Deep Brain Stimulation (DBS) in patients with Parkinson's disease (PD)

A Scandinavian Movement Disorder Society, ScandMODIS consensus document April 2023

PD-patients in advanced stage of the disease should be referred to a Movement Disorder Clinic where a comprehensive and unbiased evaluation can be made by a neurologist specialized in movement disorders with a vast experience of adjusting oral medication and in the use of deep brain stimulation (DBS) and continuous pump administration of dopaminergic drugs (subcutaneous apomorphine or levodopa, levodopa intestinal gel).

Background (references 3,4,5,8,9,11,13,15,17,19,20,21,22,24,25,26,27,28,29)

- Patients with Parkinson´s disease, who no longer can be improved by optimizing the oral/transdermal medical treatment, have shown significant benefits from treatment with DBS (Deep Brain Stimulation) in STN, or alternatively in GPi. If troublesome tremor not responding to medical treatment is present, DBS in Vim or PSA/Zi can be effective treatment options.
- DBS improves cardinal motor symptoms; bradykinesia, rigidity, and tremor and reduces motor fluctuations
- DBS decreases use of medication and reduces levodopa-induced dyskinesia
- DBS increases quality of life
- There is a tendency to operate patients at an earlier time of disease than before

Criteria for referral to a specialized Movement Disorder Centre for possible device-aided treatment (references 11,15,25).

- Patients with levodopa responsive Parkinson's disease
- Preferably with a duration of Parkinson´s disease > 4 years
- **Moderate to severe on-off motor fluctuations

and/or

- **Moderate to severe dyskinesia

and/or

- Medically refractory **moderate to severe tremor
- ** Defined as moderate to severe impact on quality of life
- *Patients with tremor-dominant PD can be treated with Vim or PSA/Zi DBS also >75 years of age

Exclusion criteria (references 1,2,6,7,10,16,18,26)

- Dementia
- Significant medically resistant psychiatric disease (e.g. severe depression)

- Significant medical conditions with limited life expectancy
- Conditions that prevent surgery or MRI

Patient eligible for DBS

Patient eligibility for DBS is determined at the Movement Disorder Centre after:

- Brain imaging
- Neuropsychological assessment of cognitive function and psychiatric symptoms
- Levodopa challenge test
- NB

– Cardiac pacemaker is not a contraindication for DBS
– It is not necessary for the patient to be awake during surgery
– It is not always necessary to remove all hair

Expected outcome of DBS treatment (reference 14, 22)

Expected outcome corresponds to the effect of an optimal levodopa dosage on the motor symptoms

- Significant reduction of on-off motor fluctuations
- Significant reduction of dyskinesia
- Tremor reduction
- Decreased use of medication depending on surgical target, see below
- Improved quality of life
- Levodopa unresponsive symptoms will usually not improve:

  Axial symptoms e.g. postural instability
  Freezing of gait (especially ON-freezing)
  Dysarthria

Surgery in Parkinson's disease

Target

• The subthalamic nucleus (STN) to treat the cardinal symptoms tremor, rigidity and hypokinesia and reduce motor fluctuations. Substantial reduction of medication is usually obtained leading to significant reduction of dyskinesia
• The internal part of globus pallidus (GPi) is an alternative target to treat cardinal symptoms and especially dyskinesia, however, often results in much less or no reduction of medication
• The ventral intermediate nucleus of thalamus (Vim) or the posterior subthalamic area (PSA)/Zona incerta (Zi) to treat tremor only (29)

• The electrodes are implanted bilaterally and connected to a subcutaneous lead and impulse generator (IPG) usually localized beneath the clavicle
• Each electrode has several contacts and stimulation contact and parameters are adjusted by computer telemetry

Complications

• Surgical complications

- Intracranial hemorrhage
- Seizures
- Deep Venous Thrombus
- Pulmonary Embolism

• Hardware complications

- Infections
- Skin erosions
- DBS lead-migration and fractures

Side effects (references 7,9,12,23,27,29)

These are often current dependent and may be reduced by redirecting the direction of current (if segmental electrodes are used)

• Worsening of dysarthria
• Sometimes worsening of gait and balance especially patients > 65 years of age
• Eyelid apraxia
• Dystonia
• Psychiatric symptoms (usually transient, treatable and potentially preventable)

– Confusion
– Psychosis
– Depression
– Increased risk of suicide
– Mania
– Apathy (can be permanent)

• Neuropsychological symptoms

– Reduced verbal fluency (can be permanent)
– Increased impulsivity (can be permanent)

Patient management and follow-up

• During the first 3-6 months frequent controls in the outpatient clinic to adjust stimulation parameters and medication to obtain maximum effect of stimulation
• In patients with directional leads stimulation may if necessary be redirected to optimize effect and/or avoid side effects
• Shared control (referral neurologist and DBS centre) of symptoms and disease development and stimulation effect
• Battery replacement every 3-5 years if relevant
• Rechargeable battery available, replacement after 15 years or more
• Ongoing DBS is a contraindication for MRI. However MRI can be performed in most cases if the MRI/neurostimulator guidelines elaborated by the manufacturer are followed
• Diathermy including shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy are contraindicated
• It is safe, however, to perform diagnostic ultrasound examination in a patient with DBS
• In case of surgery in patients with DBS monopolar electrocoagulation should be avoided. Bipolar is recommended.

If a patient with DBS needs examination by ECG, EEG or EMG the DBS can be temporarily switched off during the procedure to avoid disturbance of the examination.

MRgFUS

MRI-guided focused ultrasound ablation (MRgFUS) has been introduced as an alternative method, e.g., in patients that for medical or other reasons are not eligible for DBS. Small, but permanent unilateral lesions are made by ultrasound. Equipment for MRgFUS are at present available in Finland and Denmark, but centers in Norway and Sweden will soon follow. Thalamus-Vim has been the most common target with unilateral lesions, but treatment of medication-resistant tremor of PD is to date recommended only within registries (29). Promising results have also been reported after ultrasound pallidotomy or subthalamotomy in PD patients (30), but future randomized longitudinal studies are needed to clarify long-term efficacy, side effects and safety regarding bilateral treatment.

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