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Patrizio Prati Neurologo, Torino
Emanuele Puca Neurologia, San Benedetto del Tronto
Michele Ragno Neurologia, San Benedetto del Tronto
Sara Renzi Neurologia, San Benedetto del Tronto
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Enzo Sanzaro Neurologia, Vittoria (RG)
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Roman Sztajzel Neurologia, Ginevra (Svizzera)
Nicola Tambasco Neurologia, Perugia
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PRESIDENTE DEL CONGRESSO

Michele Ragno

Direttore U.O. di Neurologia
Ospedale Madonna del Soccorso, San Benedetto del Tronto

Local steering committee

T. Carboni, G. D'Andreamatteo, F. Di Marzio, R. Gobbato,
C. Paci, E. Puca, S. Renzi, S. Sanguigni



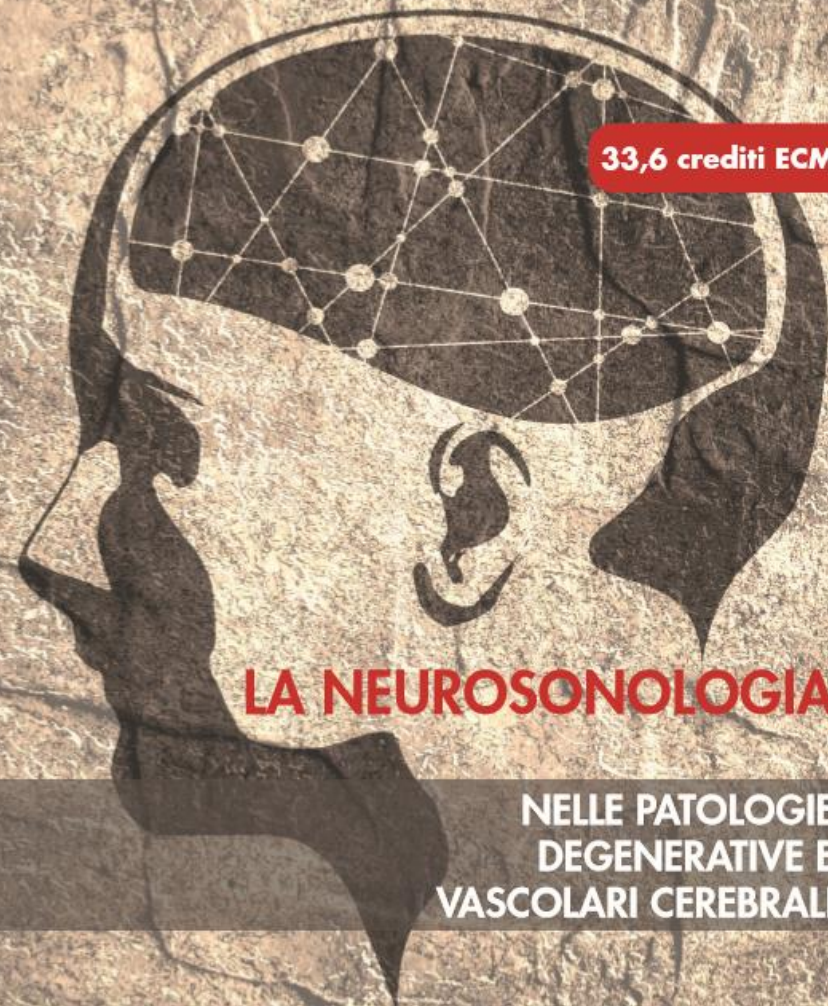
con il
patrocinio di



6-7-8 NOVEMBRE 2017

San Benedetto del Tronto (AP)

33,6 crediti ECM



LA NEUROSONOLOGIA

NELLE PATOLOGIE
DEGENERATIVE E
VASCOLARI CEREBRALI

UNITÀ OPERATIVA DI NEUROLOGIA

LA DBS:

APPLICAZIONI E METODOLOGIA

Riccardo Antonio Ricciuti



San Benedetto del Tronto, 6-7-8 Novembre 2017

DEEP BRAIN STIMULATION FOR MOVEMENT DISORDERS DISEASES STARTS FROM DISTANCE

LESIONAL AGE



STIMULATION AGE

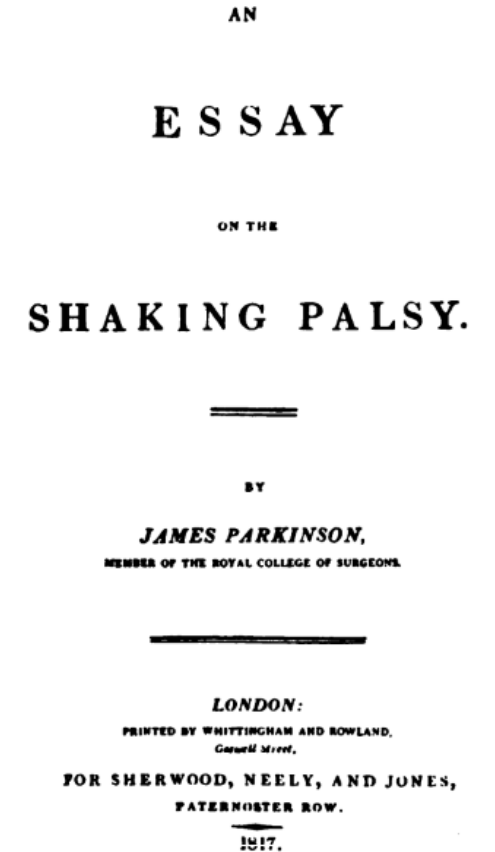
Surgical treatment, past and present, in Parkinson's disease. Laitinen L
Acta Neurol Scand Suppl. 1972; 51():43-58.

'When one sets out to make a historical survey of surgical attempts to relieve the tremor and rigor in Parkinson's disease, one cannot help feeling that it would have been a far easier task to list those nervous structures which have not been attacked'

J. PARKINSON (1817)

1921 with bilateral cervical rhizotomy by Leriche

1937 Bucy performed the first motor cortectomy in a tremor patient, and subsequently introduced lesioning of the corticospinal tract at different levels



PRE – STEREOTACTIC AGE

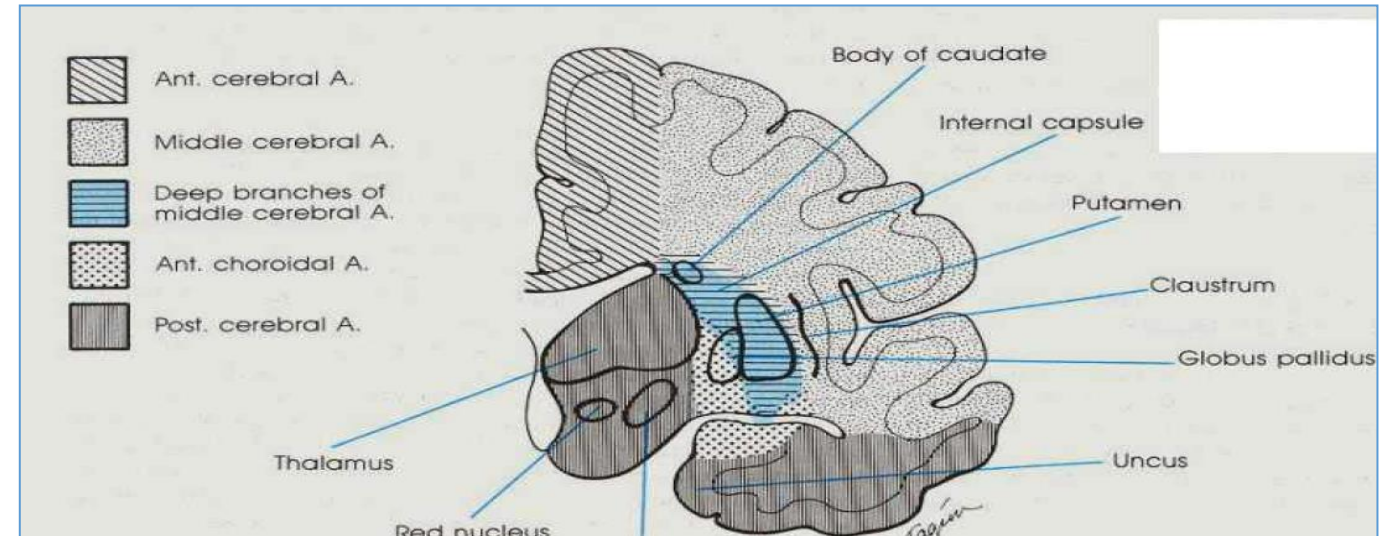
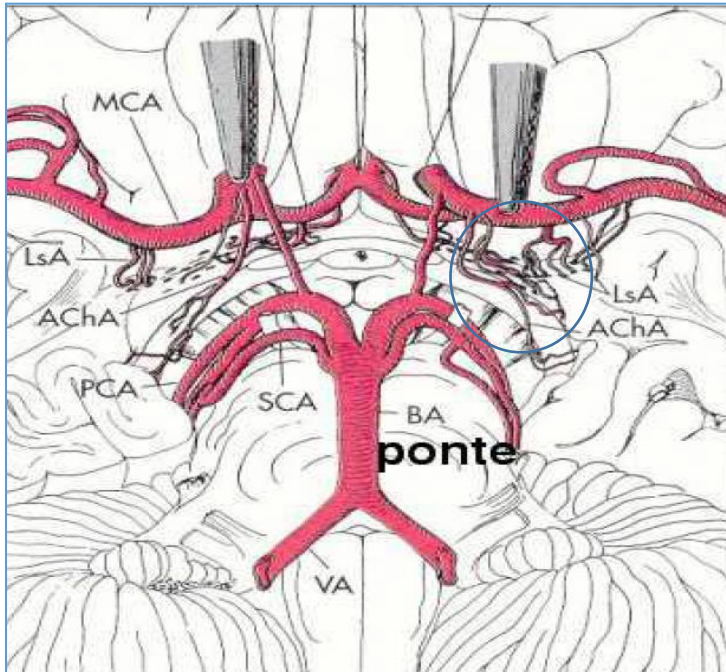
'30 – '40 (MEYERS):

TRANSVENTRICULAR APPROACH TO CAUDATE NUCLEUS AND INTERNAL CAPSULA

PEDUNCOLECTOMY

'50 (PAUL COOPER):

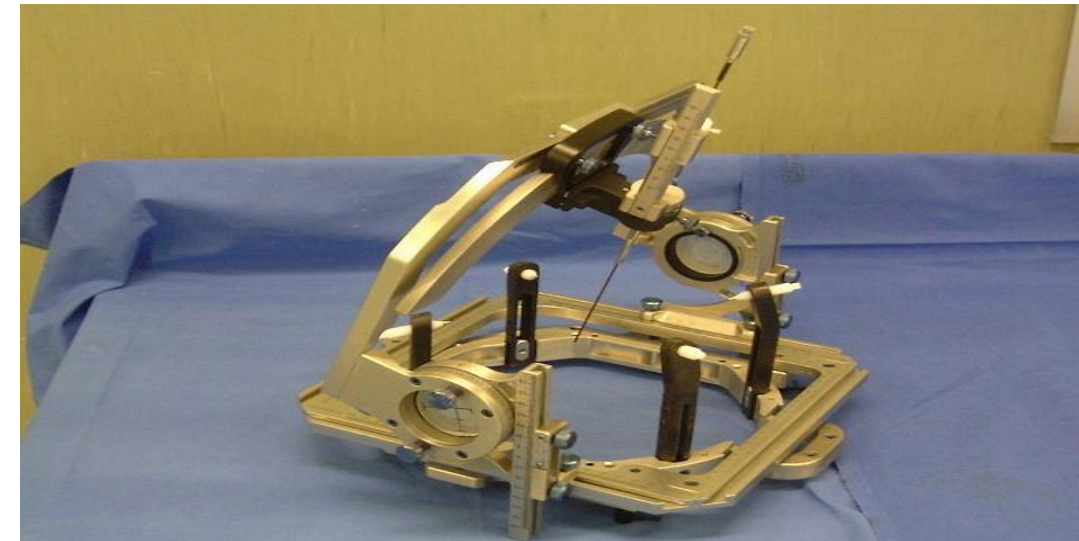
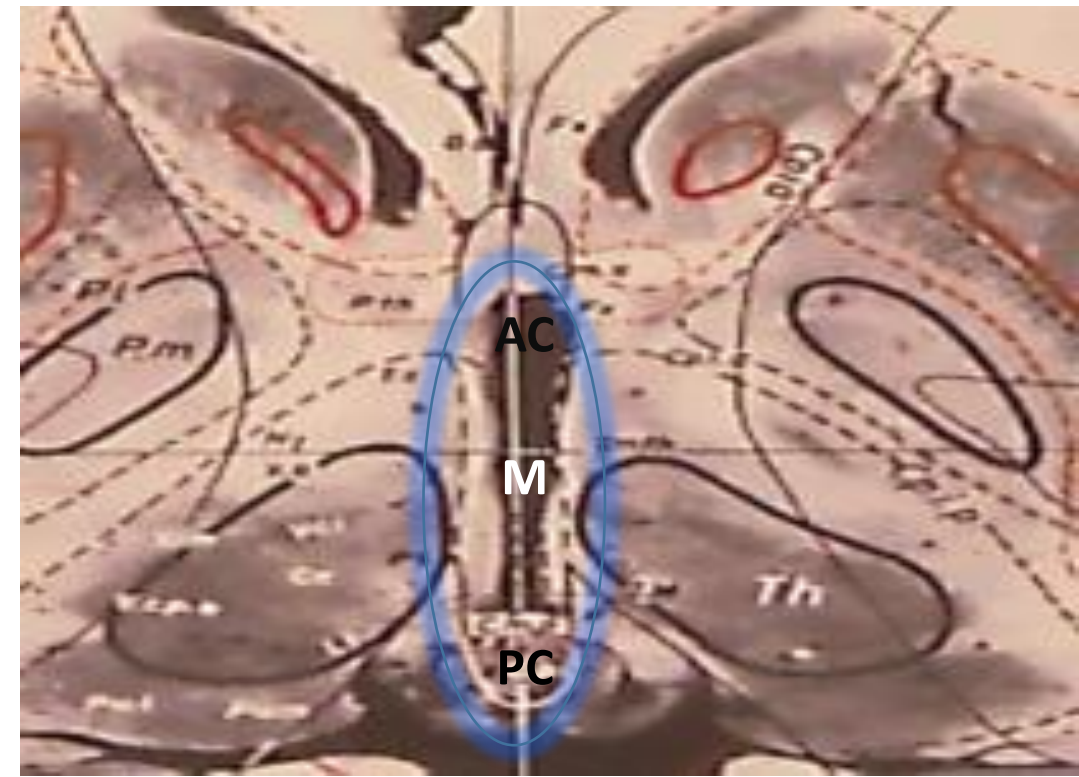
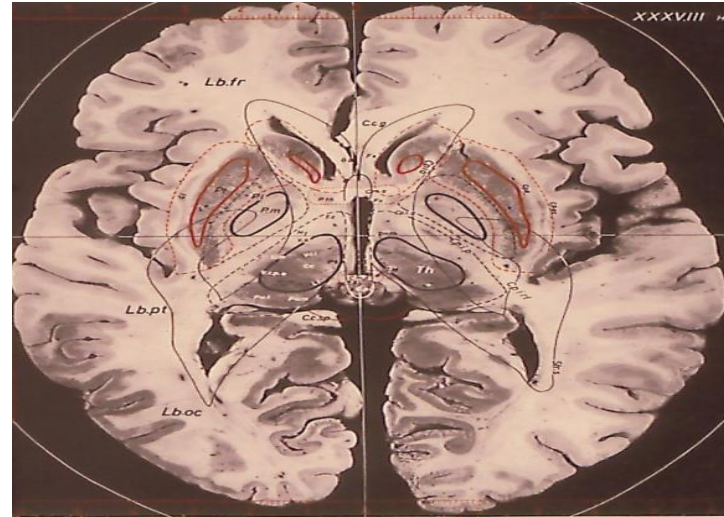
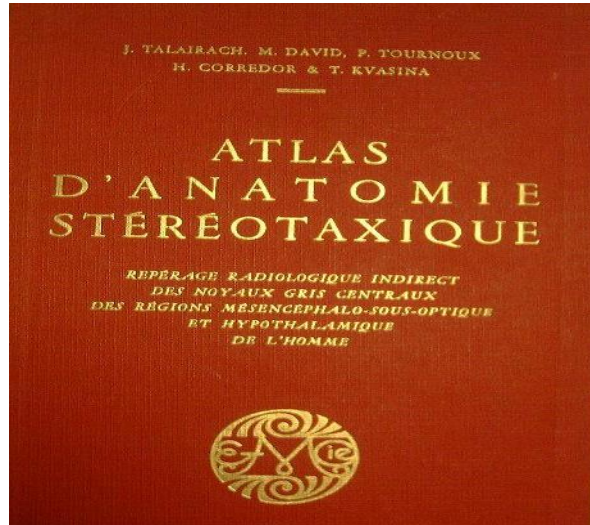
ACCIDENTAL LIGATION OF ANTERIOR CHOROIDAL ARTERY INDUCING GP AND ANSA LENTICULARIS ISCHEMIA



'52 (GUYOT AND BRION):

SUBFRONTAL APPROACH TO BASAL GANGLIA

STEREOTACTIC AGE



' 46 – ' 54 (SPIEGEL):

PALLIDOANSOTOMY

' 51 – ' 54 (HASSLER
AND RIECHERT):

THALAMOTOMY (voa, vop)

' 53 (NARABAYASHI):

THALAMOTOMY (vim)

' 54 (LEKSELL):

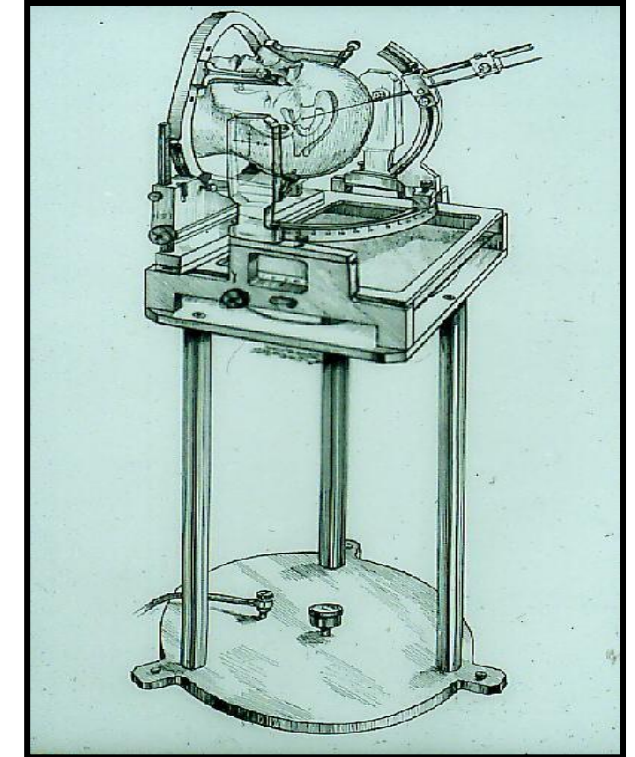
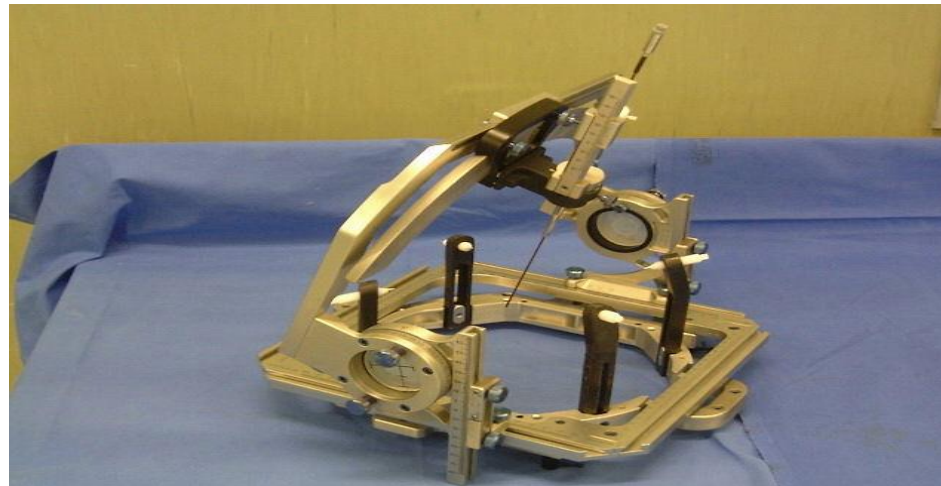
PALLIDOTOMY (Vpl)

' 87 – ' 92 (LAITINEN):

PALLIDOTOMY (Vpl)

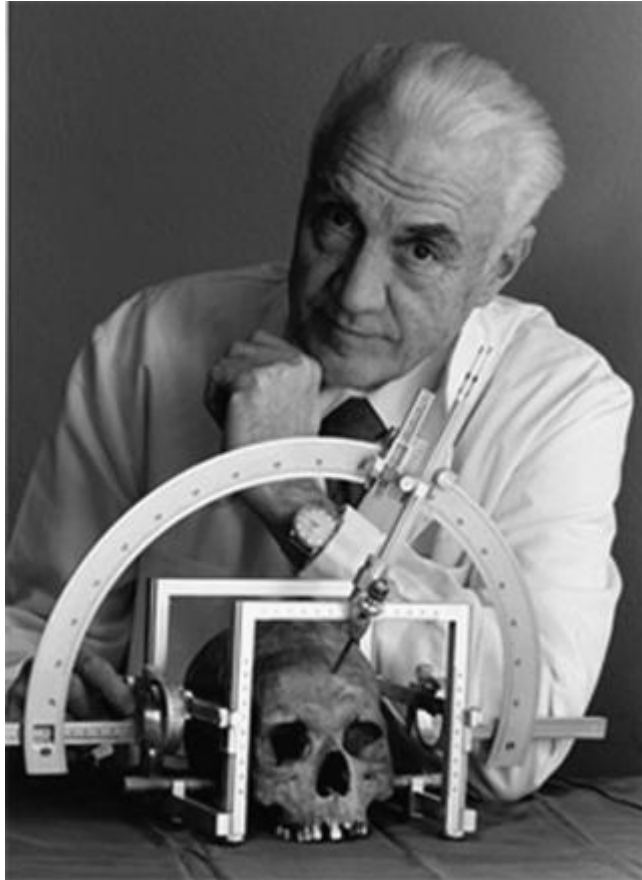
DBS IN MOVEMENT DISORDERS

'77 (MUNDINGER):	VL, Zi	DISTONIA, TREMOR
'78 (MUNDINGER):	PL	DISTONIA, SPASTICITY
'80 (BRIOE):	VL	TREMOR (SM)
'82 (SIGFRIED):	VL	TREMOR
'83 (ANDY):	VL	TREMOR
'87 (BENABID):	Vim	TREMOR
'92 (SIGFRIED):	Gpi	PARKINSON
'93 (BENABID):	Gpi, STN	PARKINSON



FRAME

FRAMELESS



Lars Leksell
Arco Isocentrico



2013



PRO

NOT ABLATIVE SURGERY (DOESN'T CREATE A LESION)

LESS PERSISTENT COLLATERAL RISKS

STIMULATION REVERSIBILITY IN PRESENCE OF SIDE EFFECTS

HFS MODULATION

BILATERAL PROCEDURES

HIGH FREQUENCY STIMULATION

CONS

HIGHER COSTS

NEUROSTIMULATOR SUBSTITUTION

INFECTIONS

RECHARGEABLE
DEVICE

WHAT IS BEING STIMULATED ?

BECAUSE THE EFFECTS PRODUCED BY DBS ARE SIMILAR TO THOSE PRODUCED BY MAKING A LESION IN THE SAME REGION, IT HAS BEEN PROPOSED THAT THE OVERALL EFFECT OF DBS IS TO **INHIBIT** THE NEURAL ACTIVITY IN THE REGION STIMULATED

HFS DOESN'T CREATE A LESION. ALL SYMPTOMS CONTROLLED BY THE STIMULATION ARE ONLY TEMPORARILY, CONTEMPORARY TO THE DURATION OF STIMULATION

MECHANISMS

INHIBITION OR DISRUPTION OF THE PATHOLOGICAL OUTFLOW BY HFS IN DBS
(INHIBITION OF NEURONAL SOMATIC STRUCTURES AND EXCITATION OF NEURAL FIBER BUNDLES)

DEPOLARISATION BLOCK

BLOCKADE OF MEMBRANE ION CHANNELS

STIMULATION EVOKED RELEASE OF γ -AMINOBUTYRIC ACID (Microdialysis studies)

DECREASE GLUTAMATE OUTPUT FROM STN

JAMMING OF THE NEURONAL MESSAGE TRANSITING THROUGH THE STIMULATED STRUCTURE



NEUROPROTECTION?

SURGERY FOR MOVEMENT DISORDERS

W
H
I
C
H

T
A
R
G
E
T
S

THALAMUS (Vim)

GPI

STN

PPN

VENTROINTERMEDIUS NUCLEUS OF THALAMUS (Vim)

TREATMENT ALTERNATIVE THAT CAN BE CONSIDERED FOR PD PATIENTS SUFFERING FROM **TREMOR** IN WHOM OTHER FEATURES OF PARKINSON DISEASE ARE NOT A SOURCE OF DISABILITY

PROBABLY VIM DBS CAN BE AN OPTION FOR PATIENTS PREVIOUSLY TREATED WITH STN OR GPI DBS WHO CONTINUE TO HAVE (OR DEVELOP) SEVERE TREMOR DESPITE GOOD CONTROL OF OTHER MOTOR SYMPTOMS OF PD

SURGICAL THERAPY FOR ESSENTIAL TREMOR PATIENTS

FUS (Focused ultrasound stimulation) under MRI create a tansitional lesion. Utilized in older patients

GLOBUS PALLIDUS INTERNUS (GPI)

IMPROVEMENT OF TREMOR, RIGIDITY, BRADYKINESIA

IMPROVEMENT OF DYSKINESIA AND MOTOR FLUCTUATIONS

DOESN'T PERMIT TO REDUCE THERAPY IN PARKINSON'S DISEASE

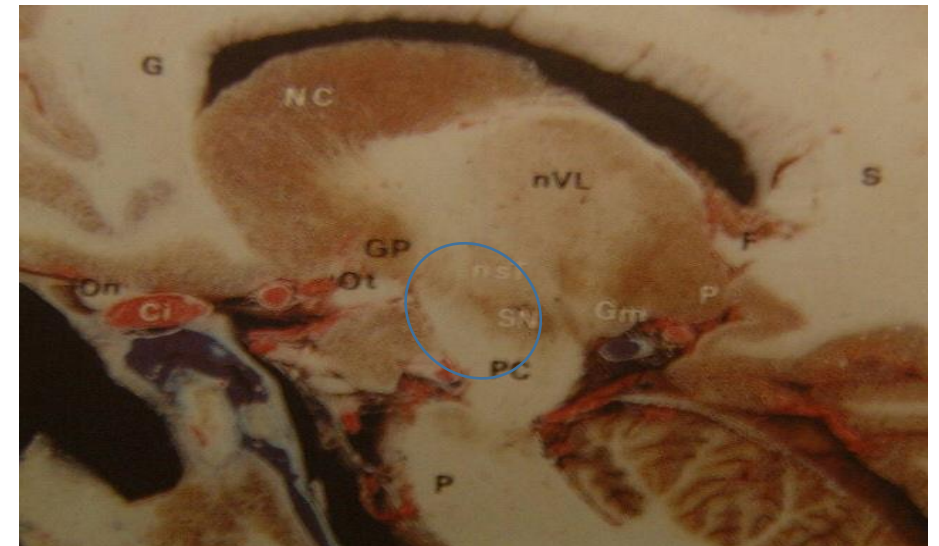
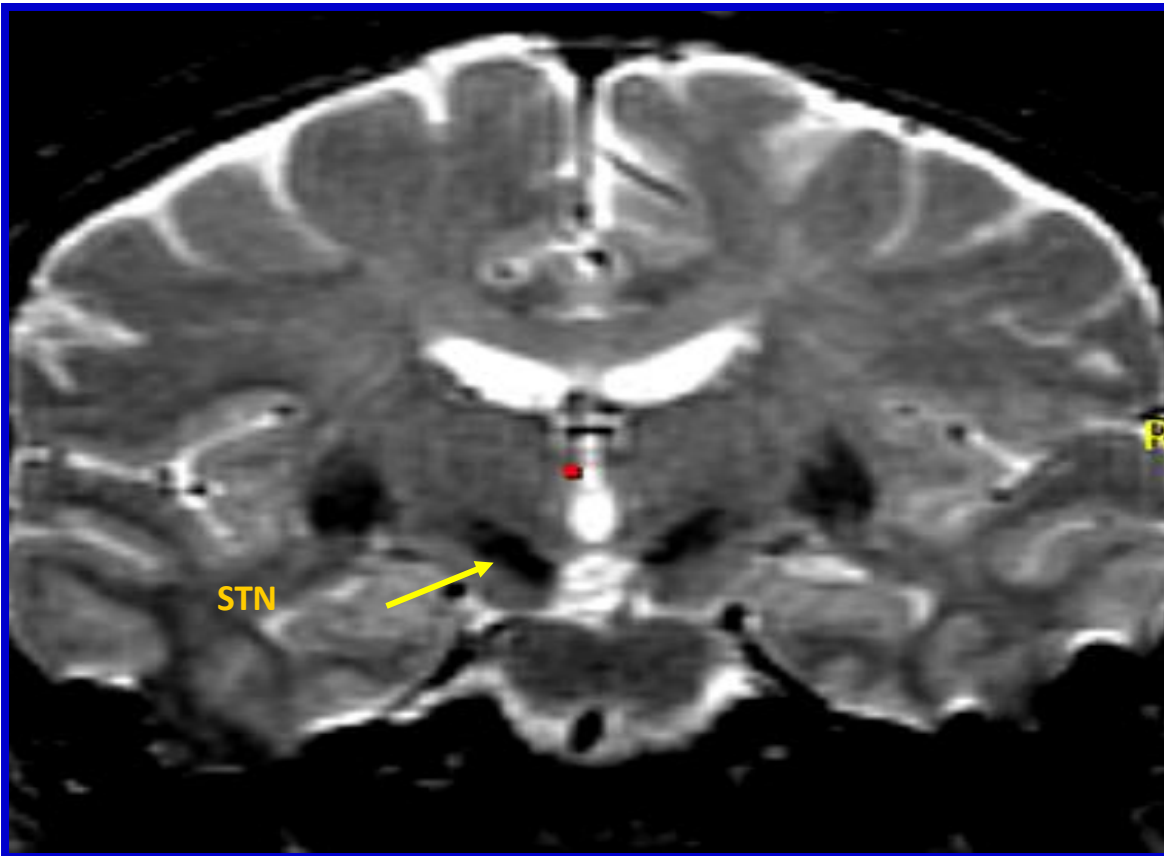
SURGICAL THERAPY FOR PD, DYSTONIC PATIENTS DYT 1 + (SENSORIMOTOR PART OF GPI) AND GILLES DE LA TOURETTE SYNDROME

SUBTHALAMIC NUCLEUS (STN)

IMPROVEMENT OF DYSKINESIA AND MOTOR FLUCTUATIONS

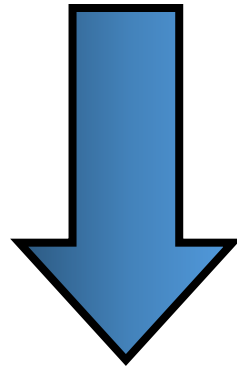
REDUCTION OF THERAPY (LEDD)

MORE COMMON TARGET IN
PARKINSON'S DISEASE



HFS for Parkinson's Disease

Subthalamic Nucleus



- Larger connections with BG
- Direct influence on GPI and SNr

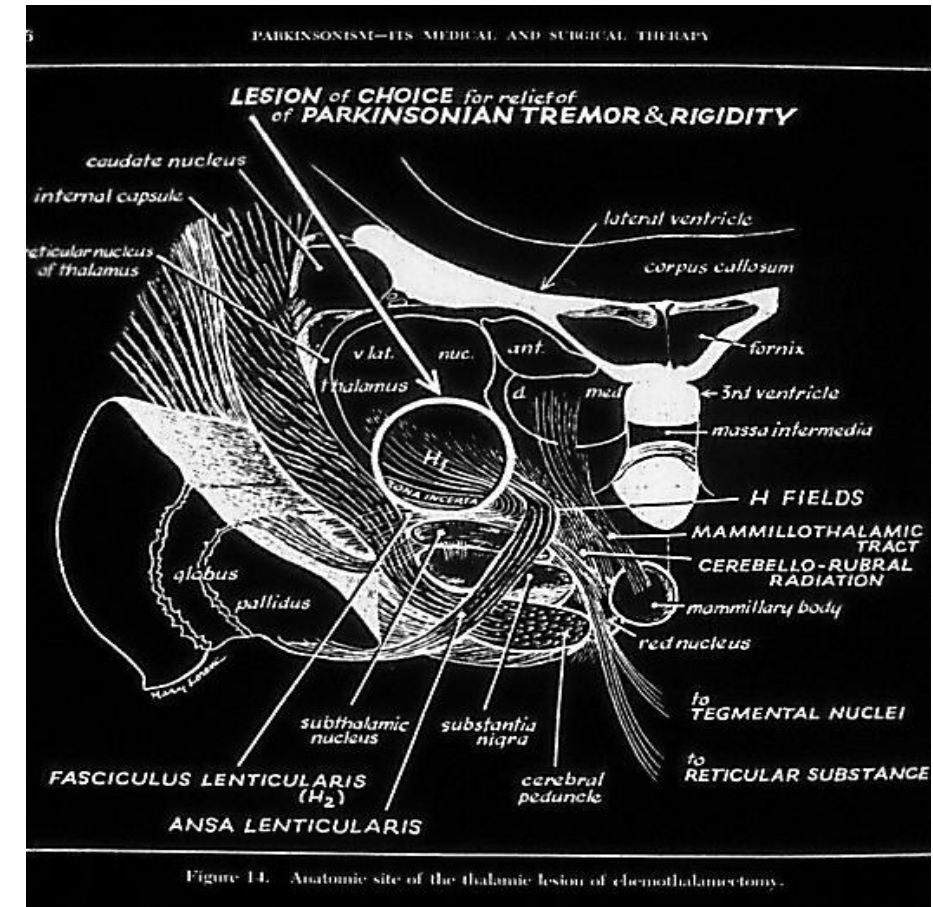


Figure 14. Anatomic site of the thalamic lesion of chemothalamectomy.

PEDUNCOLOPONTINE NUCLEUS (PPN)

FREEZING, DIFFICULTY WITH GAIT INITIATION AND LOSS OF BALANCE DOESN'T RESPOND TO L-DOPA THERAPY OR HFS-STN

PPN STIMULATION SEEMS IMPROVE THESE FEATURES OF GAIT
AND POSTURAL DYSFUNCTION

PPN DBS FOR THE TREATMENT OF PD-RELATED GAIT AND
POSTURAL DYSFUNCTION REMAINS INVESTIGATIONAL AND
REQUIRES FURTHER EVALUATION BEFORE CONSIDERING IT A
MAINSTREAM OPTION

ELIGIBILITY: critical points

	INDICAZIONI/compatibilità	CONTROINDICAZIONI	NOTE
DIAGNOSI	Diagnosi Probabile MP	Parkinsonismi atipici	UKBBcr.; Gelb '99
DURATA MALATTIA	≥ 5 anni		
ETA'	<70 anni ?		Comorbidità, ↑ Rischi
SEVERITA' MALATTIA	STADIO CLINICO sec Hoehn & Yahr ('67) _ UPDRS III score? La severità della malattia è correlata all' outcome e alla disabilità		No consensus su specifica scala di valutazione e sul CUT-OFF. La disabilità è influenzata da fattori personali e ambientali.
RISPOSTA A LEVODOPA	>30% UPDRS III (tremore = eccezione)	Disordini motori non L-dopa responsivi	LD challenge predittore dell' effetto della STN-S
ABILITA' COGNITIVE	Sdr disesecutiva lieve ? MCI?	demenza	No consensus su test
CONDIZIONE EMOTIVO/COMPORTAMEN TALE	Depressione lieve, sdr psicotiche gestite con bassi dosaggi di neurolettici o sospendendo dopaminoagonisti	Condizioni psichiatriche gravi ed instabili, depressione maggiore	No consensus su criteri di esclusione.
NEUROIMAGING	<i>RMN encefalo</i>	Atrofia cerebrale severa, vasculopatia cerebrale	OK per Meningiomi non sintomatici (Broggi '01)
COMORBIDITA'		Patologie che limitino l' aspettativa di vita	

FACTORS INFLUENCING OUTCOME

CANDIDATE SELECTION TO SURGICAL INTERVENTION

- **Inappropriate selection conditions more than 30% failures (*Okun, 2005*)**

ELECTRODES POSITIONING

STIMULATION PARAMETERS PROGRAMMING

SURGICAL EXCLUSION CRITERIA

STEREOTACTIC BRAIN OPERATIONS IN THE PAST

SIGNIFICANT BRAIN ATROPHY

INCREASED BLEEDING TENDENCY

REDUCED INFECTION DEFENSE

RELEVANT CEREBROVASCULAR DISEASE

ACUTE PSYCHOSIS (BENIGN AND/OR HALLUCINATIONS IN THE PAST ARE NO EXCLUSION CRITERION)

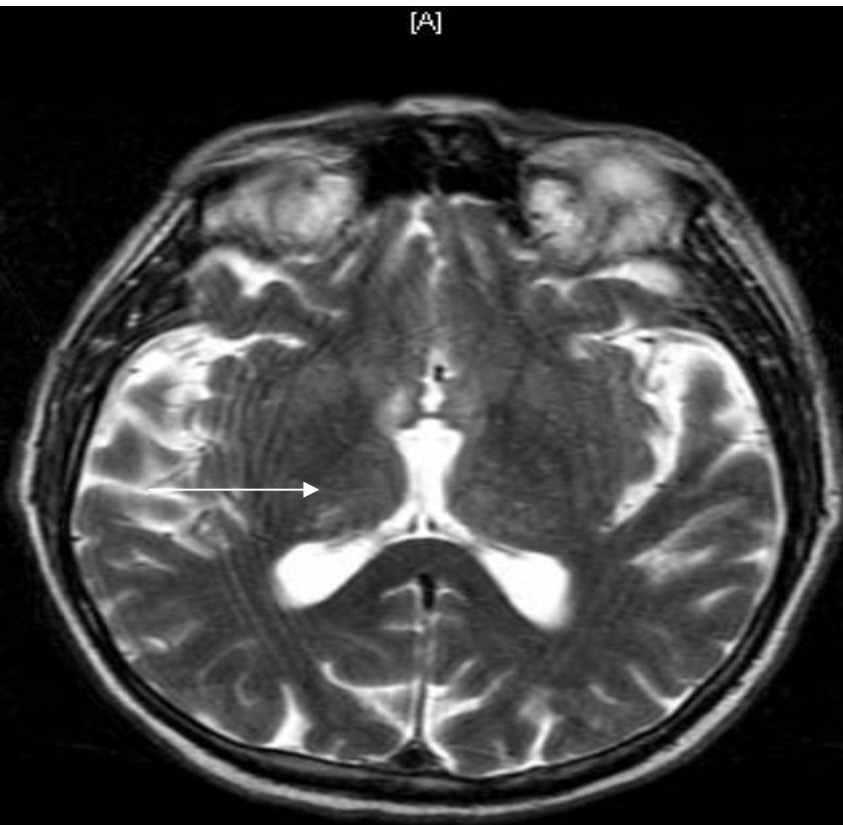
A PHYSICAL AND/OR MENTAL ILLNESS (E.G., CANCER WITH REDUCED LIFE EXPECTANCY)

ABUSE OF DRUGS OR ALCOHOL

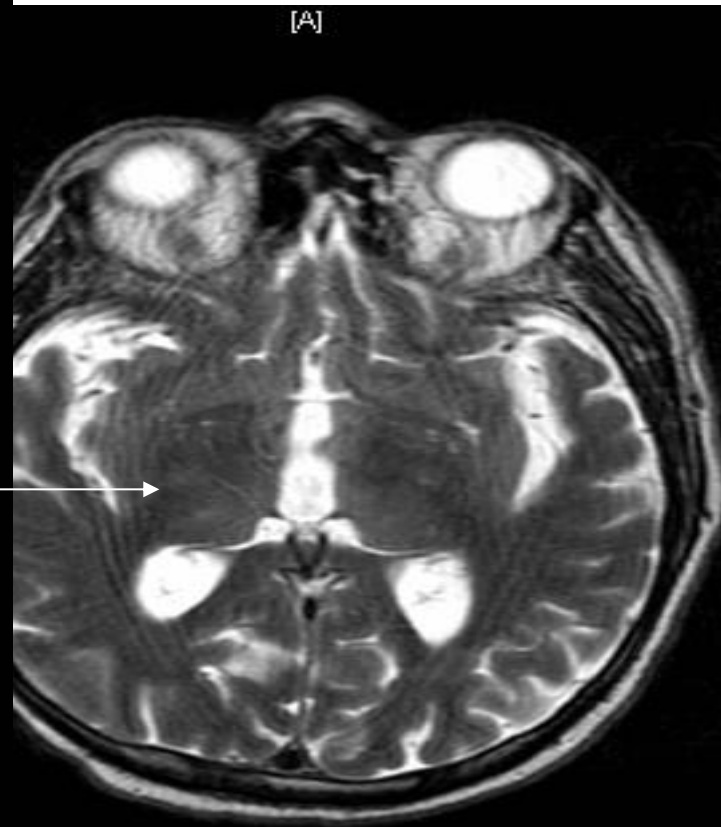
FEMALE STUDY PARTICIPANTS OF CHILD- BEARING AGE WITHOUT ADEQUATE CONTRACEPTION

WOMEN DURING PREGNANCY OR LACTATION

SURGICAL EXCLUSION CRITERIA



[P]



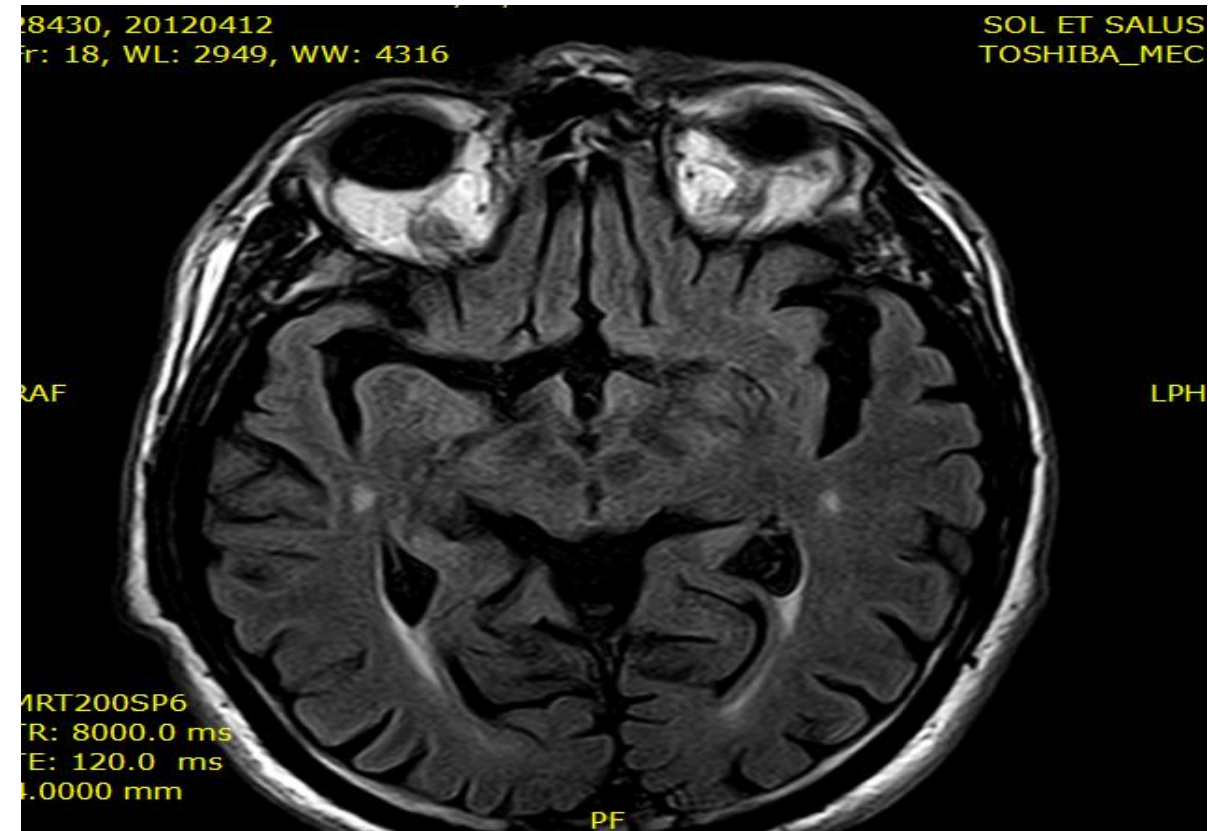
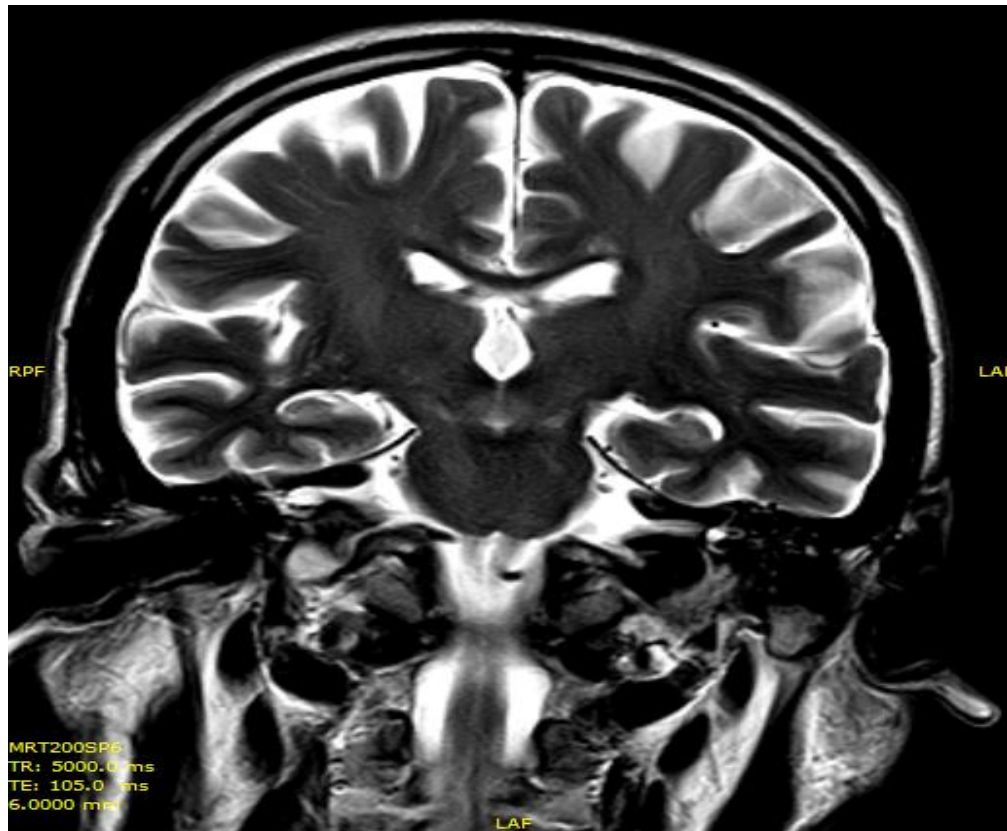
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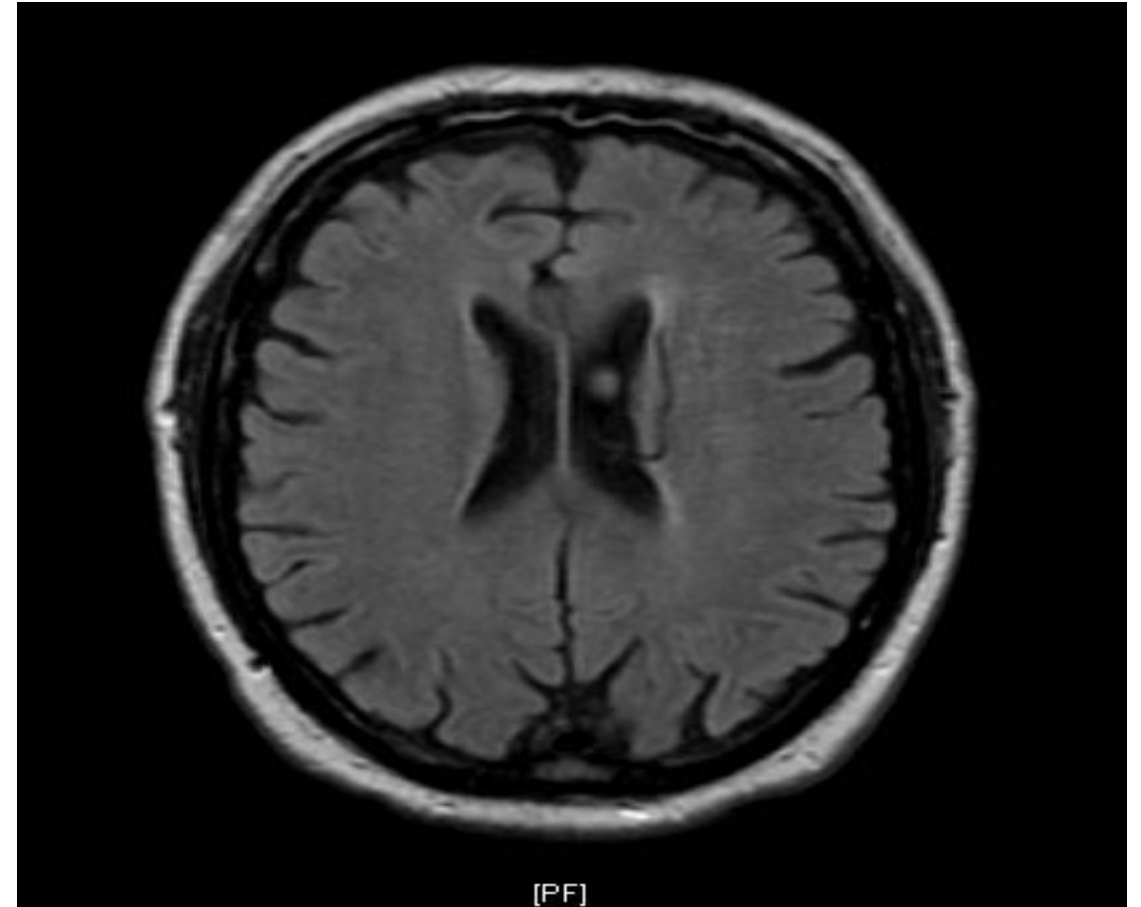
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VASCULAR ENCEPHALOPATHY AND CORTICAL
ATROPHY

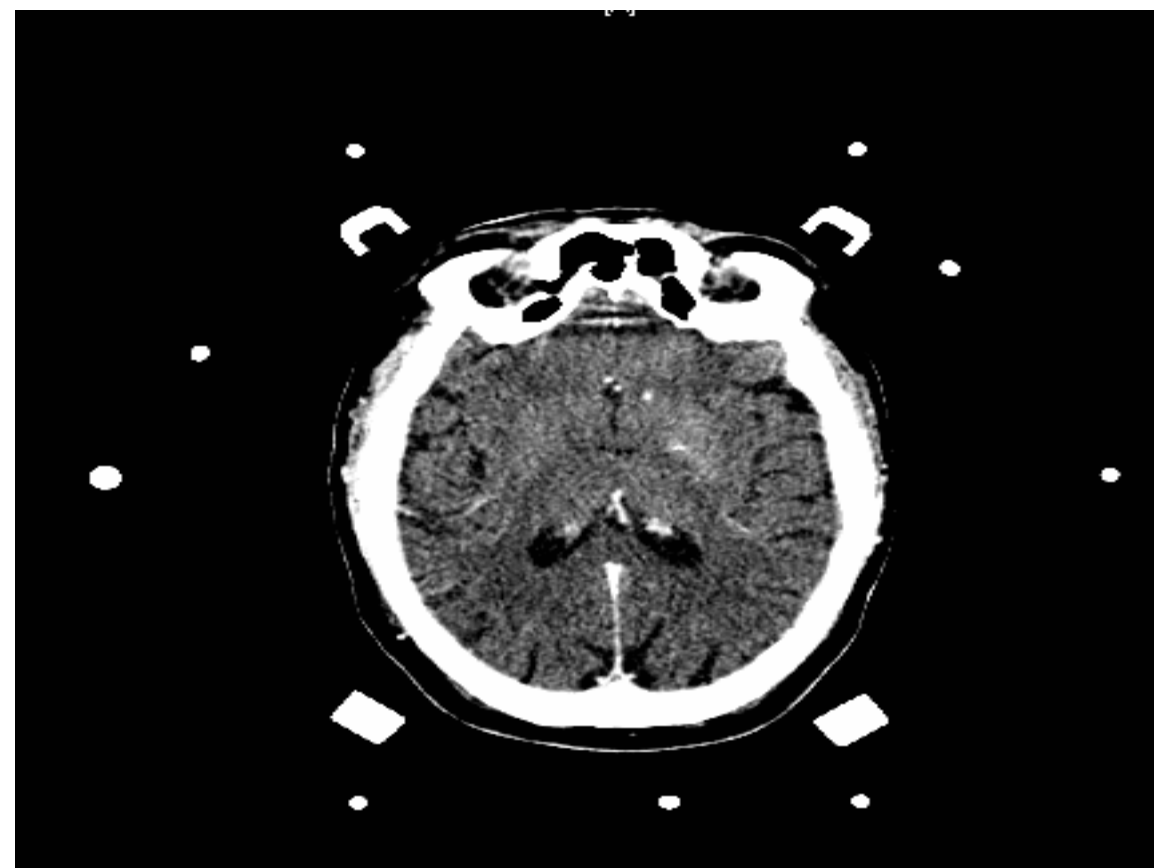
SURGICAL EXCLUSION CRITERIA



CORTICAL ATROPHY



Venous angioma with cerebral interna vein flow



THE PRECISION OF THE IMPLANT IN DBS IS ASSURED BY FULFILLING THE FOLLOWING REQUIREMENTS:

- The use of a high precision surgical instrument, such as a **stereotactic** apparatus or **frameless navigation**
- The correct and accurate definition of the **anatomical (theoretical)** target
- The functional **electrophysiological** confirmation of the target obtained with micro recording and stimulation

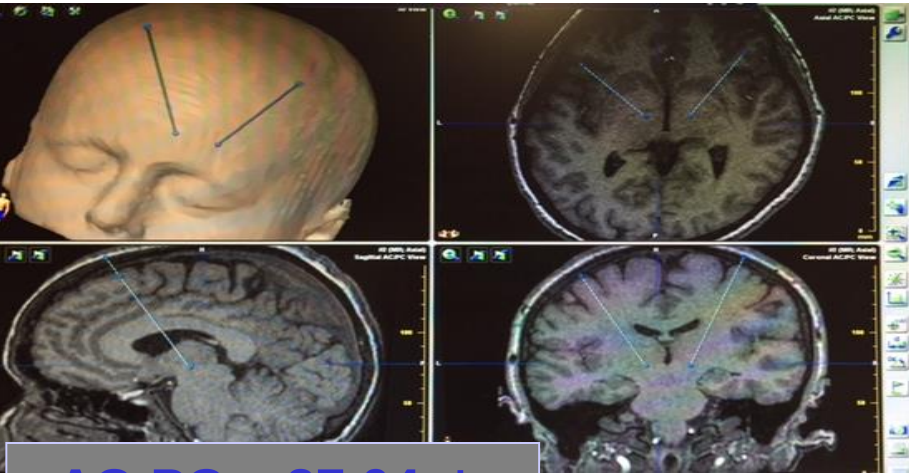
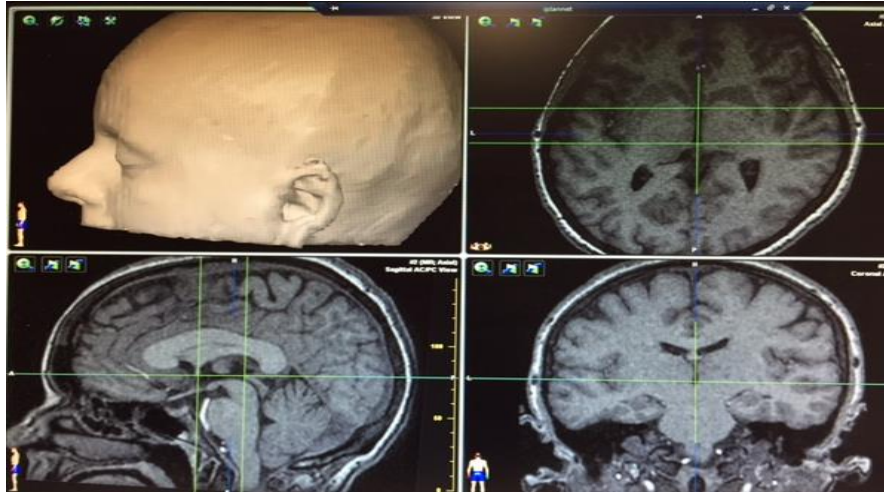
TARGET SELECTION

- Ventriculography

- CT

- TC/MRI - Neuronavigation

TARGETING (STN)



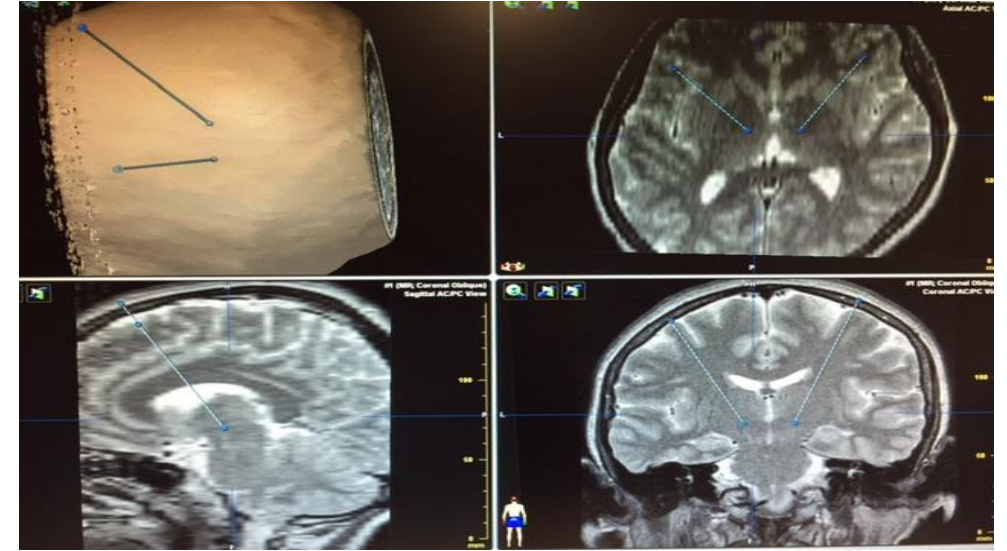
AC-PC = 27.04 ± 1.36

X = 11.5 ± 1.3

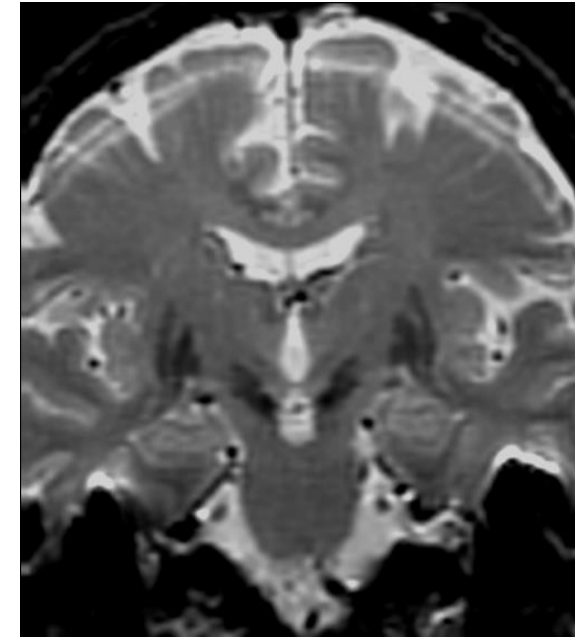
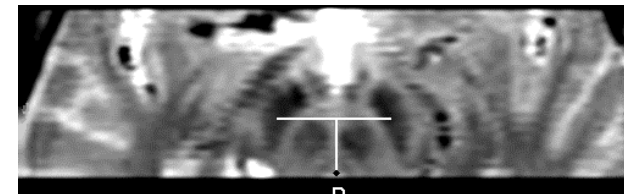
Y = 12.6 ± 1.7

Z = 2.99 ± 1.6

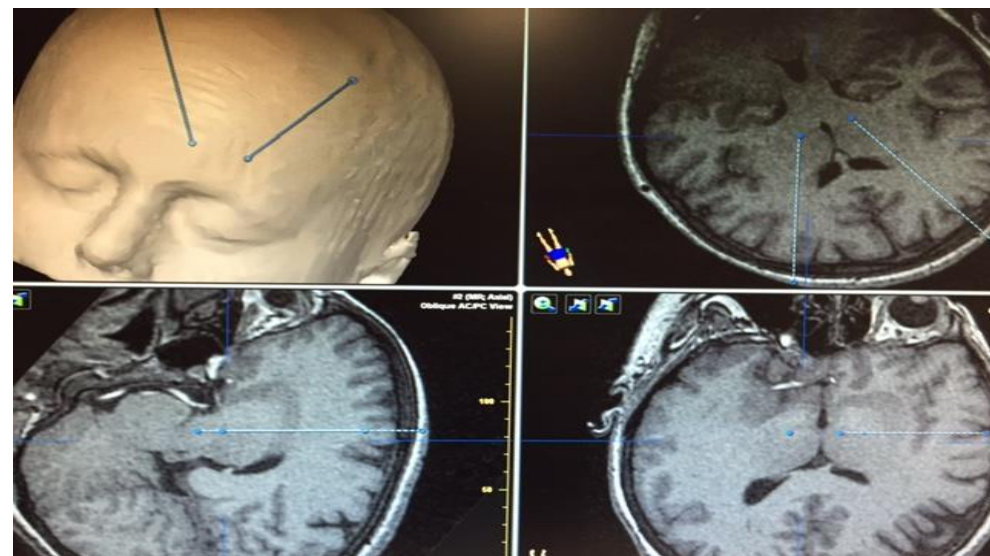
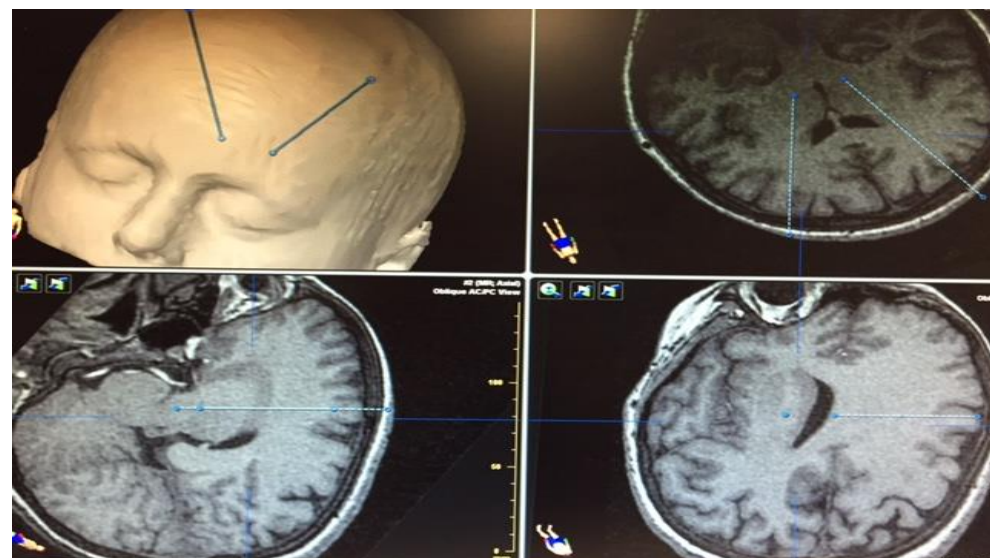
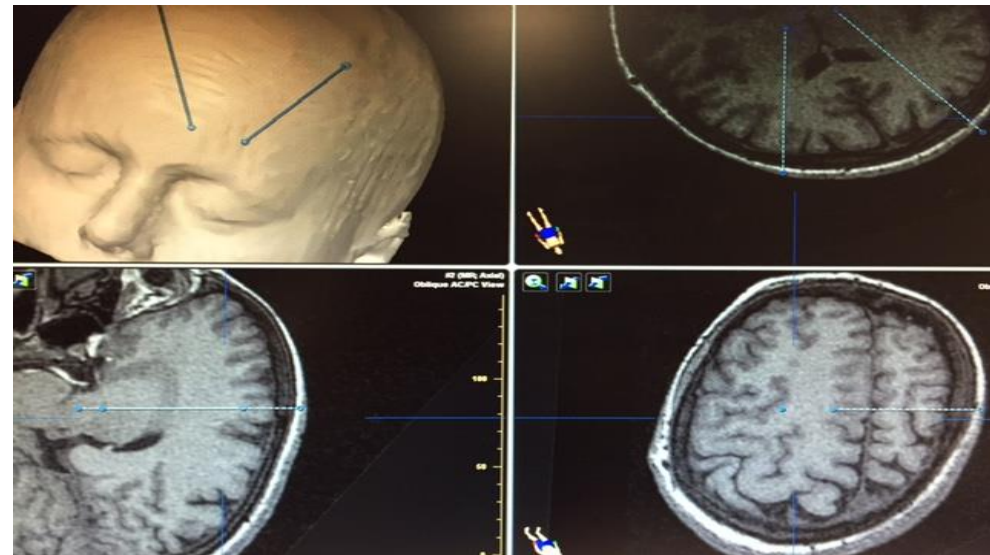
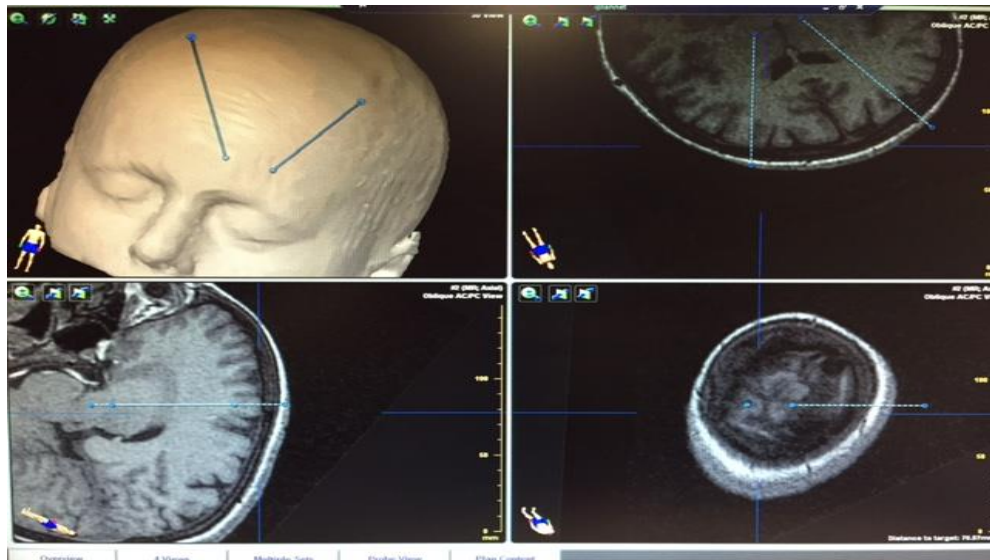
Indirect localization
(AC – PC)



Direct localization (RMN T2
2 MM coronal/ INVERSION
RECOVERY)



SURGICAL APPROACH



INTRAOPERATIVE FUNCTIONAL ELECTROPHYSIOLOGY

INTRAOPERATIVE MICRORECORDING (MER)

MICRO/MACRO STIMULATION

THERAPEUTIC WINDOW

INTRAOPERATIVE FUNCTIONAL ELECTROPHYSIOLOGY

INTRAOPERATIVE MICRORECORDING

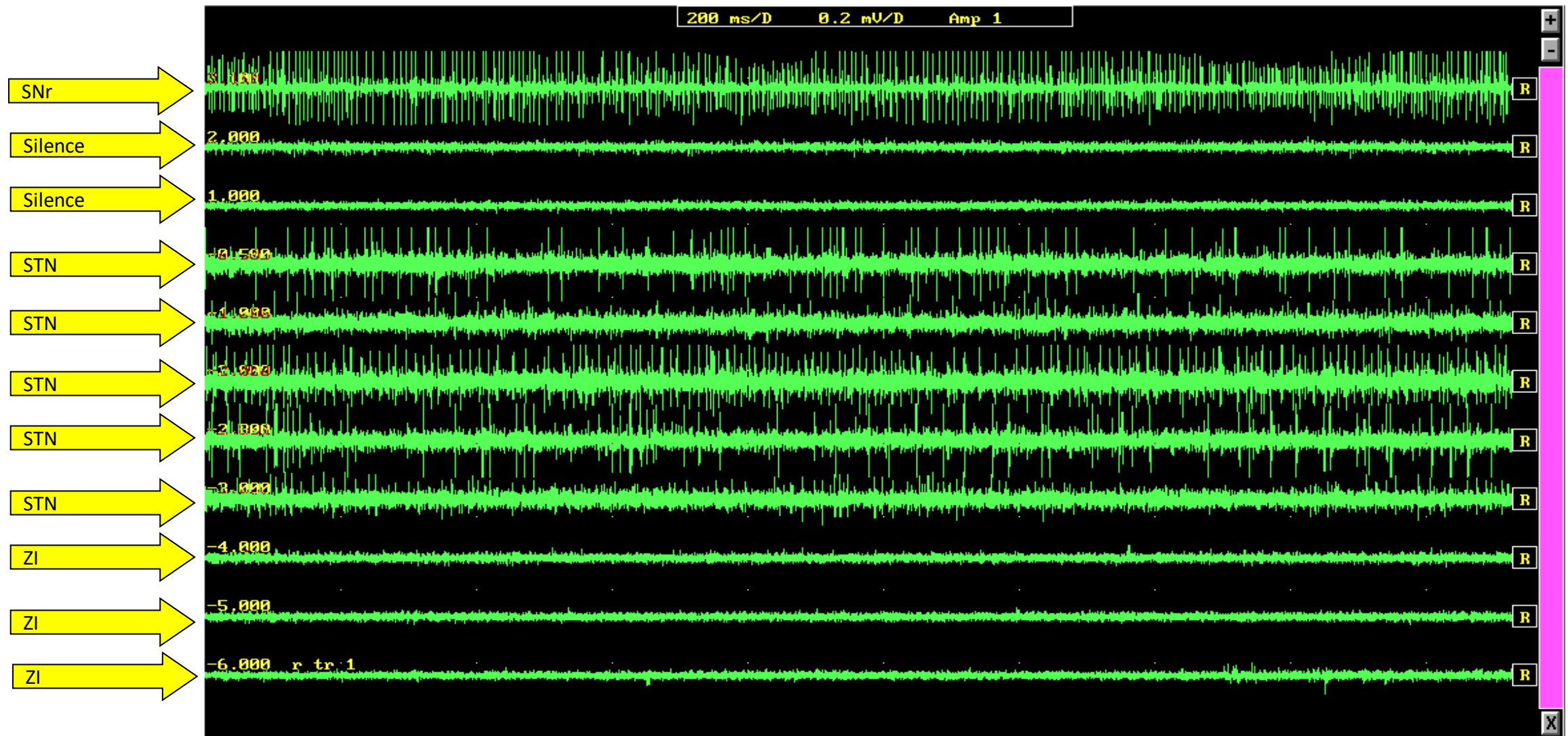
ADVANTAGES

Microelectrode recordings provide physiological information about **nuclear boundaries** based on characteristic neuronal discharge patterns and stimulus responsiveness

This information has the advantage of being **independent from patient** cooperation and can also be obtained under **general anaesthesia**

Microelectrode recordings also allow parallel or sequential explorations by several passes through the target structure to delineate the optimal site for implantation, because they cause **minimal microlesioning effects** in contrast to larger macrostimulation probes

TYPICAL STN RECORDING TRACT



INTRAOPERATIVE FUNCTIONAL ELECTROPHYSIOLOGY

INTRAOPERATIVE MICRORECORDING

LIMITS

- The extension of the **operative time**
- The potential increase of the **risk of bleeding**, due to the multiple tracks usually performed

INTRAOPERATIVE FUNCTIONAL ELECTROPHYSIOLOGY

INTRAOPERATIVE MICRORECORDING

SINGLE TRACK ENTRY

IF

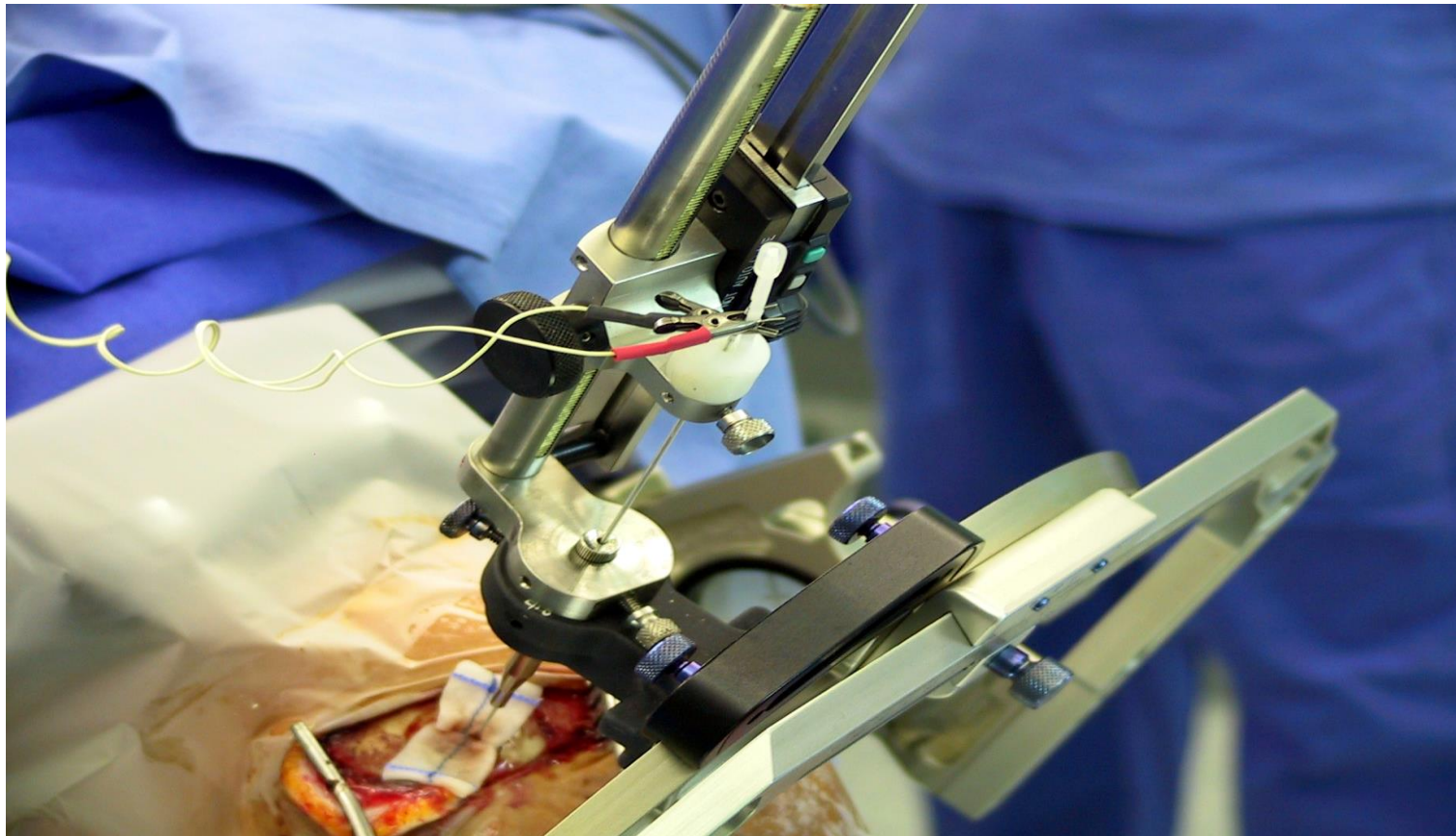
GOOD REGISTRATION



MACROSTIMULATION

INTRAOPERATIVE FUNCTIONAL ELECTROPHYSIOLOGY

INTRAOPERATIVE STIMULATION



STIMULATION PARAMETERS

- ✓ type: monopolar > bipolar
- ✓ frequency: 130-185 Hz
- ✓ amplitude: ≈ 3.6 V
- ✓ width: 60-150 μ s

(Benabid and Pollak, 1998)

MACROSTIMULATION TEST

AIMS

- To selectively interfere with the neuronal system altered by the disease, looking for the best positive effects on symptoms
- To check and prevent possible side effects

The **final position** of the lead is usually accepted when a positive and satisfying effect on the clinical symptoms is observed without side effects at a current amplitude inferior to 3 V

INTRAOPERATIVE FUNCTIONAL ELECTROPHYSIOLOGY FOR TARGETING CONFIRMATION

FINAL TRAJECTORY IS SELECTED BASED ON THE
RESULTS OF MICRORECORDINGS AND STIMULATION

THE MOST USEFUL CRITERIA ARE THE LENGTH OF AN INDIVIDUAL TRAJECTORY OF ACTIVITY, THE BURSTING PATTERN OF ACTIVITY FOR MICRORECORDING, INDUCTION DYSKINESIA, IMPROVEMENT IN PARKINSONISM TIME-LOCKED TO STIMULATION AT LOW INTENSITY, AND HIGH THRESHOLD FOR SIDE EFFECTS FROM MICROSTIMULATION

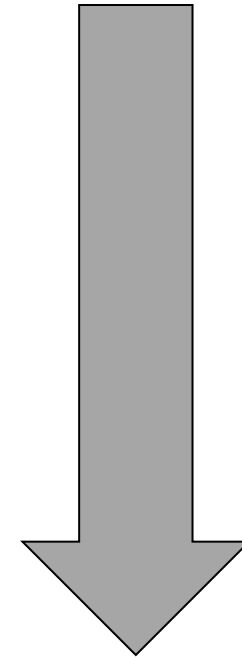
OPEN QUESTIONS

STN as the “best” target

Targeting

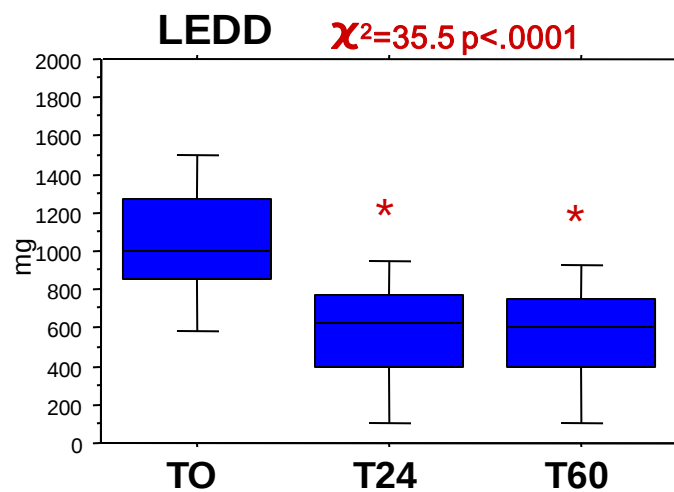
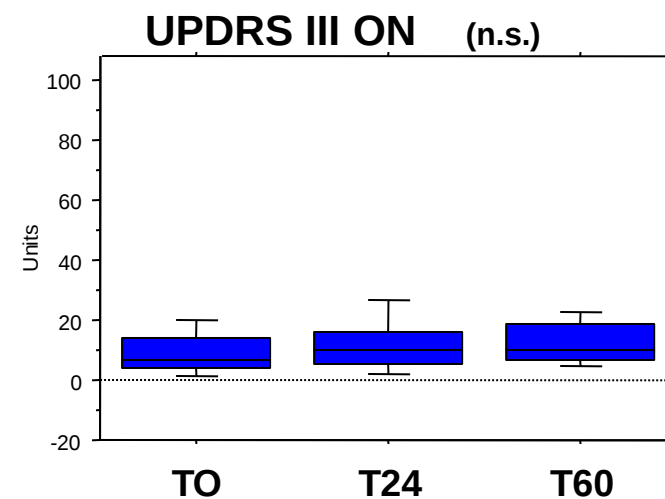
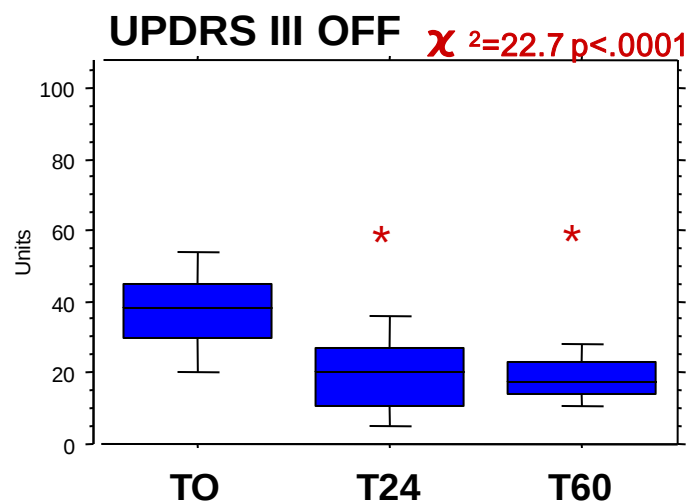
Patient’s selection

Analysis of effects and results

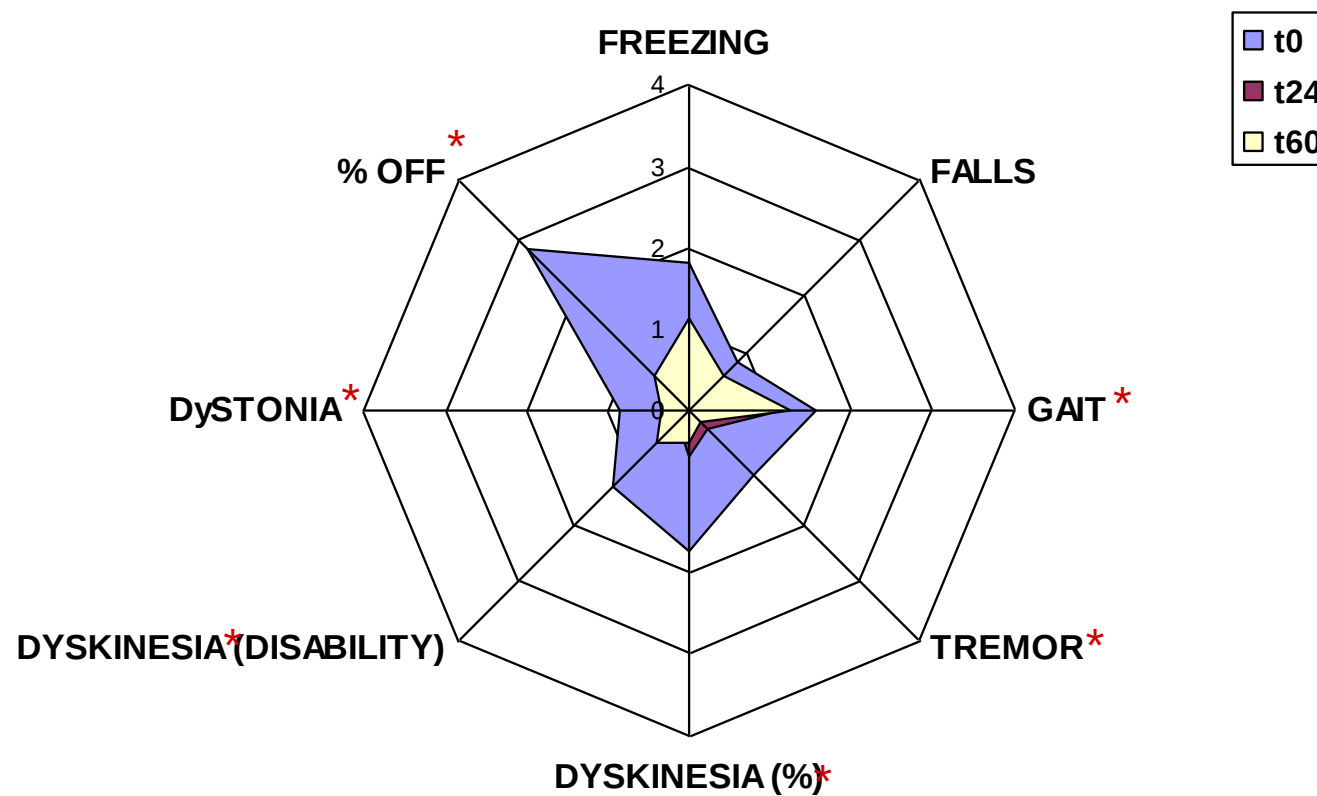


“TAILORED” SURGERY

FOLLOW-UP 5 ANNI: **persistenza del beneficio motorio**

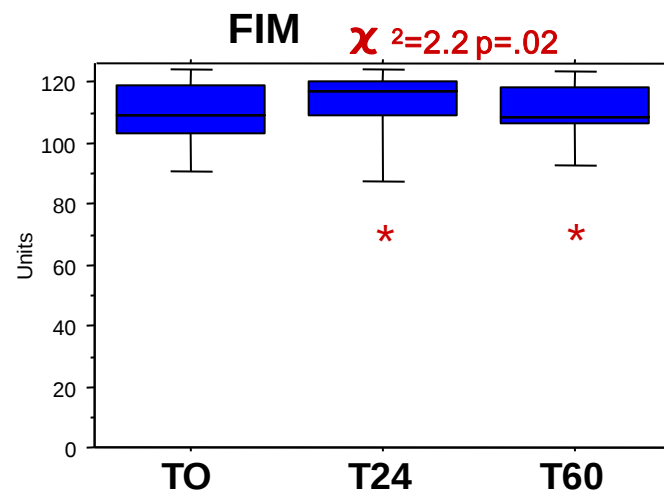
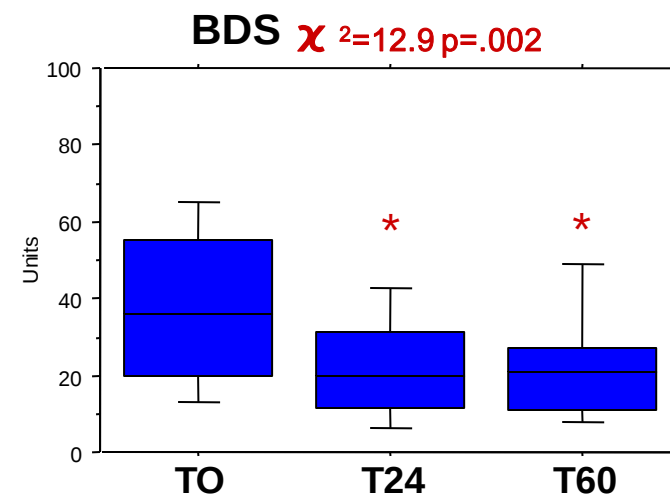
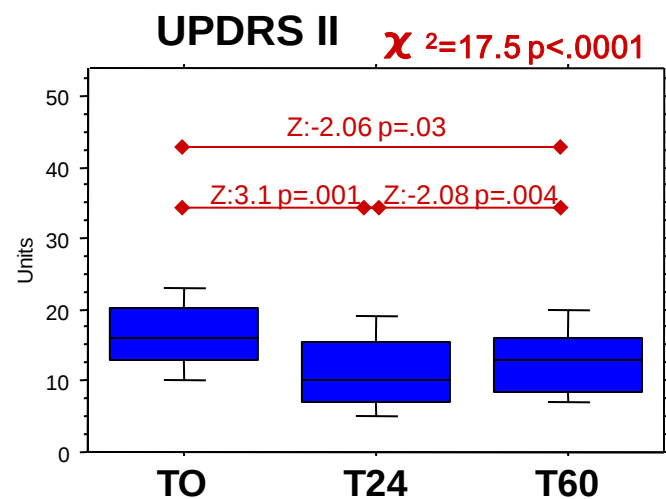


FOLLOW-UP 5 ANNI: **sintomi motori**



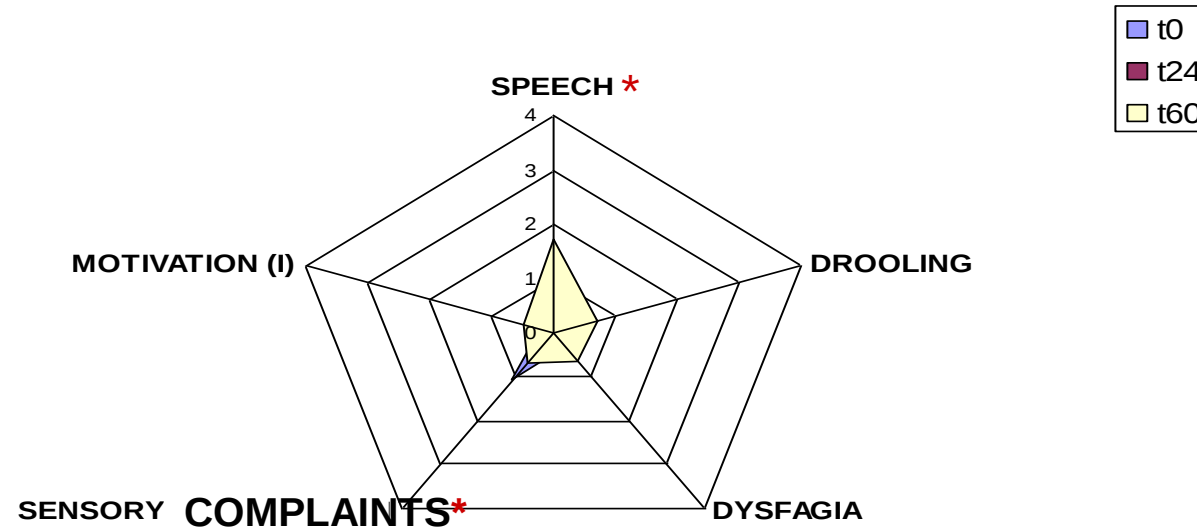
Items da UPDRS III e UPDRS IV

FOLLOW-UP 5 ANNI: FUNCTIONAL OUTCOME



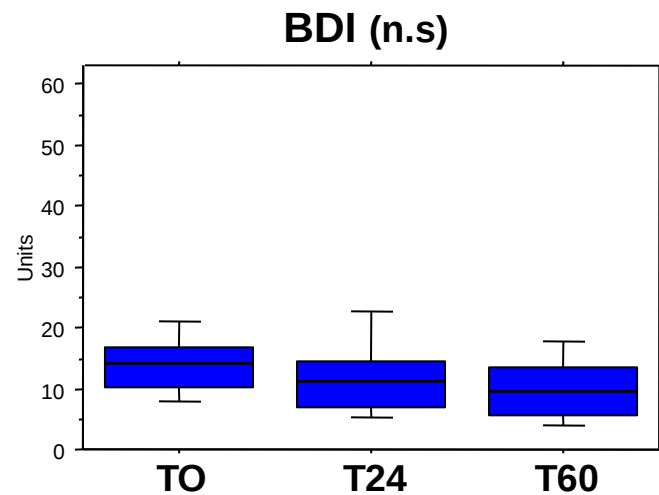
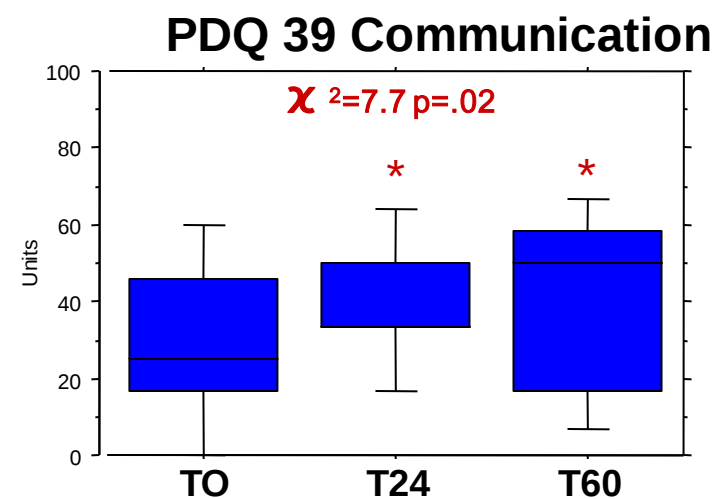
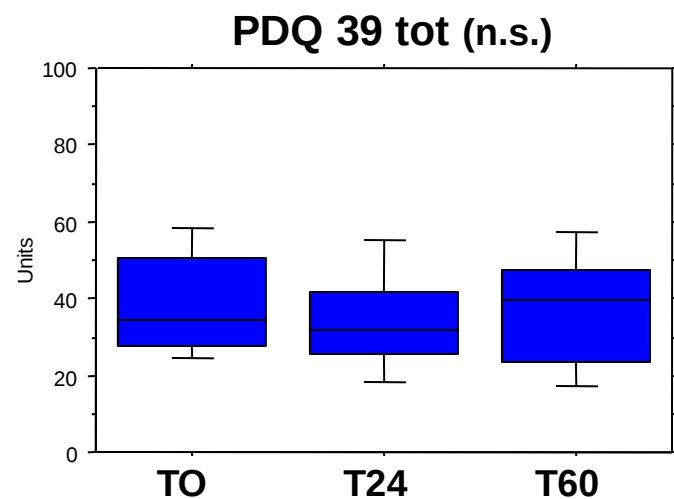
ANCONA – DBS (Malattia di Parkinson)

FOLLOW-UP 5 ANNI: **sintomi non motori**



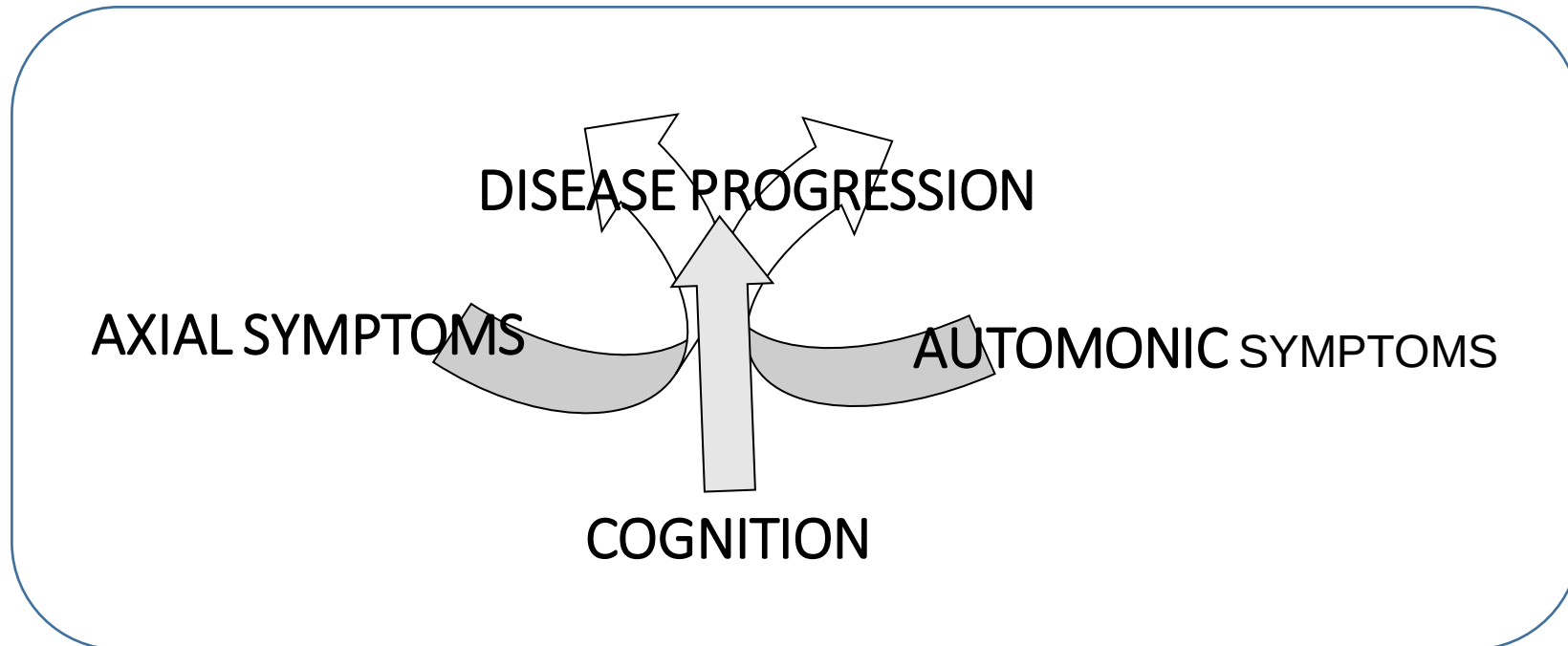
Items from UPDRS II and UPDRS I

Follow.up 5 anni: QoL & depressione



CONCLUSION

- MOTOR CLINICAL BENEFIT IS STABLE WITH TIME (> 10 YS)
- FUNCTIONAL OUTCOME SHOWS A PROGRESSIVE DECLINE



CONCLUSION

DBS IS USEFULL IN MOVIMENT DISORDER DISEASES (ET, DYSTONIA AND PARKINSON'S DISEASE).

WHILE IN ET AND DYSTONIA DBS CAN OBTAIN A STABLE CONTROL ABOUT THE DISEASE, IN PARKINSON'S PATIENTS THE DISEASE PROGRESSES BUT MOTOR SYMPTOMS ARE AGAIN CONTROLLED WITH TIME.

DBS REPRESENT A FEATURE ABOUT PARKINSON'S DISEASE TREATMENT.

BECAUSE IN PARKINSON'S DISEASE PATIENTS DBS REPRESENT A SYMPTOMATIC TREATMENT, YOUNGER ONES CAN TAKE MAJOR BENEFITS FROM ITS APPROACH. RIGHT CLINICAL SELECTION IS MANDATORY TO ACHIVE A GOOD RESULT.

SURGICAL TECHNIQUE IS IN CONTINUE EVOLUTION.

**RIGHT SELECTION
FOR
RIGHT PATIENT**

T ogether

E veryone

A chives

M ore





THANK YOU

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