

Functional Neurosurgical Program

Movement Disorders Surgery

On completion of 100 DBS surgeries

Surgical Treatment for Parkinson's disease in India



Parkinson's disease affects 150 000 patients in France, whose population is about 50 millions. There are probably several million people affected by this disease in India. The medical treatment is remarkably efficient in a large number of patients. However, 10 to 20 percent of these patients will eventually not be adequately controlled by this medication. Since

20 years, surgery has been reintroduced, particularly using the new method of deep brain stimulation at high frequency (introduced in 1994), which has the advantages of being adaptable, reversible, and has a very low morbidity and mortality. Particularly few teams in India have been performing it with the highest qualification. The drawback of this surgery is that it needs an expensive hardware. However, it has been proven that the long term cumulative cost of medication over a similar period of time might be even higher than the cost of the surgery and of its implanted components. It is clear that progress in technology will make these equipments more easily available, because of the reduced costs. There is no doubt that the Indian industry will be soon able to produce these stimulators at a very affordable price, thereby helping the usage of this method to aid advanced Parkinsonian patients in developing countries.

Another alternative of making a lesion in the surgical target which is used for deep brain stimulation, particularly in the subthalamic nucleus, has to be considered as a valid option. It requires an even more careful surgical practice. I personally know Dr. Paresh Doshi in Mumbai, who has been trained at my institution for this particular surgery and whom I visited on two occasions in Mumbai. **As the father of the method**, I'm proud to see that it has been expanded around the world and that particularly in India, it has been and it is successfully applied in a routine fashion. I'm proud to see that this method is helping seriously affected patients in India, and I am confident that this will continue.

Professor Alim Louis Benabid, M.D., Ph.D.

Head of Functional Neurosurgery at the University Hospital of Grenoble, Professor of Biophysics.

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Jaslok Hospital & Research Centre

Message from Dr. Paresh K. Doshi



Dear Colleague,

It gives me great pleasure to bring this **second newsletter** to you. As mentioned earlier, this newsletter will focus on the surgical treatment of Movement Disorders. Movement disorders are the third common neurological diseases after stroke and epilepsy. The prevalence of

Parkinson's disease, the commonest movement disorder, is 8-22/10000. This newsletter coincides with World Parkinson's Day which is observed on 11th April every year.

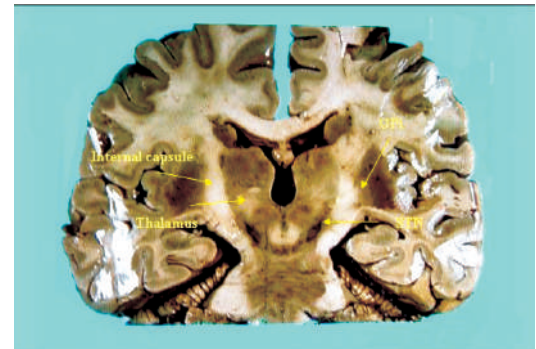
We started movement disorders surgery in 1997. We initially performed pallidotomies and thalamotomies for PD. However, in 1999, six years after the first published report of bilateral subthalamic nucleus (STN) stimulation for advanced PD by Prof. Benabid, we felt the need for introducing STN stimulation in our surgical armamentarium. I traveled to France and Austria to learn the finer aspects of these surgeries and performed the first STN stimulation in October 1999. Since then we have performed around 165 movement disorders surgeries including 104 cases of deep brain stimulation (DBS). The number of DBS surgeries, one of the most complex of all neurosurgeries, is not only highest in India but also in South East Asia. These surgeries have been performed in strict confirmation to international standards and protocol. The necessary clinical expertise and infrastructure have been comparable to the best centres in the world. In this newsletter I plan to bring to you the current understanding about movement disorders surgery, our philosophy of treatment and our results.

Dr. Paresh K. Doshi

In-charge, Stereotactic & Functional Neurosurgical Program
Jaslok Hospital and Research Centre, Mumbai.

There are three target nuclei groups used for modulating /controlling movement disorders, viz Ventro Intermedius nucleus (Vim) of thalamus, Globus pallidus internus (Gpi) and the Subthalamic nucleus (STN). (Fig. 1)

Two types of surgeries are practiced for MD, one is lesion and the other is DBS. DBS involves implantation of electrodes in one of the target nuclei, which is connected by a subcutaneous wire to a pacemaker implanted in the infraclavicular region. The advantage of this surgery is the flexibility of external programming, which helps to titrate the stimulation to suit individual patient requirement. Lesion involves selective destruction of one of the target nuclei. (Fig. 2, 3, 4) The advantages and disadvantages of lesion and DBS have been summarized in Table I.

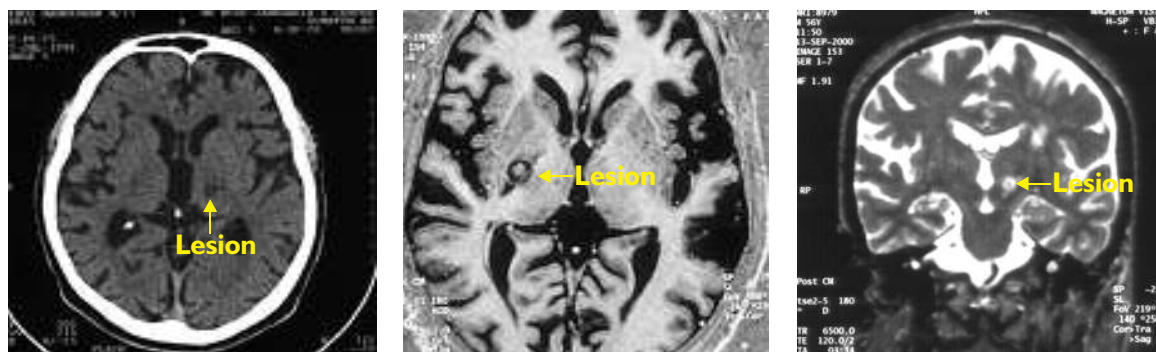


(Fig. 1) Movement Disorder surgery targets

The three common MD that can be treated surgically include PD, Tremors and Dystonia.

Tremors:

PD and essential tremor (ET) are the most common causes of tremors. Eight out of ten patients with PD tremors and most of ET patients, can be conservatively managed with medical treatment. Patients with intractable ET or PD tremors can be offered surgical treatment. Other forms of tremors that can be controlled by surgery include multiple sclerosis tremors, rubral tremors, post stroke tremors, etc. We prefer Vim as target for all kinds of tremors except for PD tremor, where we use STN as our target. A lesion or DBS in this area can achieve good tremor control.



(Fig. 2, 3 and 4): Thalamotomy, Pallidotomy and STN lesion

Parkinson's Disease:

This is the most common surgically treated movement disorder. We divide PD into three stages. The first stage is early PD. During this stage the disease could be managed with medical treatment however, 20% of the patients (especially with tremors) who do not respond to conservative treatment can be offered surgery. Stage 2 of PD is the period when the medical treatment starts losing its efficacy, is associated with side effects like hallucinations and dyskinesias and causes wide fluctuations of off and dyskinetic state. Most of our patients have been operated at this stage. Usually, one encounters this stage after 5 or more years of disease. Besides dyskinesias and motor fluctuations, some of the other symptoms for which we have operated patients in this stage include, severe pain and hallucinations. **Surgery usually resolves dyskinesias, pain and hallucinations. The 'On' period is extended to cover 80% of the day and the remaining 20% is associated with mild disabilities.** As the disease is fairly advanced at this stage it requires

'This is a serious and dedicated centre providing state of the art surgery for patients with movement disorders.'

Professor Marwan I. Hariz, M.D., Ph.D. Edmond J. Safra Chair of Functional Neurosurgery
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bilateral surgery, which could be either STN stimulation or lesioning. A recent review published by the Paris group has concluded that even in early PD patients surgery

improves quality of life by 24% as compared to marginal deterioration seen with best medical treatment¹. Third stage of the disease is the most advanced stage when the patient is virtually bed bound and barely responds to medical treatment, and has significant side effects. Surgery may or may not be possible in this case.

Dystonia

Dystonia is defined as an involuntary movement disorder characterized by repetitive, patterned, or sustained muscle contractions causing twisting movements or abnormal postures. Primary dystonia is a disease of young people, with most cases commencing in childhood, though some do not appear till the age of 10 years; adult onset is rare². Secondary dystonia occurs due to variety of disorders ranging from hereditary neurological syndromes like Wilson's disease and Huntington's disease, to perinatal cerebral injury causing cerebral palsy or later on in the life secondary to head trauma, brain stem lesions or brain tumors. Selection of suitable candidate for dystonia surgery is extremely crucial. Patients with primary generalized dystonia benefit the most from surgery, whereas secondary dystonias have variable outcome. The current target for dystonia is Gpi. We prefer Pallidal stimulation for bilateral disease and Pallidotomy for unilateral disease.

Our Setup:

MDS is a surgery of ultimate precision. It involves targeting small group of nuclei e.g. STN (7x9x5mm), not only located deep in the brain but surrounded by very vital areas like pyramidal tract, optic tract, etc. To accomplish this precision surgery we have undertaken elaborate training, developed a team of highly competent specialist and established appropriate infrastructure. The surgery is accomplished with the most elaborate and accurate stereotactic system, supported by microelectrode recording (MER) equipment and 3T MRI. To the best of our knowledge this setup has no parallel in India.

	Lesion	DBS
Hospital stay	4 days	10 days
Follow up	Local	Needs to visit specialized centers
Reversibility	None	Completely reversible
Titribility	No	Yes
Cost	Aordable	Costly

Table 1

Surgical Protocol:

We have a strict protocol for presurgical evaluation. Patients are admitted two days prior to surgery. Various MD disability scores are assessed along with the video recording of the patient. When required we perform neuropsychiatric evaluation also. Typically the patient stays in the hospital for four days for lesional surgeries and for eleven days for deep brain stimulation. Follow up visits are usually scheduled at the end of a month and once a year thereafter. Once on stable programming parameter the follow up is maintained with the reffering cetre/neurologist. Patient is expected to visit us once every year if convenient.

Surgery:

It would not be possible for me to cover the technical details of the surgery but I shall try and provide an overview. The surgery is performed in awake condition using local anesthetic agents only. All surgeries are performed with a senior anesthetist monitoring the vital parameters and comfort of the patient. Target localization is independently performed using CT and MRI scans. Physiological confirmation of the defined target is achieved by intraoperative MER performed in four to five trajectories. Once two or three trajectories with good recordings have been identifies we perform stimulation to assess the response. During this test there is instantaneous improvement in the tremors and rigidity time locked with the stimulation. The trajectory yielding the best response is than evaluated for any side effects. The trajectory with best response and least side effects is than selected for permanent electrode implantation or performing a lesion. All the surgeries are performed with a neurologist in OR to monitor and perform neurophysiological evaluation.

'If there is a miracle in life, it has to be this. (Seeing postoperative results of PD surgery)' H.E Nawal Kishore Sharma, Governor of Gujarat

Results:

Table 2 gives the breakup of the movement disorders surgery performed between 1998 till date.

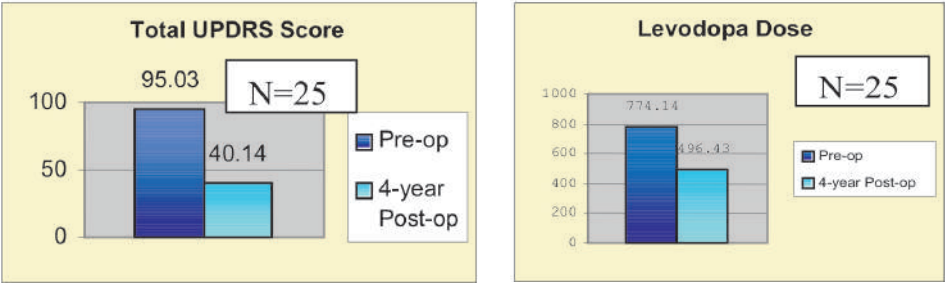
We have analyzed our four-year surgical results of Bilateral STN stimulation³ in 25 patients. We found that there was 52.45 % improvement in UPDRS, 35 % reduction in L-dopa dose and 35.37 % improvement in activities of daily living. (Fig 5,6). We had 3 cases of infection, two instances of misplaced lead and one case where we could not complete surgery due to intraoperative confusion. There was one incidence of hemorrhage. Some of the other side effects that we encountered included hyper sexuality⁴ and depression⁴. though none of them was significant to warrant discontinuation of the therapy. **We have operated on 10 patients above the age of 70 years and there are 11 doctors including surgeons who have benefited from this surgery.**

	Tremors	Dystonia	PD
Thalamotomy	16		
Thalamic Stimulation	6		2
Pallidotomy		4	33
Pallidal Stimulation		4	1
STN Lesion			8
STN Stimulation			91

Table 2

Of the patients undergoing surgery for tremors there has not been any major morbidity. Four patients had recurrence of tremor following thalamotomy. Only one patient (multiple sclerosis) had partial response to thalamic DBS.

As expected, dystonia surgery has offered mixed response. Of the two primary dystonia patient one responded well and other had moderate relief. Out of six patients with secondary dystonia 4 got good improvement. Besides a single case of infection there has been no other morbidity in this group.



(Fig. 5) Four years follow up of STN DBS

Neural Transplant:

This is one of the most promising fields for research in PD. Neural transplant program was started with transplantation of fetal mesencephalic cells in PD patients in 1987. Till the program was called off, 350 patients had undergone transplantation. Initial results of this trials were promising, however, the double blind studies revealed only 16-34% improvement and some of these patients

developed uncontrolled dyskinesias forcing to stop the trials. The second attempt was made using Glial Derived Neurotrophic Factor (GDNF) infusion into the putamen. Once again the phase I results could not be confirmed by phase II study, besides, it also stimulated antibody formation and raised suspicion of cerebellar degeneration forcing the researchers to take another look at this trials⁵. Stem cells are the most promising form of neural transplant tissue. Including us, number of researchers are working in this field, which hold great promise.

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Research Project:

We have completed one research project on selection of most optimal surgical therapy for movement disorders. As a result of this

"In 2006, with my husband we visited South Africa to be with our daughter for our first grandchild's birth. God bless, but I would be the last person to retire for bed after the midnight feed and managing meals for five of us during the day. I know that without the ticker, the pace-maker, it is not possible".
Mrs. Katy Merchant, MBA Teacher.

project we have been able to rationalise our approach to MD surgery. There are two ongoing research project related to accurate targeting and hardware complications of DBS with a funding of Rs. 10,00,000. We also offer fellowship training in Stereotactic and Functional Neurosurgery for post Mch. students.

'Thanks a million for contribution of DBS to medical field. But for this surgery which you performed on me, I would have been a living corpse.'
Mrs. Mendes, Teacher.

About Dr. Paresh Doshi

- ★ Trained in Stereotactic Surgery at the National Hospital for Neurology and Neurosurgery, Queen square, London
- ★ Training in Movement Disorders surgery from reputed centers in Sweden, Austria, France and Denmark under Prof. Benabid, Prof. Alesch, Prof. A Bosch and Prof. Marwan Hariz.
- ★ Over 10 publications on Movement Disorders in peer reviewed journal
- ★ First Indian neurosurgeon to perform Deep Brain Stimulation surgery in India.

'It's been a year now since the operation. That awful rigidity has almost gone, I take less medication, I sleep soundly, and my moods are more even. Mr. Mathew Thomas, Reader's Digest July 2002.

Dr. Paresh K. Doshi

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