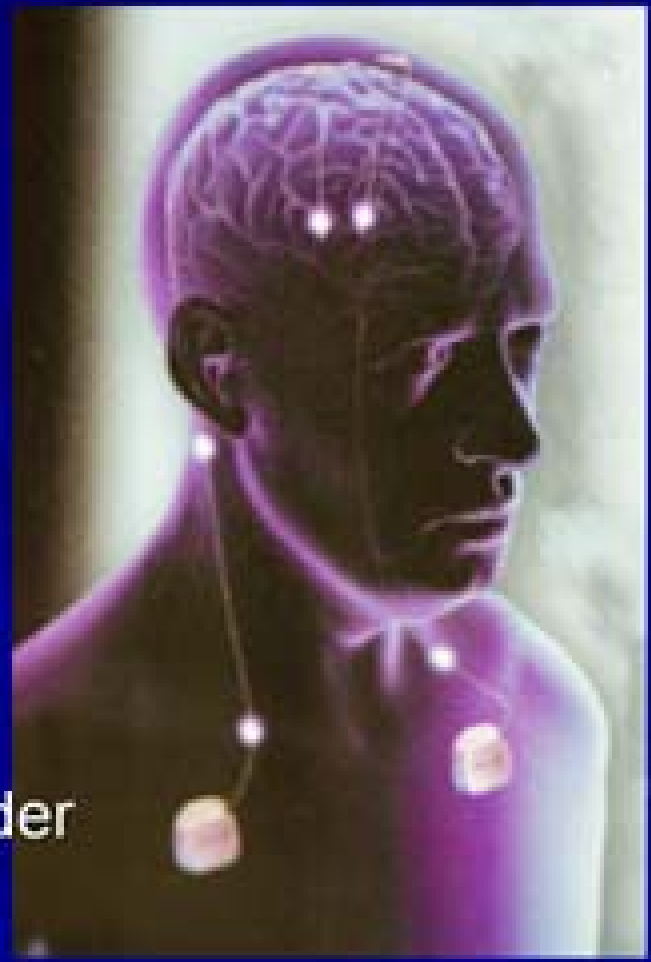
Membrane potential shows induced polarization

McIntyre, et al. *J Neurophysiol* 91: 1457–1469, 2004

Why Deep Brain Stimulation?

Symptomatic treatment when medication is ineffective for:

- Parkinson's Disease
- Tremor syndromes
- Pain syndromes
- Primary dystonia
- DOPA responsive dystonia
- Tardive dyskinesia
- Tourette's Syndrome
- Anorexia Nervosa
- Obsessive-compulsive disorder
- Depression



DBS for Parkinson's Disease

Symptoms of Parkinson's Disease

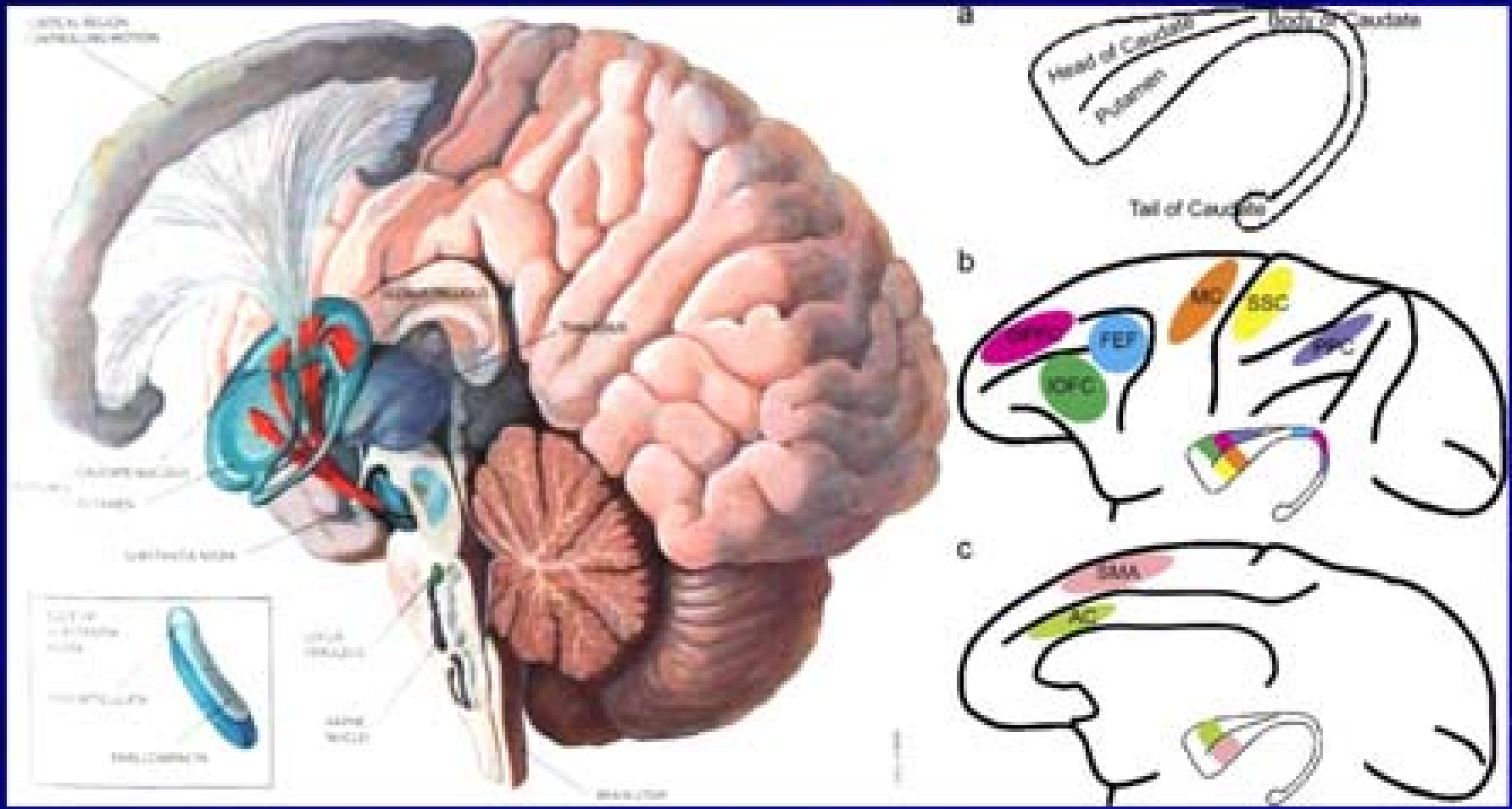
- tremor
- rigidity
- slowed gait (bradykinesia)
- motor block or "FOG"

- depression
- dementia
- orthostatic hypotension
- dysphagia
- medication complications:
  unpredictable ON/OFF states, dyskinesias.

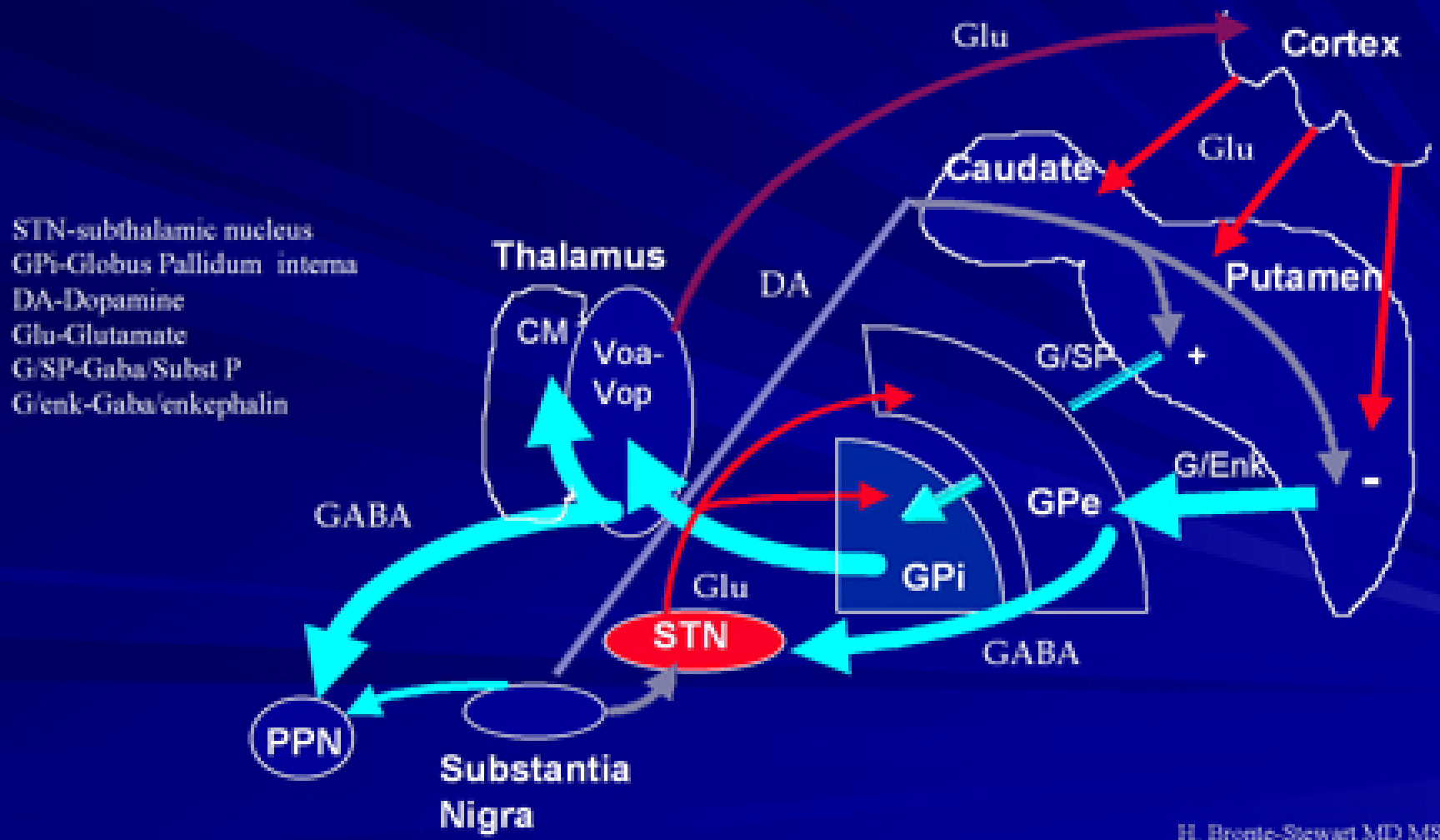
Selection Criterion for Surgery

- response to dopamine
- minimal to moderate dementia
- minimal radiographic brain atrophy.
- evaluate and treat psychiatric conditions.
- minimal dysautonomia.

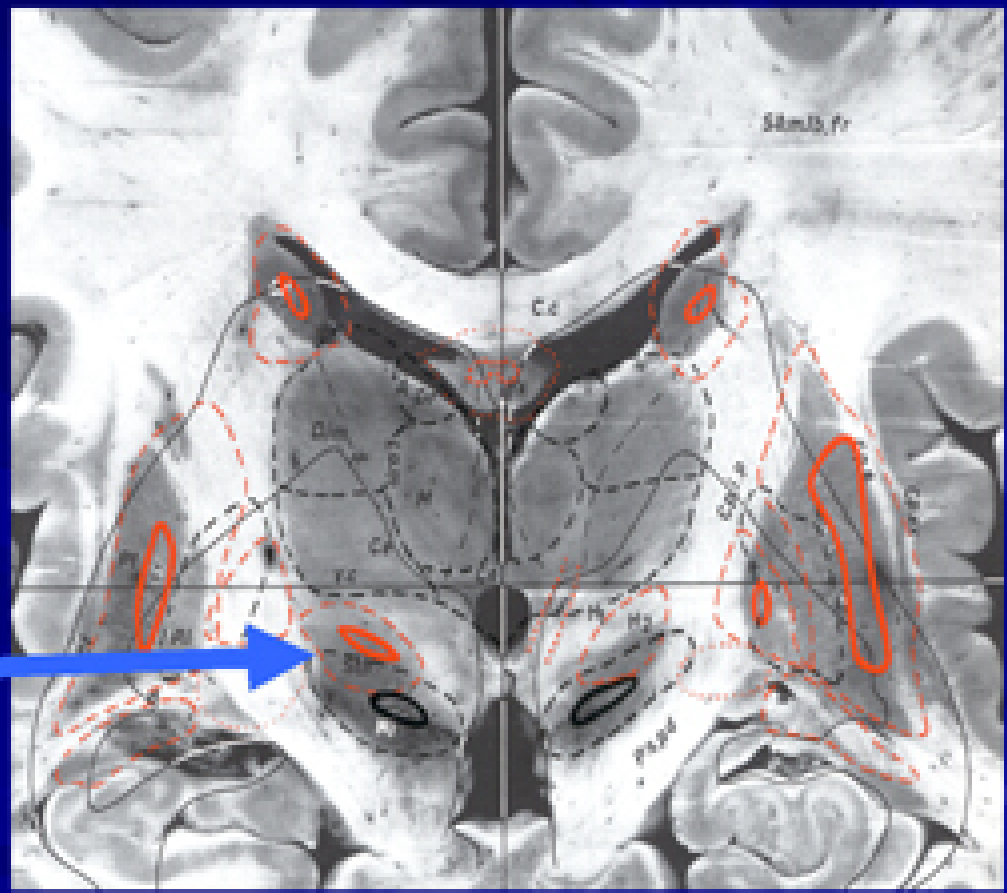
Nerve Pathways Regulating Movement



Neuroanatomical Pathways of Basal Ganglia



Deep Brain Stimulation (DBS) for Parkinson's Disease



Target:
Subthalamic nucleus

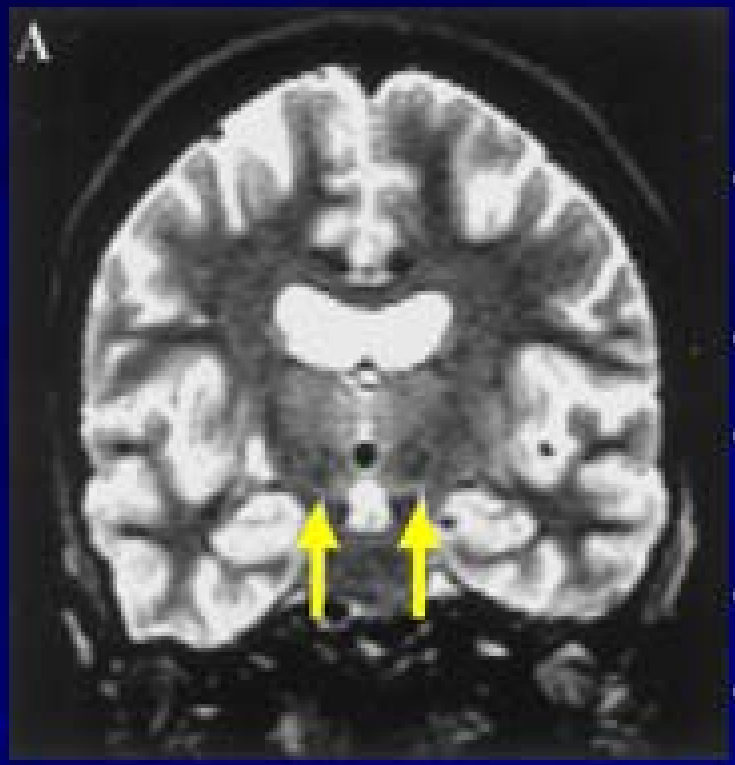
STN dimensions: 9 x 7 x 5 mm

Deep Brain Stimulation Surgery at Kaiser Redwood City

PD Patient Evaluation/Screening Process

- Initial 1 hr consultation & MRI
- Exclusionary criteria?
- If anxiety related surgical risk factor noted, refer patient for relaxation training
- Diagnostic evaluation - 1 hr to overnight
- 2nd appointment(s) for further:
  - medication
  - diagnostic studies
  - monitoring
- Neuropsychological testing - 4 hrs
- Case discussed by Review Board
- Follow up appointment to discuss recommendations & surgery option(s) – 1 hr
- Schedule surgery
- Presurgery MR & CT imaging
- Perioperative instructions – 1 hr
- Post-surgical in-patient care – 3 days
- Stimulator programming at 2, 6, 12 months – 4 hrs

Steps to insure targeting accuracy

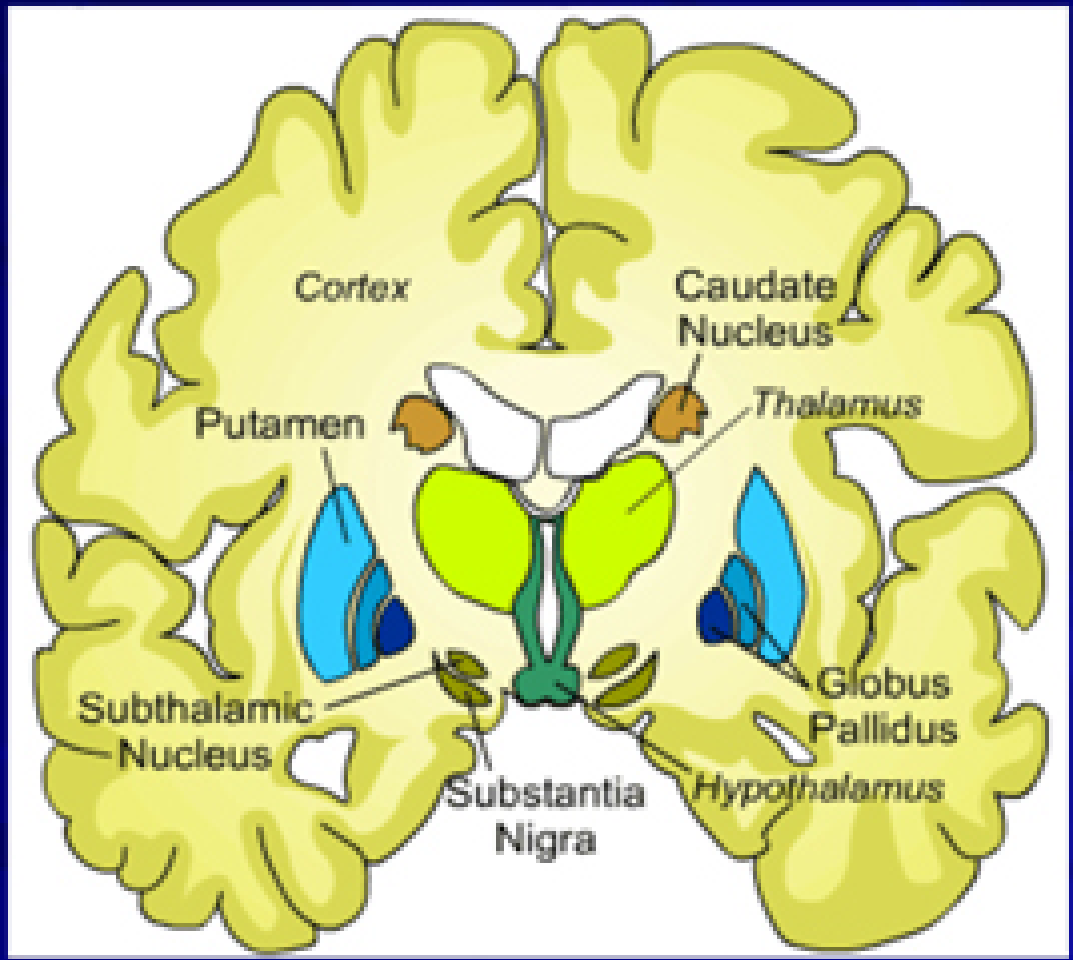


Coronal T2 MRI showing STN
Zonenshayn: Neurosurgery, 47(2). 2000.282-294

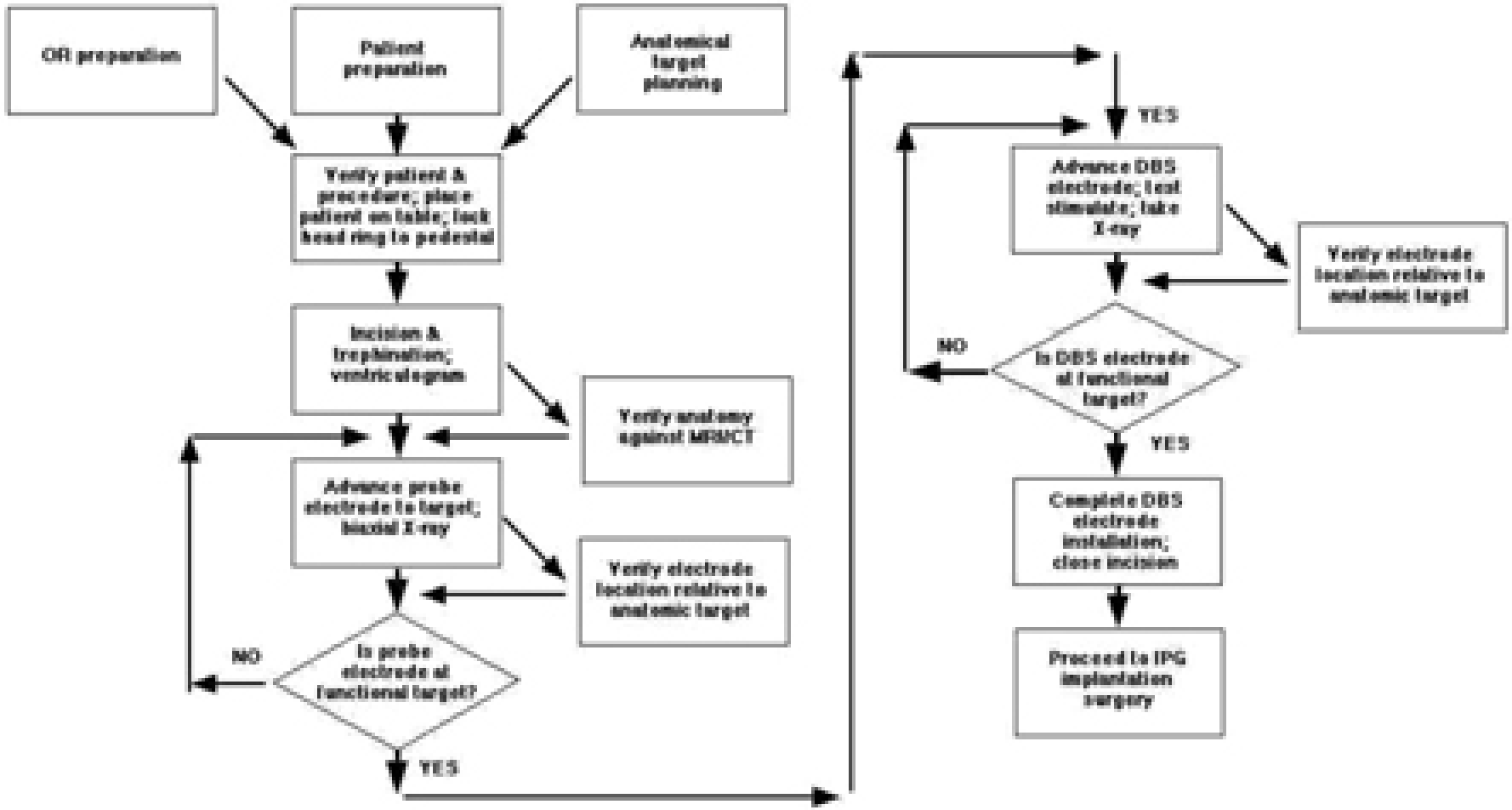
Accuracy of +/- 0.5 mm requires:

- MRI localization of STN relative to anterior & posterior commisures
- Fuse MRI & CT for bone landmarks
- Ventriculogram at surgery start as reference to MRI
- Bilateral plane X-ray to locate electrode
- Recording multiunit neuron signals at known electrode depths
- Repeat X-ray & recording for each track

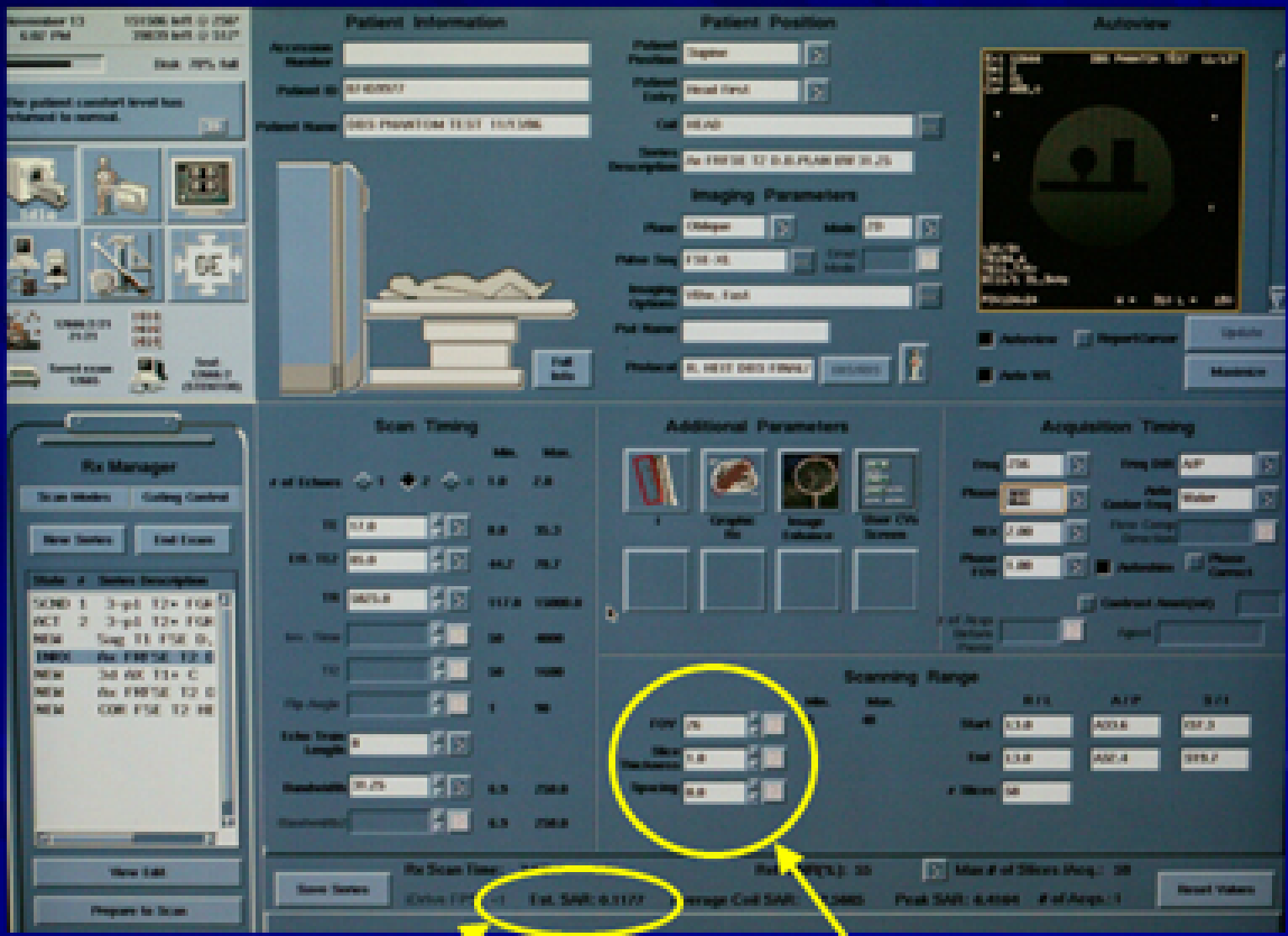
Stages of DBS surgery



DBS Surgery Workflow

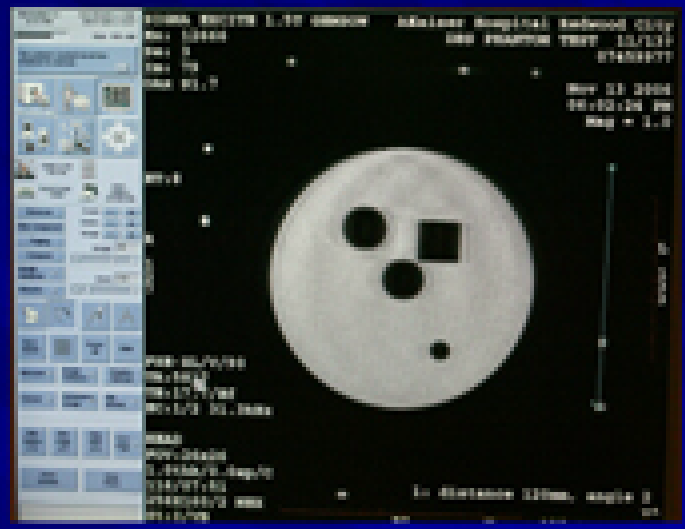


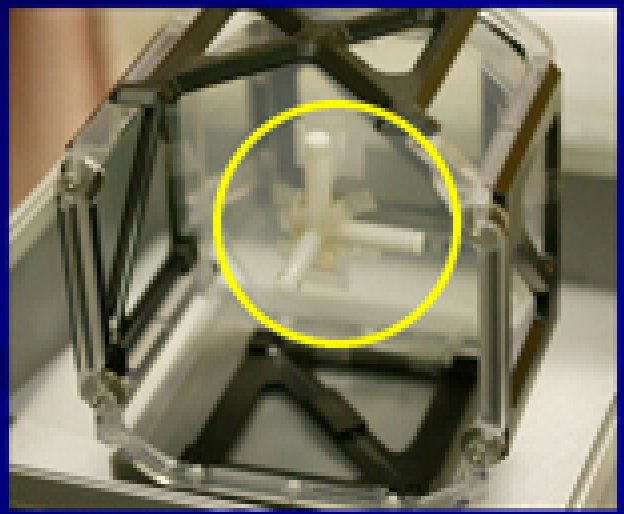
Magnetic Resonance Imaging

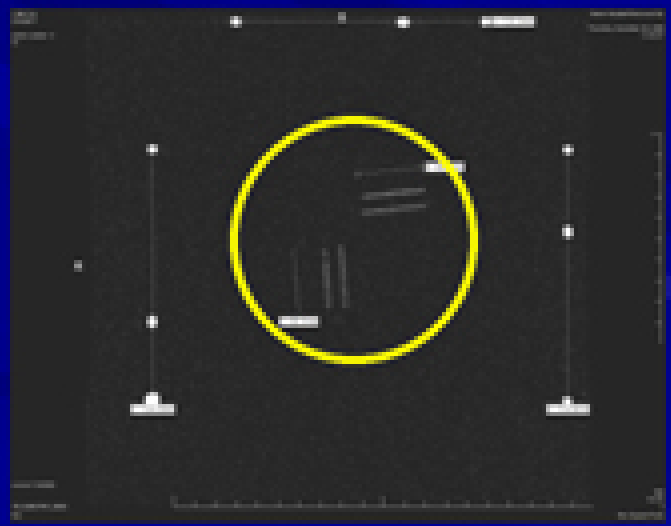


MRI dimensional accuracy & resolution assessed by imaging of phantoms

Radionics geometric phantom







3-axis 1 mm spacing custom phantom

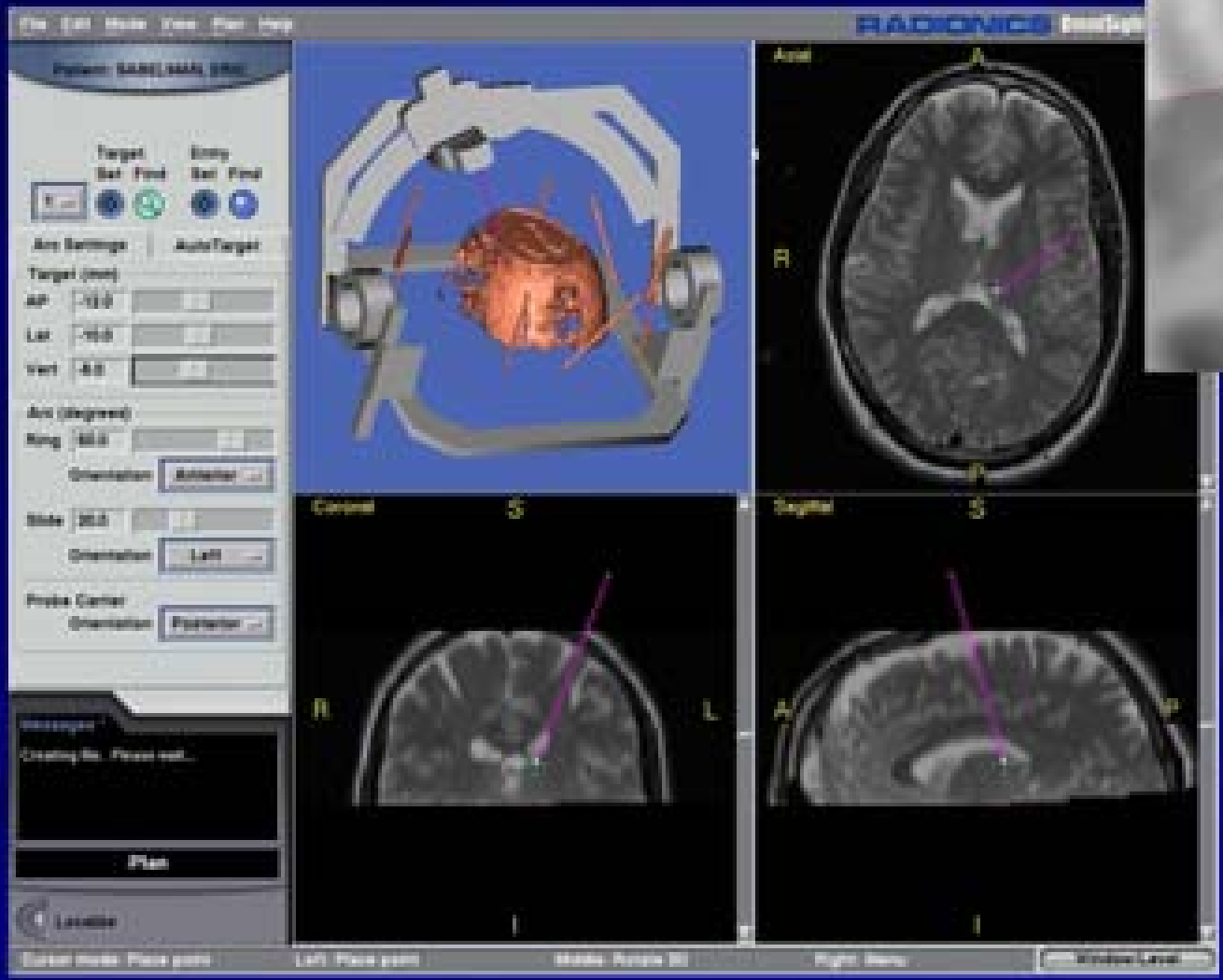
Head restraints to minimize involuntary movement

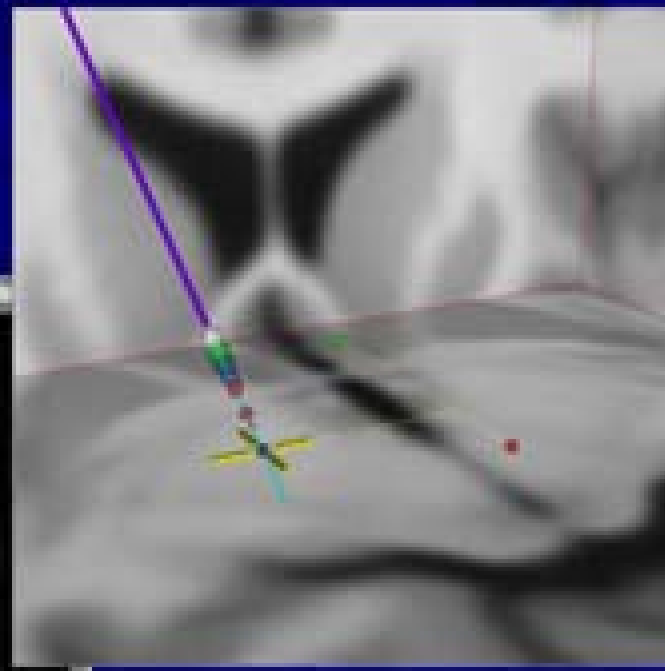
MRI

CT

Patients may be unmedicated and subject to tremor

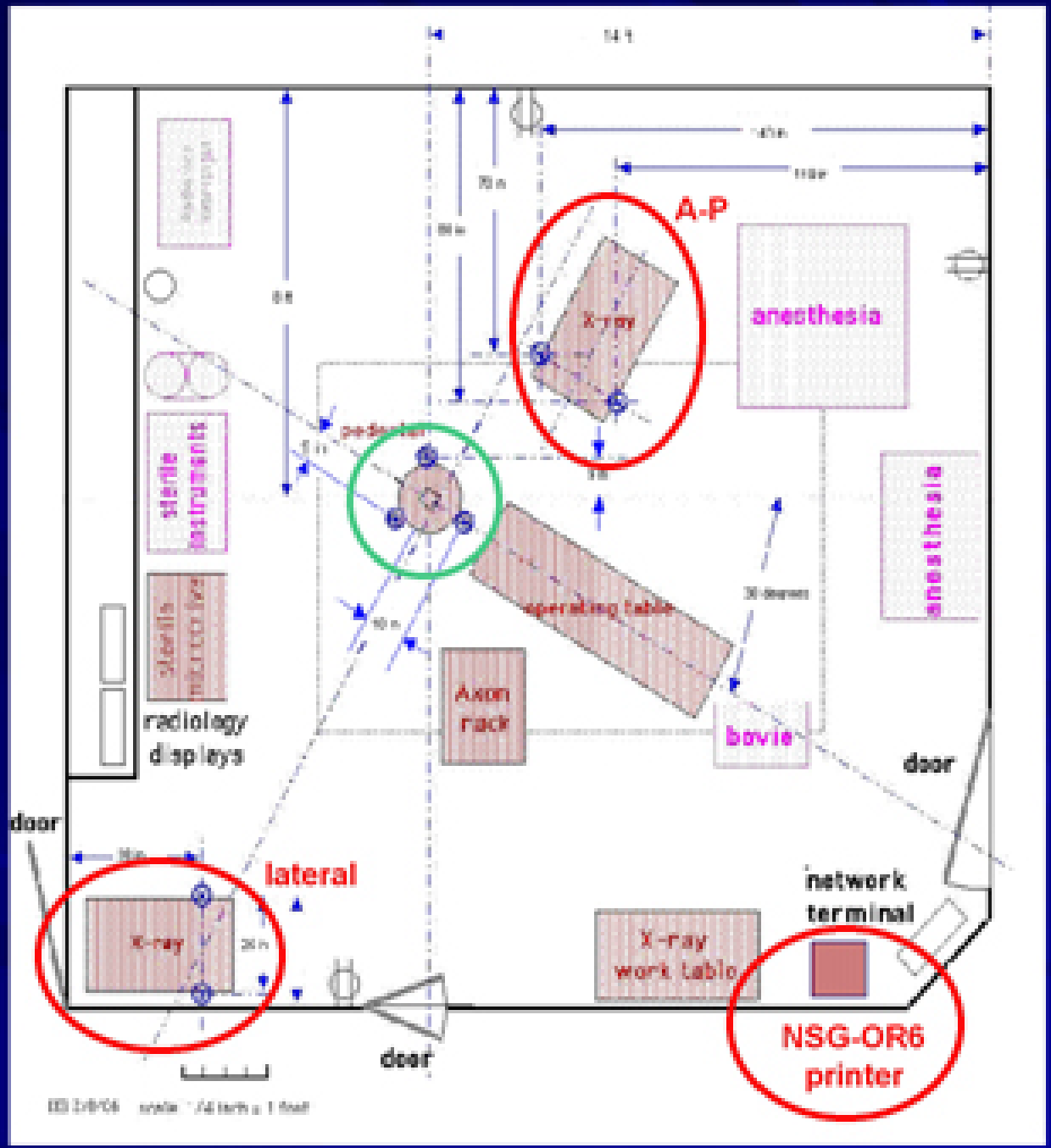
Target Planning – Fused MR+CT Images





MR-CT fusion

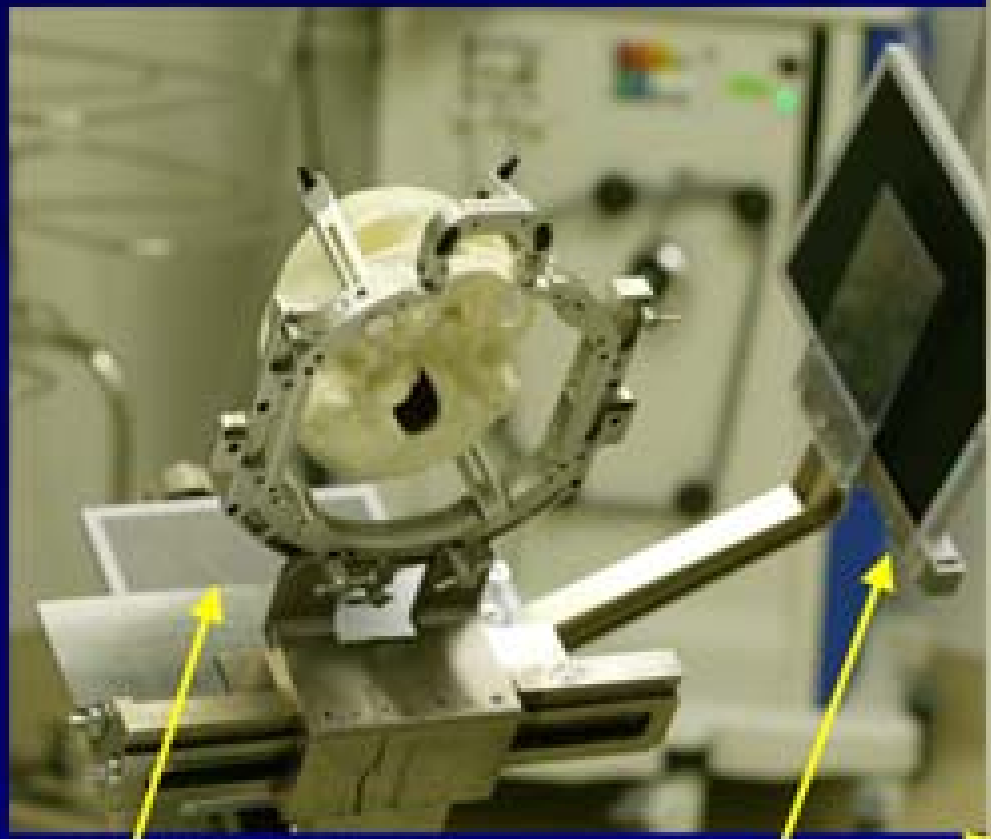
- Minimizes MRI distortion artifact
- Identifies anatomic shift since earlier MRI



Operating room setup for DBS surgery:

RWC
OR-6 floor plan
showing
stereotactic
floorstand (green)
&
intraoperative CR
X-ray units &
printer (red)

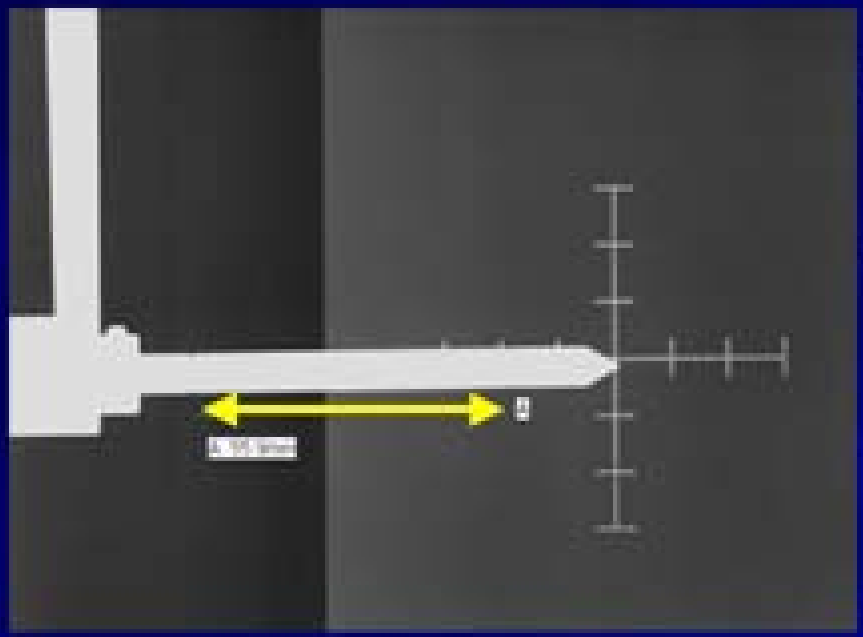
A-P CR X-ray



A-P X-ray cassette

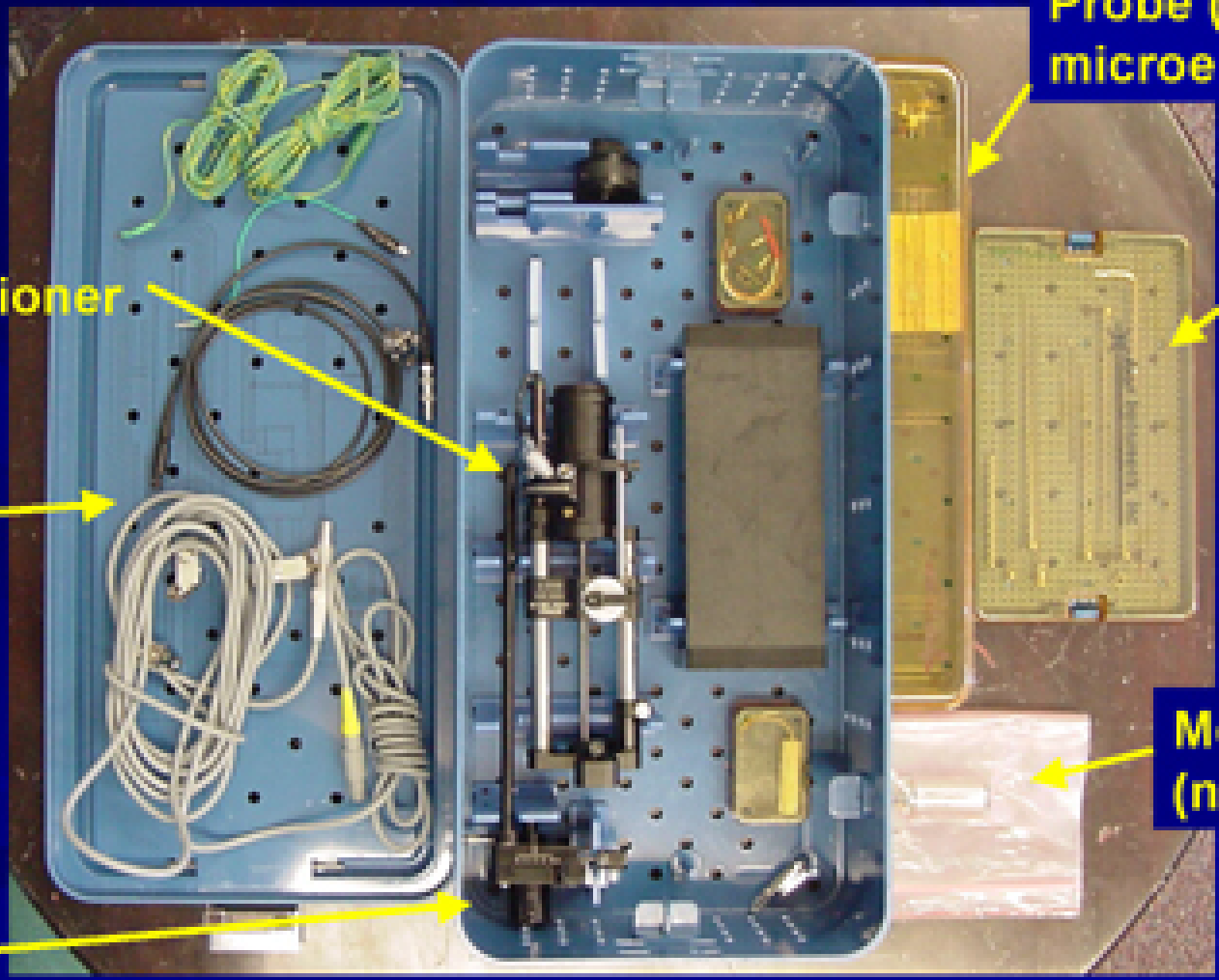
Lateral X-ray cassette

Lateral CR X-ray



Magnification and alignment calibration tool
(notches on pin = 50 mm)

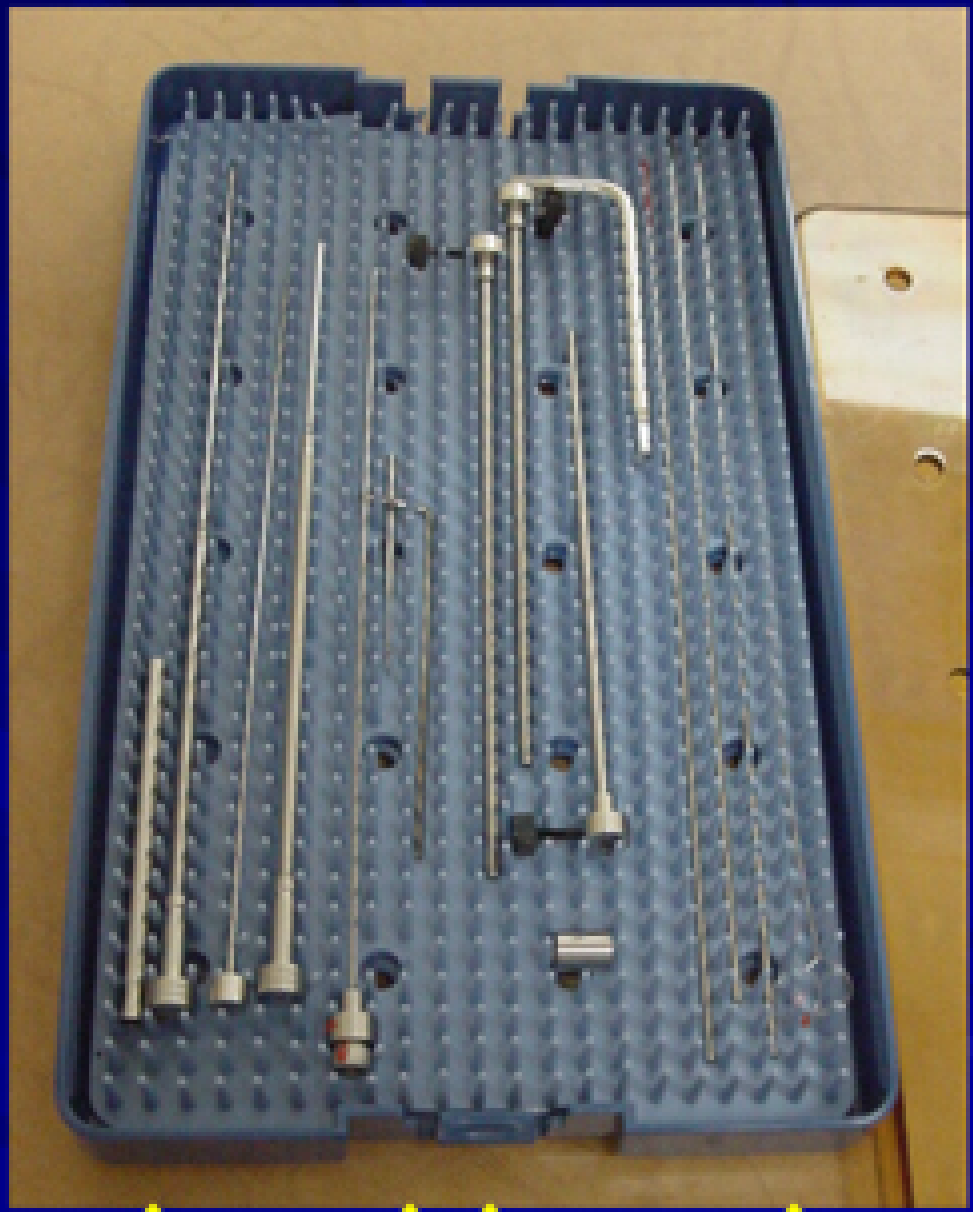
Axon DBS Instrument Set



NOTE: micropositioner is custom-made and not replaceable

Microelectrode & DBS Guide Tubes (cannulas)

NOTE: guide tubes are custom-made and not replaceable – electrode placement accuracy depends on guide tube straightness and concentricity



In the Operating Room

- DBS specialty team
  - Neurosurgeon
  - Nurse practitioner
  - Bioengineer/physicist
- Hospital staff
  - Anesthesiologist
  - Scrub tech
  - Circulating nurse
- Hospital services
  - Perioperative
  - Radiology

CRW stereotactic arc

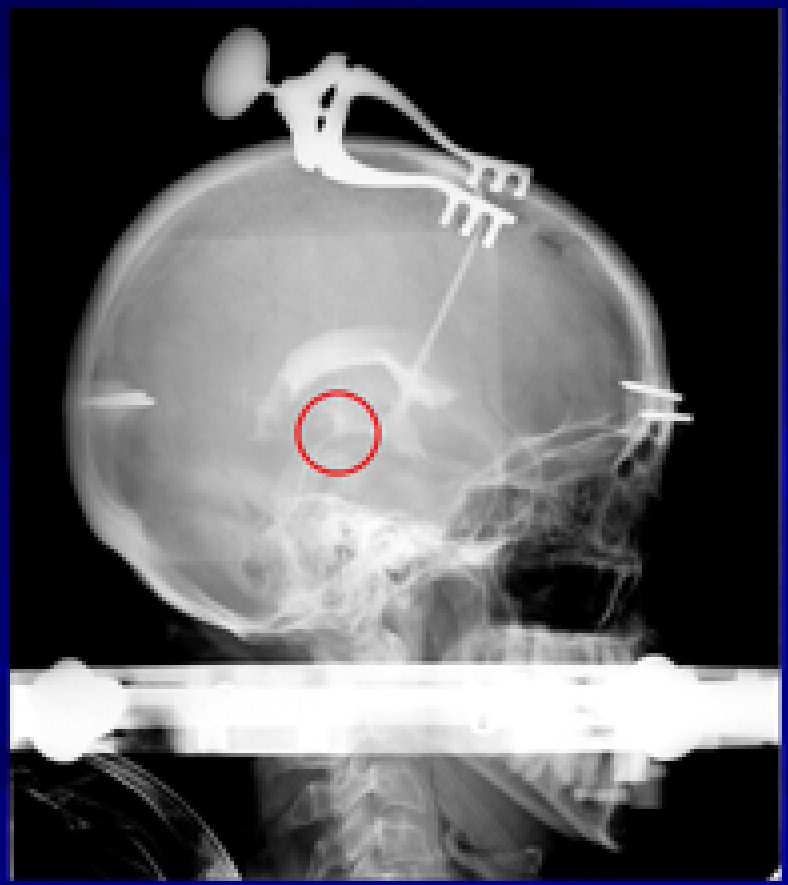
Arc on 3-D calibration phantom

Max acceptable mismatch = +/- 0.5 mm

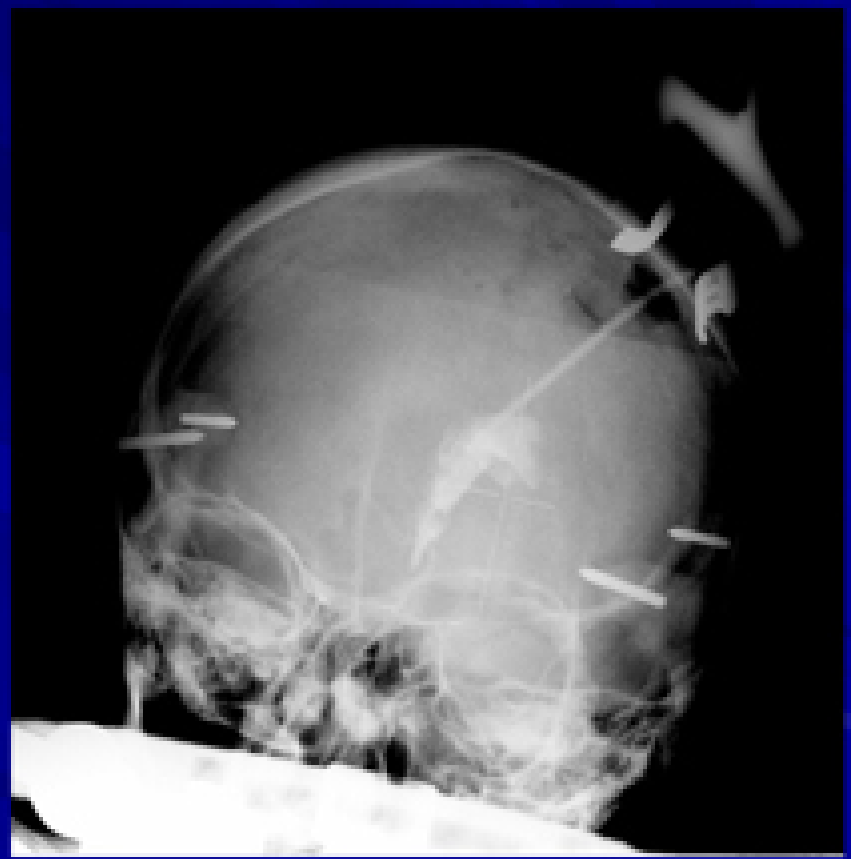
Placing CRW arc on head ring

Ventriculogram

Allows intracranial anatomic identification of posterior commisure (circle) to update presurgical imaging, providing a reference for subsequent mapping tracks

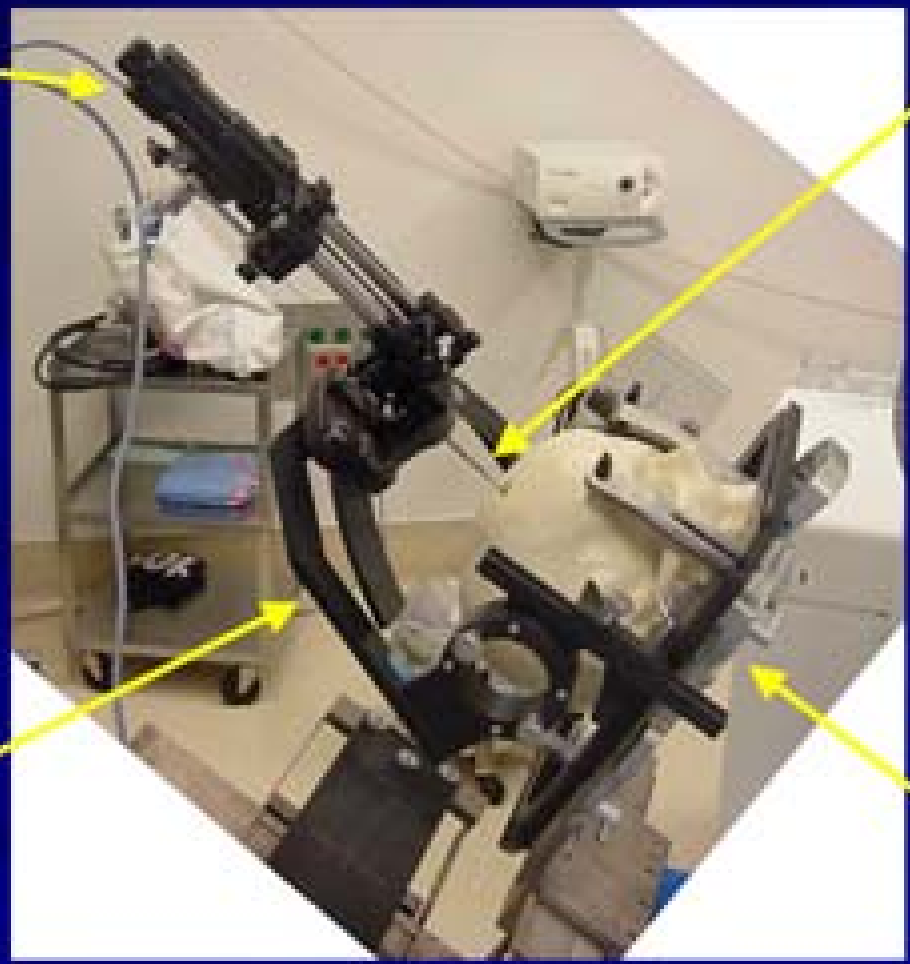


Lateral view

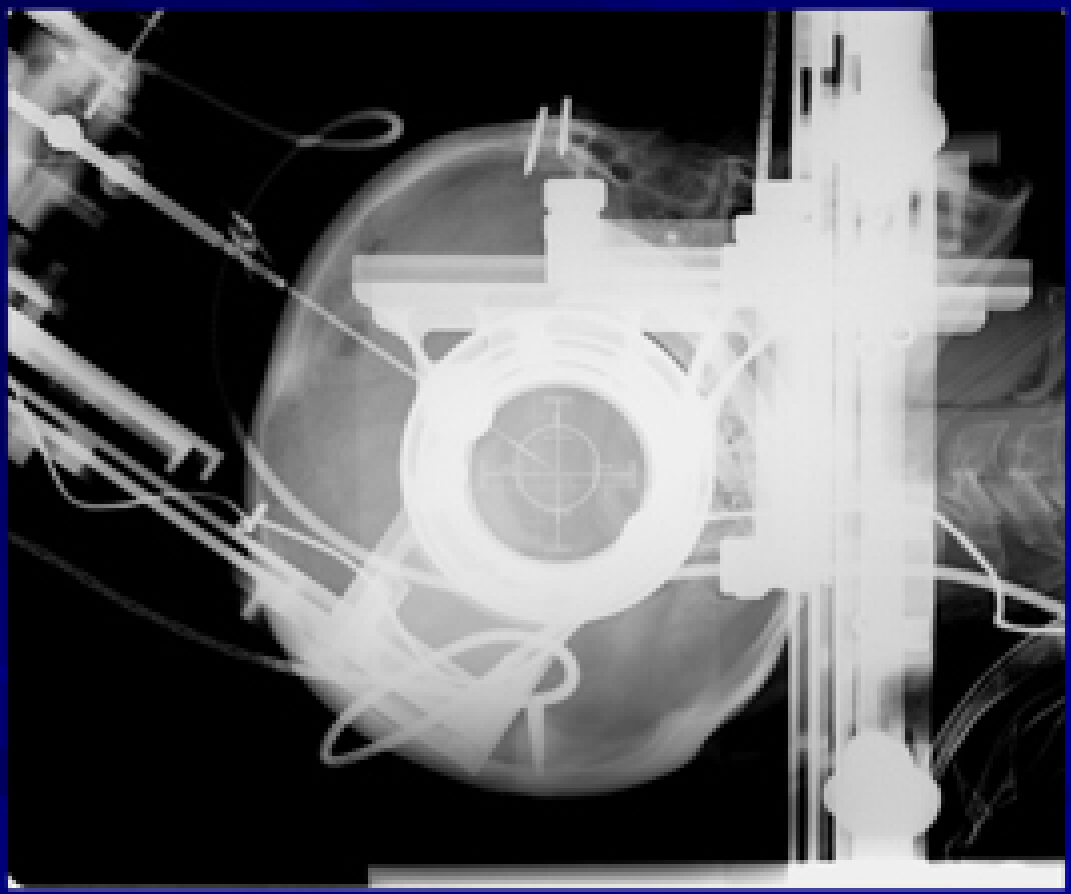


A-P view

Axon Instruments micropositioner on stereotactic arc



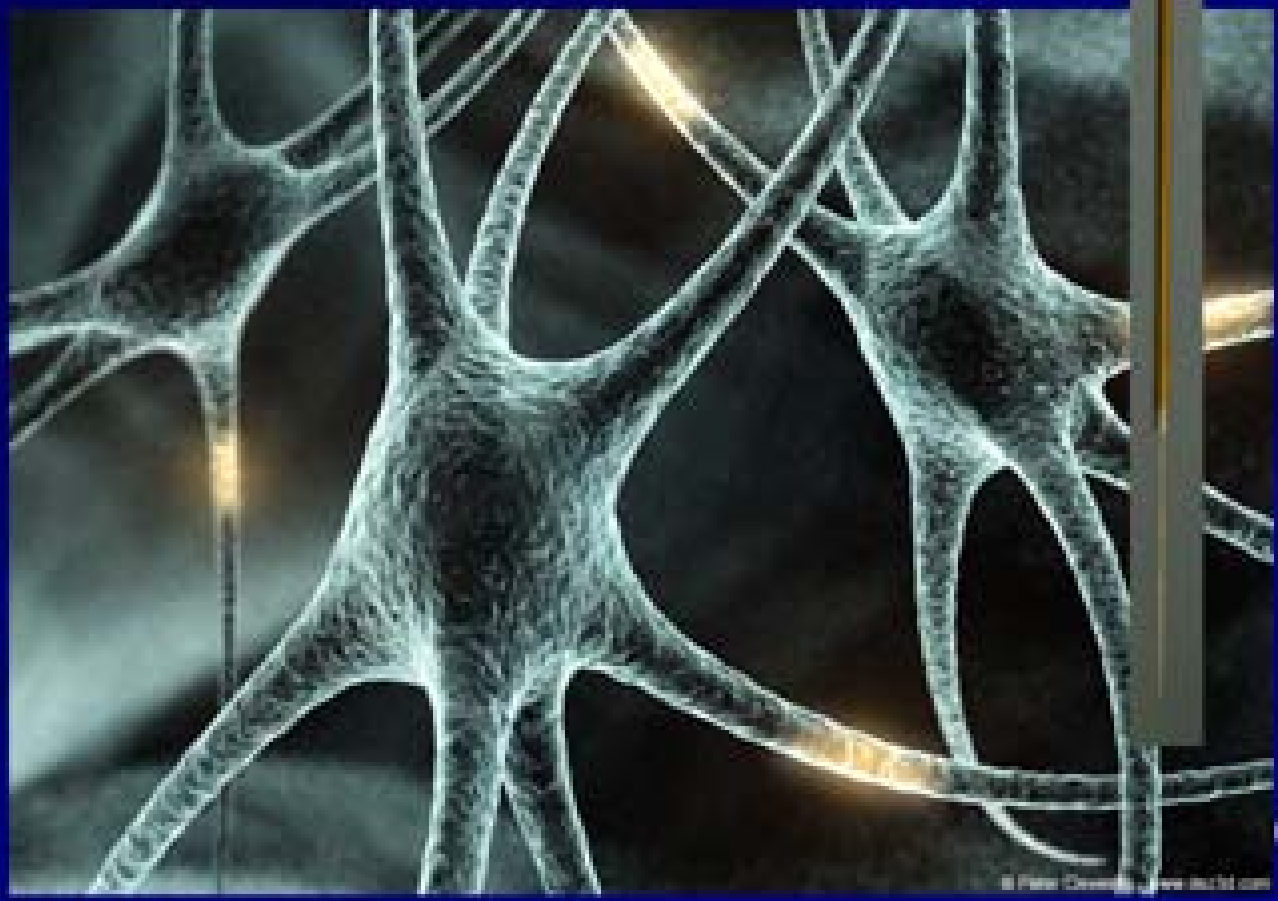
Probe Microelectrode Placement



Lateral view

A-P view

Probe (mapping) microelectrode



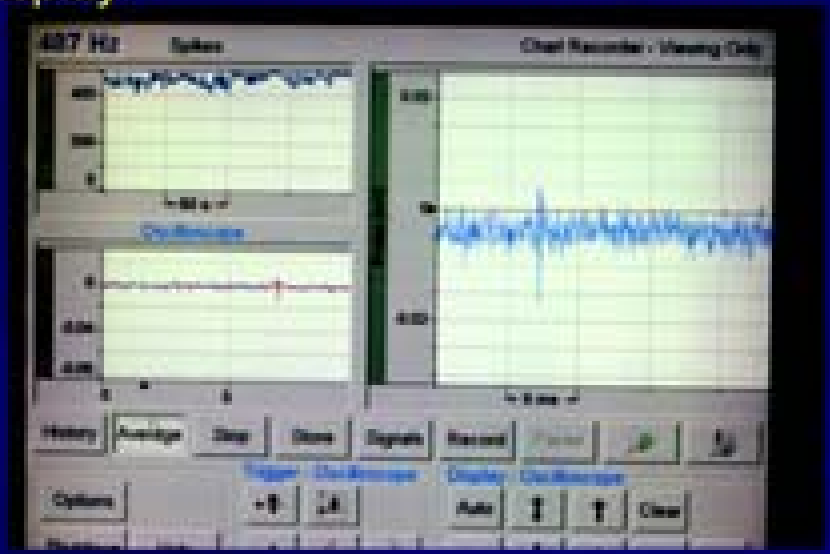
Nerve signal to amplifier

Coaxial electrode has 0.125 mm diameter core for recording that can be retracted into a 0.56 mm diameter outer electrode

(pictures not to same scale)

Axon Instruments “Guideline 3000”

Display

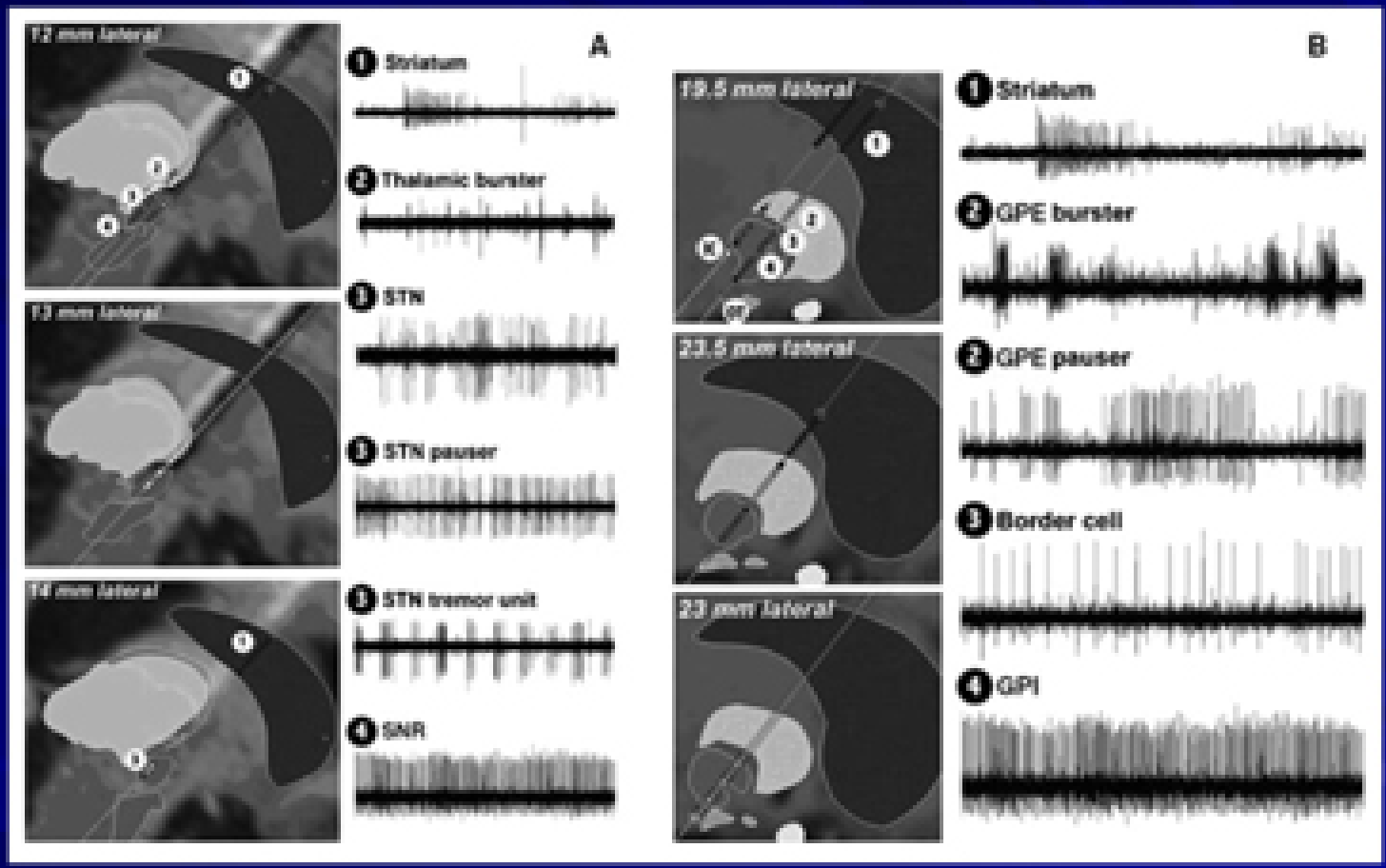


Micropositioner panel

Amplifier panels

Micropositioner control

Nerve Signal Recording

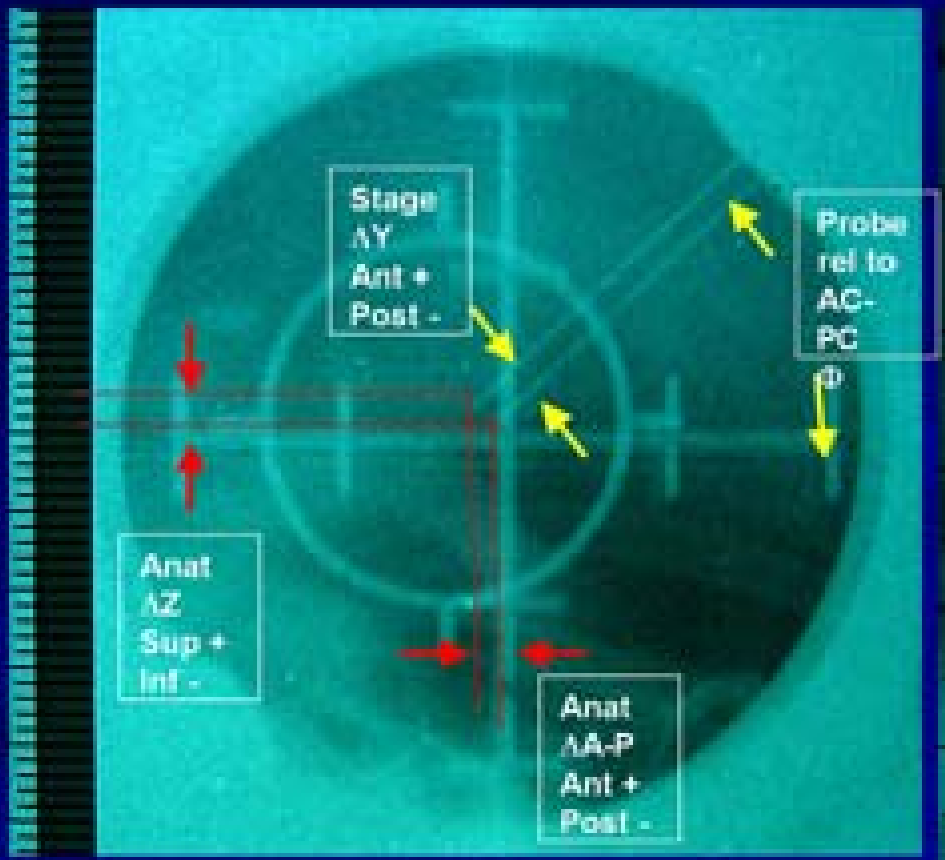


Microelectrode recordings for STN DBS (A) and GPI DBS (B) showing different fireing rates and patterns of structures in electrode trajectories on different planes. GPE=globus pallidus externus; STN=subthalamic nucleus; SNR=substantia nigra pars reticulata; GPI=globus pallidus interna; OT=optic tract; IC=internal capsule

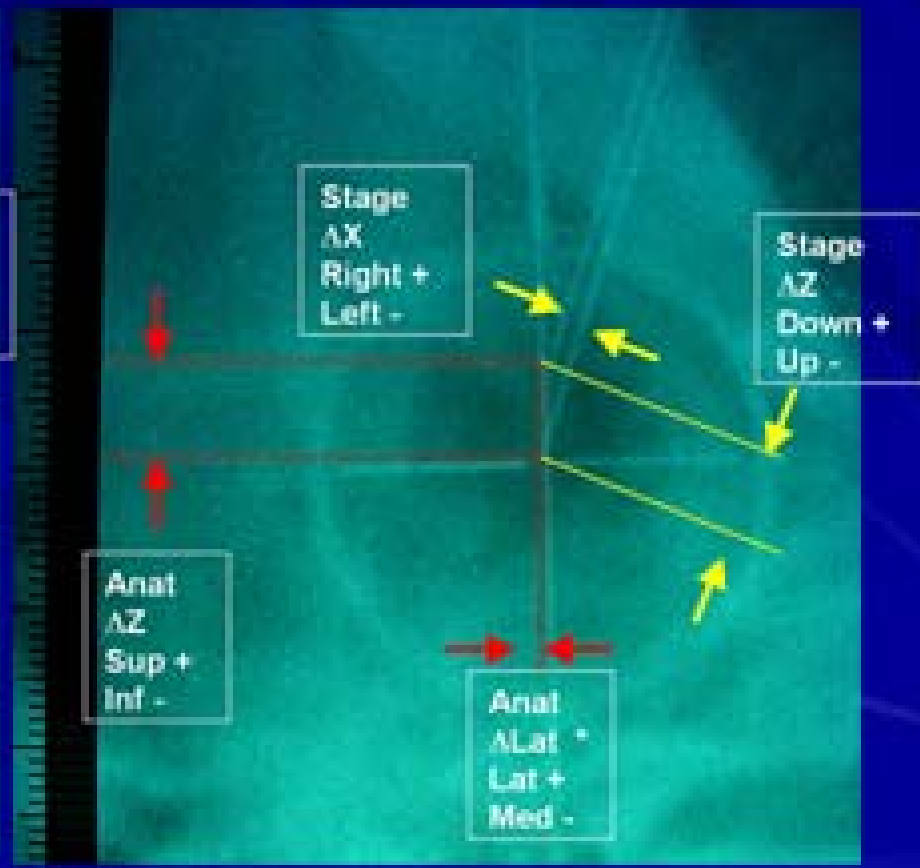
Intraoperative Microelectrode Navigation

Subsequent electrode tracks are overlaid onto Track #1

- "stage" refers to XY-stage (headstage), also to "surgeon's eye" coordinates of probe tip
- "anat" refers to anatomical coordinates relative to mid-Anterior/Posterior Commisure line

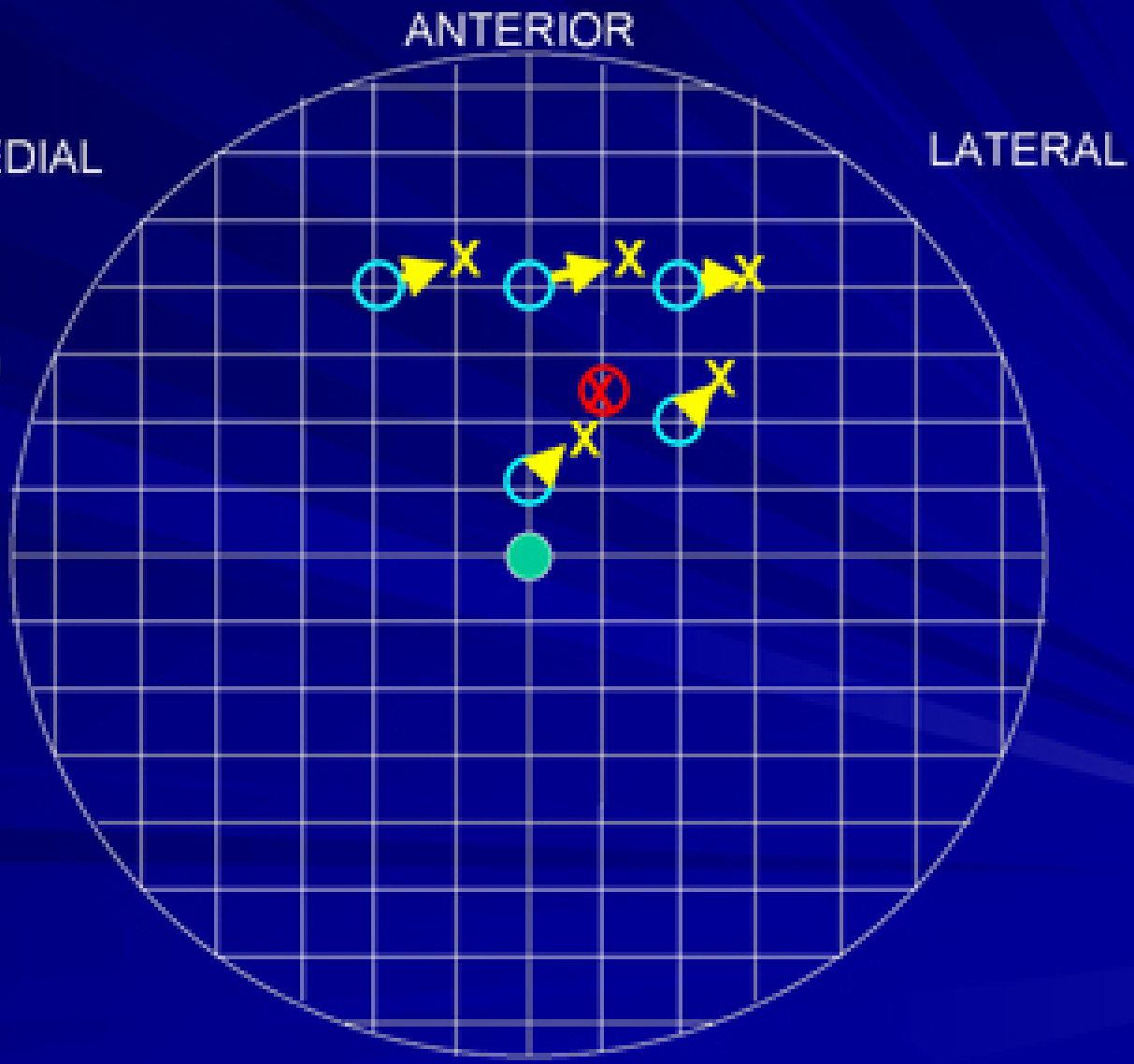


Lateral view



A-P view

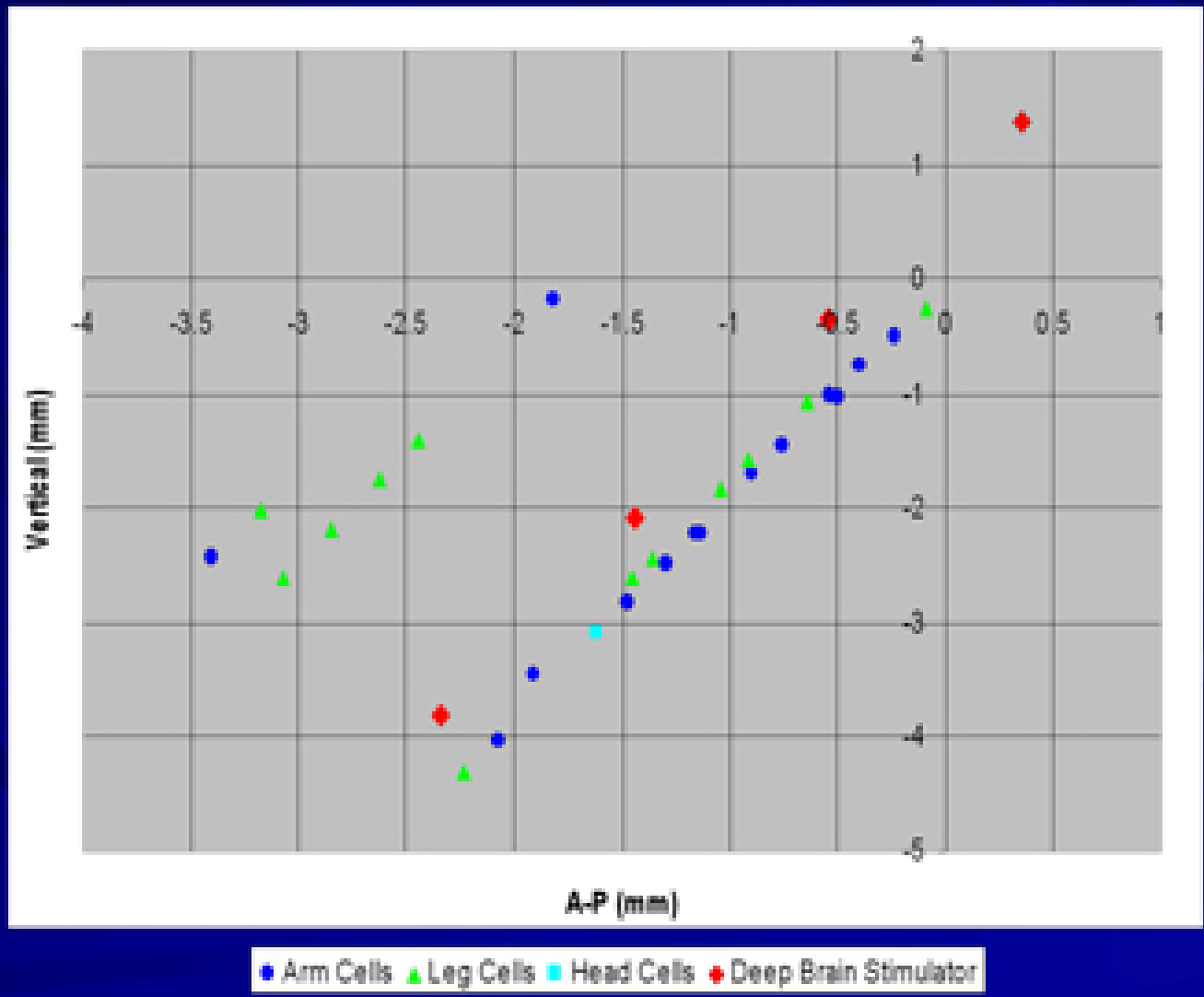
X-Y Grid Electrode Mapping
"Surgeon's Eye" view



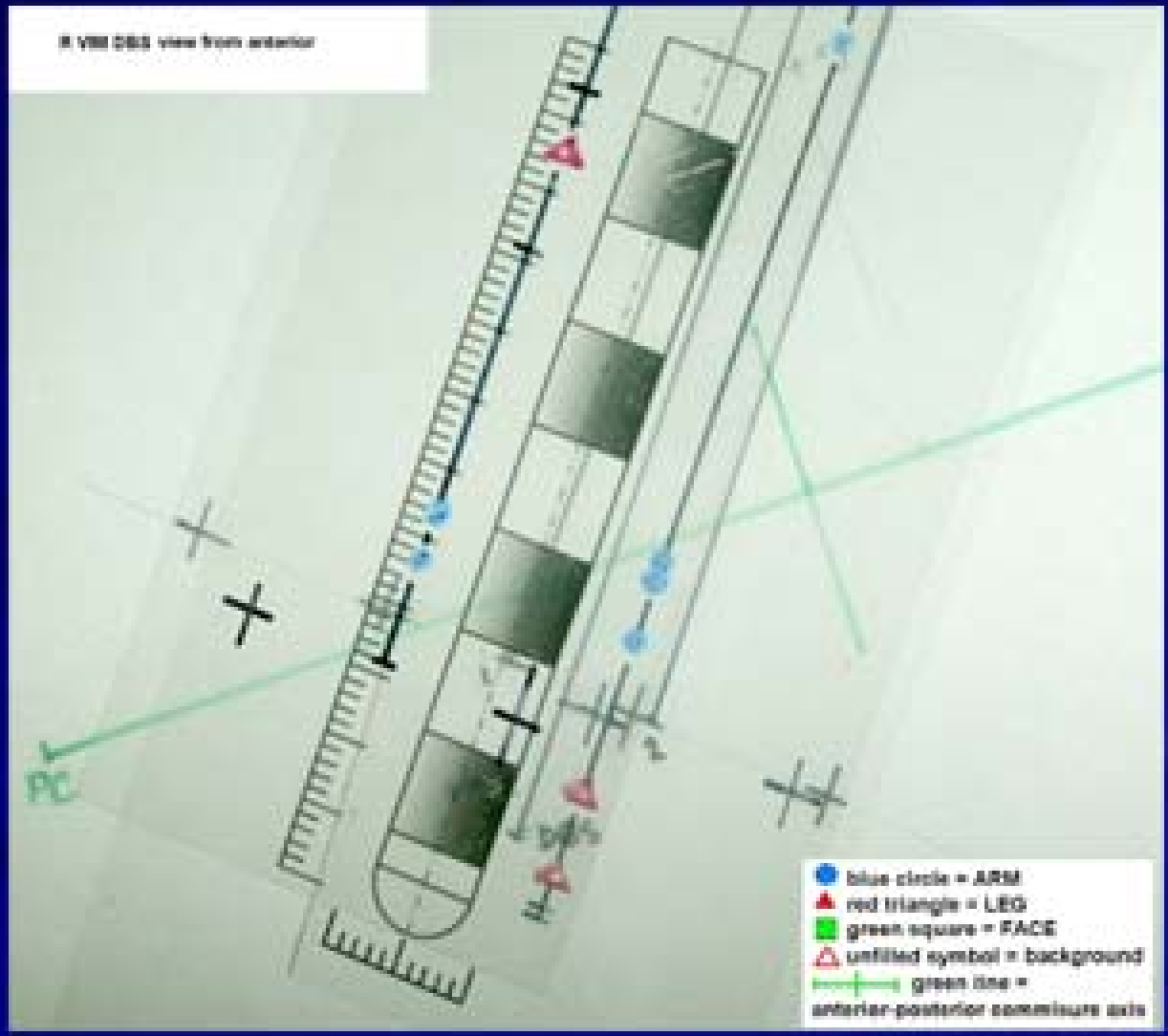
Key:

- Circles=intended microelectrode path (X-Y stage setting)
- X=measured stimulator or probe position
- Central dot represents initial stereotactic target
- each box is 1 mm
- ARROWS INDICATE DRIFT FROM INTENDED POSITION
- Red circle is DBS position (no drift)

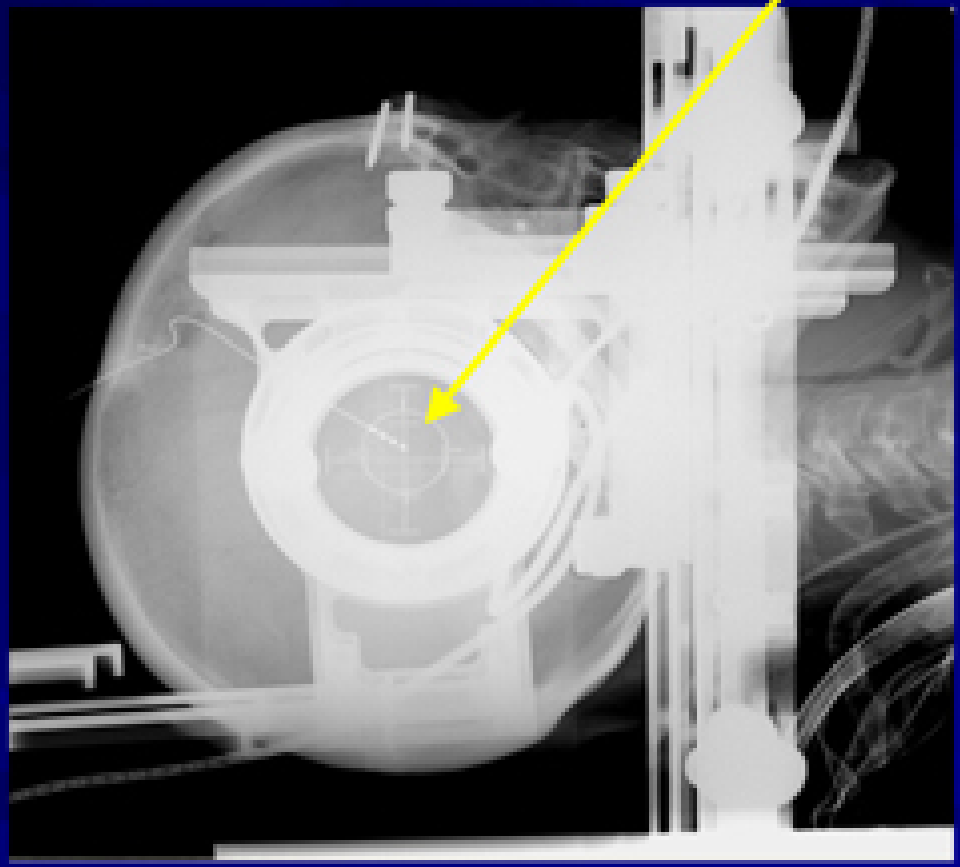
Microelectrode mapping of STN



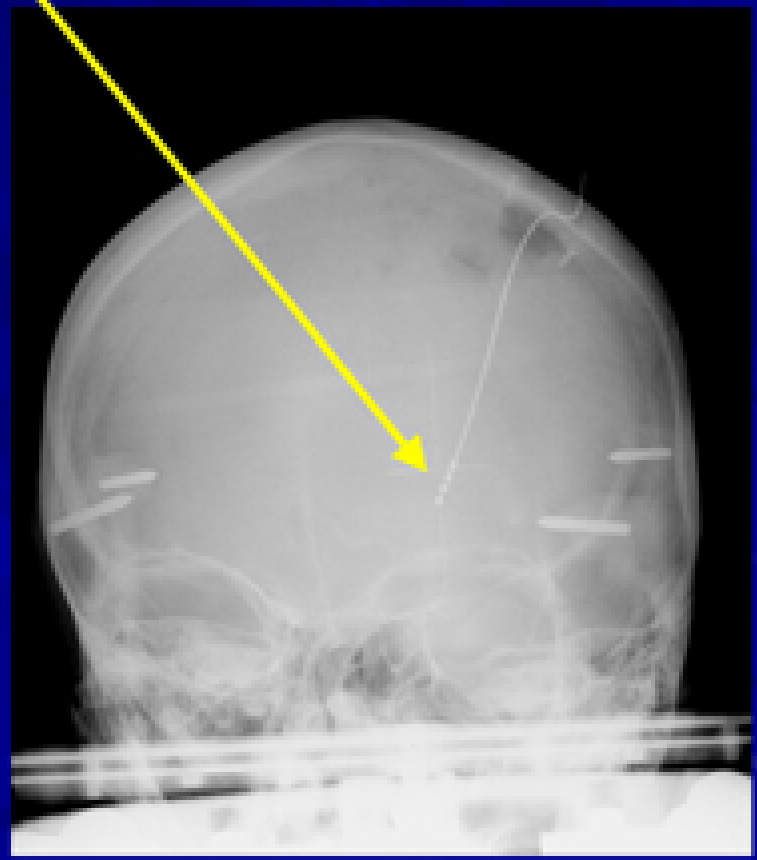
3-D location to aid programming



DBS electrode at final target



Lateral view

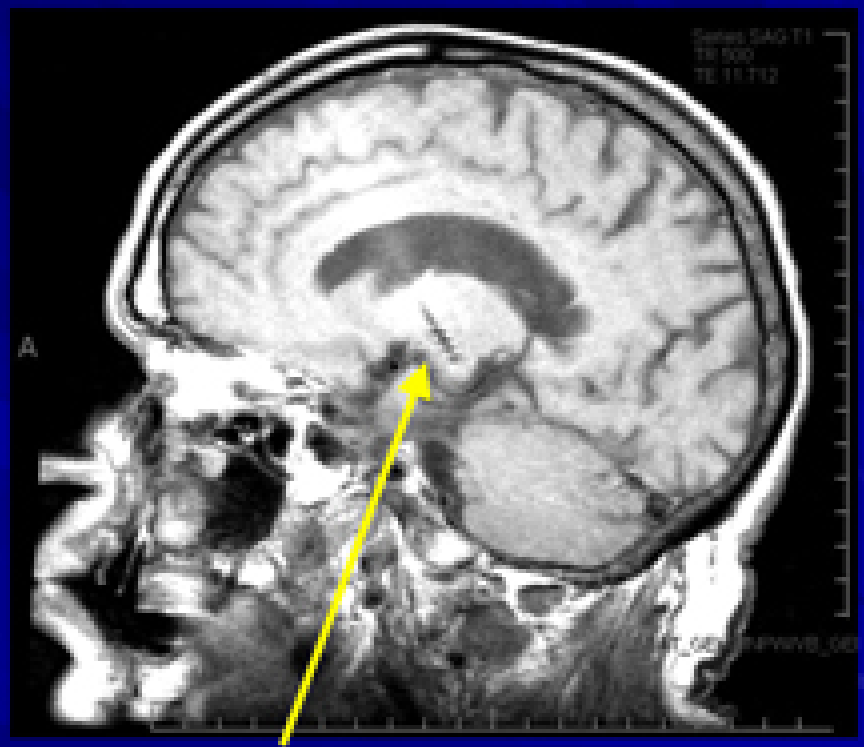


A-P view

Post-surgical electrode location confirmation

CT

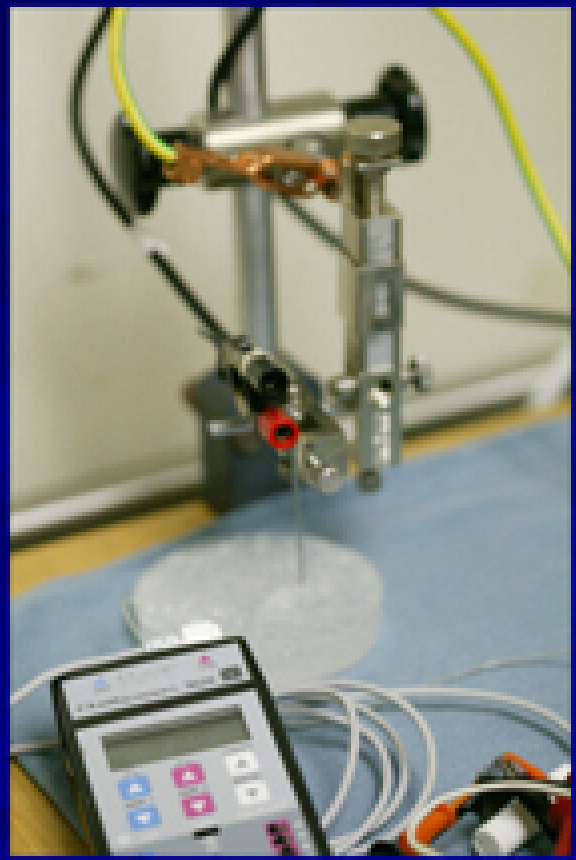
Cable to implantable pulse generator



Head MRI after DBS – questionable safety?

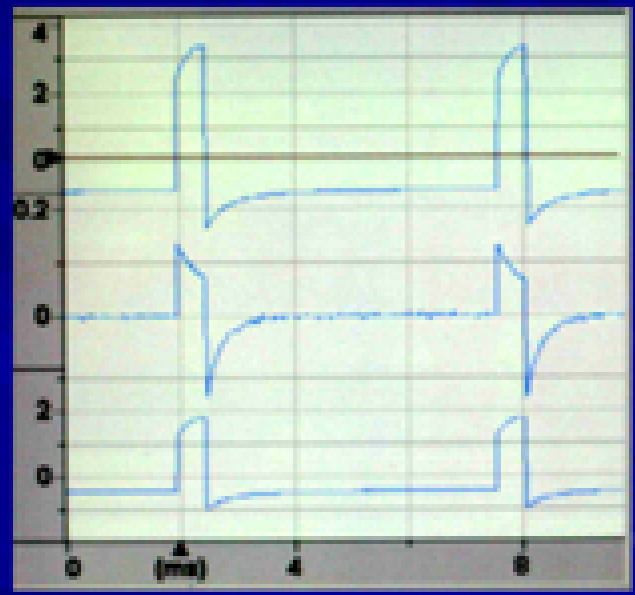
Test stimulation after DBS implantation

Medtronic implantable pulse generator (IPG)



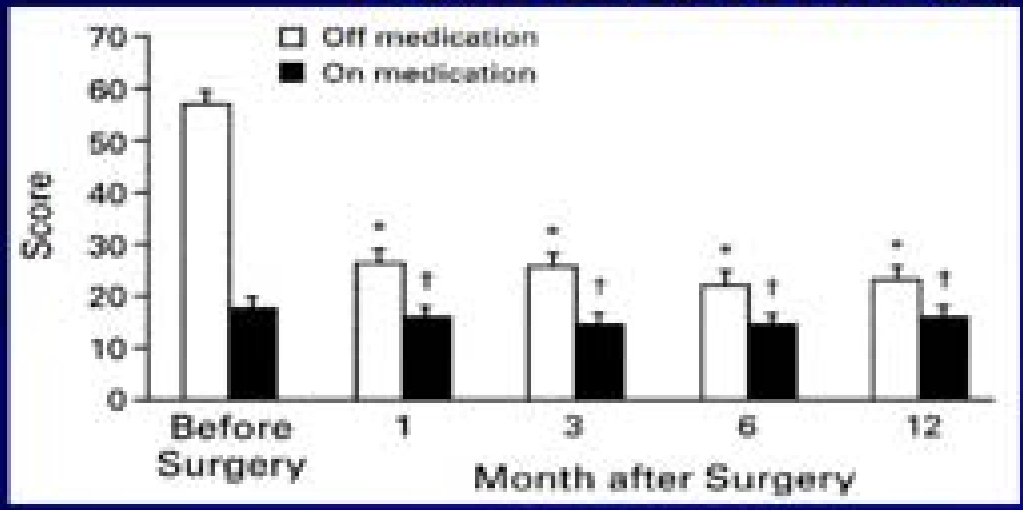
Medtronic 3628 stimulator test

Top: voltage at DBS connector
Middle: current between contacts
Lower: voltage in saline gel



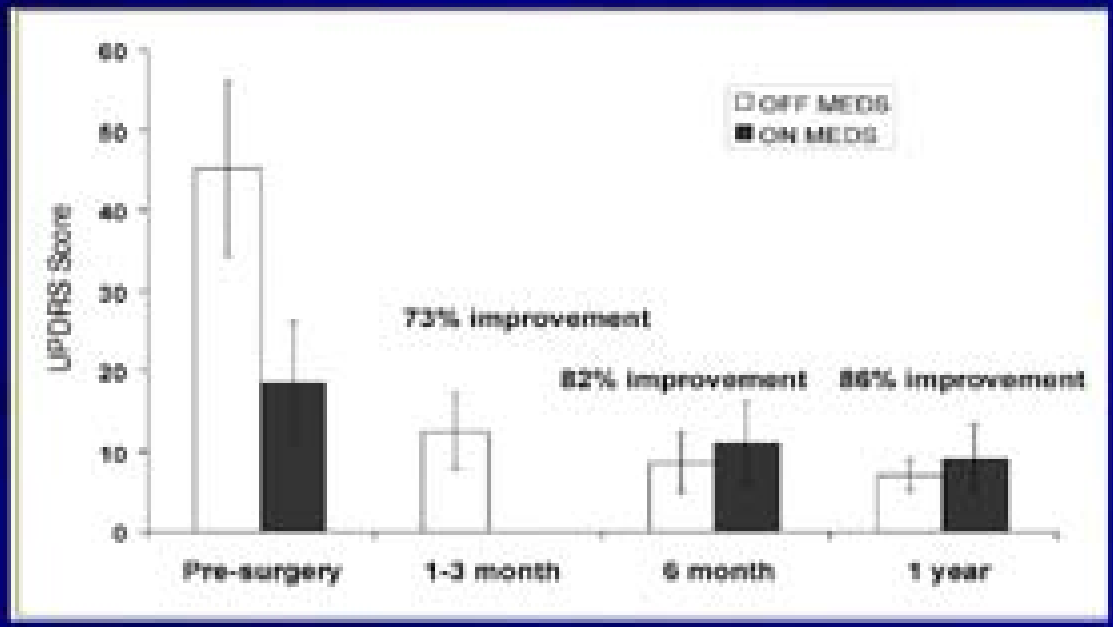
Does DBS help?

Efficacy - UPDRS Motor Outcome from Bilateral STN DBS



University of Grenoble [Limousin, et al., *NEJM*, 1998]

Similar results at Univ of Navarra, Spain [Rodrigues-Oroz, et al, *Neurology*, 55(suppl 6): S45-S51, 2000] and Presbyterian Hospital of Dallas (Sanghera, et al., *J Neurosci Nurs*, 36: 301-311, 2004)



Stanford University Data
n= 18 at 6 months,
n= 14 at 12 months.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neurosurgeon
nurse-practitioner or physician's assistant

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