Original Research Paper

Volume-8 | Issue-11 | November-2018 | PRINT ISSN No 2249-555X

Neurosurgery

CLINICAL OUTCOME OF THE PATIENTS WITH SUBTHALMIC NUCLEUS DEEP BRAIN STIMULATION – WITH CALCULATED AND VISUAL TARGETS IN PARKINSONISM .

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ABSTRACT

Objectives: The purpose of this study was to evaluate the efficacy of Deep Brain Stimulation (DBS) at subthalmic nucleus in patients of Parkinsonism.

Patients and Methods: Total 30 patients down with idiopathic Parkinson's disease with excellent motor 'On' state after levodopa challenge response with disability were studied. The target(STN) was localised using 3 tesla MRI[Visual target] and calculated target on the basis of the AC and PC .The final targets achieved were finalized with MER with inomed software. Patients were informed about the study and benefits. Confidentiality of the participants was maintained at all the levels.

Results: Percent improvements in parameters like tremors, rigidity and dyskinesia was carried out preoperatively and post-operatively in both the target groups. The comparison of the effects of the stimulation on the different contacts at calculated group and the visual group showed that , in the visual target group the improvement was 88%, 75% and 58 % respectively in tremors, rigidity and dyskinesia in on state and in the calculated target group 62%, 46% and 58% improvement respectively in tremors, rigidity and dyskinesia in on state. There was statically significantly more improvement in visual target group in tremors ($p=0.040$) and rigidity ($p = 0.032$) than calculated group and insignificant ($p = 0.265$) improvement of dyskinesia between the 2 groups. The improvement in rigidity, tremor and the dyskinesia due to subthalamic nuclei stimulation correlated well with the improvement of the other sensory and motor parkinsonian symptoms.

Conclusion: Our results clearly suggested that the visual target with MER gave better clinical results than calculated targets with MER and the outcome of the patients showed significant improvement with least need of the medications.

KEYWORDS : DBS; Parkinsonism; calculated targets, visual target , response of DBS on STN.

INTRODUCTION

Electrical stimulation of motor cortex in primates was first performed by Fritsch and Hitzig in 1870. First cortical stimulation on human was performed by Bartholow. Since then electrical stimulation of the brain has played an increasing role in the investigation of brain functions and eventually for treatment of neurological diseases. In the 1970's and beginning of the 1980's it became evident that long term levodopa treatment eventually could have disabling complications such as levodopa induced dyskinesias1 . Other complications were the alleviation of motor symptoms for a period of time (ON stage) and then a sudden change into a stage where the patients were completely rigid and akinetic (OFF stage). Hence, there was a need to find an alternative method to ablative surgical methods, without irreversible side-effects. This resulted in the reappearance of chronic DBS in the treatment of movement disorders. The pioneering work started in 1987 and was led by Alim-Louis Benabid and Pierre Pollak2 Deep brain stimulation (DBS) was not for Parkinson's disease, until 1987 when two group2, 3 independently reported results of chronic thalamic stimulation for parkinsonian tremor with nearly all patients having significant tremor suppression. Contemporary surgical approaches to Parkinson's disease introduced in the early 1990s were built on advancements in understanding of the pathophysiology of Parkinson's disease. This understanding stemmed from physiological and neuroanatomical studies in the MPTP primate model of Parkinson's disease. Seminal reviews by others3,4 have put forth a model of basal ganglia function on the basis of the hypothesis that there were segregated circuits within the basal ganglia thalamocortical system each of which served a different function. Separate motor, limbic, associative, and oculomotor circuits were proposed. The "motor" circuit was thought to participate in the control of movement and to be intimately involved in the development of the motor symptoms associated with Parkinson's disease.

Traditionally, deep brain stimulation (DBS) surgery is performed using frame-based stereotaxy with help of physiologic mapping with microelectrode recording. The aim of this retrospective study was to compare the clinical outcomes of advanced PD patients following bilateral STN DBS in terms of the positioning of their electrodes when target is taken in two different ways – Calculated and Anatomical or visual targets in Parkinsonism. Electrode was passed to the calculated target and visual target in selected cases. The final positioning of the electrode checked by impedance monitoring, depth recording, and elicitation of evoked potentials and stimulation of presumed target.

2. MATERIALS AND METHODS:

This study was carried out at the Indraprastha Apollo Hospital, Sarita Vihar New Delhi in collaboration with Radiology department. Over 30 patients suffering from Parkinsonism were adopted in this study. 15 patients were studied with calculated target for stimulation and 15 patients were studied as visual target for stimulation . Inclusion criteria were: a diagnosis of idiopathic Parkinson's disease, age 30-75 years, good levodopa response, severe drug induced dyskinesia, no falls when "on" [pulls test], good bulbar function [particularly on "on" state]. Exclusion criteria were patients with pacemaker; patients with significant depression, patients with drug induced hallucinosis, postural instability and dysphonia, patients with significant psychotic symptoms. The final targets achieved in both the groups were finalised with MER with inomed software. Approval from the Ethical Committee was taken. 30 patients were studied. This was a prospective, open level study. Patients were informed beforehand about the study and benefits. Confidentiality of the participants was maintained at all the levels.

Study design

The BRW (Brown –Robert-Wells) frame was utilized, this has i) an N-shaped picket fence localizer ring ii) an arc- guidance frame and iii) a phantom base to confirm the target before applying the setting to the patient. For calculating the co-ordinates, MRI of the brain in stereotactic format was performed in neuroradiology department (Apollo hospitals, Delhi) and the data was stored in the computer. Thereafter the patients were mildly sedated and four points on the scalp was infiltrated with local anesthesia (Lidocaine). The ring is then fastened to the patient's skull with four pins, inserted through the anesthetized regions. The localizing ring was then attached to the base ring. The patient was again taken to the neuroradiology department where a CT brain was performed. The image obtained in conjunction with the localizing ring allowed us to compute the exact three dimensional position of the region of interest by the intersection of two projections (Fig 1).

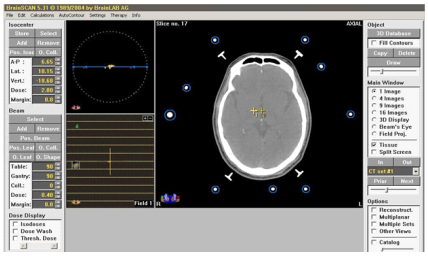


Fig 1 CT scan images used for merging in the frame link software

Well-established Cartesian (x, y, and z) target coordinates, relative to the mid-commissural point were used for planning electrode placement by frame link by Brain lab 5.31 software. Stereotactic target coordinates were discerned from frame link software that merges the MRI of the patient's brain with a brain atlas using plain CT. Once imaging was completed and a safe trajectory established, the patient was returned to the operating room. The size and position of the STN were highly variable. We had chosen two different ways for choosing the targets for DBS of the STN. These are anatomical [Visual] Targeting and calculated targeting. In anatomical [Visual] Targeting we used an imaging technique T2-weighted, non-volumetric fast acquisition 3 Tesla MRI, the STN was identified on both axial, sagittal and coronal slices. Sections selected were where the nucleus was seen at its maximum size from MRI, it was taken as visual target. The Coordinates were obtained by brain scan 5.31 software by brain lab, and the distance from the midpoint of AC-PC commissure was taken in all the x, y and z axis. In calculated targeting fusion of the CT and the MRI images were done on the frame link software, Axial slices obtained were parallel to the IC (AC-PC) plane. The sub thalamic nucleus target chosen was 12 mm lateral to midcommissural point, 2 mm posterior to midcommissural point and 6 mm below the AC–PC line on both sides. This point was taken as the calculated target (Fig 2)

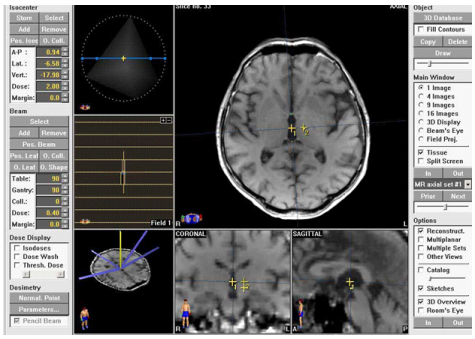
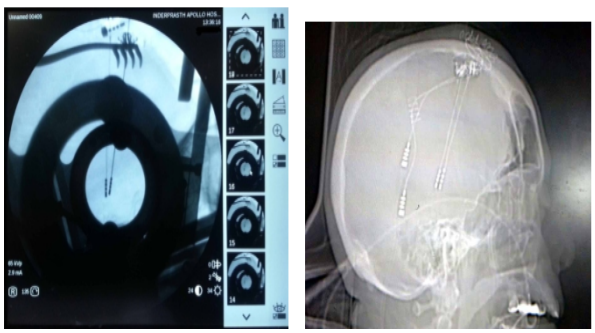


Fig 2 Localising the calculated target and getting the coordinates

Surgical technique

The patient was brought to the operating room. The frame fixed to the operating table with the head only slightly elevated above the chest to avoid air embolism. A small patch of hair shaved over the appropriate region. The stereotactic arc brought into the target position. After local anaesthesia, burr holes were made. Electrode was passed to the calculated target and visual target in selected cases. The final position of the electrode was checked by impedance monitoring, depth recording, and elicitation of evoked potentials and stimulation of presumed target. Lesion was made at the specified target (Fig 3)



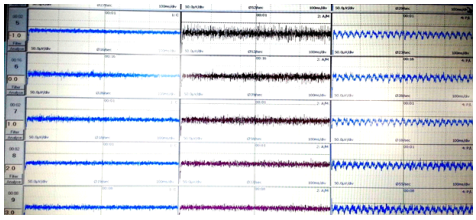


Fig 3) Final position of the target is checked by electrode checked by impedance monitoring, depth recording, and elicitation of evoked potentials and stimulation of presumed target.

Clinical rating scales

The clinical improvements of the patients were studied preoperatively and postoperatively considering the tremors, rigidity and dyskinesia/akinesia calculated accordingly to the UPDRS score. The Unified Parkinson Disease Rating Scale (UPDRS) is designed to monitor Parkinson Disease disability and impairment.

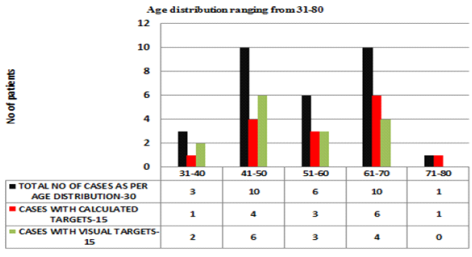
Statistical significance:

Statistical analysis of the data was performed by using Statistical Package for the Social Sciences Version 20 SPSS version 20 , Paired T Test, Wilcoxon signed rank test and by R software with KW Test , Mann Whitney and t-stat ,To indicate statistical significance p value<0.01 for paired t test and <0.05 for Wilcoxon signed rank test , KW Test , Mann Whitney and t-stat was taken.

3 RESULTS:

Patients' characteristics / clinical outcomes.

30 patients with idiopathic Parkinson's disease with excellent motor 'On' state after levodopa challenge response with disability were enrolled in this prospective study. A total of 53 points were stimulated. The mean age was 54.66 years and the age range was 38- 72 years. Out of 30 patients, 13 (43.34%) patients were of 50 years or below. The mean age of presentation for females was 58 years, where as in females in whom calculated target of STN was taken mean age was 53.5 years, and where visual target of STN taken mean was 59.8 years. The mean age of presentation for males was 48.3 years, where as in males in whom visual target of STN was taken, mean age was 57 years, and where calculated target of STN was taken mean was 48.3 years. Age range for females was 47- 66 years and for males it was 38- 72 years (Fig 4). Out of 30 patients 7 (23.34%) were female and 23 (76.66%) patients were males. 2 females and 13 males were studied with visual target for DBS surgery. 5 females and 10 males were studied with calculated target for DBS surgery.



AGE DISTRIBUTION-30	31-40	41-50	51-60	61-70	71-80
TOTAL NO OF CASES AS PER	3	10	6	10	1
CASES WITH CALCULATED TARGETS-15	1	4	3	6	1
CASES WITH VISUAL TARGETS-15	2	6	3	4	0

In the visual target group, 5 out of 15 patients had unilateral stimulation of the STN (3 left sided and 2 right sided) and 10 patients had bilateral stimulation. Similarly, in the calculated target group out of 15 patients, 2 patients had unilateral left sided stimulation of the STN and 13 patients had bilateral stimulation.

The final target stimulated after the MER in calculated and visual targets.

In calculated target group, 26.7% (4 patients at 7 STN's.) it was necessary to modify the stereotactical coordinates to reach the target, always by a vertical correction with mean of 5.62 mm on the right side and 5.75 mm the left side. The final target in this group after MER was 2 mm posterior, 12 mm lateral and 5.62±0.506mm inferior to the midcommisural point on the right side (Table1). In visual target group, a significant percentage 73.34 %, (11 patients at 19 STN's) of the accuracy of the target were confirmed by MER and adjustment was done . Our surgical target is based on the Schaltenbrand and Wahren

atlas coordinates with variation to the vertical axis whereas in Visual targets groups, the necessity to variation for the reaching of the STN in visual group was in significant percentage of cases 87% (13 patients) and only 13 % (2 patients) had accuracy. The calculated target group from the MRI targets were 1.18 ±1.07 mm posterior, 12.1± 0.86 mm lateral and 5.33 ±1.03 mm inferior to the midcommisural point on the right side and 1.20±1.06mm posterior, 11.73±1.66 lateral and 5.35±1.07 mm inferior to the midcommisural point on the left side. The final target after the MER was 5.49±0.39 mm inferior on the left side and 5.41±0.41mm inferior to the midcommisural point on the right side (Table 2). In 6 patients the best MER was obtained at 1 mm above the visual target at 11 STN's and 1 mm below the calculated target in 6 patients at 11 STN's. In one individual the target was taken 2 mm down at both right and left STN's (Table 3.1 and 3.2) Comparison of tremors, rigidity and dyskinesia preoperatively and postoperatively in patients with different targets.

The comparison of the effects of the stimulation on the different targets showed that , In the visual group the improvement was 88%, 75% and 58 % respectively in tremors, rigidity and dyskinesia in on state. In the calculated target group it was only 62%, 46% and 58% in tremors, rigidity and dyskinesia respectively. There was statically significantly more improvement in visual target group in tremors (p=0.040) and rigidity (p = 0.032) than calculated group and insignificant (p = 0.265) improvement of dyskinesia between the 2 groups charts {5a, 5b , 6a ,6b, 7a and 7b}

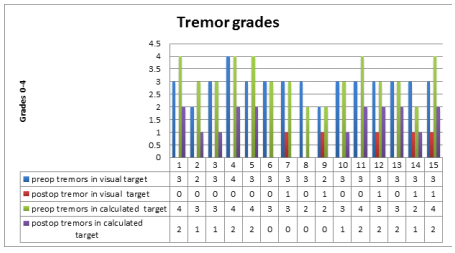


Fig 5 (a) Comparison of tremors in the patients preoperatively and postoperatively with different targets.

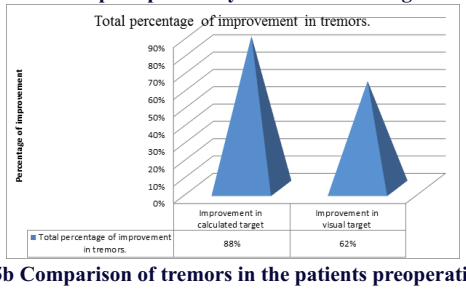


Fig 5b Comparison of tremors in the patients preoperatively and postoperatively with different targets.

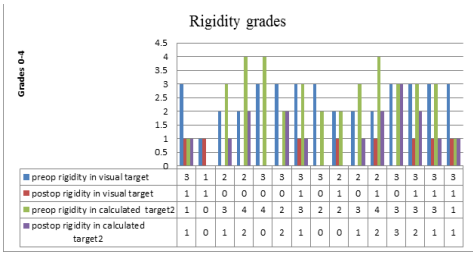


Fig 6a. Comparison of rigidity in the patients preoperatively and postoperatively with different targets.

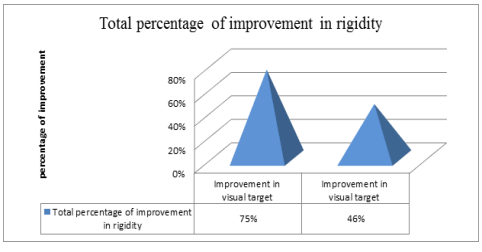


Fig 6b. Comparison of rigidity in the patients preoperatively and postoperatively with different targets.

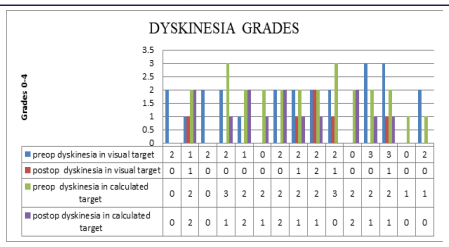


Fig 7b. Comparison of dyskinesia in the patients preoperatively and postoperatively with different targets.

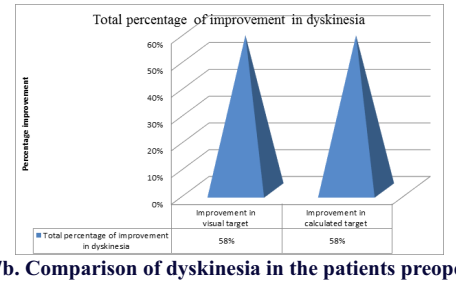


Fig 7b. Comparison of dyskinesia in the patients preoperatively and postoperatively with different targets.

Statistical significance

One sample test for the probability testing was applied wherein testing at 0.01 on 99% confidence limit was carried out. Since the P value at calculated targets is equal to 0.019 so we accept the null hypothesis therefore we say that the calculated targets are more close after the MER also. Whereas the p value at visual targets is equal to 0.000 so we fail to accept the null hypothesis and we conclude that MER points are significantly differ from visually obtained points, so calculated targets are better than visual targets (Table 4). Wilcoxon method for testing the clinical improvement was applied wherein the testing at 95% confidence limit was done.

DISCUSSION

We describe the clinical outcomes of STN DBS at subthalmic nucleus when target is taken in two different ways – Calculated and Anatomical or visual targets in a series of 30 advanced Parkinson's disease patients with excellent motor 'On' state. Overall the surgery was well tolerated, with the exception of one patient developed thalamic bleed; the patient was managed with conservative treatment. The visual target of the subthalamic nuclei 5-7 were the closest to the final target, confirmed by microelectrode recording5, 7, as similarly reported , visual target as possibly more accurate 8, 9,10, 11,. Patients achieved the best results in Unified Parkinson's Disease Rating Scale scores in both “on and off” state12. The improvement in rigidity, tremor and the dyskinesia due to subthalamic nuclei stimulation correlated well with the improvement of the other sensory and motor parkinsonian symptoms13. A trajectory of 50˚-60˚was used14, which correlated with the alignment of the subthalamicnuclei. An accuracy of 73.34 % was achieved in localising the subthalamic nuclei, confirmed with microelectrode recording. The best results were achieved in the dorsolateral portion of the subthalamic nuclei 15, 16. The dorsolateral portion of the nucleus seems to be involved in the sensorimotor circuits14, 17 so had better postoperative results in Unified Parkinson's Disease Rating Scalein the calculated group. The ventral portion of subthalamic nuclie which was better visualised in the magnetic resonance imaging is associative areas and has connections with the limbic system18. Consequently the results in the visual group were not as good as the calculated group if all the coordinateds anr modified as per MER but this increases the chances of the bleeding and complications . The surgery was well tolerated14, 16, barring one patient who developed a thalamic bleed14, 16 and he also improved with full recovery.

It is likely that there were several unavoidable errors in this study e.g the estimation of the positions of the electrodes based on the fused images of magnetic resonance imaging /computed tomography, direct visualisation of subthalamic nuclei on account of image fusion, inter-evaluator errors, and errors in plotting the electrodes in the brain atlas based on the fused images19,20. Secondly there are distortions in the magnetic resonance imaging which may lead the displacement of the targets in the visual group17. Thirdly the calculated targets are fixed whereas there are variations in the visual targets with change of posture and after dural incision with CSF drainage. Fourthly, it is rare that all

the borders of the subthalamic nuclei are visualised with precision, while the commissures are always clearly identified14, 17.

Finally, the long-term outcome of the patients who underwent programming after subthalamic nuclei deep brain stimulation needs to be assessed. Our results clearly suggested that the visual target with MER21, 22 gave better clinical results than visual targets with MER.

Final Calculated Target in 'mm'

Table 1: Data shows the final target stimulated after the MER in calculated targets

Right side			Left side		
AP	Lateral	Vertical	AP	Lateral	Vertical
2	12	6	2	12	6
2	12	5	2	12	5
_	_	_	2	12	6
2	12	6	2	12	6
2	12	5	_	_	_
_	_	_	2	12	6
2	12	6	_	_	_
2	12	6	2	12	6
2	12	5	2	12	5
2	12	5	2	12	5
2	12	5	_	_	_
2	12	6	2	12	6
2	12	6	2	12	6
2	12	6	2	12	6
2	12	6	2	12	6

Empty cell means unilateral stimulation on other side

Table 2: The final target stimulated after the MER in visual targets

Final Visual Target in 'mm'					
Right side			Left side		
AP	Lateral	Vertical	AP	Lateral	Vertical
2.3	11.16	5	2.32	11.16	5
-1	12.94	5.21	-1	12.95	5.23
_	_	_	2.2	6.54	5.57
1.5	11.15	5.66	1.6	11.15	5.66
1.8	12.9	5.06	1.7	12.9	5.06
2.5	13	5	2.4	13.2	6
2.2	12.16	5.08	2.2	12.16	5.08
0.9	11	5	0.9	11.2	5.23
1	11.29	6	1	11.29	5.97
1	11.14	5.83	1	11.11	5.84
_	_	_	0.2	11.56	5.12
-0.3	12.89	5.22	-0.3	12.88	5.24
1.5	12.97	5.34	1.8	12.96	5.34
0	13	6	0	13.2	6
2	11.78	6	2	11.78	6.01

Empty cell means unilateral stimulation on other side

Table 3.1: 3.2

	Calculated Target AP Right	Calculated Target Lateral Right	Calculated Target Vertical Right	Final Calculated Target right after MER	Calculated Target AP Left	Calculated Target lateral Left	Calculated Target Vertical Left	Final Calculated Target Left after MER	
N	Valid	14	14	14	13	12	12	12	12
	Missing	16	16	16	17	18	18	18	18
Mean		2.00	12.00	6.00	5.62	2.00	12.00	6.00	5.75
Mode		2	12	6	6	2	12	6	6
Std. Deviation		.000	.000	.000	.506	.000	.000	.000	.452
Minimum		2	12	6	5	2	12	6	5
Maximum		2	12	6	6	2	12	6	6

		Visual Target AP Right	Visual Target Lateral Right	Visual Target Vertical Right	Final Vertical Visual Target Right after MER	Visual Target AP LEFT	Visual Target Lateral LEFT	Visual Target Vertical LEFT	Final Visual Target Vertical Left after MER
N	Valid	13	13	13	15	15	15	15	13
	Missing	17	17	17	15	15	15	15	17
Mean		1.1846	12.1062	5.3392	5.4907	1.2013	11.7360	5.3567	5.4154
Mode		1.00[a]	13.00	4.00[a]	5.23[a]	1.00[a]	13.20	5.00	5.00[a]
Std. Deviation		1.07148	.86727	1.03874	.39092	1.06249	1.66233	1.07711	.41828
Minimum		-1.00	11.00	4.00	5.00	-1.00	6.54	4.00	5.00
Maximum		2.50	13.00	7.00	6.02	2.40	13.20	6.97	6.00

a. Multiple modes exist. The smallest value is shown

Table 4 : One-Sample Test showing significance statistical significance of the calculated targets.

	Test Value = 0					
	t	df	Sig. (2-tailed)	Mean Difference	99% Confidence Interval of the Difference	
					Lower	Upper
MER at visual	2.646	14	.019	.333	-.04	.71
MER at calculated	7.897	14	.000	.93333	.5815	1.2852

REFERENCES:

1. Schwartz, A., Rosenberg, G., Spencer, A., Barbeau, A., Mars, H. & Libman, I: The effects of levodopa therapy in patients with Parkinson's disease. I. Clinical response. Can Med Assoc J, (1972) 107, 973-6.
2. Hassler, R., Riechert, T., Mundinger, F., Umbach, W. & Ganglberger, J.A: Physiological observations in stereotaxic operations in extrapyramidal motor disturbances. Brain, (1960) 83, 337-50.
3. Bechtereva, N. P. & Hughes, H. K. Implanted electrodes: experimentation on humans: Am J Psychiatry, (1971) 127, 1422-3.
4. Benabid, A. L., Pollak, P., Louveau, A., Henry, S. & De Rougemont, J: Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson disease. Appl Neurophysiol, (1987) 50, 344-6.
5. , Egidi M, Pesenti A, Rohr M, Rampini P, Locatelli M: Do intraoperative microrecordings improve subthalamic nucleus targeting in stereotactic neurosurgery for Parkinson's disease? J Neurosurg Sci. 2003 Mar;47(1):56-60.
6. , Meuli R, Maeder P, Vingerhoets F, Ghika J, Villemure JG:Subthalamic nucleus deep brain stimulation for Parkinson's disease: magnetic resonance imaging targeting using visible anatomical landmarks. Stereotact Funct Neurosurg. 2003;80(1-4):76-81.
7. , Mitchell RD, Mocroft P, Westby GW, Milner J, Pall H:Targeting the subthalamic nucleus for deep brain stimulation: technical approach and fusion of pre- and postoperative MR images to define accuracy of lead placement. J Neurol Neurosurg Psychiatry. 2005 Mar; 76(3):409-14.
8. Littlechild P, Varma TR, Eldridge PR, Fox S, Forster A, Fletcher N et al,. Variability in position of the subthalamic nucleus targeted by magnetic resonance imaging and microelectrode recordings as compared to atlas co-ordinates. Stereotact Funct Neurosurg. 2003;80(1-4):82-7.1
9. Slavin KV, Thulborn KR, Wess C, Nersesyan H: Direct visualization of the human subthalamic nucleus with 3T MR imaging.AJNR Am J Neuroradiol. 2005 Jan;27(1):80-4.
10. , Khan S, Gill SS:Comparison of atlas- and magnetic-resonance-imaging-based stereotactic targeting of the subthalamic nucleus in the surgical treatment of Parkinson's disease.Stereotact Funct Neurosurg. 2008;86(3):153-61.
11. Daniluk S, G Davies K, Ellias SA, Novak P, Nazzaro JM: Assessment of the variability in the anatomical position and size of the subthalamic nucleus among patients with advanced Parkinson's disease using magnetic resonance imaging.Acta Neurochir (Wien). 2010 Feb;152(2):201-210
12. Limousin P, Krack P, Pollak P,et al. Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease.N Engl J Med 1998;339:1105–11
13. Schaltenbrand G, Wahren W. Atlas for Stereotaxy of the Human Brain. Stuttgart, New York: Thieme; 1977.
14. Starr PA, Christine CW, Theodosopoulos PV, Lindsey N, Byrd D, Mosley A, Marks WJ Jr: Implantation of deep brain stimulators into the subthalamic nucleus: technical approach and magnetic resonance imaging-verified lead locations. J Neurosurg. 2002 Aug;97(2):370-87.
15. , Thulborn KR, Wess C, Nersesyan H: Direct visualization of the human subthalamic nucleus with 3T MR imaging.AJNR Am J Neuroradiol. 2005 Jan;27(1):80-4.
16. Kahn, Pierre-Francois, Benoit Dawant, Laura Allen , Koa Chris , Charles P David, Konrad Peter: Deep Brain Stimulation in Early Stage Parkinson's Disease: Operative Experience from a Prospective, Randomized Clinical Trial:–J Neurol Neurosurg Psychiatry. 2012 Feb; 83(2): 164170.
17. Hamel W, Fietzek U, Morsnowski A,Schrader B, Herzog J, Weinert D et al,. Deep brain
18. stimulation of the subthalamic nucleus in Parkinson's disease: evaluation of active electrode contacts. J Neurol Neurosurg Psychiatry. 2003 Aug; 74(8): 1036–1046.
19. Lanotte M M, Rizzone M, Bergamasco B, Faccani G, Melcarne A, Lopiano L : Deep brain stimulation of the subthalamic nucleus:anatomical, neurophysiological, and outcome correlations with the effects of stimulation. J Neurol Neurosurg Psychiatry 2002;72:53–58
20. ,Chao-Chin Lee, Sheng-Huang Lin, Yue-Long Hsin, Tien-Wen Lee, Pao-Sheng Yen, et al: Microelectrode recording can be a good adjunct in magnetic resonance image–directed subthalamic nucleus deep brain stimulation for parkinsonism. Surgical NeurologyVolume 65, Issue 3, March 2006, Pages 253–260
21. Lanotte M M, Rizzone M, Bergamasco B, Faccani G, Melcarne A, Lopiano L : Deep brain stimulation of the subthalamic nucleus:anatomical, neurophysiological, and

outcome correlations with the effects of stimulation. J Neurol Neurosurg Psychiatry 2002;72:53–58
22. Guridi J , Rodriguez MC, Lozano,Moro, Albanese,Nuttin et al;Targetting the basal ganglia for deep brain stimulation in Parkinson's disease: Neurology 2000;55(Supll);S21-S28
23. Hamani C, Richter EO, Andrade-Souza Y, Hutchison W, Saint-Cyr JA, et al:Correspondence of microelectrode mapping with magnetic resonance imaging for subthalamic nucleus procedures. Surg Neurol. 2005 Mar;63(3):249-53; discussion 253.