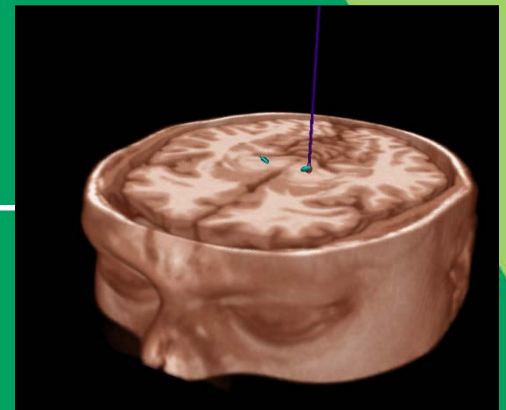


# Deep Brain Stimulation and Movement Disorders

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June 27, 2017



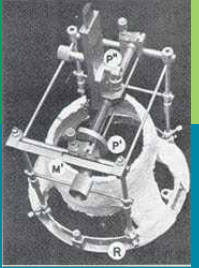
# OBJECTIVES

- Understand the role of Deep Brain Stimulation (DBS) in movement disorders
- Understand the rationale for patient selection, benefits as well as risks of DBS in movement disorders

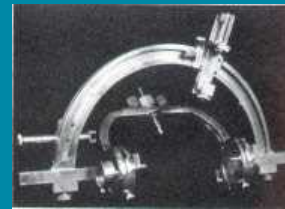
# HISTORY.....

- 
- 1900 yrs
- 46 AD: Application of electric ray (torpedo torpedo) to cranium to cure headaches
  - 19<sup>th</sup> century: Aldini stimulated exposed cortex and evoked motor response (grimacing prisoner)
    - 1880s: topography studies by surgeon Horsley
  - 1950s: eloquent mapping of sensory and motor cortices by Penfield and colleagues
  - 1938: Electroshock by Cerletti for psychosis
  - 1950s Electrical stim for pain, functional stim for behavioral disorders

20 yrs




- 1947 Spiegel and Wycis fashioned the first human stereotactic frame
- 1949 Leksell fashions an arc-quadrant frame which still continues to be used



<http://www.neurosurgery.org/cybermuseum/stereotactichall/stereoarticle.html>

- Early stimulation studies (1950s-60s)
  - Delgado for seizures and psychosis
  - Bektherva for hyperkinetic movement disorders
  - Sem-Jacobsen for epilepsy and schizophrenia
  - Cooper for epilepsy, cerebral palsy and spasticity
- Micro electrode recordings Abel-Fessard 1961
- 1967: Introduction of levodopa, political pressures—functional neurosurgery briefly takes a back seat

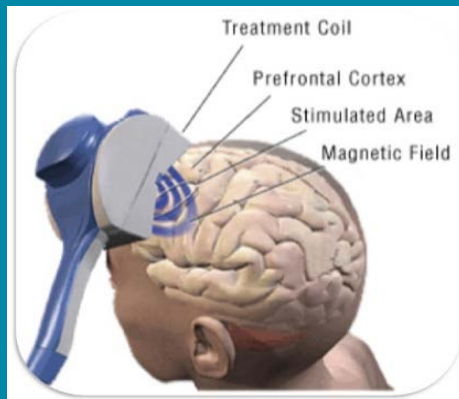
- 
- 20 yrs
- 1991 Benabid, Blond and Siegfried report effects of thalamic DBS on tremor
  - 1990s Laitinen DBS to Gpi for parkinsons
  - 1994 Pollack and colleagues demonstrated effects on STN DBS in Parkinsons
  - FDA APPROVAL
    - 1997 ET
    - 2002 for PD (STN and GPi)
    - 2003 Humanitarian device exemption for dystonia (generalized and segmental)
    - 2009 HDE for OCD (ant limb IC)

# NEUROSTIMULATION

## MODULATION OF THE NERVOUS SYSTEM USING IMPLANTED/ EXTERNAL DEVICES



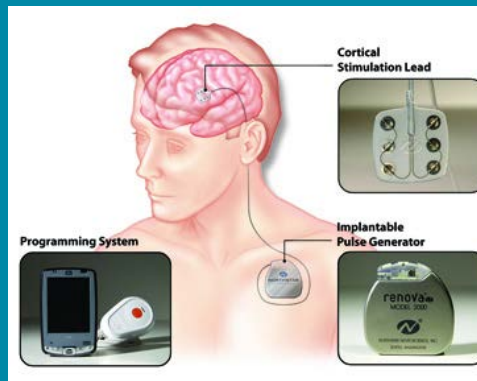
### TRANSCRANIAL MAGNETIC STIMULATION



<http://etkinlab.stanford.edu/images/rTMScoil.jpg>



### CORTICAL STIMULATION



[http://www.medgadget.com/2008/01/brain\\_stimulation\\_device\\_for\\_stroke\\_victims\\_fails\\_clinical\\_trial.html](http://www.medgadget.com/2008/01/brain_stimulation_device_for_stroke_victims_fails_clinical_trial.html)



### DEEP BRAIN STIMULATION



<http://professional.medtronic.com/pt/neuro/dbs-md/edu/presentations-downloads/index.htm#.WB4kaYWcHcw>

# CONDITIONS DBS IS USED FOR

FDA approved for Parkinson's & Essential tremor

Humanitarian device exemption (HDE) for Generalized/  
segmental dystonia (genetic) and for OCD

# MOTOR SYMPTOMS OF PARKINSONS

- Rigidity
- Tremor
- Bradykinesia
- Gait disorder



# MOVEMENT DISORDERS AND THEIR IMPACT

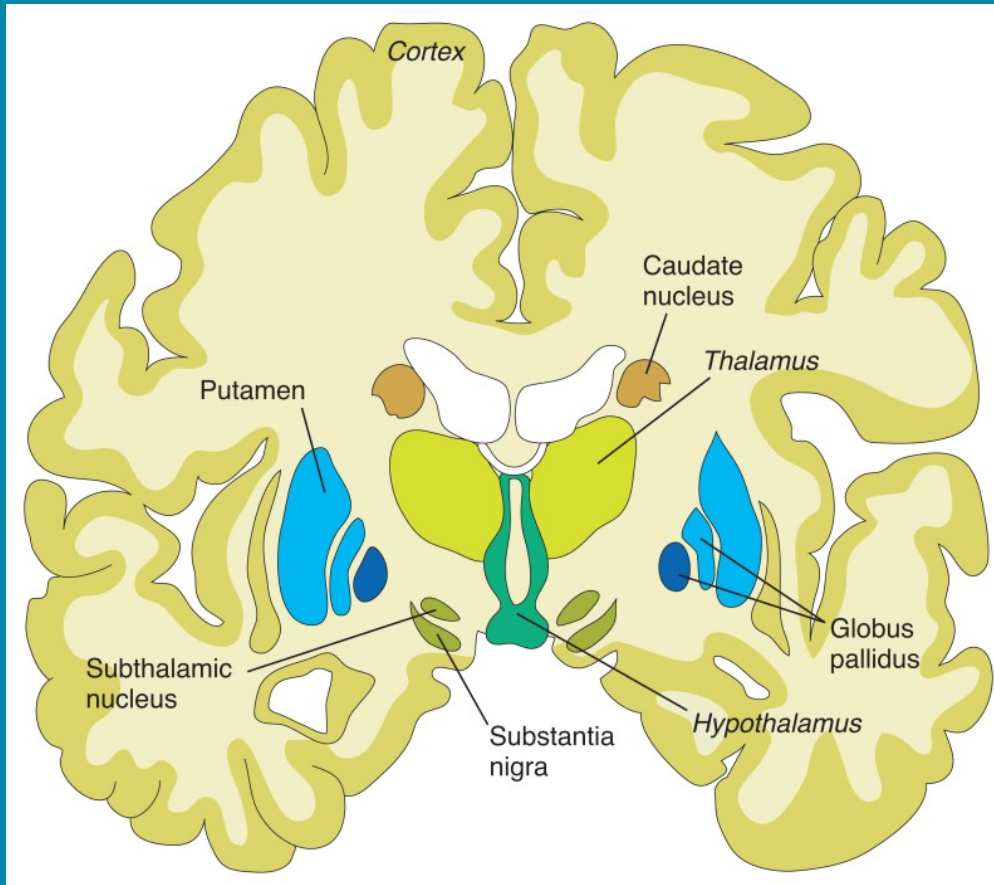
## PARKINSONS

- 1 MILLION people are currently diagnosed with PD in the United States
- 1 in 100 Americans over the age of 60
- 1.6% of Medicare beneficiaries

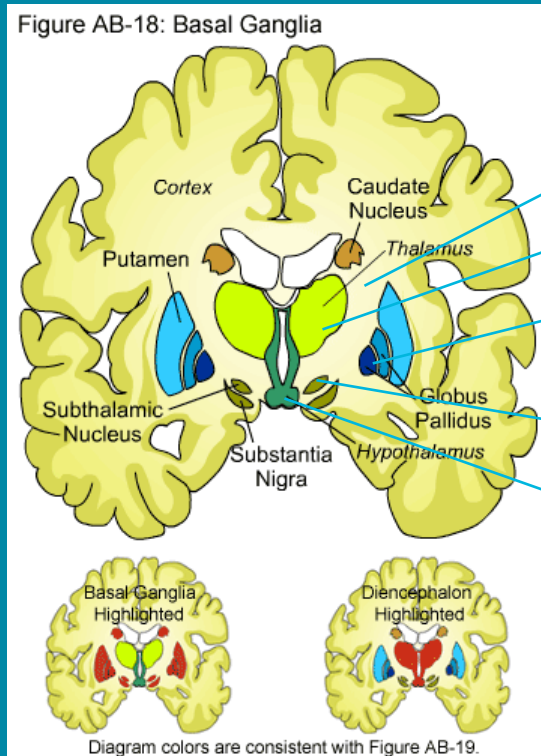
## ESSENTIAL TREMOR:

- Most common movement disorder
- 0.4 to 3.9 % of the population, incidence maybe higher (Severe enough to warrant diagnosis)
- QUEST Scores higher than in PD
- DYSTONIA: limited data due to multiple forms

# BASAL GANGLIA STRUCTURE



# DBS-WHAT IS THE TARGET?



ANTERIOR LIMB INTERNAL CAPSULE- OCD

THALAMUS- TREMOR

GLOBUS PALLIDUS INTERNA- PARKINSONS/  
DYSTONIA

SUBTHALAMIC NUCLEUS- PARKINSONS

HYPOTHALAMUS- CLUSTER HEADACHE

[http://web.stanford.edu/group/hopes/cgi-bin/hopes\\_test/sites/hopes/files/f\\_ab18bslgang.gif](http://web.stanford.edu/group/hopes/cgi-bin/hopes_test/sites/hopes/files/f_ab18bslgang.gif)

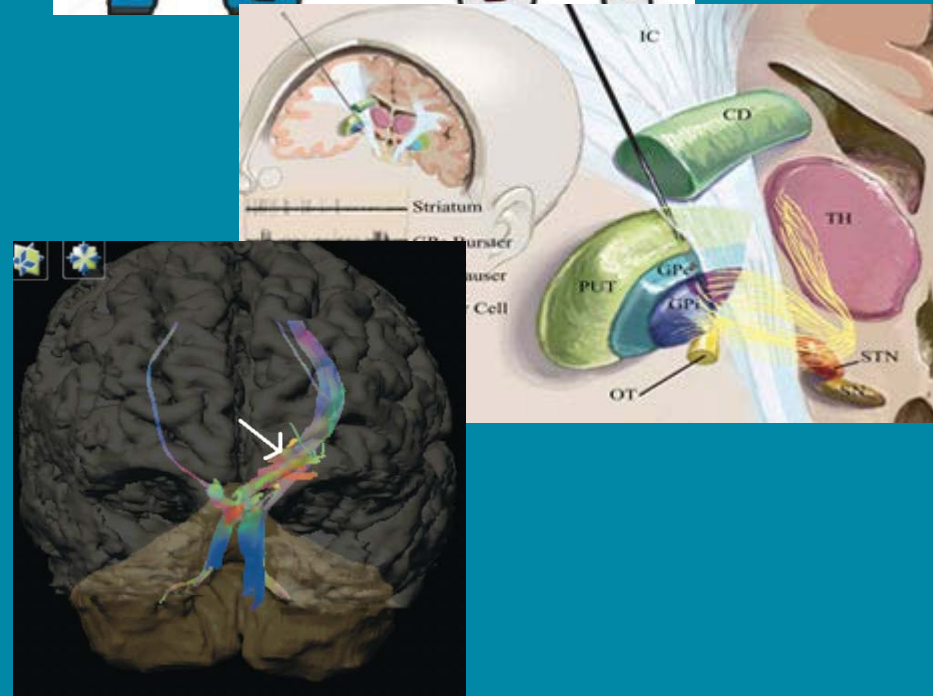
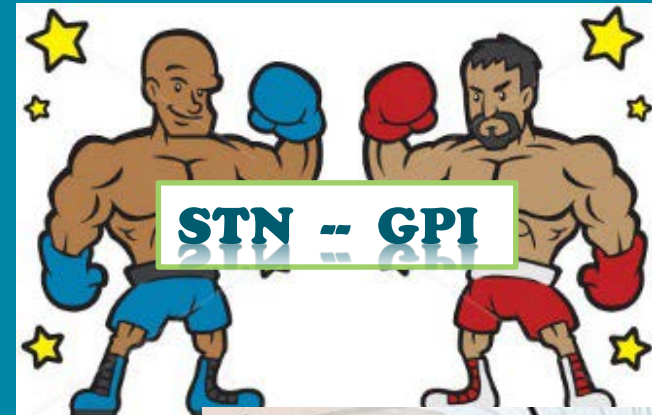
# STN vs. GPI

LANCET 2013

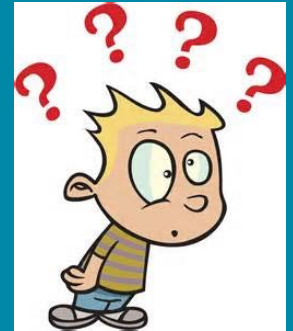
Subthalamic nucleus versus globus pallidus bilateral deep brain stimulation for advanced Parkinson's disease: a randomized controlled trial.

## INTERPRETATION:

Although there was no difference in the primary outcomes, findings suggest that STN could be the preferred target for DBS in patients with advanced Parkinson's disease



# HOW DOES DBS WORK?



- Short answer----- We don't know!!
- Long answer
  - Initially thought to be similar to lesioning, inhibits electrical activity
  - Data suggests differential effects based on stim rate and location
    - High frequency stim works, frequencies lower than 50 Hz doesn't
    - Axon stimulation (excitatory-capsule) vs neuronal stim (inhibitory)
    - ? Modulation more than inhibition

# WHY SHOULD YOU CONSIDER DBS

- PARKINSONS (PD):

- Tremor inadequately controlled by medications
- DBS with significant advantage over best medical therapy for motor fluctuations

On state without dyskinesias ~ 4hrs

Off state decreased by ~ 2-4 hrs

Improved PDQ 39 ~ 25%

Benefits sustained upto 10 yrs

- ESSENTIAL TREMOR:

- better than standard meds, improves ADLs, functional impact (60% or more improvement in tremor scores)

- GENERALISED DYSTONIA (HDE) (limited data):

- DYT-1 responds really well, role of meds in generalized dystonia again limited

# PATIENT SELECTION

- PARKINSONS:

- PD and not Parkinson plus / drug induced parkinsonism
- Ideally with motor fluctuations and maximum medical therapy, though emerging data for early implantation (EARLY STIM)
- Not demented, screen mood disorders
- Comorbidities (cardiac/ vascular/ coagulation disorders)

- ESSENTIAL TREMOR:

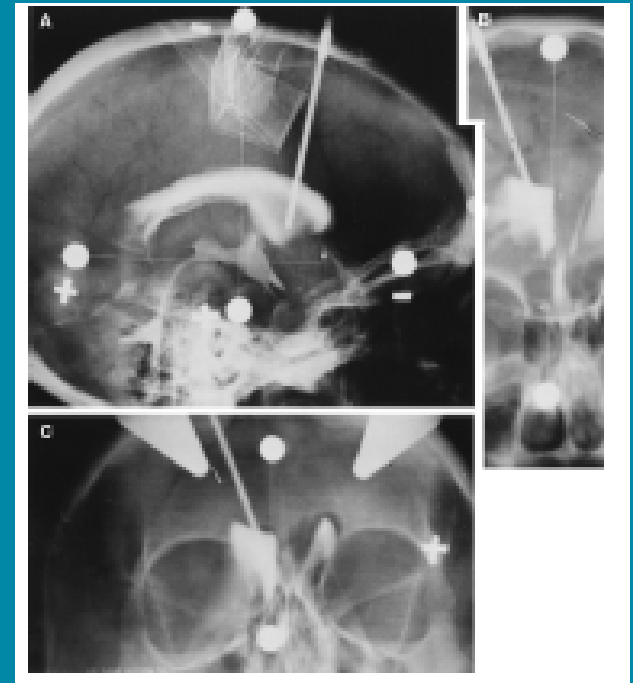
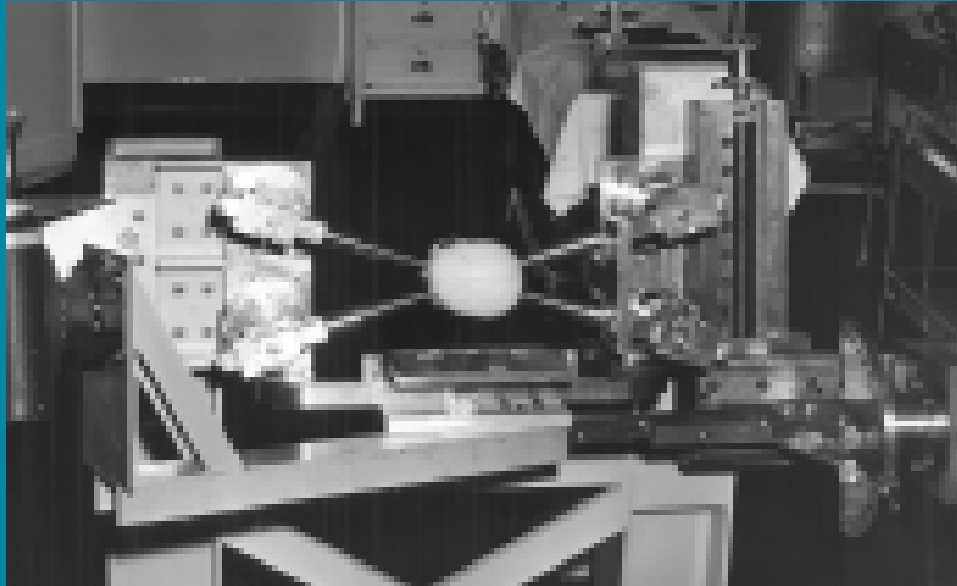
- Tremor affecting quality of life/ function (moderate to severe tremor)
- Ideally should have tried first line meds (beta blockers/ primidone)
- Not demented

- DYSTONIA:

- Case by case, through IRB, ideally generalized/ genetic torsion dystonia

OTHE INFLUENCING FACTORS: age, poor levodopa response in PD, family/ social support

# EARLY STEROTACTIC SURGERY





# DBS PROCEDURE

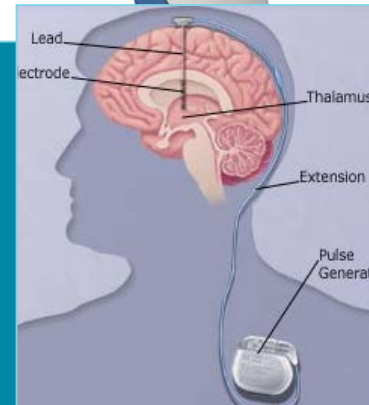
## Stage I – Implant electrode

- Frame placement
- CT with frame
- CT/MR fusion & targeting
- Micro-electrode recording
- Macro Stimulation
- Implantation



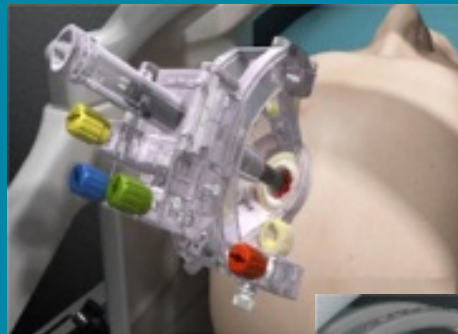
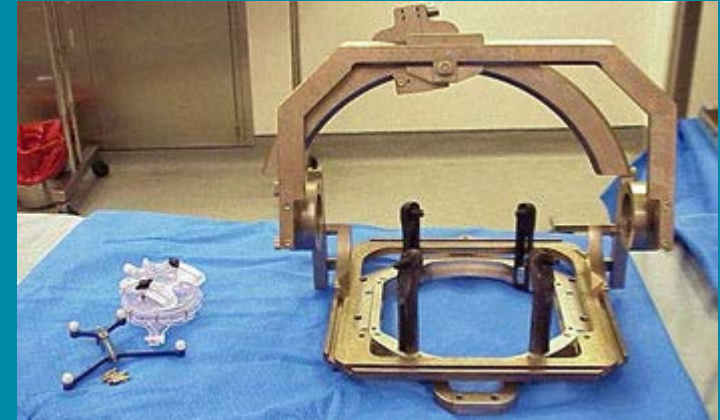
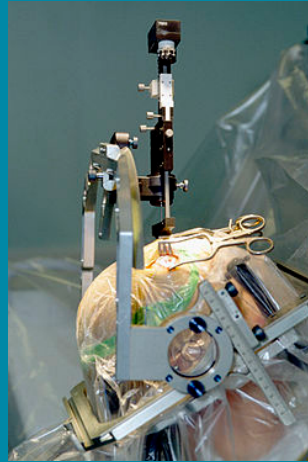
## Stage II

- Pulse Generator Placement



# CURRENT DBS SURGERY OPTIONS

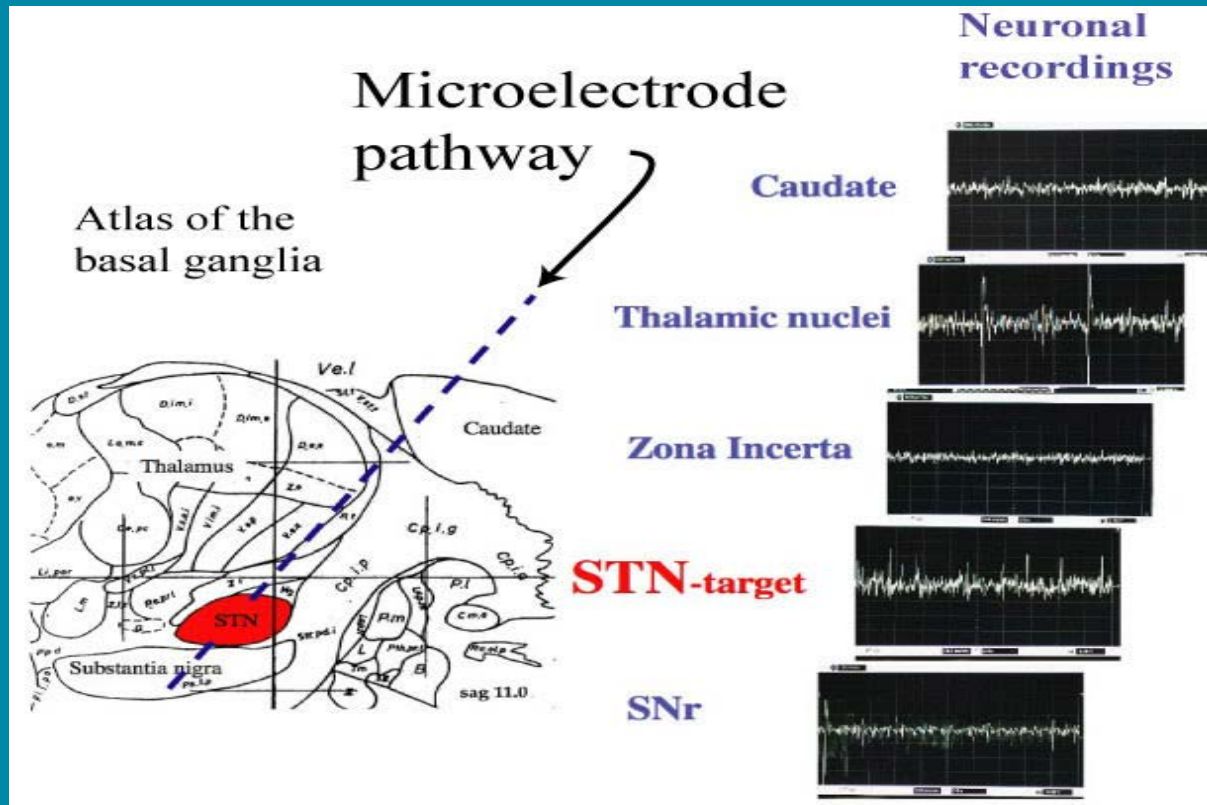
- **AWAKE:**
  - Frame bases
    - With MER
  - Frameless
    - With MER
- **ASLEEP:**
  - Frameless
    - MRI Guided
    - CT Guided



# ROLE FOR MICRO-ELECTRODE RECORDINGS

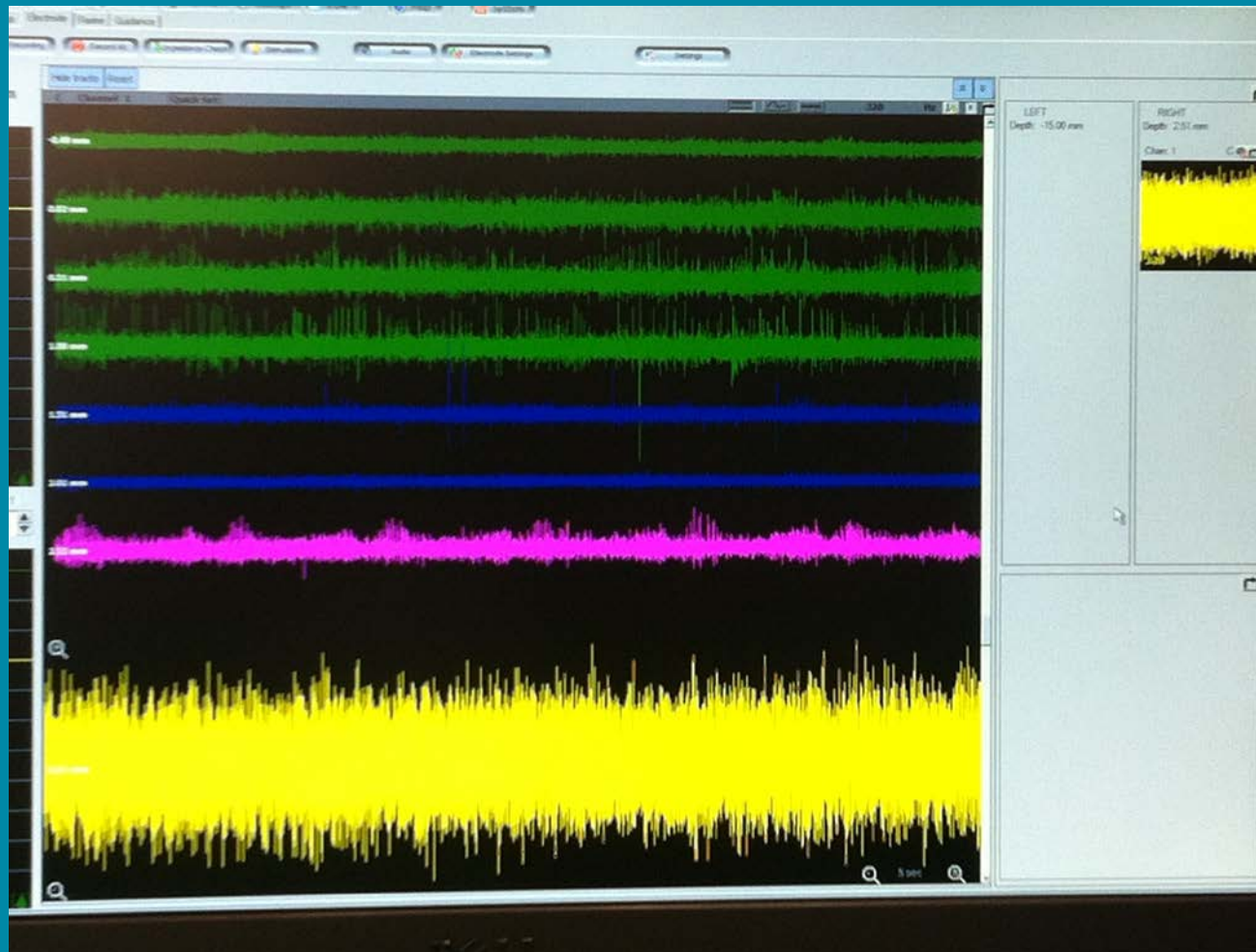
- Target localization is a combination of anatomic and physiologic localization
  - Anatomic (MRI-CT fusion and coordinates)
  - Physiologic (confirms intended anatomic target)
- MER (microelectrode recording)
  - Allows for confirmation of intended functional target (Vim thalamus, dorsolateral STN, Gpi)
  - Allows intra operative revision of intended stereotactic plan

# DBS TRAJECTORY



[http://cmpl.columbia.edu/wp-content/uploads/2015/11/MER\\_trajectory.jpg](http://cmpl.columbia.edu/wp-content/uploads/2015/11/MER_trajectory.jpg)

# MICROELECTRODE RECORDINGS





# MACROSTIMULATION

## STIMULATION THROUGH THE LEADS :

- Goal to map out effects (improve tremor, rigidity)
- Map side effects (capsule, medial lemniscus, 3 rd nerve fascicles)
- In some cases, mainly useful to map side effects (such as Dystonia)



# PROGRAMMING

## Four variables

- Active contact in electrode (0,1,2,3-mono, bipolar/ double negative and so on)
  - Amplitude of charge ( in volts)
  - Frequency (in hertz)
  - Pulse width (in microseconds)
- Contributes to infinite combinations but we start with tried and tested ones
    - Low frequency (dystonia)
    - High and mid range frequencies( PD and tremor)
    - Higher pulse width (dystonia/ sometimes tremor)
  - Programming can take 3-6 mo or longer



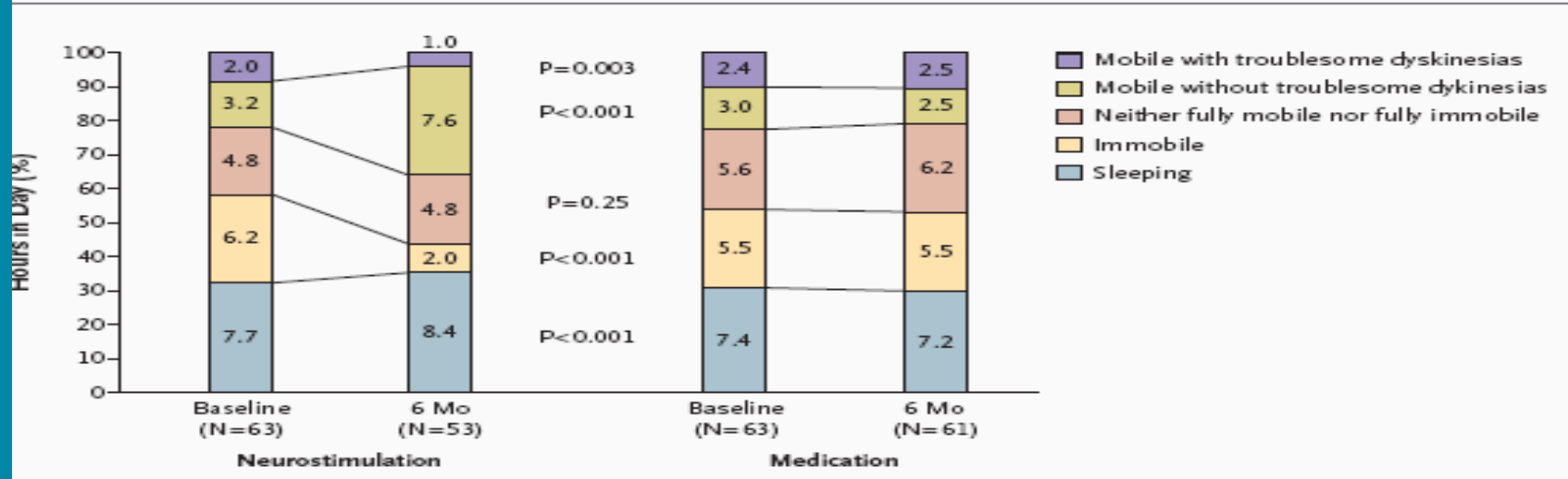
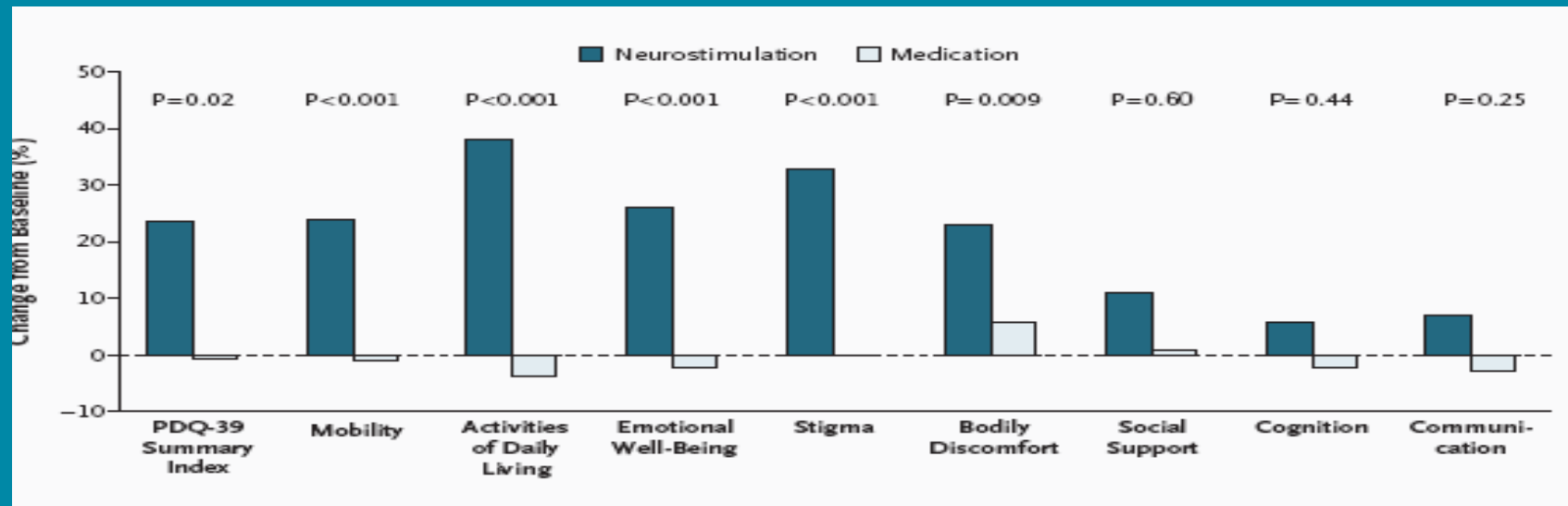
# OUTCOMES

Deuschl, NEJM Aug. 2006

- Randomized trial of DBS for PD
- 156 patients
- DBS + Rx *vs.* Rx alone
- End points: 6 mo PDQ-39 & UPDRS-III
- Outcomes *avored DBS*
  - PDQ 75% vs. 25% (p<0.001)
  - UPDRS 85% vs. 13% (p<0.001)



# OUTCOMES



# RISKS

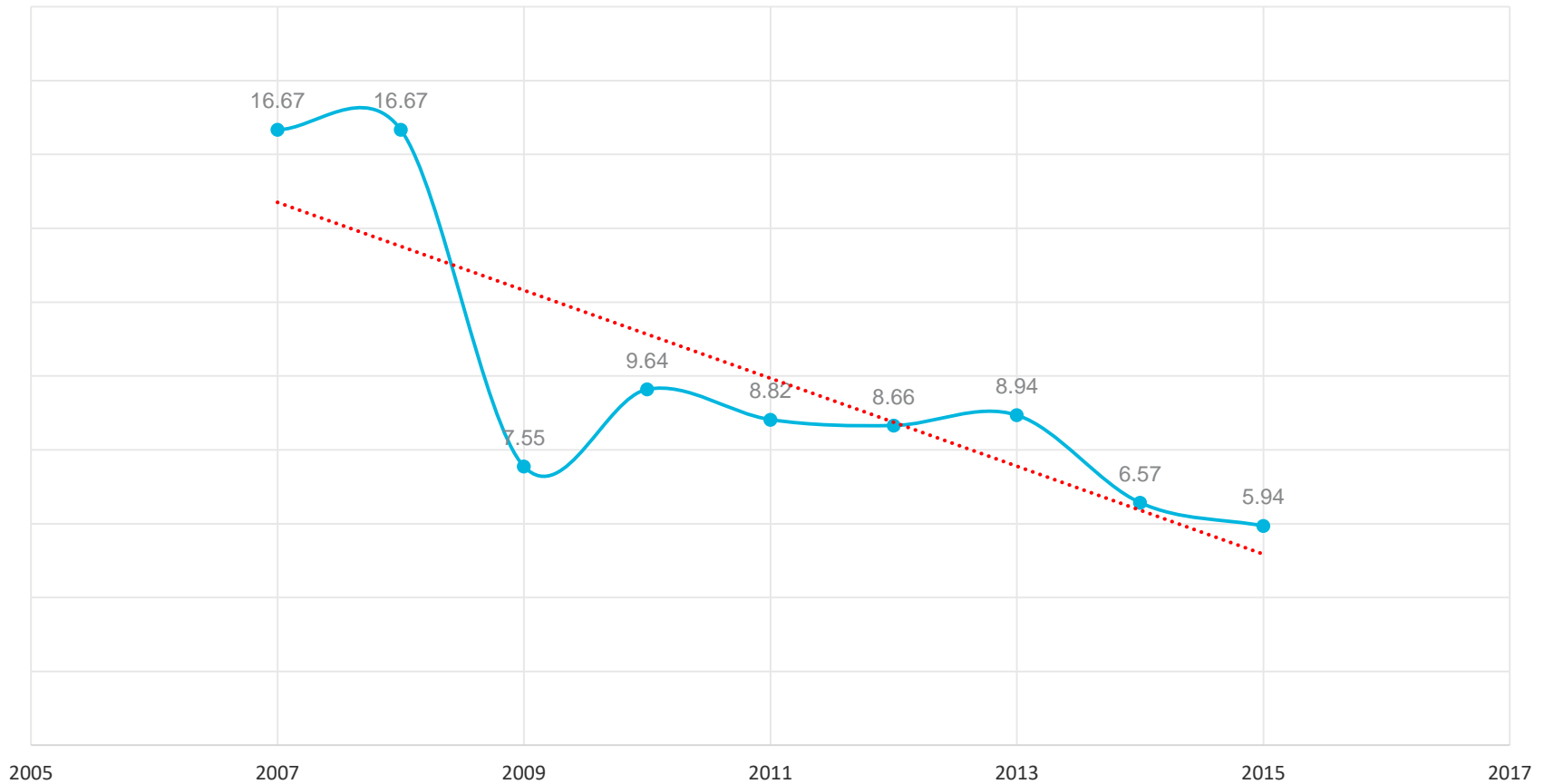
Goodman, et al 2006

100 Consecutive patients / 191 implanted devices

– <b>Infections</b>		<b>7 (3.7%)</b>
– Cerebral infarct		1
– <i>Intracerebral hemorrhage</i>	<i>1</i>	
– Subdural hemorrhage	1	
– Air embolism	1	
– Wound hematomas	2	
– Skin erosions	2	
– Seizures		3
– Electrode revisions		6 (3.1%)
– <b>Mortality</b>	<b>0</b>	
– <b>Permanent deficits</b>	<b>0</b>	
– <b><u>TOTAL</u></b>		<b><u>24 (13%)</u></b>

# ANNUALIZED VM COMPLICATION RATE

2007-2015



# RISKS DBS vs MEDICATION

**Table 4. Adverse Events during the Six-Month Study.\***

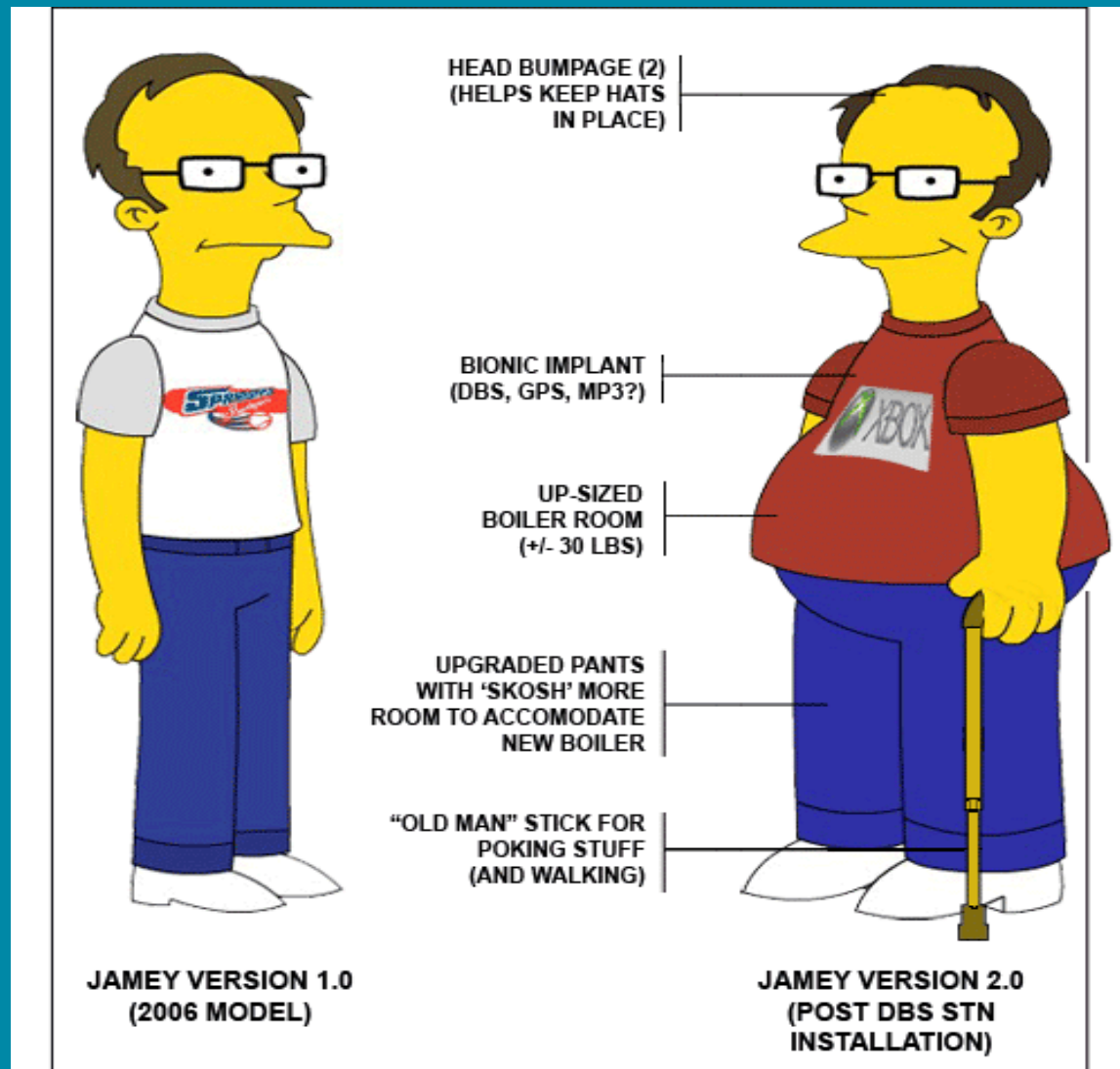
Event	Neurostimulation Group <i>no. of events</i>	Medication Group
<b>Serious adverse event†</b>		
Death	3	1
Perioperative cerebral hematoma	1	0
Suicide 5 mo after surgery	1	0
Car accident during psychotic episode	0	1
Pneumonia	1	0
Readmission to the hospital	7	2
Worsening of mobility	3	1
Infection at the stimulator site	2	0
Erroneous stimulator shut-off	1	0
Vertebral fracture from fall	1	0
Hip fracture from fall	0	1
<b>Total nonserious adverse events‡</b>	77	96
Mild	35	8
Moderate	32	39
Severe	10	49

Deuschl 2006

# **LIMITATIONS OF SURGERY**

- Improvement limited by patient's best condition "on" medications
- Little effect on autonomic dysfunction
- Little effect on depression
- Akinesia, speech, postural stability, freezing of gait, and cognitive function worsen within 1 to 5 years
- Unknown (likely no) alteration in natural history of Parkinson's Disease

# OTHER RISKS



# THINGS TO REMEMBER

- DBS systems now (fully implanted Medtronic Activa system) are **WHOLE BODY MRI COMPATIBLE**
- Microwave, shortwave and ultrasound diathermy contraindicated
- Can be used in conjunction with pacemakers, as long as devices are compatible
- Newer devices not affected by household electronic equipment

# FUTURE OF DBS



## DEVICE RELATED:

- Battery life
- ? Remote monitoring
- Constant current
- ?Responsive neurostimulators
- ?Record data

## EXPANDING THE HORIZON:

- Early PD
- Tourettes
- Cluster headaches
- ?Memory
- Epilepsy
- OCD

## PROCEDURE RELATED:

- Awake vs asleep
- Miniature pulse generators
- CSF Glucose as power supply