Palex

Constant Improvement

PRESENTE Y FUTURO DE LOS ULTRASONIDOS GUIADOS POR RM (MRgFUS)

Andrés Lozano

University Professor and RR Tasker Chair in Functional Neurosurgery. University of Toronto. Canada

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Servicio de Neurocirugía. Hospital Universitario Ramón y Cajal, CINAC (HM Puerta del Sur). Madrid

-Simposium patrocinado por PALEX-

Presenta: Jorge Guridi Legarra

Servicio de Neurocirugía. Clínica Universidad de Navarra. Pamplona

Exablate

SOUND TREATMENT



VII CONGRESO
DE LA SOCIEDAD ESPAÑOLA
DE NEUROCIRUGÍA FUNCIONAL
Y ESTEREOTÁCTICA

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DE NEUROCIRUGÍA FUNCIONAL
Y ESTEREOTÁCTICA
24 – 26 DE NOVIEMBRE DE 2021



ORGANIZA: senfe

MADRID

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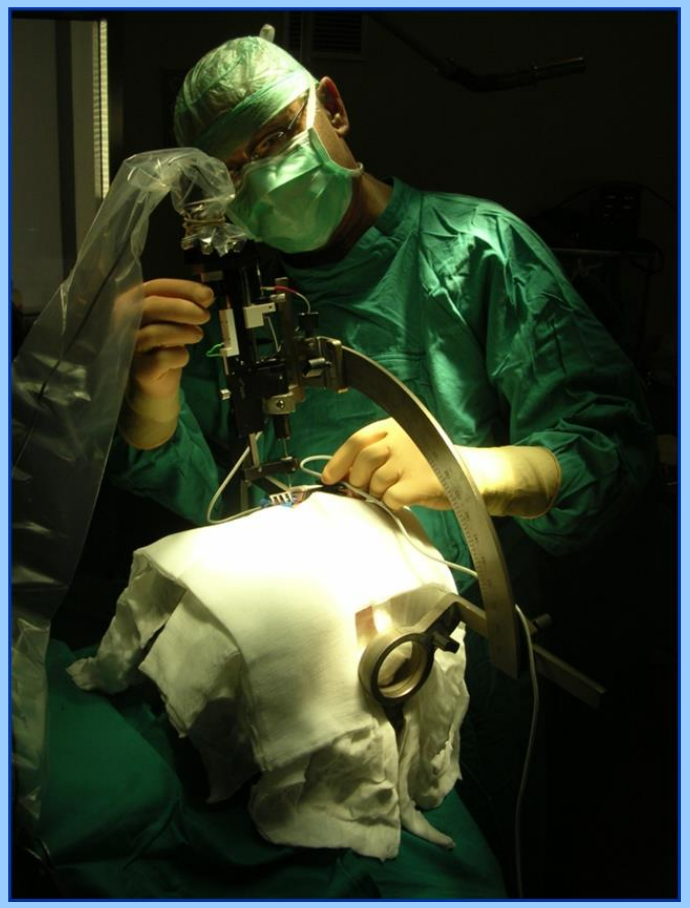
Conflicto de intereses

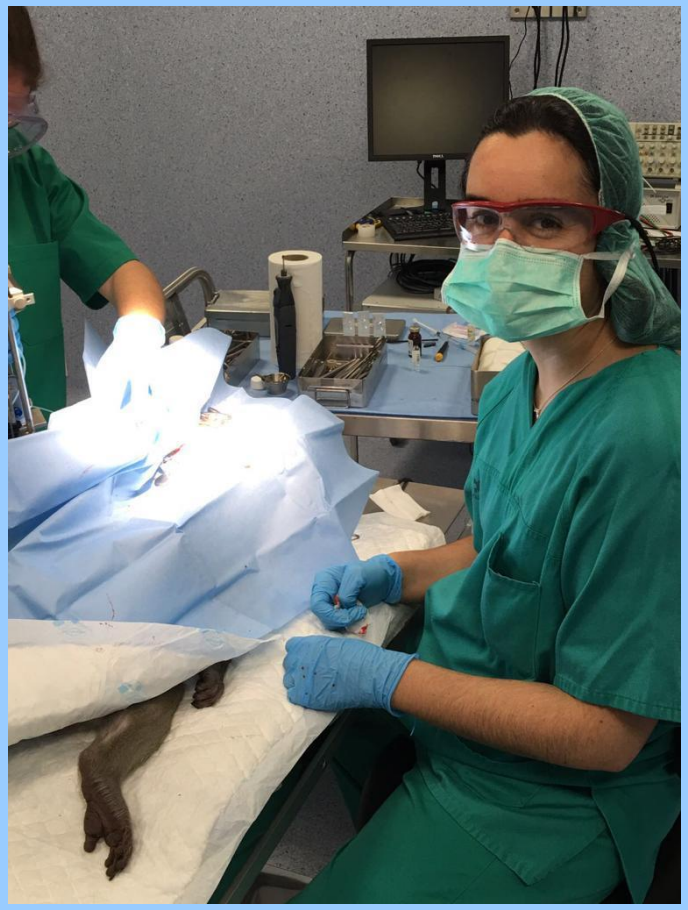
-Financiación de gastos en congresos y remuneración por charlas por Boston Scientific, Medtronic, Abbot e Insightec.



Conflicto de intereses

-Experiencia previa de más de 300 casos intervenidos de estimulación cerebral profunda como primer neurocirujano





Introduction

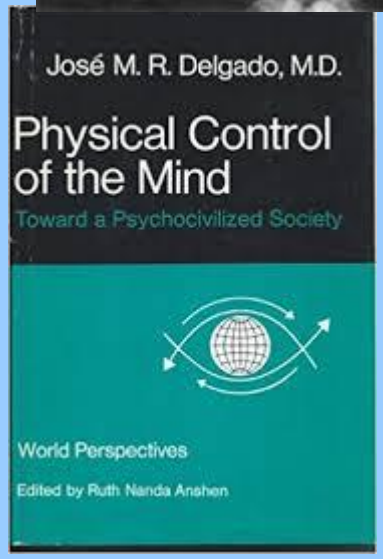
- **Ramón y Cajal hospital long history in functional neurosurgery**

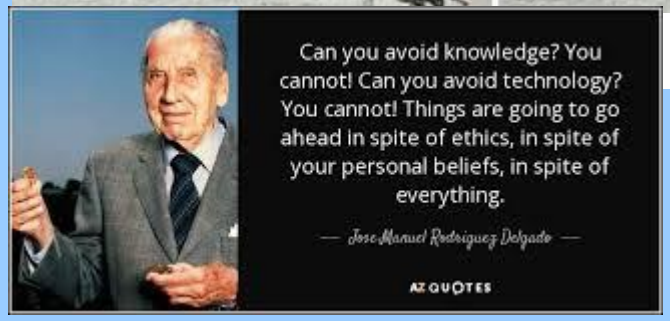


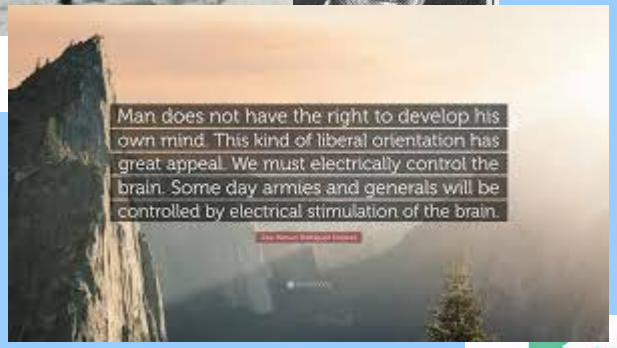




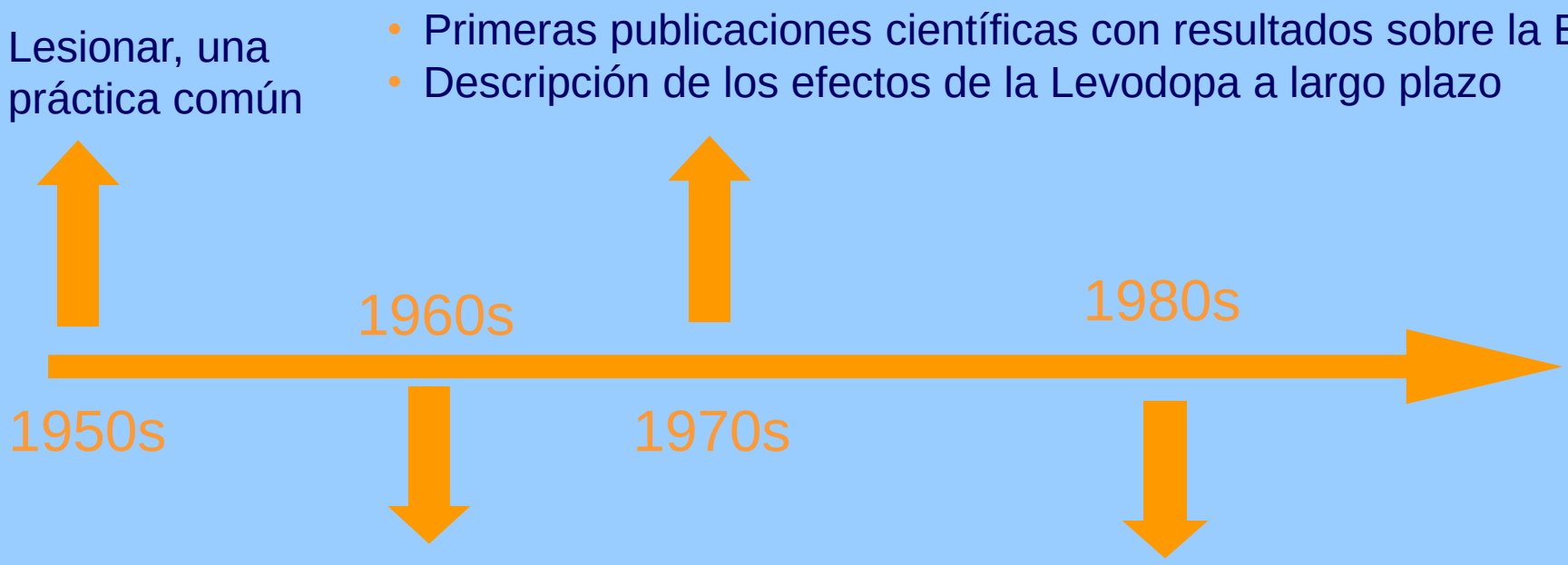








Antecedentes históricos



1. Benabid AL *et al,* 1987

Antecedentes históricos

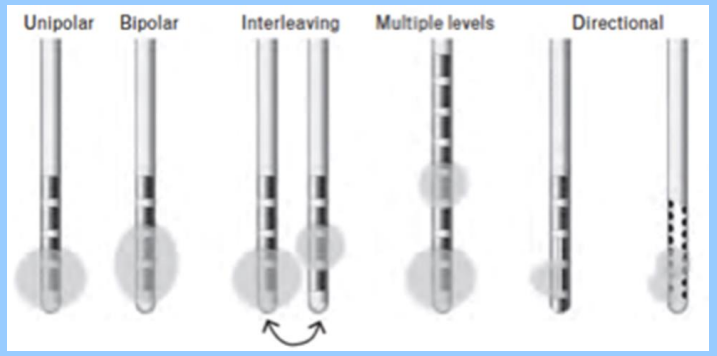
Terapia Ampliamente disponible

Complicaciones del hardware y estimulación



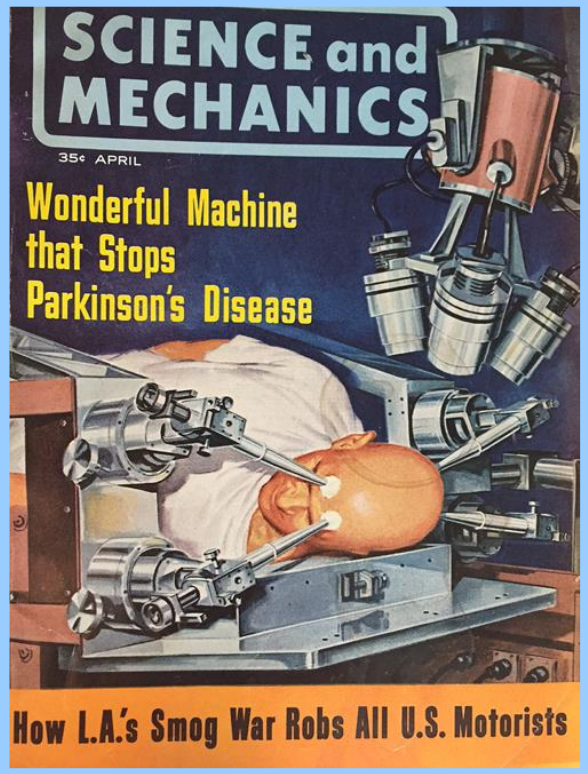
1990s

2000s



Introducción

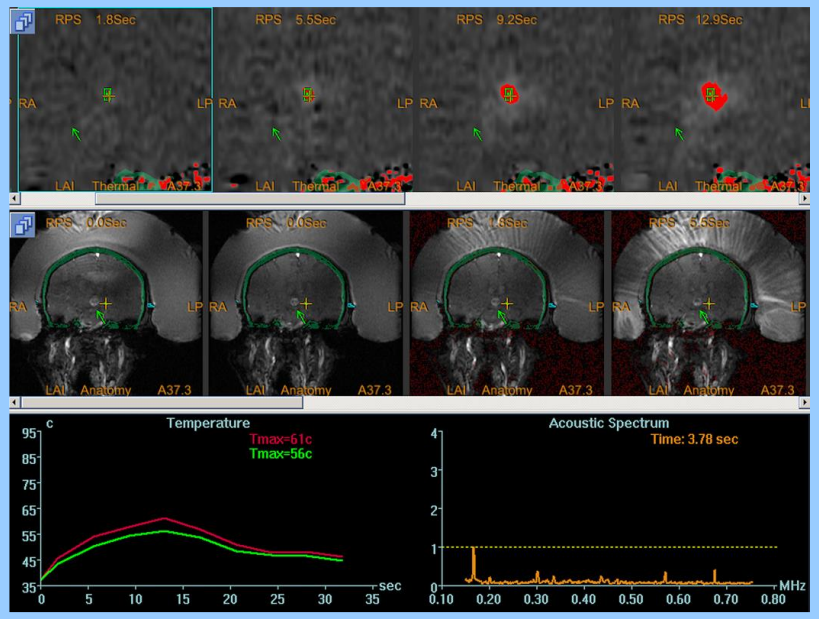
- Los primeros en realizar lesiones con ultrasonidos para el tratamiento de trastornos del movimiento y dolor fueron los hermanos Fry y Russell Meyers.
- Estos procedimientos requerían la realización de una craneotomía para obtener una adecuada ventana acústica.

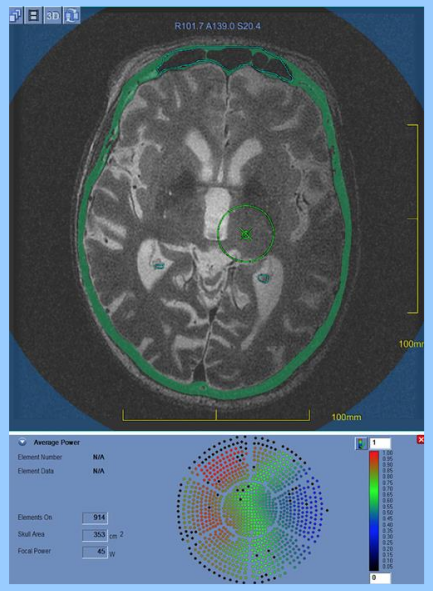


Meyers y Fry. Science Abril 1963

Introducción

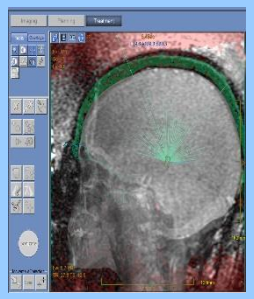
- Las recientes mejorías en el diseño del ultrasonido focal han derivado en la forma de un transductor multielemento, la Tac craneal y los agoritmos aplicados permiten la compensación del grosor y densidad ósea craneal para minimizar la desviación y absorción de ultrasonidos.
- Combinando la tecnología de ultrasonidos con la Rm y la termografía acoplada se obtiene una monitoriación en tiempo real del proceso de realización de la lesión.







Materiales y métodos



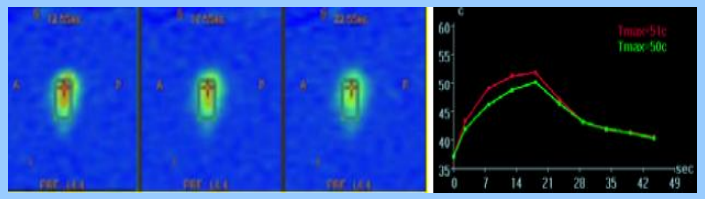
1. Planning Preop: fusion de MRi y Ct fusion and marcado de "non pass regions"



2. Marco para fijar cabeza



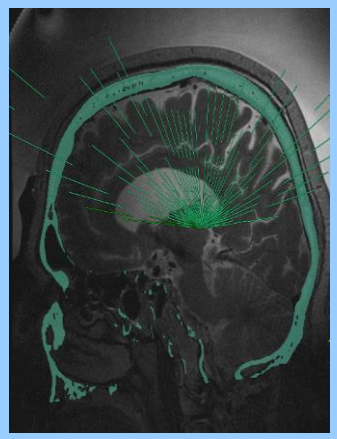
3. Mri, Target selection



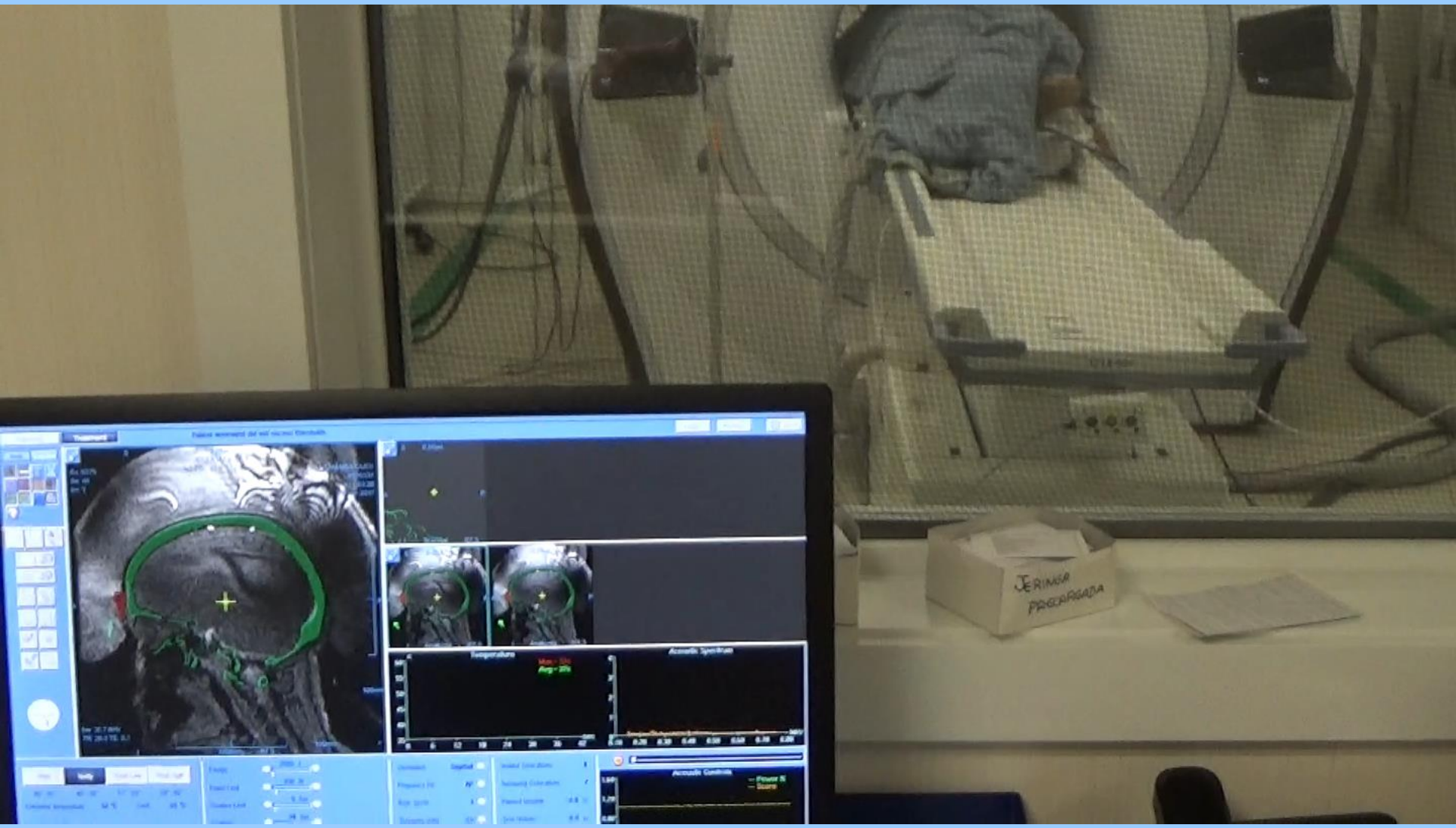
4. Calibrado del transductor



5. Confirmar target



6. Lesión: ±60ºC


JERINGA
PRECARGADA

Pronóstico y complicaciones. Serie CINAC

283 casos
HIFU en
5 años

- -160 Vim unilaterales
- -6 Vim bilaterales
- -4 Retratamientos de Vim
- -103 Stn unilaterales
- -5 Stn bilaterales
- -2 Retratamientos Stn
- -9 Palidotomía unilateral

27 LIFUS

Rango de edad 21-91 años

The CINAC experience: non-ET tremors (n=2)



¿Parkinson's disease?

tremor and thalamotomy (n=)

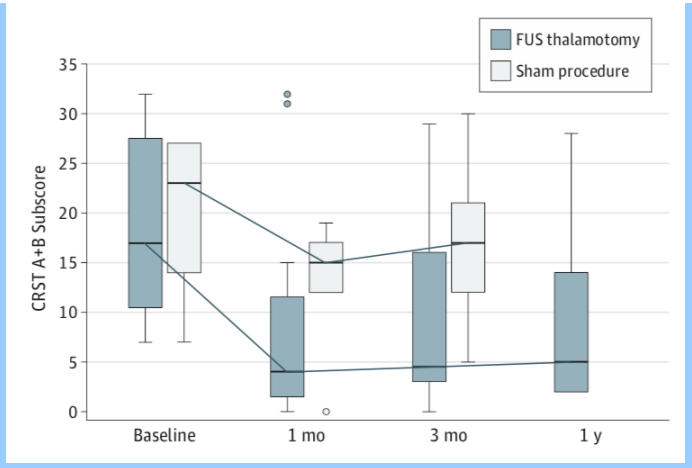


JAMA Neurology | Original Investigation

Safety and Efficacy of Focused Ultrasound Thalamotomy for Patients With Medication-Refractory, Tremor-Dominant Parkinson Disease

A Randomized Clinical Trial

Bond et al. *JAMA Neurol* 2017

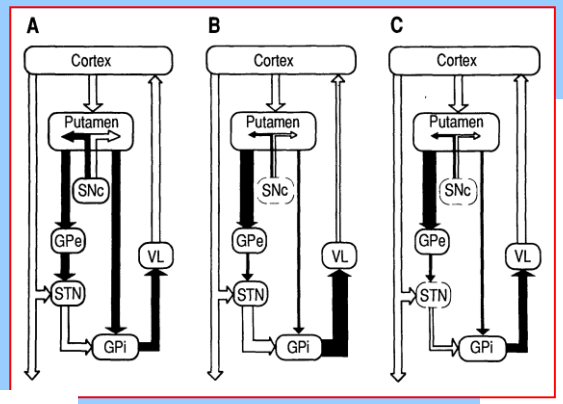


Parkinson's disease

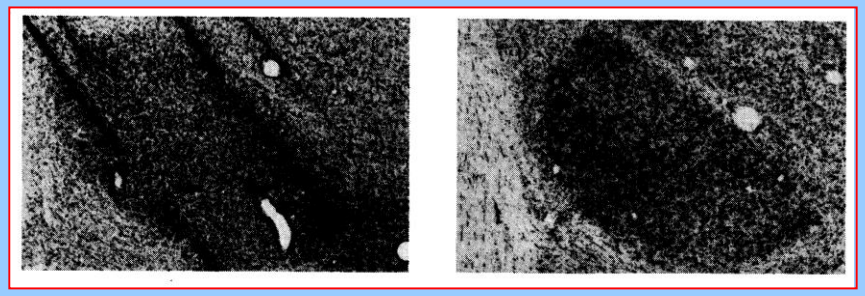
¿what about the other cardinal motor features?

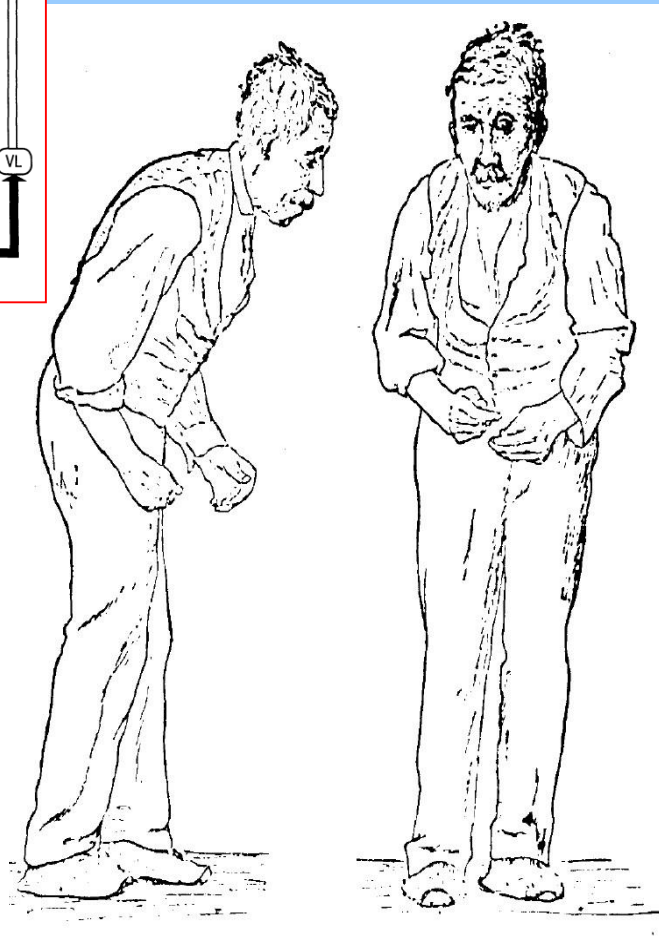
Reversal of Experimental Parkinsonism by Lesions of the Subthalamic Nucleus

HAGAI BERGMAN, THOMAS WICHMANN, MAHLON R. DELONG



SCIENCE, VOL. 249 21 SEPTEMBER 1990





Guridi J, Herrero MT, Luquin R, Guillen J, Obeso JA.. Subthalamotomy improves MPTP-induced parkinsonism in monkeys. Stereotact Funct Neurosurg. 1994;62(1-4):98-102.

¨Cuban experience¨

1)Unilateral subthalamotomy .

Obeso JA, Alvarez L, Guridi J, Teijeiro J, Juncos JL, Rodriguez MC, et al: Lesion of the subthalamic nucleus (STN) in Parkinson's disease. **Neurology 48:**A138, 1997

Alvarez L, Macias R, Pavón N, López G, Rodríguez-Oroz MC, Rodríguez R, et al: Therapeutic efficacy of unilateral subthalamotomy in Parkinson's disease: results in 89 patients followed for up to 36 months. **J Neurol Neurosurg Psychiatry 80:**979–985, 2009

2)Bilateral subthalamotomy.

Alvarez L, Macias R, Lopez G, Alvarez E, Pavon N, Rodriguez-Oroz MC, et al: Bilateral subthalamotomy in Parkinson's disease: initial and long-term response. **Brain 128:**570–583, 2005

3)Anatomic and neurophisiological studies of stn nucleus.

López-Flores G, Miguel-Morales J, Teijeiro-Amador J, Vitek J, Pérez-Parra S, Fernández-Melo R, et al. Anatomic and neurophysiological methods for the targeting and lesioning of the subthalamic nucleus. Cuban experience and review. Neurosurgery 2003; 52: 817-31.

Subthalamotomy for Parkinson's disease: Clinical outcome and topography of lesions

Rafael Rodriguez-Rojas[1,2], Maylen Carballo-Barreda[3], Lazaro Alvarez[3], Jorge Guridi[4], Nancy Pavon[3], Ivan Garcia-Maeso[3], Raul Macías[3], Maria C. Rodriguez-Oroz[2,5], Jose A. Obeso[1,2*]

Stn published lesions

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Gill SS, Heywood P: Bilateral subthalamic nucleotomy can be accomplished safely. **Mov Disord 13 (Suppl 2):**201, 1998
Gill SS, Heywood P: Subthalamic nucleus lesions, in Lozano AM (ed): **Movement Disorder Surgery.** Basel: Karger, 2000, Vol 15, pp 188–195

Patel NK, Heywood P, O'Sullivan K, Love S, Gill SS: MRI-directed subthalamic nucleus surgery for Parkinson's disease. **Stereotact Funct Neurosurg 78:**132–145, 2002
Patel NK, Heywood P, O'Sullivan K, McCarter R, Love S, Gill SS: Unilateral subthalamotomy in the treatment of Parkinson's disease. **Brain 126:**1136–1145, 2003

Coban A, Hanagasi HA, Karamursel S, Barlas O: Comparison of unilateral pallidotomy and subthalamotomy findings in advanced idiopathic Parkinson's disease. **Br J Neurosurg 23:** 23–29, 2009

Vilela Filho O, da Silva DJ: Unilateral subthalamic nucleus lesioning: a safe and effective treatment for Parkinson's disease. **Arq Neuropsiquiatr 60:**935–948, 2002
Vilela Filho O, Silva DJ, Souza HA, Cavalcante JE, Sousa JT, Ferraz FP, et al: Stereotactic subthalamic nucleus lesioning for the treatment of Parkinson's disease. **Stereotact Funct Neurosurg 77:**79–86, 2001

Parkin S, Nandi D, Giladi N, Joint C, Gregory R, Bain P, et al: Lesioning the subthalamic nucleus in the treatment of Parkinson's disease. **Stereotact Funct Neurosurg 77:**68–72, 2001


REV ARGENT NEUROC | VOL. 27, N° 2 : 67-71 | 2013 NOTA TÉCNICA

Subtalamotomía por Radiofrecuencia:
Aspectos Técnico-Quirúrgicos

Sergio Pampin, Santiago Driollet Laspiur, Fernando Leiguarda, Juan Pablo Travi, Dario Adamec
Hospital Prof. Alejandro Posadas

Su PC, Tseng HM, Liu HM, Yen RF, Liou HH: Treatment of advanced Parkinson's disease by subthalamotomy: one-year results. **Mov Disord 18:**531–538, 2003

Tseng HM, Su PC, Liu HM, Liou HH, Yen RF: Bilateral subthalamotomy for advanced Parkinson disease. **Surg Neurol 68 (Suppl 1):**S43–S51, 2007

Merello M, Tenca E, Pérez Lloret S, Martín ME, Bruno V, Cavanagh S, et al: Prospective randomized 1-year follow-up comparison of bilateral subthalamotomy versus bilateral subthalamic stimulation and the combination of both in Parkinson's disease patients: a pilot study. **Br J Neurosurg 22:** 415–422, 2008

"Focused ultrasound subthalamotomy in patients with asymmetrical Parkinson´s disease. A pilot sudy"

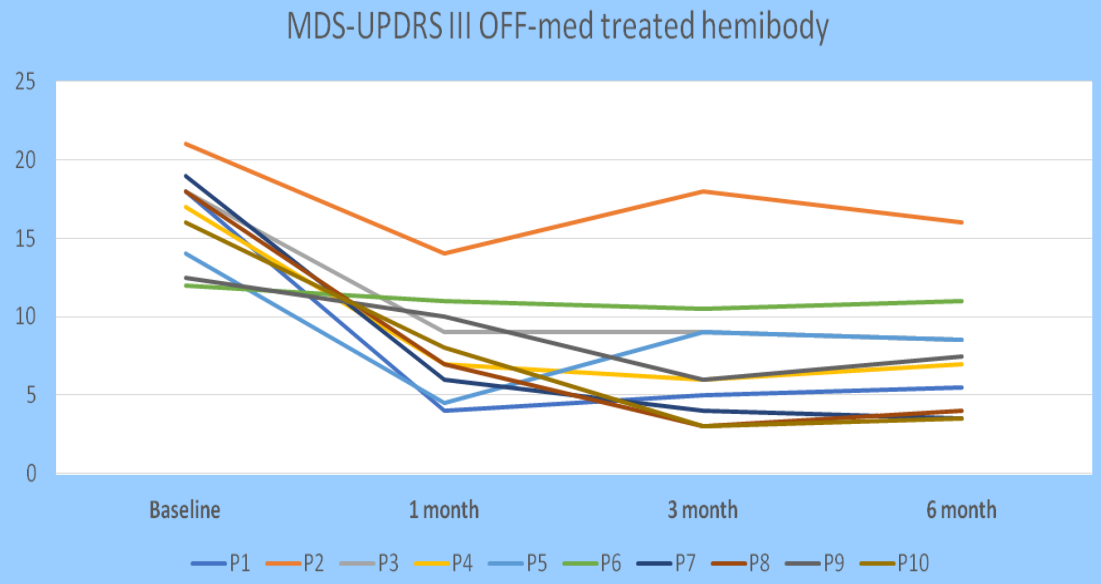

THELANCETNEUROLOGY-D-17-00398 0941
S1474-4422(17)30403-9
Embargo: November 24, 2017—23:30 (GMT)
Doctopic: Primary Research
1/TLN0398
Articles
JG
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Focused ultrasound subthalamotomy in patients with asymmetric Parkinson's disease: a pilot study

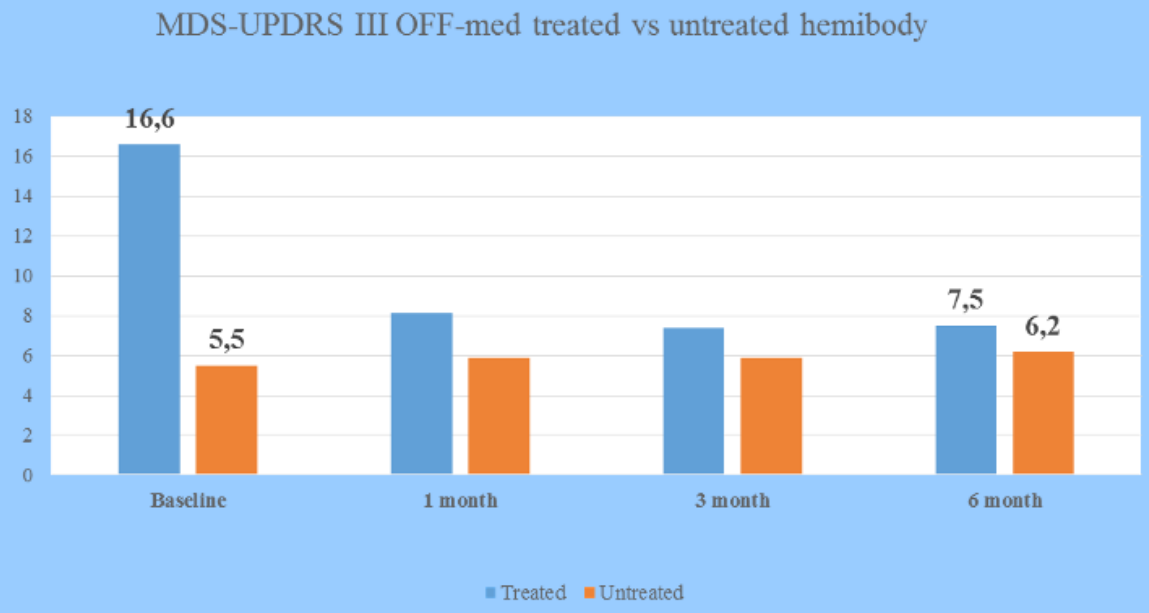
Raul Martínez-Fernández, Rafael Rodríguez-Rojas, Marta del Álamo, Frida Hernández-Fernández, Jose A Pineda-Pardo, Michele Dileone, Fernando Alonso-Frech, Guglielmo Foffani, Ignacio Obeso, Carmen Gasca-Salas, Esther de Luis-Pastor, Lydia Vela, José A Obeso

Results

PRIMARY OUTCOME

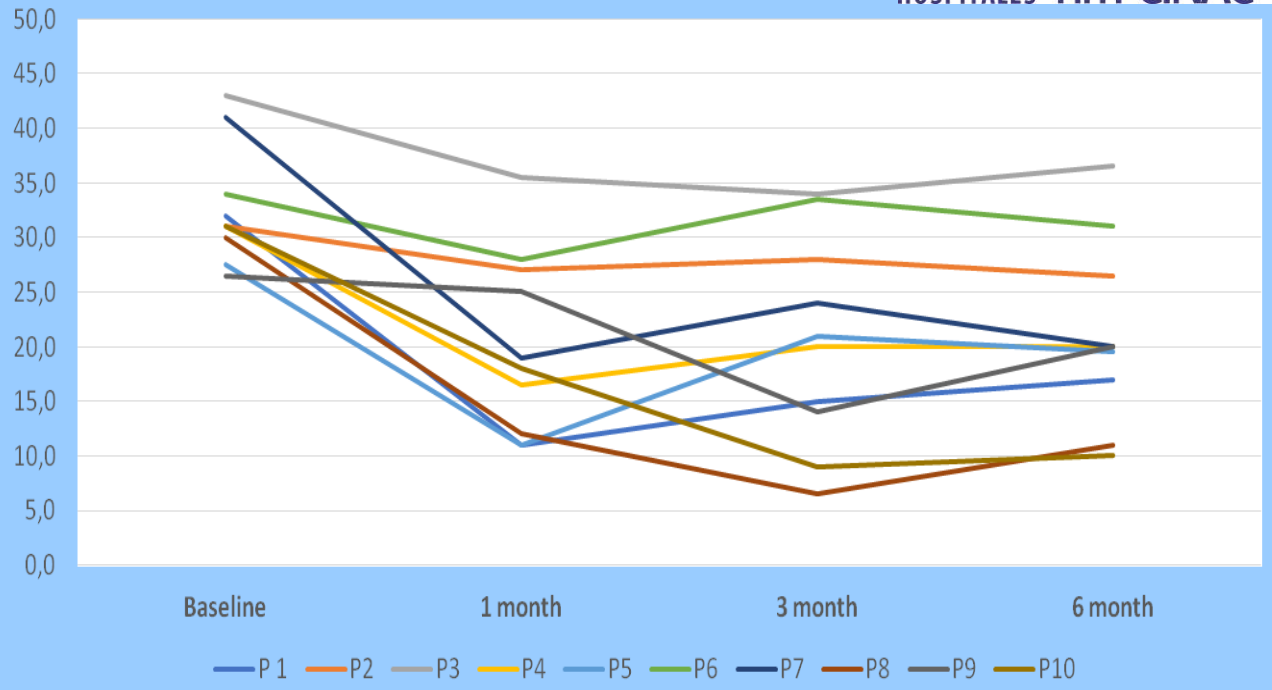


6 patients >50% ↓



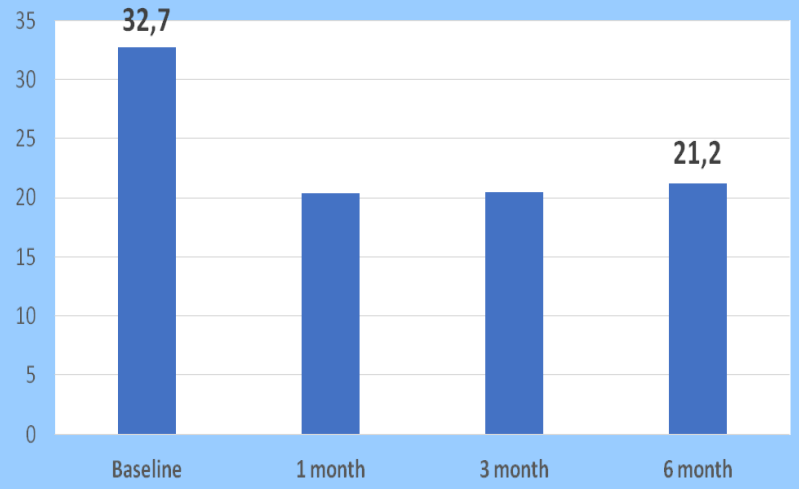
↓ 53% (p<0.005)

TOTAL MDS-UPDRS III OFF-med

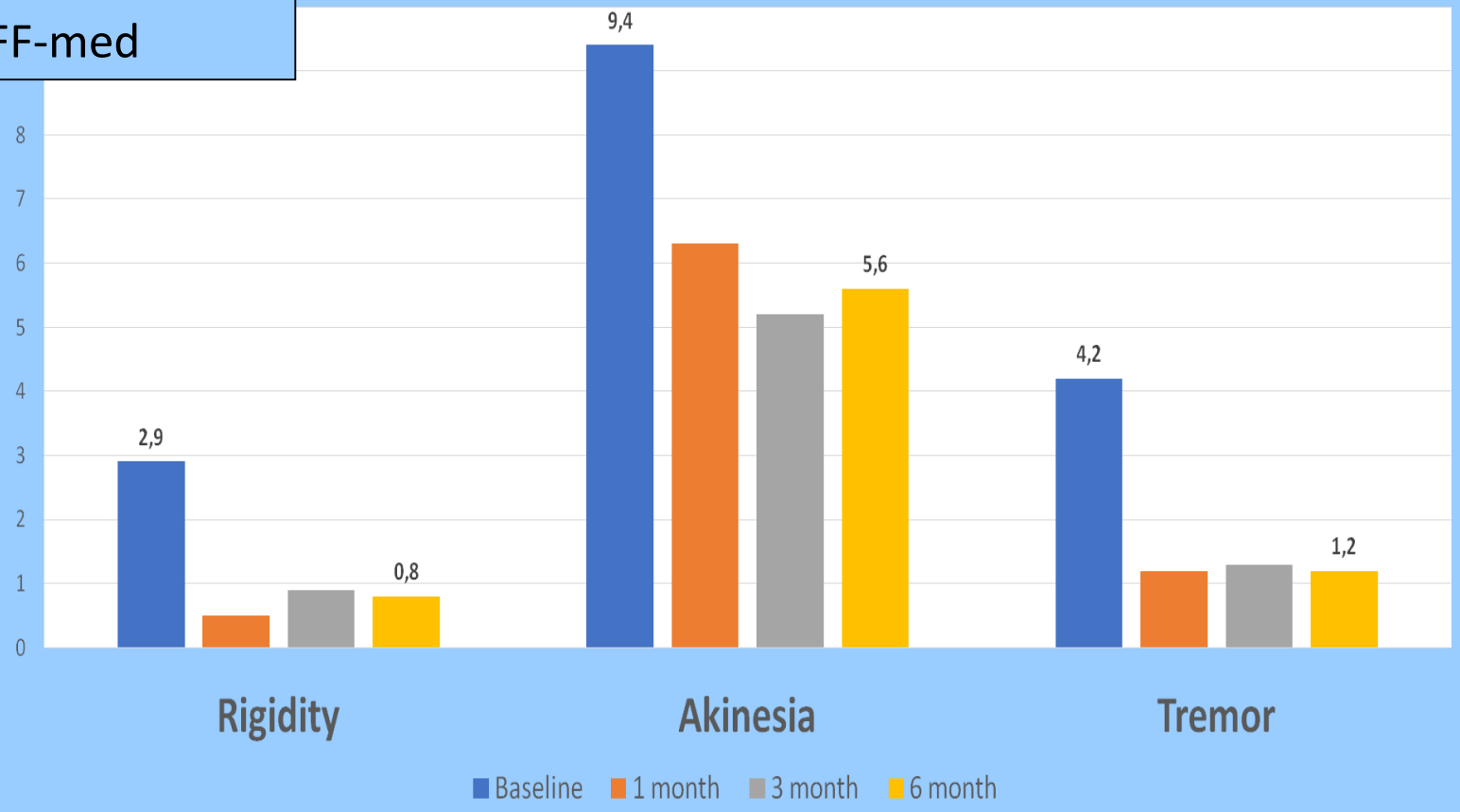


Todos los pacientes mejoraron

35% Reduction ($p<0.005$)



MDS-UPDRS III
subitems
OFF-med



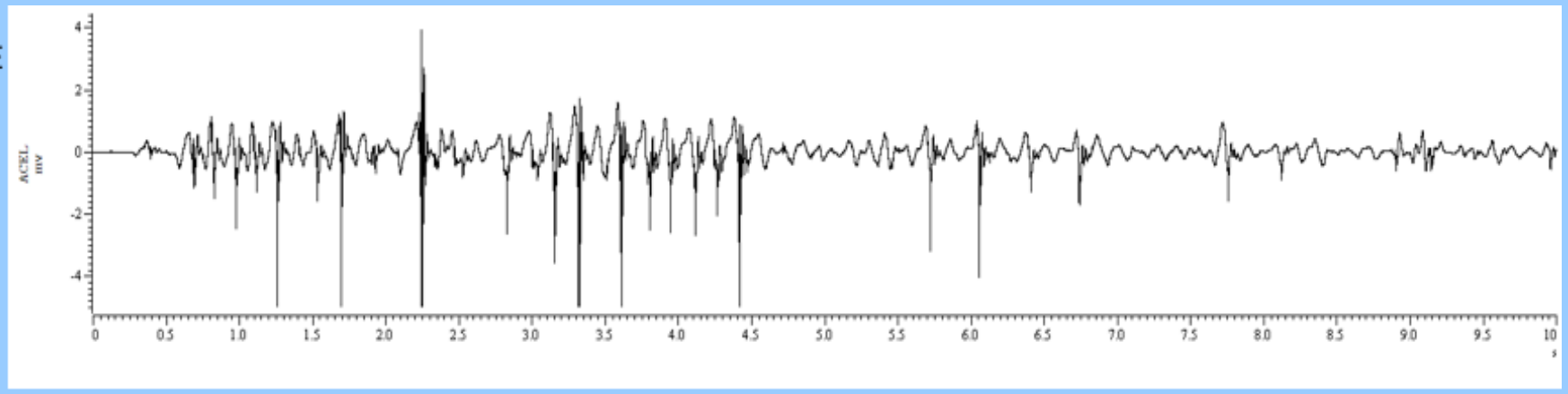
↓ 71%
(p=0.005)

↓ 36%
(p=0.01)

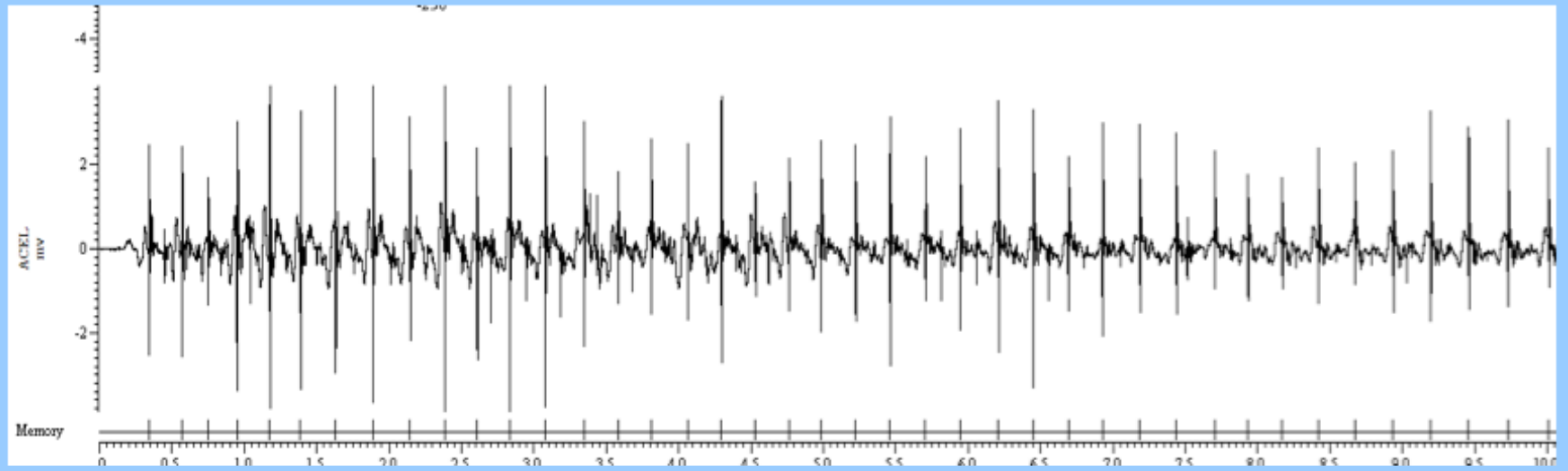
↓ 77%
(p=0.007)

MOVEMENT ANALYSIS (EMG)

PRE



6M



Structural Neuroimaging (3T MRI)

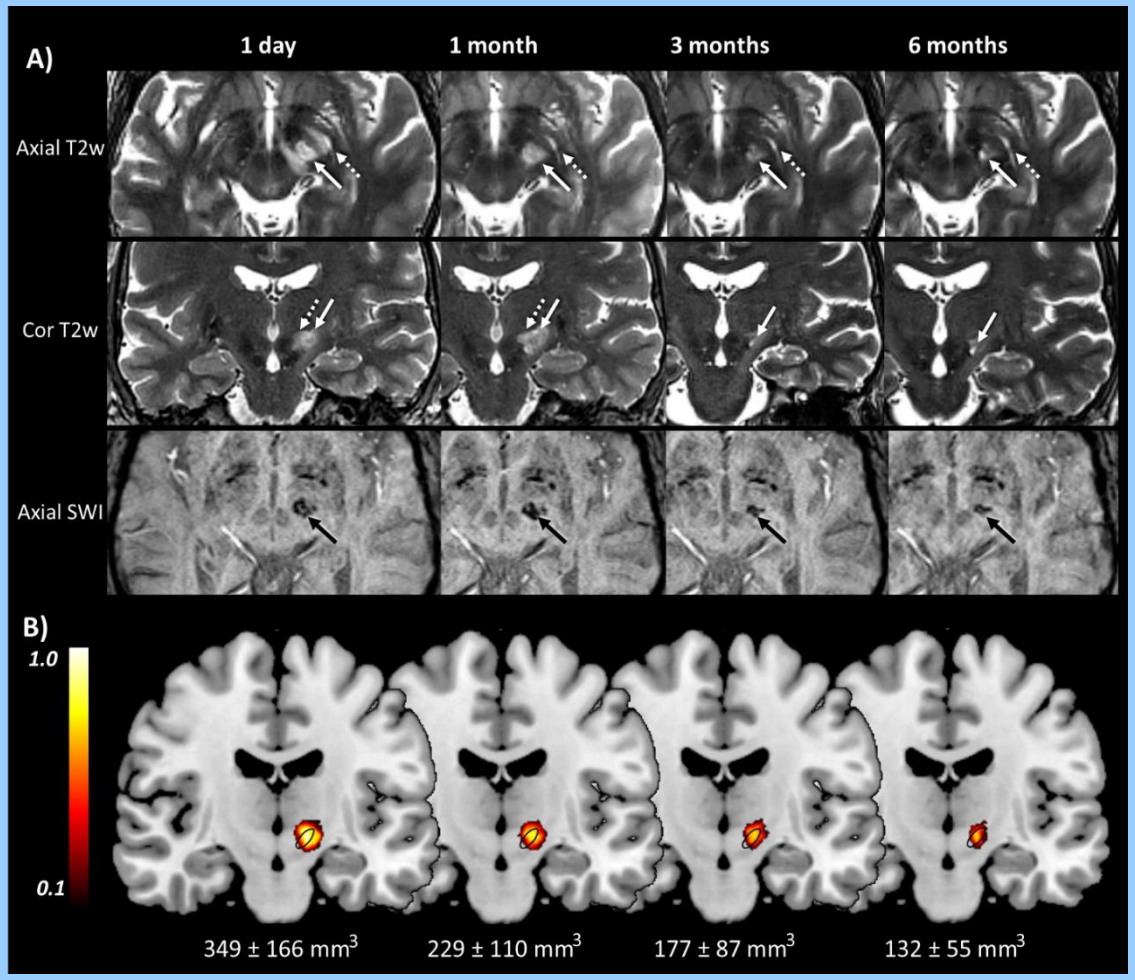
TARGET INDIRECTO: Stn Target (desde pto intercomisural):

-X: 12

-Y: 3

-Z: 4

Ajuste DIRECTO visual



Seguridad -Primary endpoint

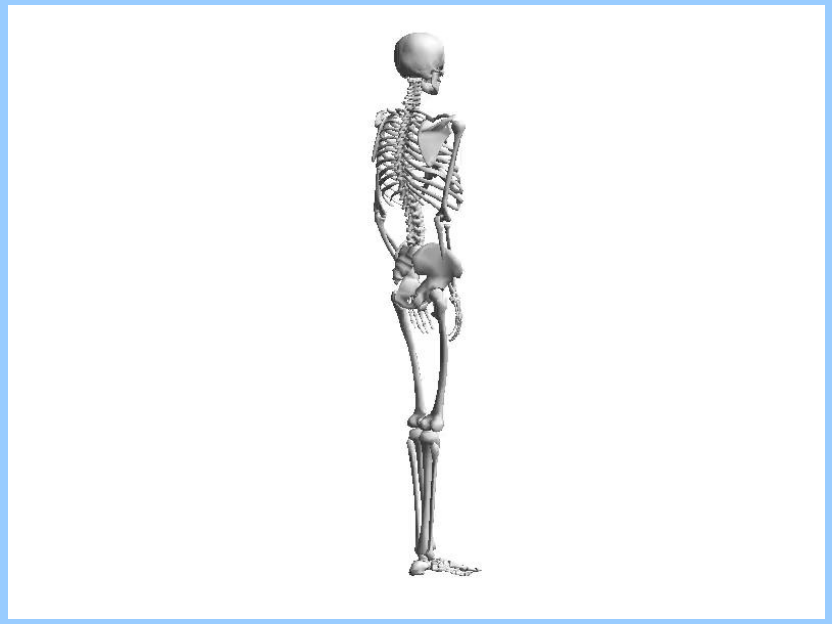
- Ataxía de la marcha leve y asimetría facial (n=1) estaban presentes al día siguiente del tratamiento y desaparecieron en el seguimiento.
- Cambios moderados del comportamiento (impulsividad, desinhibición y alegría desmesurada) aparecieron en dos pacientes pocos días después del tratamiento y desaparecieron durante el primer mes.
- Aumento de peso (n=2), fatiga (n=1) y ansiedad (n=1) fueron reportadas durante los primeros 6 meses.
- Las pruebas congnitivas a los 3 months post-tratamiento no demostraron ningún emporamiento ni deficit en ningún subdominio cognitive.
- Todos los pacientes (10) fueron dados de alta en menos de 48h.

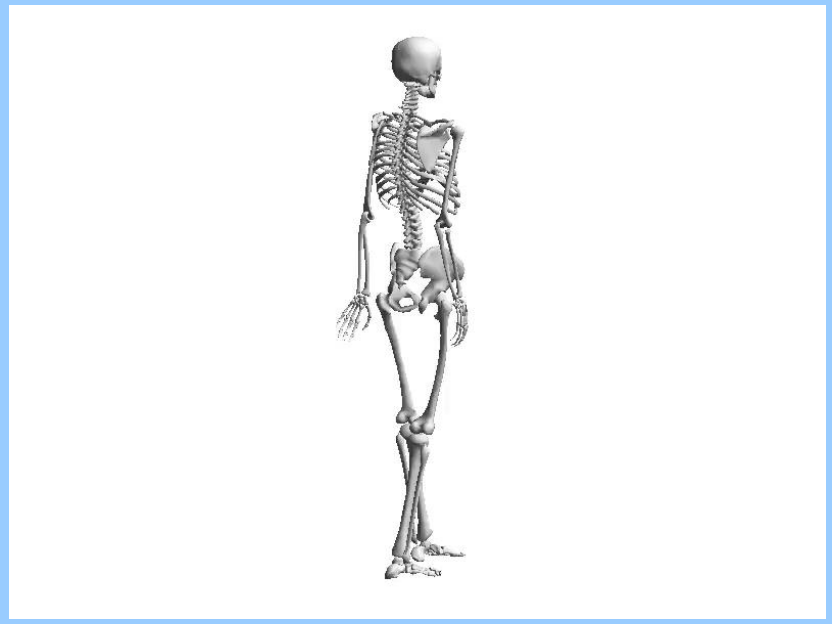
Baseline vs 5 days post right subthalamotomy





Baseline vs 5 days post right subthalamotomy





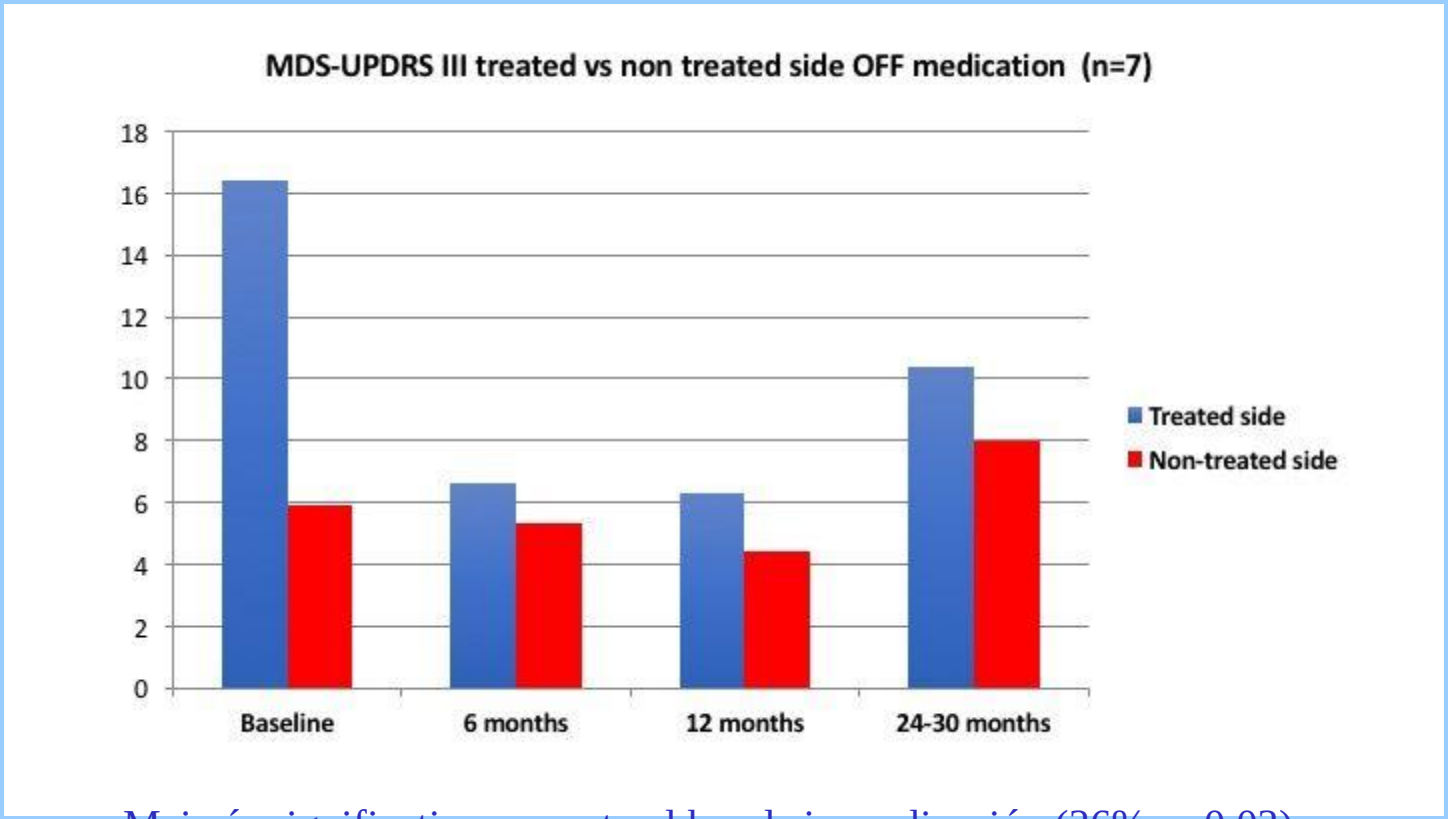
KINETIKOS


BASELINE
(OFF-MED)

Conclusiones

- La subtalamotomía unilateral mediante ultrasonidos fue bien tolerada y mejoró los síntomas cardinales motores de la E. de Parkinson. Hacen falta estudios controlados randomizados con mayor número de pacientes para confirmar esta evidencia preliminar en el tratamiento de la E. de Parkinson.

Resultados a largo plazo (30m)



Mejoría significativa respecto al basal sin medicación (36%;p=0.03)

Longterm results (30m)

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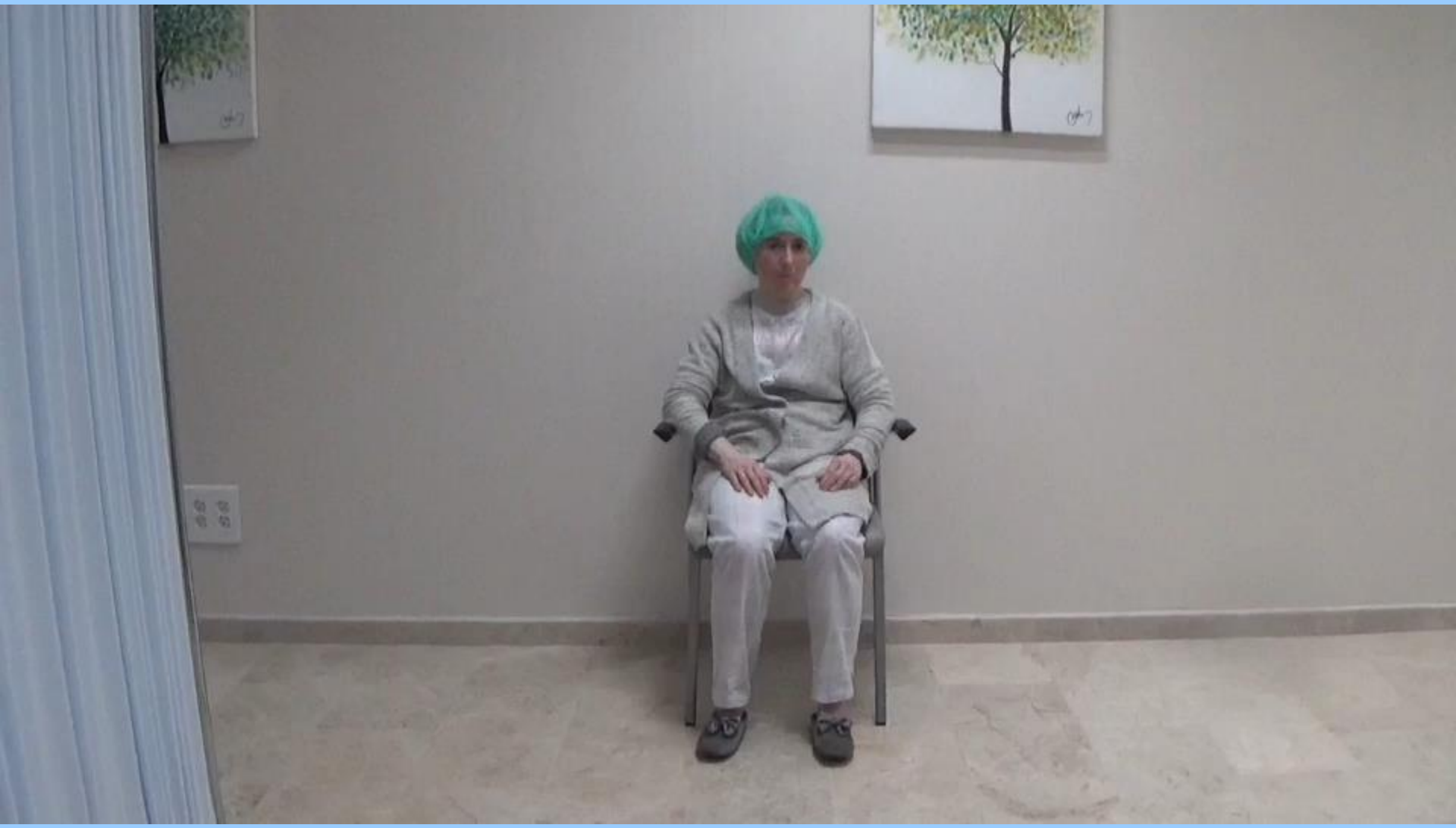
Table 2. Effect of unilateral subthalamotomy on the MDS-UPDRS III scores.

	Baseline *(mean ± SD)*	**Long-term follow-up**	**Change (%)**	**p<0.05 §**
Off medication				
MDS-UPDRS III total	31.5 ± 4.7	27.1 ± 6.5	- 15 %	0.128
MDS-UPDRS III treated side (t.s)	16.4 ± 2.4	10.7 ± 3.1	**+ 36 %**	**0.028**
MDS-UPDRS III non-treated side	5.9 ± 4.7	8.4 ± 3.3	**- 36 %**	**0.034**
MDS-UPDRS III rigidity (t.s)	2.8 ± 0.7	1.6 ± 0.8	**- 48 %**	**0.026**
MDS-UPDRS III bradykinesia (t.s)	8.9 ± 3.1	7.4 ± 2.1	- 9 %	0.292
MDS-UPDRS III tremor (t.s).	4.6 ± 1.8	1.7 ± 2.1	**- 69 %**	**0.018**
On medication				
MDS-UPDRS III total	22.0 ± 6.0	16.4 ± 2.7	- 22 %	0.063
MDS-UPDRS III treated side (t.s)	12.1 ± 1.9	6.1 ± 1.4	**- 47 %**	**0.018**
MDS-UPDRS III non-treated side	3.6 ± 2.9	5.4 ± 2.0	**+ 48 %**	**0.041**
MDS-UPDRS III rigidity (t.s)	2.2 ± 0.9	0.7 ± 0.5	**- 63 %**	**0.027**
MDS-UPDRS III bradykinesia (t.s)	6.4 ± 2.2	4.9 ± 1.6	- 17 %	0.168
MDS-UPDRS III tremor (t.s).	4.1 ± 1.6	0.7 ± 1.3	**- 89 %**	**0.017**

§ *Wilcoxon test for related samples.*

-No aumento de medicación, LEDD (620±271 VS 565±222, p=0.05).
-No aparición de efectos secundarios a largo plazo.
-No se observaron discinesias en off en el último seguimiento.





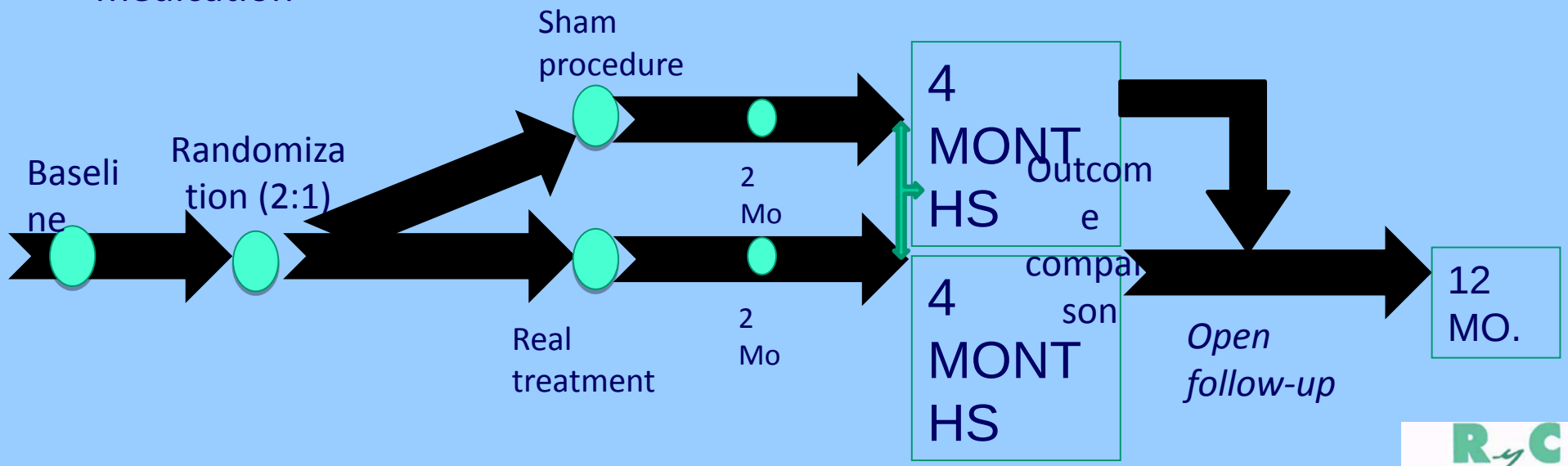
Design: Prospective, randomized, double-blind, single-site study.

Primary outcome:

Efficacy: between group differences in the MDS-UPDRS III for the treated body side

Safety

Inclusion criteria: PD Subjects with predominant motor features/disability from one side of the body (i.e asymmetry index > 1.5) non-optimaly controlled with medication



NEUROPSYCHOLOGICAL ASSESSMENT

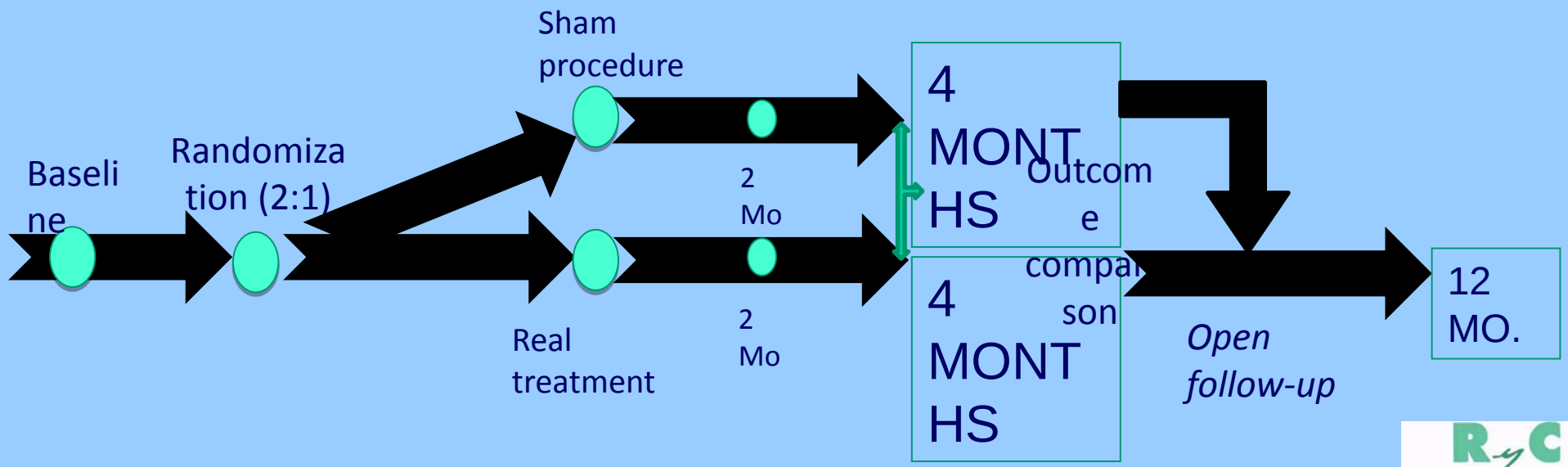
MAGNETOCEUTICAL ASSESSMENT

TEMPORAL DISCRIMINATION THRESHOLD

ELECTROPHYSIOLOGICAL ASSESSMENT

FUNCTIONAL NEUROIMAGING ASSESSMENT

KINEMATIC ASSESSMENT



BILATERAL STN

Design: Prospective, open-label, single-site study.

Primary

Safety

Prelimir PDRS III

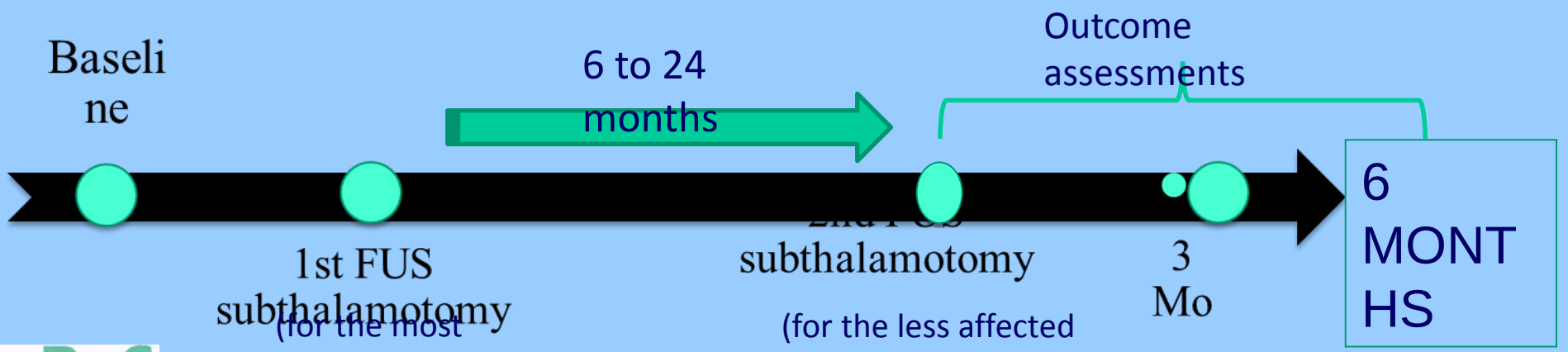
Inclusion

subthalar n motor

features i ed by an

adequate

Early HIFU in Pd



The NEW ENGLAND JOURNAL of MEDICINE

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Randomized Trial of Focused Ultrasound Subthalamotomy for Parkinson's Disease

R. Martínez-Fernández, J.U. Máñez-Miró, R. Rodríguez-Rojas, M. del Álamo, B.B. Shah, F. Hernández-Fernández, J.A. Pineda-Pardo, M.H.G. Monje, B. Fernández-Rodríguez, S.A. Sperling, D. Mata-Marín, P. Guida, F. Alonso-Frech, I. Obeso, C. Gasca-Salas, L. Vela-Desojo, W.J. Elias, and J.A. Obeso

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Focused Ultrasound Subthalamotomy (N = 27)	Sham Procedure (N = 13)
Age — yr		
Mean	56.6±9.3	58.1±8.8
Range	35–74	43–70
Sex — no. (%)		
Male	16 (59)	10 (77)
Female	11 (41)	3 (23)
Duration since diagnosis — yr		
Mean	5.6±2.5	7.3±3.8
Range	2–11	2–17
MDS-UPDRS III total score†‡		
Off-medication state	39.9±9.7	40.1±8.1
On-medication state	26.9±6.7	25.1±8.1
MDS-UPDRS III score for the more affected side of the body‡§		
Off-medication state	19.9±5.0	18.7±5.5
Rigidity	3.5±1.0	3.8±1.0
Bradykinesia	10.8±2.8	9.7±3.6
Tremor	5.6±3.0	5.2±2.2
On-medication state	14.2±4.2	11.9±5.1
Rigidity	2.6±1.1	2.6±1.4
Bradykinesia	7.9±2.9	6.4±2.9
Tremor	3.8±2.3	2.9±1.9
MDS-UPDRS IV score for levodopa-related motor complications¶	4.0±4.5	5.1±4.7
Dyskinesia	0.3±0.9	1.1±1.8
Motor fluctuations	3.0±3.1	3.5±2.8
Dystonia, in the off-medication state	0.7±1.2	0.5±1.1
MDS-UPDRS II score for activities of daily living‖	11.3±5.9	12.5±4.6
Treatment with levodopa — no. (%)**	26 (96)	12 (92)
Daily dose of levodopa equivalent — mg††	729.7±328.3	881.7±407.9
PDQ-39 summary index for quality of life‡‡	21.7±12.0	23.9±10.2

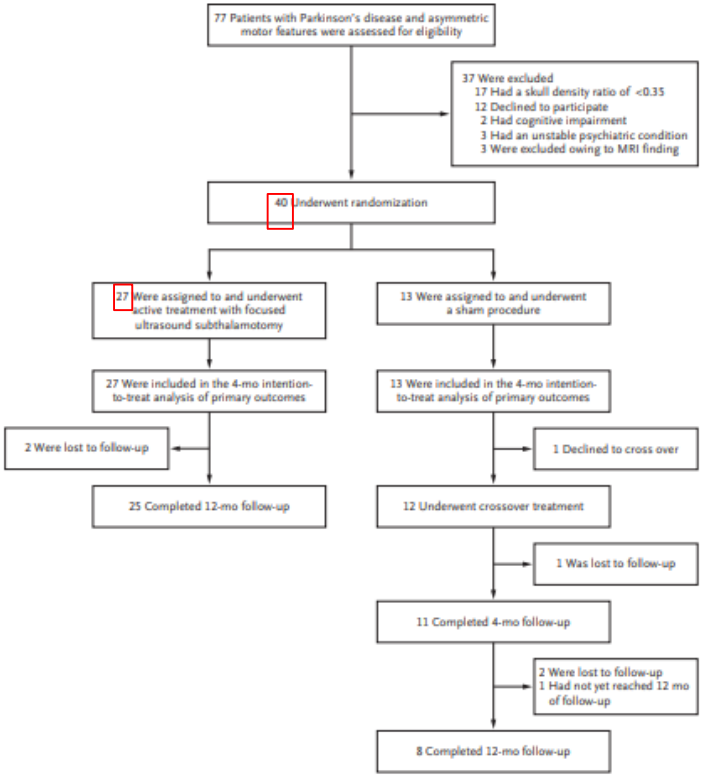
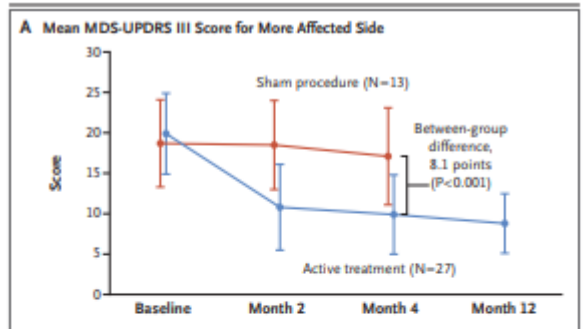


Figure 1. Enrollment and Follow-up of the Patients.

Patients who had a skull density ratio (an index of ultrasound penetration into the skull) of less than 0.35 were excluded from the trial. All 40 patients who had undergone randomization finished the blinded follow-up for the primary and main secondary outcomes (at 4 months). Of the 27 patients in the active-treatment group, 25 continued to the open follow-up phase for 12 months. Of the 13 patients in the control group (in which patients underwent a sham procedure), 12 crossed over to receive unblinded active treatment at 4 months. After undergoing the second (i.e., active) procedure, 11 patients in the crossover group completed an additional 4 months of follow-up and 8 patients completed 12 months of follow-up.



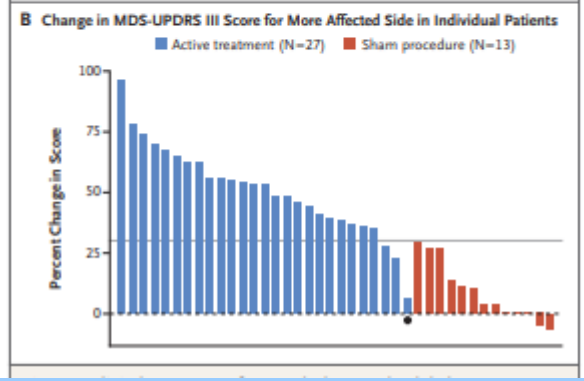


Table 2. Primary and Secondary Efficacy Outcomes, Assessed from Baseline to 4 Months (Intention-to-Treat Population).*

Outcome	Baseline		Within-Group Change from Baseline to 4 Mo				Between-Group Difference in Change
	Focused Ultrasound Subthalamotomy (N=27)	Sham Procedure (N=13)	Focused Ultrasound Subthalamotomy (N=27)		Sham Procedure (N=13)		
			mean (95% CI)	%	*mean (95% CI)*	%	*mean (95% CI)*
Primary efficacy outcome							
MDS-UPDRS III score for the more affected side, in the off-medication state	19.9±5.0	18.7±5.5	9.8 (8.6 to 11.1)	52.6	1.7 (0.0 to 3.5)	4.2	8.1 (6.0 to 10.3)†
Secondary efficacy outcomes							
MDS-UPDRS III score for the more affected side, in the on-medication state‡	14.2±4.2	11.9±5.1	6.4 (5.2 to 7.6)	46.5	0.1 (−0.3 to 0.6)	6.0	5.9 (3.8 to 8.0)
MDS-UPDRS III score for the more affected side in an unblinded evaluation							
Off-medication state	19.5±3.8	18.6±5.7	11.1 (9.9 to 12.3)	53.8	1.4 (0.3 to 2.4)	2.0	10.4 (8.3 to 12.5)
On-medication state‡	14.0±4.3	12.3±4.5	7.5 (6.4 to 8.6)	53.1	0.3 (−0.6 to 1.3)	2.9	6.6 (4.7 to 8.5)
MDS-UPDRS III subscores for more affected side							
Off-medication state							
Rigidity	3.5±1.0	3.8±1.0	1.9 (1.6 to 2.2)	60.0	0.1 (−0.3 to 0.6)	0.0	1.8 (1.3 to 2.3)
Bradykinesia	10.8±2.8	9.7±3.6	4.0 (3.2 to 4.7)	33.3	1.4 (0.3 to 2.4)	9.1	2.7 (1.4 to 4.0)
Tremor	5.6±3.0	5.2±2.2	4.0 (3.3 to 4.6)	83.3	0.3 (−0.6 to 1.3)	0.0	3.6 (2.5 to 4.8)
On-medication state‡							
Rigidity	2.6±1.1	2.6±1.4	1.3 (1.0 to 1.6)	50.0	−0.2 (−0.6 to 0.2)	0.0	1.5 (1.1 to 2.0)
Bradykinesia	7.9±2.9	6.4±2.9	2.3 (1.5 to 3.1)	27.3	0.8 (−0.3 to 2.0)	12.7	1.5 (0.1 to 2.9)
Tremor	3.8±2.3	2.9±1.9	2.7 (2.1 to 3.3)	92.9	0.0 (−0.8 to 0.9)	0.0	2.7 (1.6 to 3.7)
MDS-UPDRS II score	11.3±5.9	12.5±4.6	4.1 (2.2 to 5.9)	42.9	−1.4 (−4.0 to 1.2)	−11.8	5.5 (2.2 to 8.7)
MDS-UPDRS III total score							
Off-medication state	39.9±9.7	40.1±8.1	15.2 (13.5 to 17.0)	34.2	2.3 (−0.2 to 4.8)	6.3	12.9 (9.9 to 16.0)
On-medication state‡	26.9±6.7	25.1±8.1	8.4 (6.6 to 10.3)	33.9	−0.8 (−3.4 to 1.8)	0.0	9.2 (6.0 to 12.4)
MDS-UPDRS IV total score§	4.0±4.5	5.1±4.7	1.1 (0.0 to 2.1)	40.0	−1.2 (−2.7 to 0.3)	0.0	2.3 (0.5 to 4.1)
Dyskinesia	0.3±0.9	1.1±1.8	0.0 (−0.4 to 0.3)	NA	−0.4 (−0.9 to 0.2)	NA	0.3 (−0.3 to 1.0)
Motor fluctuations	3.0±3.1	3.5±2.8	0.9 (0.2 to 1.6)	26.8	−0.6 (−1.6 to 0.4)	12.5	1.5 (0.2 to 2.7)
Dystonia, in the off-medication state	0.7±1.2	0.5±1.1	0.2 (−0.1 to 0.5)	75.0	−0.2 (−0.6 to 0.2)	NA	0.4 (−0.1 to 1.0)
PDQ-39 summary index	21.7±12.0	23.9±10.2	7.4 (4.1 to 10.6)	38.5	1.6 (−3.1 to 6.2)	29.0	5.8 (0.1 to 11.4)
Daily dose of levodopa equivalent (mg)	729.7±328.3	881.7±407.9	−94.5 (−151.9 to −37.2)	7.5	22.5 (−60.2 to 106.4)	0.0	−117.0 (−218.0 to −16.0)
Additional analysis							
MDS-UPDRS III score for the more affected side in the open-label crossover subgroup¶	19.5±3.9	NA	11.6 (8.4 to 14.8)	68.0	NA	NA	NA

Table 3. Adverse Events.*

Adverse Event	Focused Ultrasound Subthalamotomy (N=27)				Sham Procedure (N=13)
	Total	At 24 Hr	At 2 Mo	At 4 Mo	At 12 Mo	At 4 Mo
Dyskinesia on the more affected side, in the off-medication state — no. of patients (%)						
Any event, regardless of severity	6 (22)	0	6 (22)	3 (11)	0	0
Chorea	5 (19)	0	5 (19)	3 (11)	0	0
Ballism	1 (4)	0	1 (4)	0	0	0
New-onset dyskinesia on the more affected side, in the on-medication state — no. of patients (%)	6 (22)	0	6 (22)	1 (4)	2 (7)	0
Weakness on the more affected side — no. of patients (%)	5 (19)	5 (19)	2 (7)	2 (7)	2 (7)**	0
Isolated facial asymmetry — no. of patients (%)	3 (11)	3 (11)	3 (11)	1 (4)	0	0
Speech disturbance — no. of patients (%)						
Any objective or subjective event†	15 (56)	6 (22)	12 (44)	3 (11)	1 (4)	0
Dysarthria, assessed objectively on examination	7 (26)	6 (22)	5 (19)	3 (11)	1 (4)	0
Slurred speech, as reported by the patient	8 (30)	0	7 (26)	0	0	0
Gait disturbance — no. of patients (%)						
Any objective or subjective event‡	13 (48)	8 (30)	7 (26)	2 (7)	1 (4)	0
Ataxia, assessed objectively on examination	3 (11)	2 (7)	1 (4)	0	0	0
Unsteady gait, as reported by the patient	10 (37)	6 (22)	6 (22)	2 (7)	1 (4)	0
Upper limb dysmetria — no. of patients (%)	2 (7)	0	2 (7)	0	0	0
Impulsiveness — no. of patients (%)	1 (4)	0	1 (4)	0	0	0
Weight gain — no. of patients (%)§	2 (7)	0	1 (4)	1 (4)	2 (7)	0
Somnolence — no. of patients (%)	1 (4)	1 (4)	0	0	0	0
Intraprocedural sensations or events, all transient — no. of patients (%)						
Nausea	7 (26)					2 (15)
Emesis	1 (4)					1 (8)
Dizziness	13 (48)					2 (15)
Head "tilting"	13 (48)					1 (8)
Head discomfort, such as "heat" or "pressure"	11 (41)					1 (8)
Anxiety	6 (22)					0
Pin-site head pain	16 (59)					8 (62)
Right inner ear pain	1 (4)					0
Headache	5 (19)					6 (46)
Back or neck pain	4 (15)					2 (15)
High blood pressure	7 (26)					6 (46)
Fatigue	1 (4)					1 (8)
Chest pain	0					1 (8)
Other adverse events not directly related to treatment — no. of patients (%)						
Rib fracture	2 (7)					0
Fall	2 (7)					0
Dysuria	1 (4)					0
Total adverse events, according to severity — no. of events¶	144					31
Mild	96					13
Moderate	40					16
Severe	8					2

Discusión y conclusiones

	Beric *et al*[7]	Kondziolka *et al*[8]*	Oh *et al*[9]	Umemura *et al*[10]	Limousin *et al*[6]**	Lyons *et al*[11]	This study
No of patients	86	66	79	109	111	80	262/180
No of electrodes	149	66	124	179	135	155	472/325
No of surgeries	NG	100	NG	NG	NG	160	526
Follow-up time	3.5 years†	29 months‡	33 months§	20 months§	12 months†	5 years†	35.3 months§
Aborted procedures	3.5%	—	0.9%	—	0.9%	4.9% [2.5%]	1.9% [1.0%]
Mortality	—	—	—	1.8%	—	—	—
Morbidity	6%	NG	1.3%	4.6%	—	—	0.4%
SURGERY							
ICH	3.3%	1.5%	3.6% (2.3%)	3.6% (2.2%)	2.7% (2.2%)	1.2% (0.6%)	0.4% (0.2%)
Extracranial haemorrhage	—	—	—	—	1.8%	—	2.4%
Venous infarction	—	—	—	0.9% (0.6%)	—	—	—
Seizure	2.3%	—	—	0.9%		1.2% [0.6%]	—
CSF fistula	—	—	1.3%	0.9% (0.6%)	—	—	0.8% (0.4%)
INFECTION							
Total	1.2%	10.6%	15.2%	3.7% [2.2%]	1.8%	6.2% [3.8%]	8.3% [2.9%]
Hardware removed	—	6.0%	13.9%	3.7%	1.8%	6.2% [3.8%]	6.7% [2.3%]
HARDWARE							
Lead fracture	—	15.2%	5.1%	—	—	2.5% (1.3%)	1.7%
Lead migration	3.5% (2.0%)	1.5%	5.1%	—	—	6.3% (3.2%)	2.8% (1.5%)
Extension wire**	3.5%	—	—	—	—	2.5%	1.1%
IPG malfunction	1.2%	1.5%	3.8%	—	—	13.8%	—
Local discomfort	1.2%	—	—	—	—	Some patients	6.7%*
Others††							1.7%*

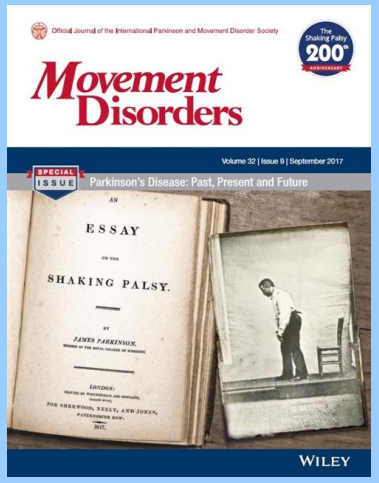
Voges, Waerzeggers, Maarout et al. J Neurol Neurosurg Psychiatry. 2006 Jul;77(7):868-72

Functional topography of the human subthalamic nucleus: relevance for subthalamotomy 2 of Parkinson's disease

Rafael Rodriguez-Rojas, PhD,1-3 Jose A. Pineda-Pardo, PhD,1-3 Jorge Mañez-Miro, MD,1 3 Alicia Sanchez-Turel, BsC,1 Raul Martinez-Fernandez, MD, PhD,1-3 Marta del Alamo1 4 , Mahlon DeLong, MD, PhD,4 Jose A. Obeso, MD, PhD1-3 5 1 6

HM CINAC (Centro Integral de Neurociencias Abarca Campal). Hospital Universitario HM 7 Puerta del Sur, HM Hospitales. Madrid, Spain. 2 8 Universidad CEU-San Pablo University, Madrid, Spain. 3 9 Network Center for Biomedical Research on Neurodegenerative Diseases (CIBERNED), 10 Carlos III Institute, Madrid, Spain. 4 11 Department of Neurology, Emory University School of Medicine, Atlanta, USA

-Caracterización topográfica, somatotópica y conexional de N. Subtalámico.
-Combinación de tractografía analítica, Rm funcional y atlas multimodales
-86 pacientes con E. Parkinson, 39 de ellos se les realizó subtalamotomía unilateral.
-23 voluntarios sanos.
-Volumen N. Subtalámico 192mm^3



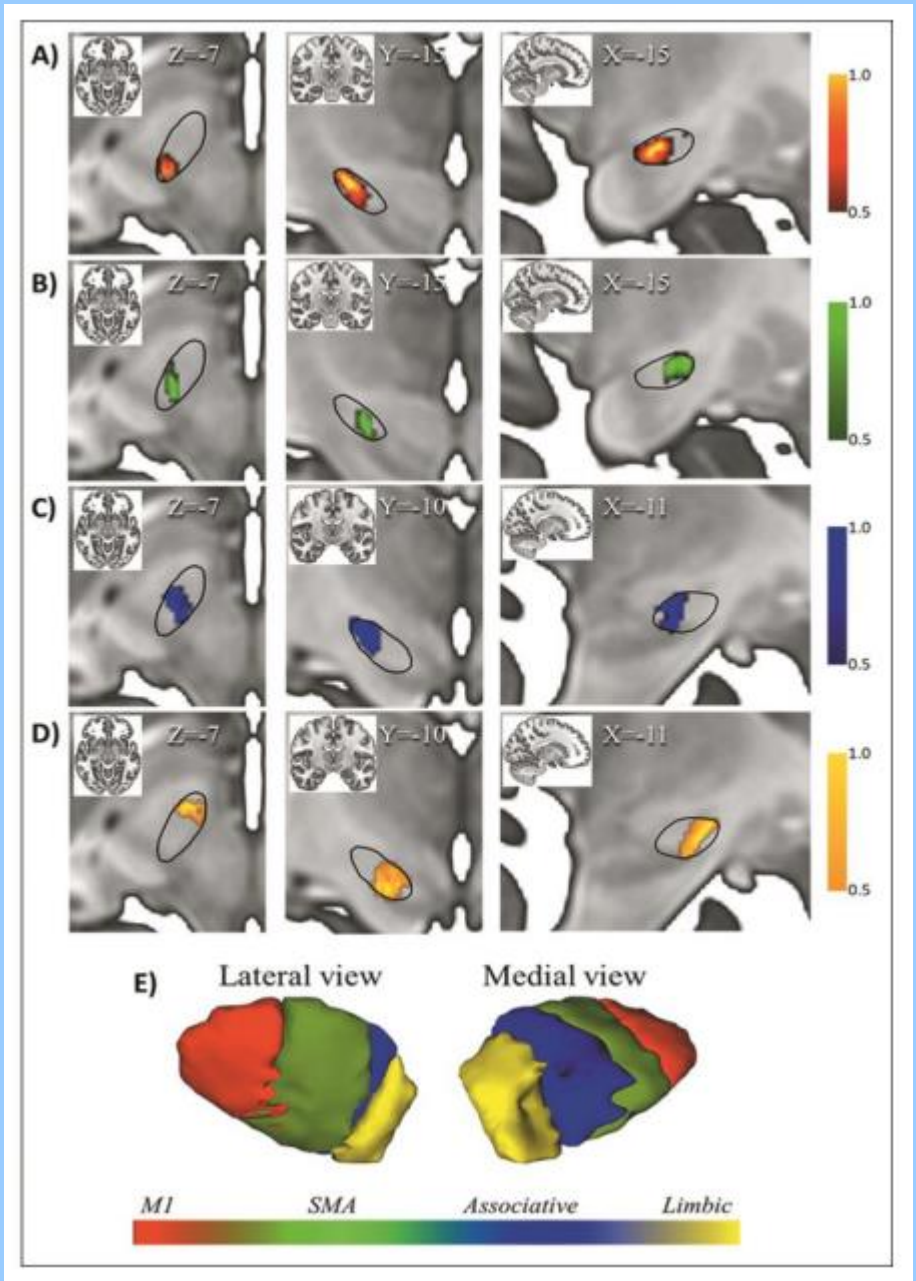


Figure 1. Connectivity-based parcellation of the STN. Intersection of tract density images for SMC (A), SMA (B), Associative (C) and Limbic (D) connections with combined STN atlas (CIT168 / Morel Thalamic / MNI-PD25), superimposed by the MNI152 template. The corresponding slice and coordinate in the MNI152 space is displayed at the top of each panel. E) Lateral and medial views of the 3D rendered right STN. Each geometrical locus was assembled according to its connectivity probabilities and color-coded as red (SMC), green (SMA), blue (associative), and yellow (limbic).

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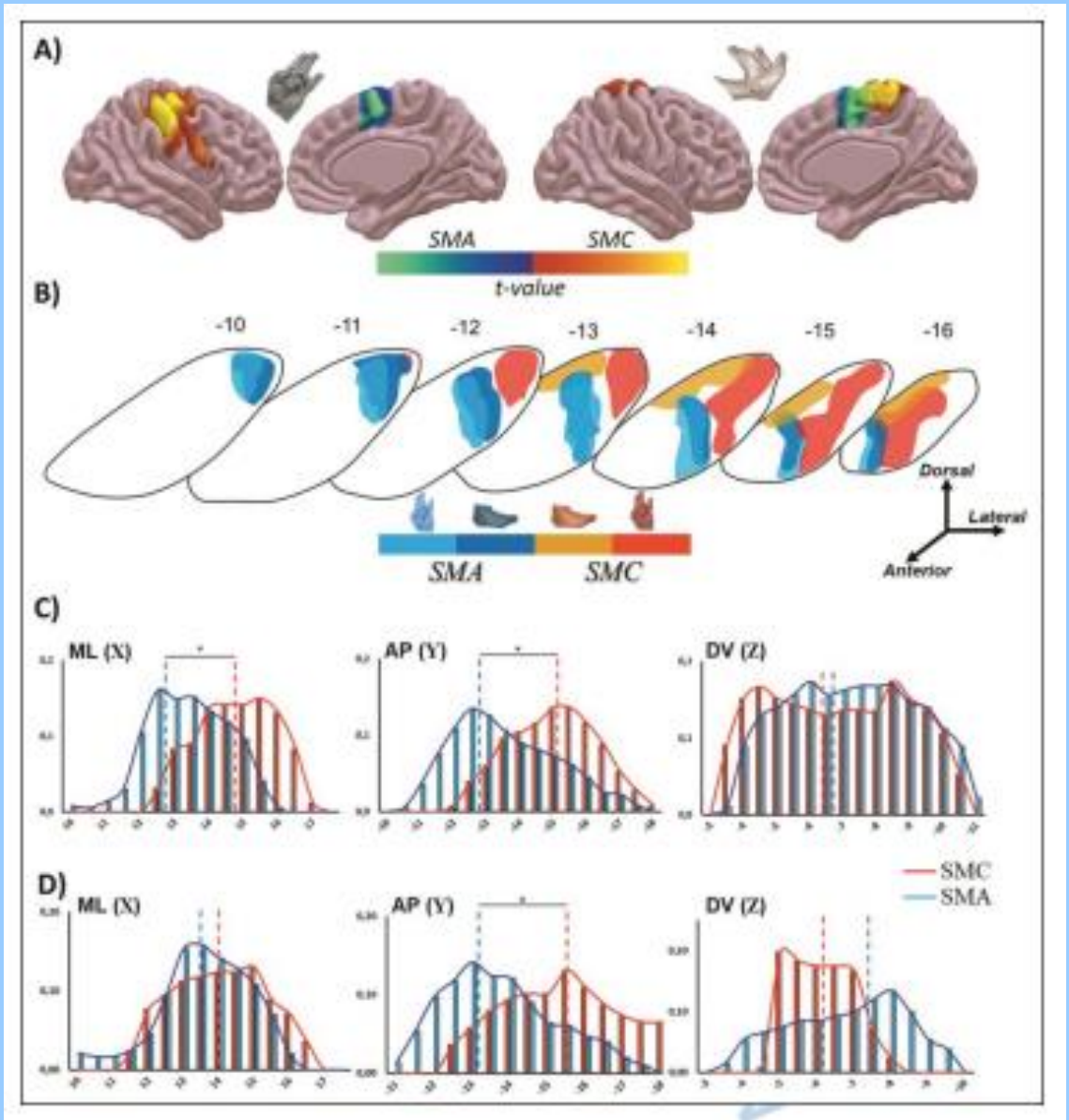


Figure 2. Distribution of fMRI-driven SMC and SMA connectivity profiles in the STN. A) Activation maps during right hand finger opposition (left panel) and foot flexion-extension (right panel) in SMC and SMA ($k > 50$, $P < 0.05$ FWE corrected), rendered on the left-hemisphere MNI152 brain mesh. (B) Coronal sections of the merged STN, depicting tractography-derived 50% thresholded maps of the functional regions resulting from the connectivity with functional cortical clusters. Histograms in the lower panels show the density of voxels in the STN, which are significantly connected with hand (C) and foot (D) cortical clusters according to MNI space coordinates, along the medial-lateral (ML), anterior-posterior (AP), and dorsal-ventral (DV) axes. Dashed vertical lines indicate median coordinates of the centroid (*significantly different at $P < 0.05$, Mann–Whitney test).

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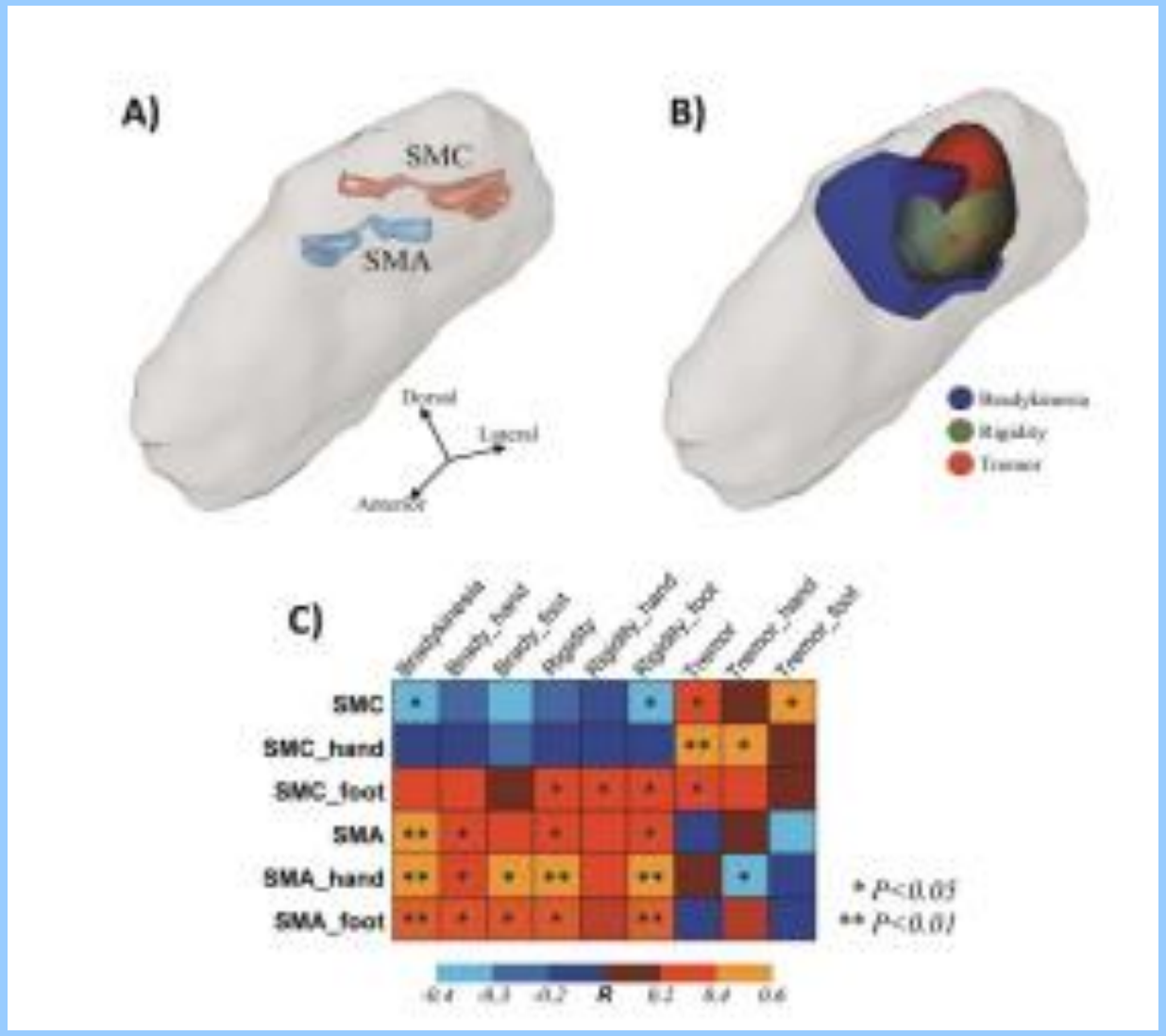
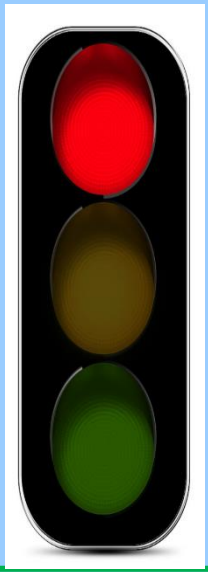


Figure 3. Functional connectivity profiles predictive of motor improvement after subthalamotomy. A) Functional topography of the STN is shown schematically in a rendered view. Hand and foot drawings depict the position of the COG of respective fMRI-based clusters. B) Rendering of effective lesions inducing >65% improvement in bradykinesia (blue), rigidity (green), and tremor (red) after tcMRgFUS-subthalamotomy. Volumes are thresholded to 0.7 (i.e. 70% of the selected patients contribute to the cluster). C) Pearson correlation heat map representing the correlation between the lesion-to-somatotopy distances and clinical efficacy. Positive and negative correlations are represented in hot and cold color maps, respectively, and discretized for visualization purposes.
Significance is indicated by * = $P \leq 0.05$, ** = $P < 0.01$.

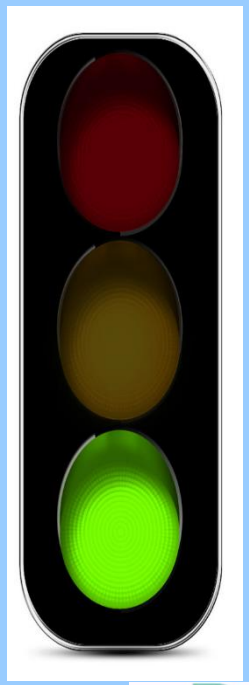
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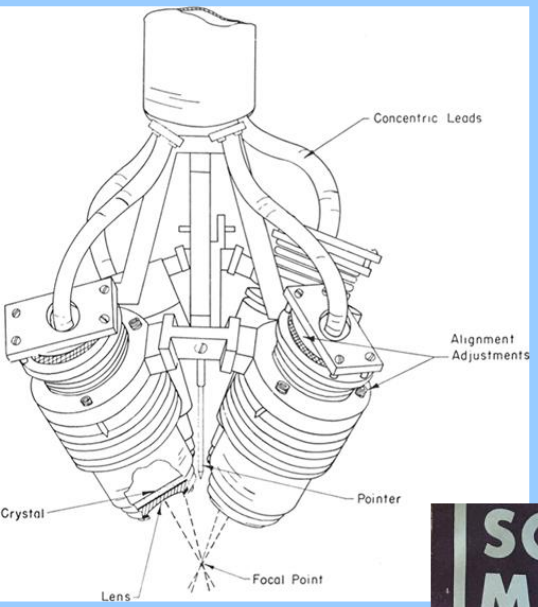
Discusión

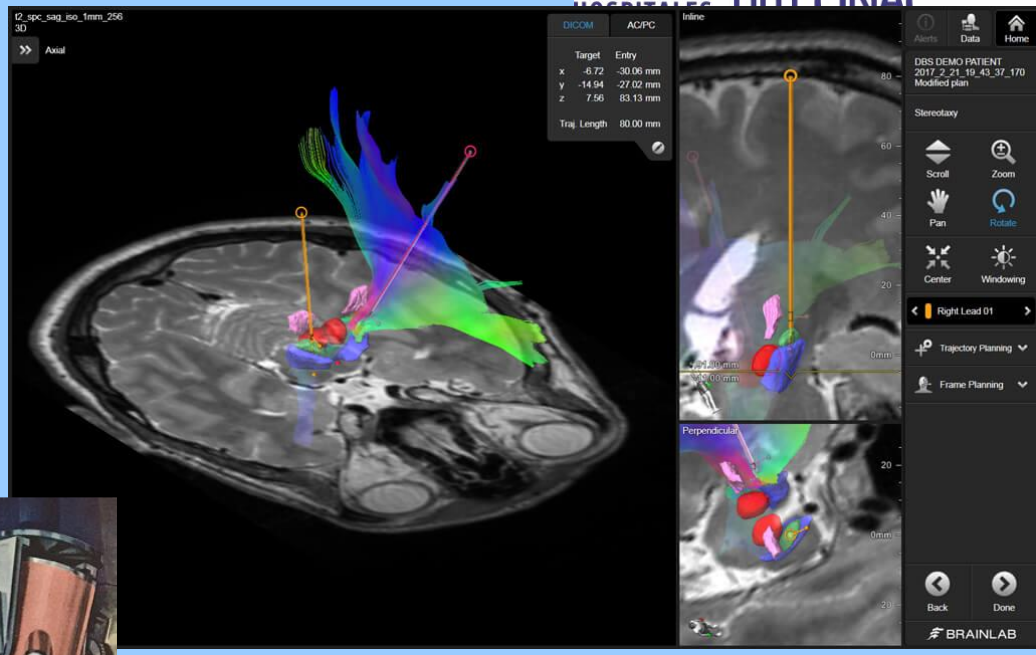


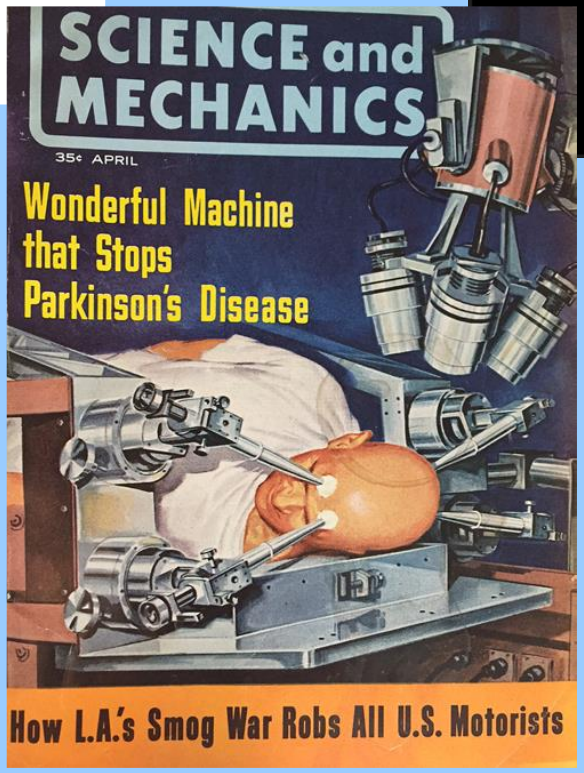
- No microrregistro
- No protocolos establecidos (número de sonicaciones, temperatura…)
- No con anestesia general.
- No seguimiento adaptativo.
- Unilateral ……..

- Imagen intraoperatoria integrada con la respuesta clínica.
- Mejor accesibilidad a las dianas, no problemas con trayectoria de acceso ni brain shift
- Menos invasivo, sin incisiones, no radiación ionizante.
- En una sesion única, corta hospitalización
- Sin implante de material: no infecciones, más barato.
- Seguimiento de pacientes más sencillo.







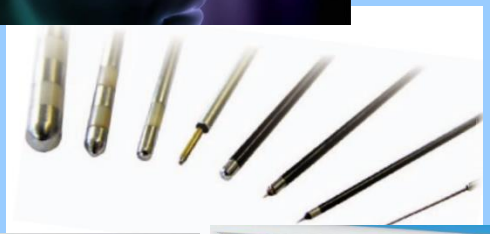


Meyers y Fry. Science Abril 1963

- No estudios comparativos con:
  - Estimulación cerebral profunda
  - Cirugía lesiva clásica
  - Radiocirugía











A COMPARISON OF CONTINUOUS THALAMIC STIMULATION AND THALAMOTOMY FOR SUPPRESSION OF SEVERE TREMOR

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(N Engl J Med 2000;342:461-8.)

A prospective single-blind study of Gamma Knife thalamotomy for tremor

Witjas et al. Neurology, 85
November 3, 2015

nature COMMUNICATIONS

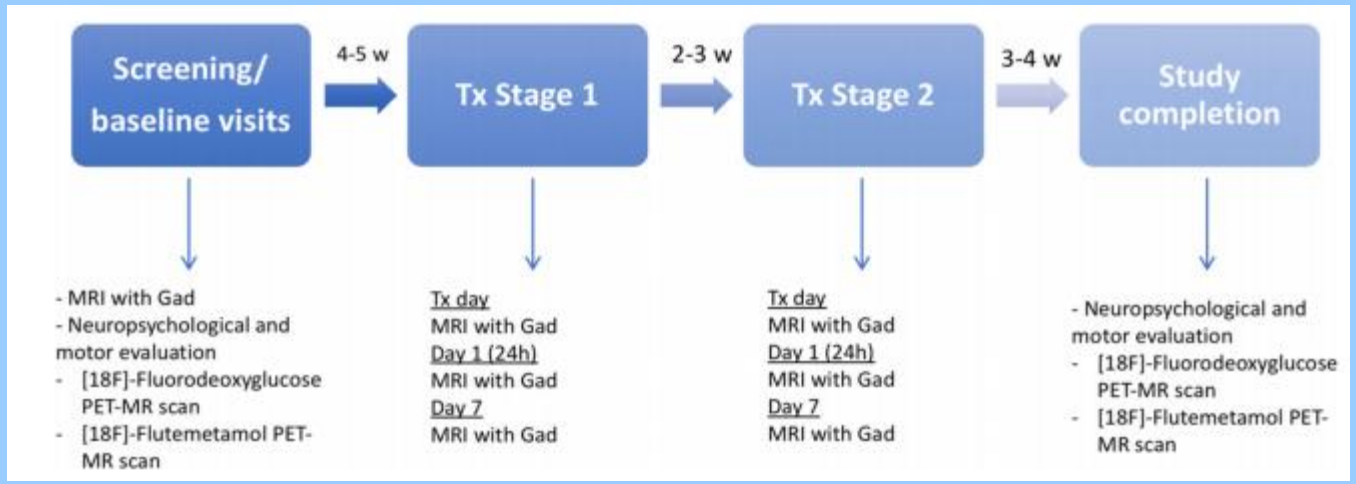
ARTICLE

https://doi.org/10.1038/s41467-021-21022-9 OPEN

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Blood-brain barrier opening with focused ultrasound in Parkinson's disease dementia

Carmen Gasca-Salas[1,2], Beatriz Fernández-Rodríguez[1,8], José A. Pineda-Pardo[1,2,8], Rafael Rodríguez-Rojas[1,2], Ignacio Obeso[1,2], Frida Hernández-Fernández[1,3], Marta del Álamo[1,2], David Mata[1,2], Pasqualina Guida[1,2], Carlos Ordás-Bandera[4], J. Ignacio Montero-Roblas[5], Raúl Martínez-Fernández[1,2], Guglielmo Foffani[1,2,6], Itay Rachmilevitch[7] & José A. Obeso[1,2]✉



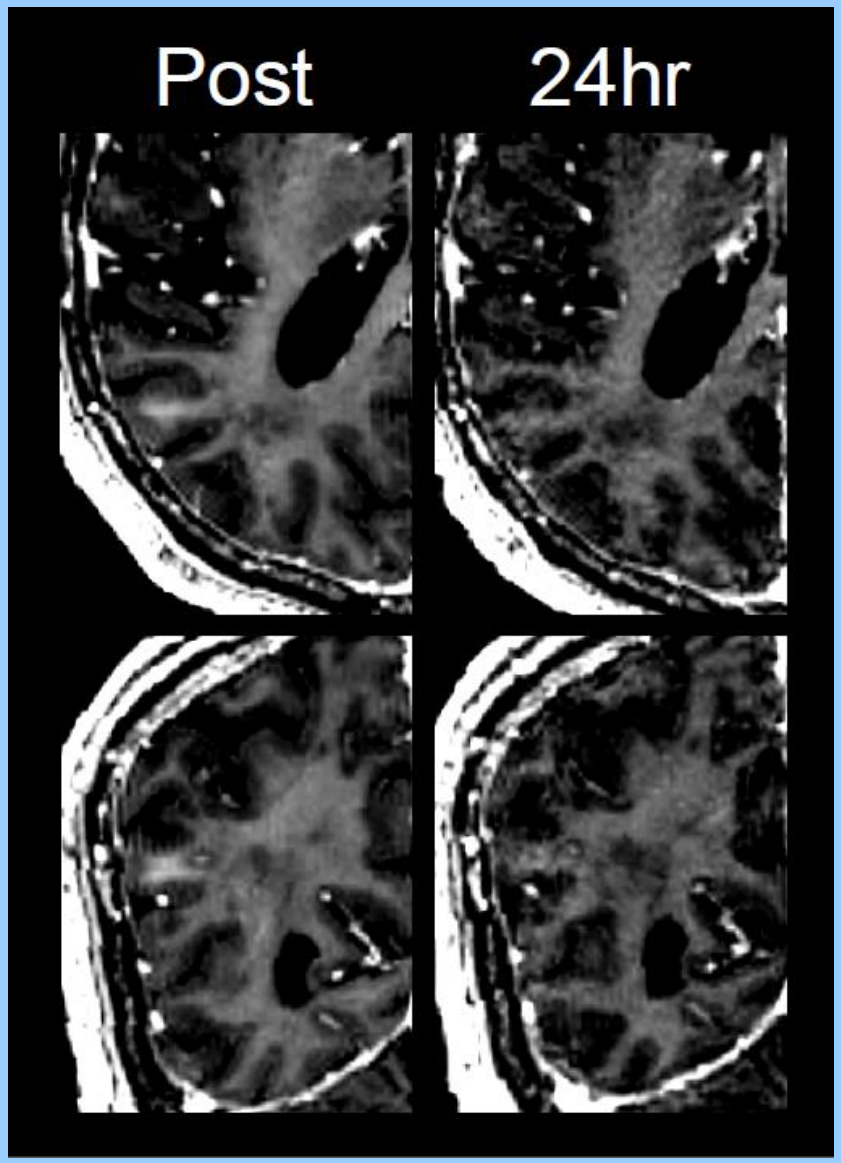
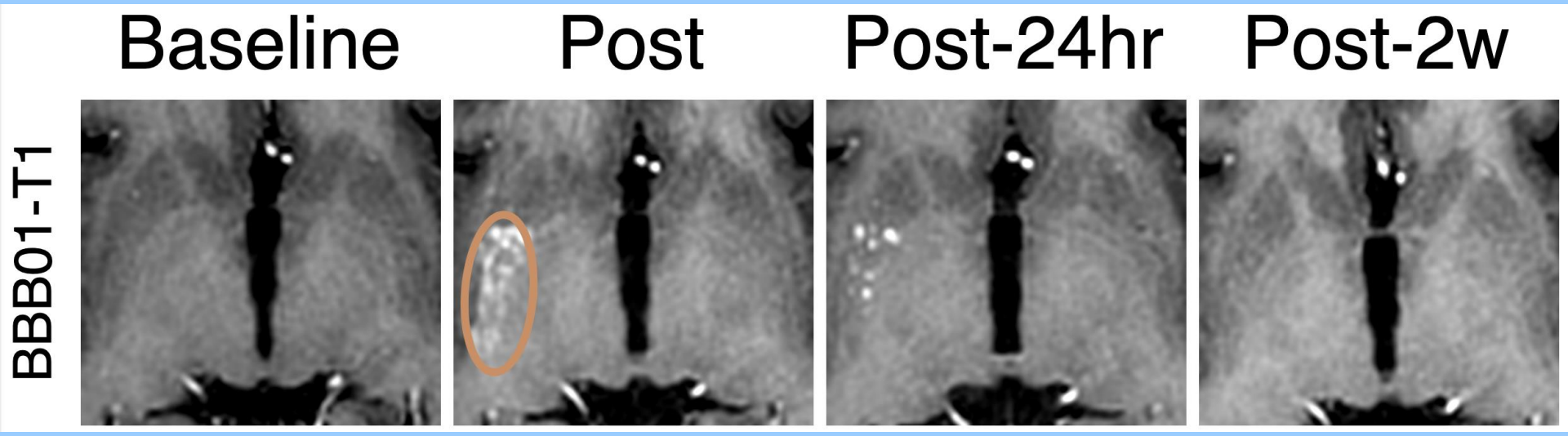


Table 2 Neuropsychological test scores.

Cognitive scores	Baseline	Post treatment (stage 2)
Screening tests		
MMSE	18.11 (3.9)	21.6 (3.4)
MoCA	14.4 (2.7)	15.00 (4.1)
Attention		
Digit span forward	3.60 (1.5)	3.40 (0.8)
Digit span backward	2.80 (0.4)	2.80 (1.3)
Memory		
Verbal memory (CERAD)		
Short term	2.80 (1.9)	4.60 (1.1)
Delayed recall	1.00 (1.2)	1.20 (1.5)
Recognition	15.40 (1.8)	17.00 (1.5)
Visual memory (WMS-IV)		
Short term	7.80 (5.2)	14.40 (10.2)
Long term	0.60 (1.3)	5.60 (6.1)
Recognition	1.40 (1.6)	2.80 (1.1)
Executive function		
Stroop test inhibition	11.40 (7.8)	17.25 (7.1)
Phonemic fluency	7.60 (4.5)	7.40 (4.6)
Language		
Semantic fluency	6.40 (2.3)	8.20 (3.3)
BNT	46.00 (7.2)	46.50 (7.8)
Visuospatial function		
JLO	10.4 (10.1)	13.8 (10.4)
VOSP silhouettes	16.6 (4.4)	19.6 (2.5)
Neuropsychiatric scales		
GDS	12.4 (5.9)	13.4 (5.5)
NPI	5.4 (3.4)	4.2 (3.1)

Data are presented as mean and standard deviation.
MMSE mini-mental state examination, *MoCA* Montreal Cognitive Assessment, *CERAD* Consortium to Establish a Registry for Alzheimer's Disease, *WMS* Wechsler Memory Scale, *BNT* Boston Naming test, *JLO* Judgment of Line Orientation, *VOSP* Visual Object and Space Perception, *GDS* Geriatric Depression Scale, *NPI* Neuropsychiatric inventory.

27 Lifus realizados



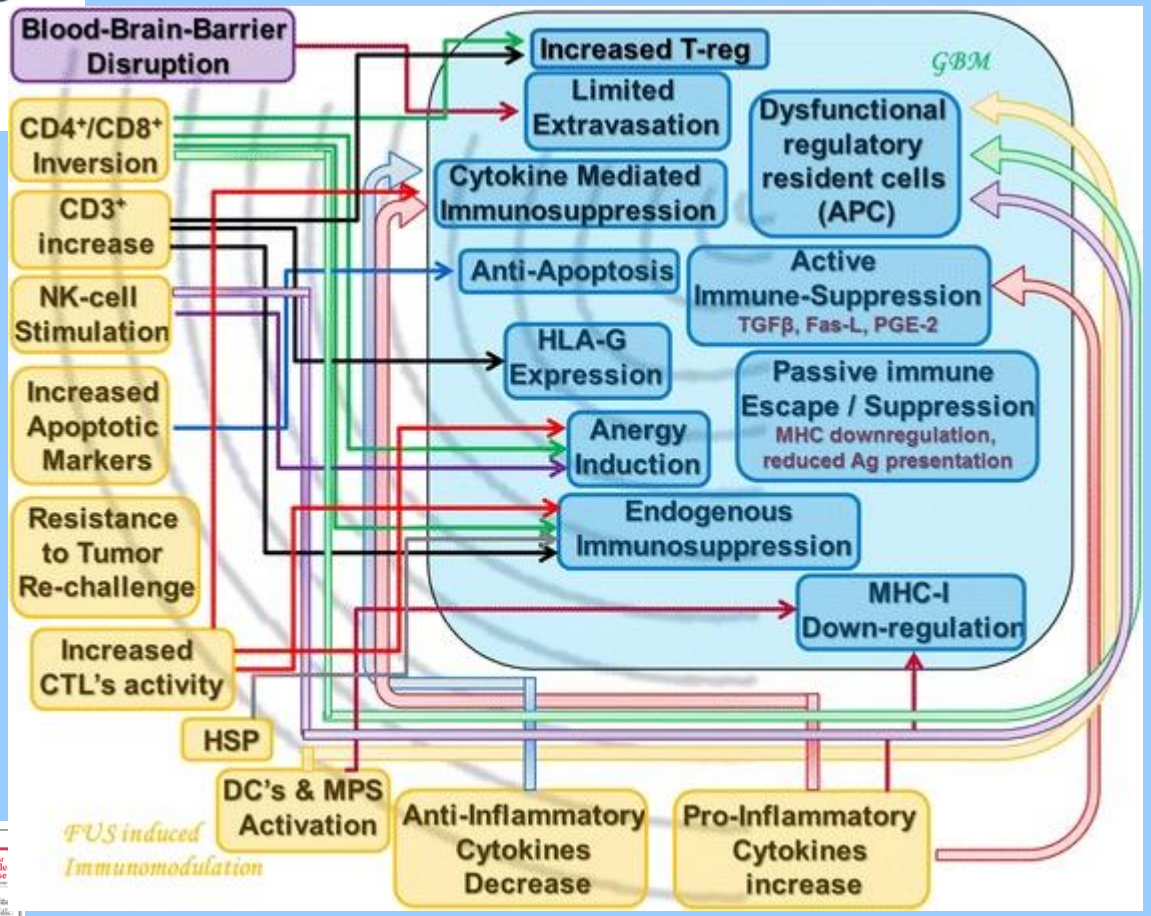
Cohen-Inbar *et al. Journal of Therapeutic Ultrasound* (2016) 4:2
DOI 10.1186/s40349-016-0046-y

Journal of Therapeutic Ultrasound

REVIEW Open Access

Focused ultrasound-aided immunomodulation in glioblastoma multiforme: a therapeutic concept

Or Cohen-Inbar[1,2*], Zhiyuan Xu[1] and Jason P. Sheehan[1]



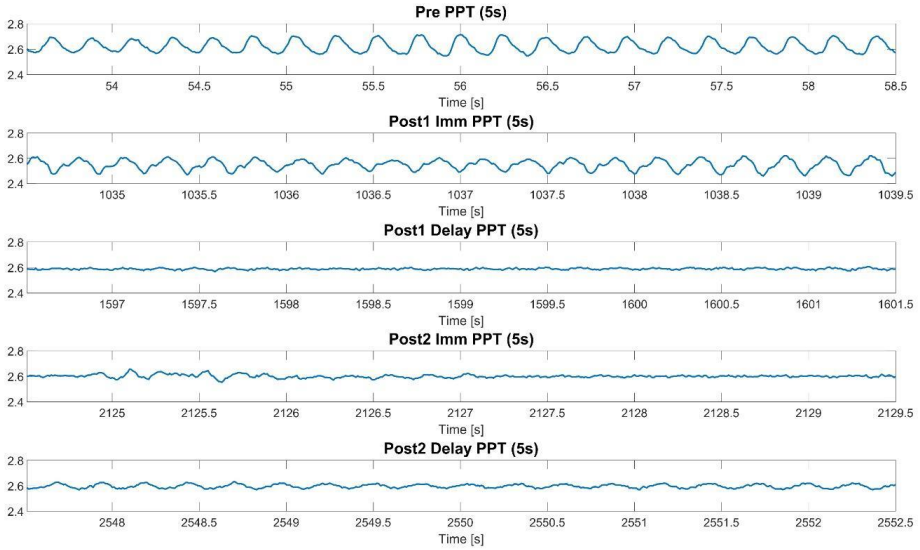
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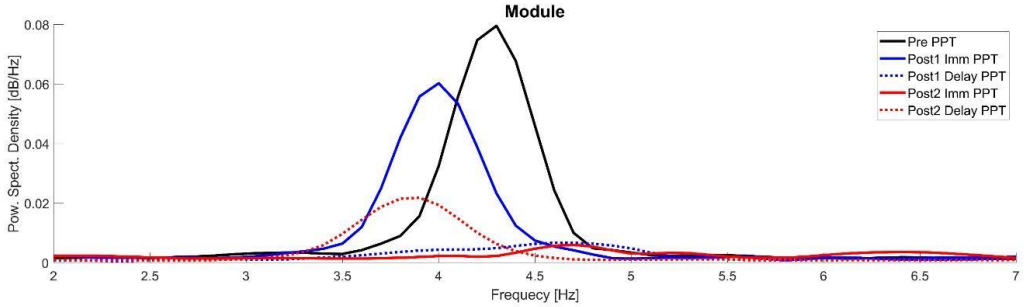
Journal of Controlled Release
Volume 295, 10 February 2019, Pages 130-139

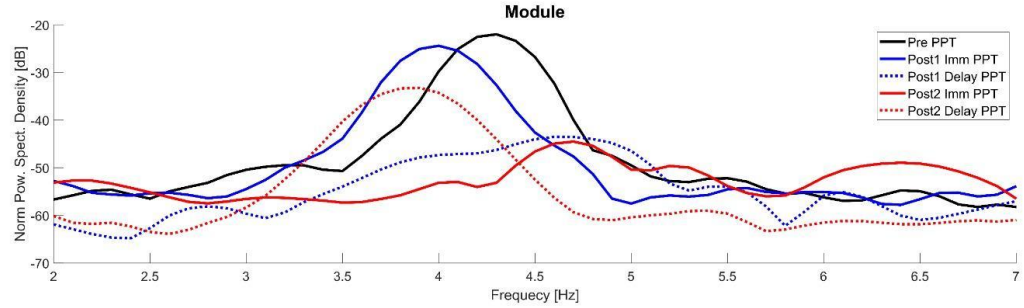
Chemotherapy sensitization of glioblastoma by focused ultrasound-mediated delivery of therapeutic liposomes

Alexandros Papachristodoulou [a, 1, 2], Rea Deborah Signorell [b, 1], Beat Werner [c], Davide Brambilla [b, 3], Paola Luciani [b, 4], Mustafa Cavusoglu [c], Joanes Grandjean [d, 5], Manuela Silginer [a], Markus Rudin [d], Ernst Martin [c], Michael Weller [a], Patrick Roth [a, *, 6], Jean-Christophe Leroux [b, 6]

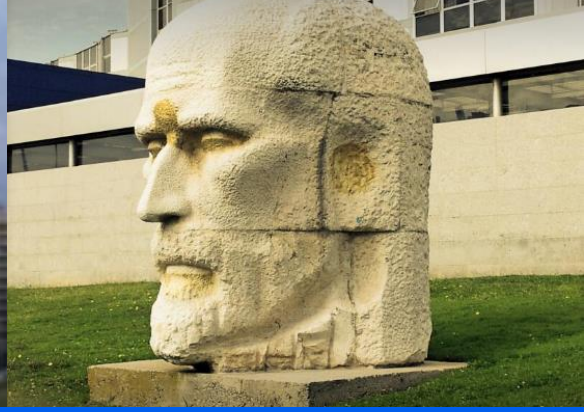
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Muchas gracias



