

# NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

## INTERVENTIONAL PROCEDURES PROGRAMME

### Interventional procedure overview of subthalamotomy for Parkinson's disease

#### Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) advise on the safety and efficacy of an interventional procedure previously reviewed by SERNIP. It is based on a rapid survey of published literature, review of the procedure by Specialist Advisors and review of the content of the SERNIP file. It should not be regarded as a definitive assessment of the procedure.

#### Date prepared

The overview was prepared by Bazian Ltd in December 2002.

#### Procedure name

Subthalamotomy for Parkinson's disease

Synonyms: lesioning of the subthalamic nucleus; subthalamic nucleotomy

#### Specialty society

Society of British Neurological Surgeons

#### Indication

Parkinson's disease.

Parkinson's disease is a chronic disease of the brain characterised by gradually worsening tremor, muscle rigidity and difficulties with starting and stopping movements. The condition is usually treated with drugs. Surgery may be considered in people who have responded poorly to drugs, who have severe side-effects from medication, or who have severe fluctuations in response to drugs (on-off syndrome).

Parkinson's disease is common, affecting about 0.5% of people aged 65 to 74 and 1-2% of people aged 75 and over. Experts believe that 1 to 10% of people with Parkinson's disease might be suitable for brain surgery.<sup>1</sup>

#### Summary of procedure

Surgery for Parkinson's disease is carried out on structures within the brain that are responsible for the modification of movements, such as the thalamus, the globus pallidus and the subthalamic nucleus. Each of these structures consists of two parts; one on the left hand side of the brain and one on the right. Surgery may be carried out on one or both sides.

Surgical treatment aims to correct the imbalance created by diminished function of the substantia nigra, the underlying abnormality in Parkinson's Disease. Surgery alters, through either destruction or electrical stimulation, the function of brain nuclei, such as the thalamus, globus pallidus or subthalamus that interact functionally with the substantia nigra. All these procedures carry the risk of stroke, confusion and speech and visual problems.

Surgery involves inserting very fine needles into the brain through small holes made in the skull. The exact points of insertion may be different in each patient. In subthalamotomy, a part of the subthalamic nucleus is destroyed using heat or radiofrequency. The procedure is usually carried out under local anaesthetic. Patients remain awake during the procedure so that effects on movements can be monitored.

## **Literature review**

### **Appraisal criteria**

We included studies on subthalamotomy in people with Parkinson's disease.

### **List of studies found**

We found one systematic review.<sup>1</sup>

We found no randomised controlled trials.

We found only case series or case reports. The table give details of the five largest.<sup>2-6</sup> including one study that was identified during the consultation process in February 2004.

References to smaller studies are given in the Annex.

## Summary of key efficacy and safety findings (1)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Nicholson T <sup>1</sup> Systematic review Search date: September 1999	<ul style="list-style-type: none"> <li>found no controlled studies</li> <li>found two case series</li> </ul> <p>Efficacy 'not yet established'</p>	Safety not yet established	<p>Search date and primary sources described</p> <p>Selection criteria for studies described</p> <p>Quality of included studies assessed: all papers had methodological limitations</p>
Yasui N <sup>2</sup> Case series Tokyo, Japan Date not stated (published 1976)  n=66 patients had subthalamotomy Inclusion/exclusion criteria not reported Follow up: 2 weeks	None reported	Cerebellar signs (reduced muscle tone and difficult placing limbs accurately) persisting after 2 weeks: 41%	<p>Uncontrolled case series</p> <p>Very limited description of surgical technique and of patients.</p> <p>Very short follow up</p>
McCarter R <sup>3</sup> Case series Bristol, UK Date not stated (published 2000)  n=12 subthalamotomy, age range 42 to 69 years (4 had subthalamic nucleus stimulator implanted on the opposite side in addition)  Inclusion criteria: <ul style="list-style-type: none"> <li>disabling motor function despite medical management</li> </ul> Exclusion criteria: <ul style="list-style-type: none"> <li>dementia or depressive illness</li> </ul> Mean follow up: 6 months (minimum 3.5 months)	None reported	<ul style="list-style-type: none"> <li>No change in overall cognitive test results</li> <li>Learning and retrieval deteriorated in 20-30%</li> <li>Spatial working memory and planning: deteriorated in 28%</li> </ul>	Uncontrolled case series

## Summary of key efficacy and safety findings (2)

Study details	Key efficacy findings	Key safety findings	Comments
<p>Alvarez<sup>4</sup> Case series Havana, Cuba Date not stated (published 2001)</p> <p>n=11, average age 60 years (range 53 to 69 years)</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> <li>• mainly axial motor manifestations</li> <li>• absent or mild levodopa-induced dyskinesia</li> </ul> <p>Follow up: 12 months</p>	<ul style="list-style-type: none"> <li>• 'average' reduction in motor ability score off medication: 50%</li> <li>• 'significant' improvements in freezing gait, postural stability and facial expression</li> <li>• bradykinesia and rigidity 'improved' bilaterally</li> <li>• tremor 'significantly ameliorated' in whole group</li> <li>• mean time to turn in bed reduced from 17 to 6 seconds</li> </ul>	<p>No intraoperative complications</p> <p>Postoperative complications:</p> <ul style="list-style-type: none"> <li>• dyskinesia: 5 people</li> <li>• chorea: 1 person</li> <li>• no cognitive, sensory, motor or speech deficits occurred</li> </ul>	<p>Uncontrolled case series</p> <p>Losses to follow up</p> <p>No patient assessment of outcome</p>
<p>Diederich N<sup>5</sup> Case series Cologne, Germany 1976 to 1985</p> <p>n=17 people</p> <ul style="list-style-type: none"> <li>• 13 combined subthalamotomy and thalamotomy</li> <li>• 1 subthalamotomy alone</li> <li>• 1 thalamotomy alone</li> <li>• 1 not known</li> </ul> <p>Minimum age at surgery 35 years – maximum age at re-examination 71 years.</p> <p>Mean follow up: 11 years</p>	<p>Only one person had subthalamotomy alone</p> <p>No efficacy data presented separately</p>	<p>No complications or adverse effects reported</p>	<p>Uncontrolled case series</p> <p>Data for thalamotomy and subthalamotomy group not reported separately</p> <p>Information of people who were dead and people who did not wish to provide information not given (17 people)</p>

Study details	Key efficacy findings	Key safety findings	Comments
<p>Patel, N<sup>6</sup> (2003)</p> <p>Case series 1997 -2000 N=21 people with advanced idiopathic Parkinsons disease. 17 had asymmetrical tremor 4 had bilateral disease</p> <p>Mean age: 60 years (range 36-73 years) Mean duration of disease: 12 years (3-24 years)</p> <p>Operation on the right side in 12 patients and on the left in 9 patients</p> <p>Follow-up: 16 patients at 6 month 15 patients at 12 months 18 patients at 24 months</p>	<p>Unified Parkinson's Disease Rating Scale (UPDRS) II – activities of daily living; III – motor examinations</p> <p>Significant reduction in the motor UPDRS III scores for patients OFF and ON medication.</p> <p>Significant reduction in the activities of daily living UPDRS II scores for patients OFF and ON medication.</p>	<p>1 patient had dyskinesia 1 patients sustained a post-operative grand mal seizure and Todd's paresis (transient)</p> <p>No patients developed sensory or speech deficits</p> <p>Cognitive assessment of 17 of the patients suggested few adverse cognitive effects of the surgery.</p> <p>(UPDRS) IV – complications of therapy</p>	<p>This study was identified during the consultation process.</p> <p>12 of the patients included in this paper were included in an earlier study<sup>3</sup></p> <p>Originally 26 patients – five lost to follow-up (two failed to attend clinic, two lived abroad and unable to return and one patient developed metastatic disease)</p>

**Validity and generalisability of the studies**

The studies were all carried out in settings appropriate to the UK.

We found only case series, all of which were small. Only one provided any efficacy data.<sup>4</sup>

**Bazian comments**

The systematic review<sup>1</sup> states that 'the Parkinson's Disease Society and the Medical Research Council are currently establishing a trial protocol for a multicentre randomised controlled trial of early compared with deferred lesioning or stimulation of the subthalamic nucleus'.

**Specialist advisor's opinion / advisors' opinions**

*Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.*

The Specialist Advisors commented that there were not enough data to assess the long-term benefits of subthalamotomy for Parkinson's disease, and that subthalamic electrical stimulation had become the preferred intervention.

This overview was amended by NICE in May 2004

## References

1. Nicholson T, Milne R. Pallidotomy, thalamotomy and deep brain stimulation for severe Parkinson's disease. Southampton: Wessex Institute for Health Research and Development; 1999 December. Development and Evaluation Committee Report No 105
2. Yasui N, Narabayashi H, Kondo T, Ohye C. Slight cerebellar signs in stereotactic thalamotomy and subthalamotomy for parkinsonism. *Applied Neurophysiology* 1976; 39: 315-320
3. McCarter RJ, Walton NH, Rowan AF, Gill SS, Palomo M. Cognitive functioning after subthalamic nucleotomy for refractory Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry* 2000; 69: 60-66
4. Alvarez L, Macias R, Guridi J, Lopez G, Alvarez E, Maragoto C et al. Dorsal subthalamotomy for Parkinson's disease. *Movement Disorders* 2001; 16: 72-78
5. Diederich N, Goetz CG, Stebbins GT, Klawans HL, Nittner K, Koulosakis A et al. Blinded evaluation confirms long-term asymmetric effect of unilateral thalamotomy or subthalamotomy on tremor in Parkinson's disease. *Neurology* 1992; 42: 1311-1314
6. Patel NK, Heywood, P, O'Sullivan, KO, McCarter, R et al. Unilateral subthalamotomy in the treatment of Parkinson's disease. *Brain* 2003; 126:1136-1145.

## Annex: References to studies not described in the table

Reference	Number of study participants
Barlas O, Hanagasi HA, Imer M, Sahin HA, Sencer S, Emre M. Do unilateral ablative lesions of the subthalamic nucleus in parkinsonian patients lead to hemiballism? <i>Movement Disorders</i> 2001; 16: 306-310	9
Rodriguez MC, Guridi OJ, Alvarez L, Mewes K, Macias R, Vitek J et al. The subthalamic nucleus and tremor in Parkinson's disease. <i>Movement Disorders</i> 1998; 13(suppl 3): 111-118	7
Su PC, Tseng HM, Liu HM, Yen RF, Liou HH. Subthalamotomy for advanced Parkinson disease. <i>Journal of Neurosurgery</i> 2002; 97: 598-606	7
Gill SS, Heywood P. Bilateral dorsolateral subthalamotomy for advanced Parkinson's disease. <i>Lancet</i> 1997; 350: 1224	2
Su PC, Tseng HM, Liou HH. Postural asymmetries following unilateral subthalamotomy for advanced Parkinson's disease. <i>Movement Disorders</i> 2002; 17: 191-194	2
Su PC, Tseng HM. Subthalamotomy for end-stage severe Parkinson's disease. <i>Movement Disorders</i> 2002; 17: 625-627	1
Klostermann W, Vieregge P, Kompf D. Apraxia of eyelid opening after bilateral stereotaxic subthalamotomy. <i>Journal of Neuro-Ophthalmology</i> 1997; 17:122-123	1