# **STN DBS under General Anesthesia**

Subjects: Others Contributor: Hye Ran Park

Bilateral subthalamic nucleus (STN) Deep brain stimulation (DBS) is a well-established treatment in patients with Parkinson's disease (PD). Traditionally, STN DBS for PD is performed by using microelectrode recording (MER) and/or intraoperative macrostimulation under local anesthesia (LA). However, many patients cannot tolerate the long operation time under LA without medication. In addition, it cannot be even be performed on PD patients with poor physical and neurological condition. Recently, it has been reported that STN DBS under general anesthesia (GA) can be successfully performed due to the feasible MER under GA, as well as the technical advancement in direct targeting and intraoperative imaging.

Keywords: general anesthesia ; intraoperative computed tomography ; intraoperative magnetic resonance imaging ; local anesthesia ; microelectrode recording ; Parkinson's disease ; subthalamic nucleus ; deep brain stimulation

## 1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease following Alzheimer's disease, characterized by bradykinesia, rigidity, resting tremor and postural instability <sup>[1]</sup>. The long-term use of anti-Parkinsonian drugs has been found to be associated with dyskinesia and symptom fluctuation. Since the introduction of deep brain stimulation (DBS) in 1980s, DBS has been accepted as a preferred surgical treatment for PD <sup>[2]</sup>. Internal globus pallidus (GPi) and subthalamic nucleus (STN) are the main stimulation targets <sup>[3]</sup>. In particular, bilateral STN DBS is known to significantly improve not only primary motor symptoms, but also non-motor symptoms, such as sensory symptoms and sleep disturbances <sup>[4][5]</sup>.

Traditionally, DBS surgery is performed under local anesthesia (LA) and conscious sedation to evaluate clinical benefit and side effects by localizing electrophysiological target using microelectrode recording (MER) and/or intraoperative test stimulation while the patient is awake <sup>[G][Z][B][9][10][11][12][13][14][15]</sup>. STN DBS has several advantages when implemented under LA. The spike features of MER can be analyzed, and symptom relief or side effects by stimulation can be evaluated with intraoperative macrostimulation. In addition, by using electrophysiological targeting using MER, it is possible to compensate for errors from planning based on preoperative imaging, which is caused by brain shift due to cerebrospinal fluid (CSF) leakage after dura opening. However, MER under LA requires PD patients to withstand surgical procedure with approximately 18 h of antiparkinsonian medication discontinued. Most PD patients are old age and have severe multiple neuro-skeleto-muscular symptoms due to comorbidity, such as spinal stenosis and herniated intervertebral disc. Moreover, patients have to wear a frame on their head during the entire procedure and undergo surgery with the frame fixed to the operation table; thus, the patients may suffer from intolerable pain and psychological sequelae. The risk of hemorrhage risk also increases if an unintended large motion occurs due to cough or tremor during surgery. Patient cooperation is one of the factors that may influence the outcome after surgery.

Because of these concerns, many authors have consistently tried STN DBS under GA and reported that the clinical outcome is not inferior compared to under LA. However, there have been no randomized trials comparing DBS surgery under LA and GA due to logistical concerns. Only class II evidence has been compared through retrospective data analysis <sup>[16]</sup>. Here, we aimed to review previously published literature on STN DBS under GA as an alternative to STN DBS under LA. The technique and clinical outcome using intraoperative imaging and MER in DBS under GA are thoroughly reviewed along with the introduction of single-center experience of our institution.

## 2. STN DBS Using Intraoperative Imaging or Microelectrode Recording Under GA

The DBS surgical procedure can be divided into two stages: the intracranial implantation of DBS electrodes and the implantation of implantable pulse generator (IPG). In the case of IPG implantation, GA is generally preferred because tunneling is required subcutaneously. For intracranial electrode implantation, the STN DBS procedure under LA and GA

are similar, but the specific details are different. The main difference between the STN DBS surgical procedure under LA and GA is the intraoperative verification method for the intended target acquisition, i.e., test stimulation or intraoperative imaging with or without MER. An accurate electrode location is a key factor to determine the postoperative prognosis after STN DBS surgery <sup>[17][18][19][20]</sup>. Image verification of the lead position is an important step, whether intra- or postoperatively <sup>[21]</sup>. For STN DBS under GA, some centers perform intraoperative verification using MER even under GA, and other centers use intraoperative imaging without MER. We reviewed each method of STN DBS under GA using intraoperative imaging or MER, respectively (Table 1).

**Table 1.** Summary data of published literature presenting clinical outcome effect of after subthalamic nucleus deep brain stimulation under general anesthesia in patients with Parkinson's disease.

| Author                 | Year | No. of<br>Patients | Age<br>(yrs) | Disease<br>Duration<br>(yrs) | Follow-<br>up<br>Months | UPDRS III Medication off |                |             |                 | LEDD     |                |             |              |
|------------------------|------|--------------------|--------------|------------------------------|-------------------------|--------------------------|----------------|-------------|-----------------|----------|----------------|-------------|--------------|
|                        |      |                    |              |                              |                         | Baseline                 | Follow-<br>up* | %<br>Change | <i>p</i> -value | Baseline | Follow-<br>up* | %<br>Change | p -<br>Value |
| Intraoperative imaging |      |                    |              |                              |                         |                          |                |             |                 |          |                |             |              |

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- Saleh et al. 64 ± 10.9 ± 5.86 \pm 5.86
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achieved with mean error close to 0.7 ± 0.3 mm <sup>[66]</sup>. The main advantage of electrode implantation using iMRI is that 41. Fiegele, T.; Feuchtner, G.; Sohm, F.; Bauer, R.; Anton, J.V.; Gotwald, T.; Twerdy, K.; Eisner, W. Accuracy of stereotactic electrode trajectory can be accurately implanted and adjusted before final placement by visualizing the intended target electrode placement in deep brain stimulation by intraoperative computed tomography. Parkinsonism & related disorders 2008, 14, 595-599.

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In the standard STN DBS procedure under LA, MER is used during surgery to obtain a signal to identify the deep 52trustaires 🖾; Kube, Onac.sicherf, alectrocherimplayitationsphyletelogicalcompanisionscionscional Mark derepibraioperinativetidest stiful Auxinssetadize and detween astignisoner elevange equiliande logalianes iteration in a standard of the standard of ne cost of using MER in STN DBS surgery is to obtain high accuracy in 53adiadraph& Gno Daterophysic Bajitan taxige NhB.; Baro Lewianto, Me Zireanta Nge Wangu 18. b Baoine a GdAth Staam B. Abult are veral im Baarkatack or Backins we build be as a constignt purple and in the end of the second state of the second s netrolininsmistic & Ralated Disardere 2017 or 4 wate 205TN DBS, about 25% (38/150) of the electrodes were found very recording taking the stand to the stand and the standard stand effectionestectationstimulationstimulations indicate that MER is esstantial 1016arpetkoeldina 1006070000 DBS surgery. Even small merge error combined with brain shift can lead to 5: Chen, S.Y., Isal, S.T., Elh, S.H., Chen, T.Y., Hung, H.Y., Lee, C.W., Wang, W.H., Chen, S.P., Lin, S.Z. Subtrialamic deep that it is sussible on inpervention. The subset in MER of feater the sensitive motion deviation of the subset of t effects and sides offer through to station 1810 Boogle of the electrode position, the effect

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Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology 2012, 123, 2406-MER 13, vince 19 the risk of the risk of the risk of the official hemorrhage and cognitive decline <sup>[82]</sup>. Binder et al. reported a bleeding rate of

STN length alone cannot predict the occurrence of stimulation-related side effect [18]. Moreover, the MER procedure 59 c Reades yo MASul Andrean Shid Mucchise 195 C .; Seier, M.; Wilhelm, J.; Vederman, A.; Burchiel, K.J. Clinical outcomes of

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Macrostonulation dependence of the patients are asleep during the operation. There is also controversy about

whether intraoperative stimulation is needed during DBS surgery. Some researchers believe that it is necessary to confirm 60. Sharma, M., Deogaonkar, M. Accuracy and safety of targeting using intraoperative "O-arm" during placement of deep the offectiveness of the stimulus in the other hand, some argued that discretion at the drug in LA makes the needles less reliable superially if it is not located in the source and in the source and it is not located in the source and difficult to distinguish from the lesion effect <sup>[86]</sup>. 61. Carlson, J.D.; McLeod, K.E.; McLeod, P.S.; Mark, J.B. Stereotactic Accuracy and Surgical Utility of the O-Arm in Deep

62: the net of the synchronic contractions of the synchronic contractic contractions of the synchronic contractions of the s [24s26g29y42n872], Experiences and redwating retanglangetine retanglangetine and the straight in the surger of STN DBS under LA with M = 0.18, as well as in dysarthria, capsular, (p = 0.18), as well as in dysarthria, capsular,

oculomotor, and sensory side effects <sup>[87]</sup>. Chen et al. also reported that there was no difference in the UPDRS III reduction 63. Aviles-Olmos, I.; Kefalopoulou, Z.; Tripoliti, E.; Candelario, J.; Akram, H.; Martinez-Torres, I.; Jahanshahi, M.; Foltynie, rate and score 6 months after STN DBS surgery between the MER group and the non-MER group. In addition to T.; Hariz, M.; Zrinzo, L. Long-term outcome of subthalamic nucleus deep brain stimulation for Parkinson's disease frequently, used imaging sequences, idirect targeting can be used with quantitative 19, see tiblity 19, or and

diffusion tensor imaging (DTI). 64. Chabardes, S.; Isnard, S.; Castrioto, A.; Oddoux, M.; Fraix, V.; Carlucci, L.; Payen, J.F.; Krainik, A.; Krack, P.; Larson, P. 2.252 utside Engrassible Dingren GASS leads using intraoperative MRI guidance: technique, accuracy, and clinical benefit at

1-year follow-up. Acta neurochirurgica 2015, 157, 729-737. STN DBS under GA has traditionally been used in patients who are unable to tolerate awake surgery including pediatric 65ationes el manpatente internation de molaneiglar el cince prestivilli soci Mardons es sitere en aprication de molaneiglar el interne diguest concern with the the base subject wis valization with high-field MRI is Stere possibility of Until Internation of the stere static and functional one of the stere static and the small-sized retrospective studies have reported that MER obtained from STN, GPi, substantia nigra in STN DBS surgery conduce PASwiftidhandsonatifeManutennerveronalsMarleSinieleds DeeppBranic Silverulatiop ditends replayed in Significations bignification control of the Nance com/pared/7wille, safe field advalled advalled advalled and a strength of typical burst pattern. Notably, the neural activity of typical burst pattern 64isappeared, whee higher allest herio danses were used R. Jowerer, the results of the set studies are controversial given the small samale submarkhetriegees weet than estimation and cherrarized were the submarket biad and the submarket same the norther and a standard and a standard and a standard and a standard a standard

doi:10.1016/j.brs.2014.04.007.

The next concern is that since intraoperative stimulation cannot be performed under GA, immediate response of clinical 68/refeater and the set of the se MEReview use the Literature Brain Sci 2018 and di: 10,3390/brainsci8010017 timulation [89]. In these studies, propofol or 62ertkitembayoi TendeedstoErtRertErrestwiteotbetieleretmoehbessielerginet signalgrhettatheservaereerguisigdistemeotatticeprocessionnesmas of exace than defon on earsing and references and related acceleration of the official action signed to the section with proposel, it did not interfere with the optimal approach to the

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discharges and spike activity patterns are an important part of the precise localization of the target nucleus. Anesthetics 73. Geevarghese, R.; O'Gorman Tuura, R.; Lumsden, D.E.; Samuel, M.; Ashkan, K. Registration Accuracy of CT/MRI have been shown to affect background activity and neuronal spike activity in a dose-dependent manner, primarily through Eusion for Localisation of Deep Brain Stimulation Electrode Position: An Imaging Study and Systematic Review. activity in variation, of v-aminobutyric acid (CABA) receptors, in addition and the same effect on neuronal Stereotact Funct Neurosurg 2016, 94, 159-163, doi:10.1159/00046609.

activity in various target nucleus. Since most anesthetics enhance the inhibitory action of GABA, this difference in GABA-74, Ivan, M.E., Varlagarda, J., Saxena, A.P., Marting Starr, P.A.; Sootsman, W.K.; Larson, P.S. Brain shift during bur input of the target nucleus plays an important role in the second se hole-based procedures using interventional MRI. J Neurosurg 2014, 121, 149-160, doi:10.3171/2014.3.jns121312.

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activity, localization of the target areas was proven possible in most studies. Nevertheless, most studies did not mention 76. Erickson, K.M.; Cole, D.J. Anesthetic considerations for awake craniotomy for epilepsy. Anesthesiology clinics 2007, the exact effect on the background activity, degree of suppression of spike activity, and the number of trajectories used for 25, 535-555, ix, doi:10.1016/j.anclin.2007.06.001.

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motion-related firing of STN, and the clinical results were similar in both groups [97]. 78. Khan, M.F.; Mewes, K.; Gross, R.E.; Skrinjar, O. Assessment of brain shift related to deep brain stimulation surgery.

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791.ePalfaota arf, psoppted and Banta Rydropole / IARS a we that clinic a kautoom Ko Trad, locations and set of the cardes over a in estimoted withing the action of the postapolities concerned by the second standard with the second standard standard standard standards and the second standard standards and the second standards and the sec England UADers 2204 Scores 1223 2010 120 1200 56211 5482009 10301 40 [92] [93]

80 through the effects of short-acting opioid receptor agonists, such as remiferitanil, on MER are not well known, some data Movement disorders 2008, 23, 1317-1320. suggest that GABAergic neurons may play a central role <sup>[98]</sup>. A few reports showed that anesthesia using propofol reduces

achemillay rate kolasks a garajka vin Mandesports Man ow Bite Chabandes showed abid of Hickan appendive minimpande compared to machantimulations at the subthalappicon value since a safe tecfinite 100 2018 shotes use [100]. In some studies, MER was properly performed without affecting the surgical outcome

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that 0006r,e10/2as3866-s196 ificant difference between the GA and LA groups in terms of MER trajectory, recorded STN depths,

postoperative, coordinates, and everall incidence of stimulation-related side effect. Under remifentanil or ketamine 33. Binder, D.K.; Rau, G.M.; Starr, P.A. Risk factors for hemorrhage during microelectrode-guided deep brain stimulator anesthesia in a significant differences were found in number of spikes detected, mean firing rate, pause index, and burst index compared to LA. However, Moll et al. observed a long interburst between abnormally long group discharges under 84. Vesper, J.; Haak, S.; Ostertag, C.; Nikkhah, G. Subthalamic nucleus deep brain stimulation in elderly patients--analysis proporti and remitentanil. of outcome and complications. BMC Neurol 2007, 7, 7, doi:10.1186/1471-2377-7-7.

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been fully elucidated, but it seems to be a reasonable option due to the non-GABA-mediated mechanism of action.
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 MER in STN or GPi [104]. Although dexmedetomidine may affect the MER result, it does not affect target localization.

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doi:10.1111/ner.12766. Some authors performed STN DBS surgery on PD patients under GA and reported favorable clinical outcomes (Table 1). 894eftersticter, AppMerantra Opareffeinsa M. Wilhases deinetasted Fronte some no H.718, aphile itheten infect Arkarkinson's Disease Rahns stearing underso directories and the human and the state of the and 22 (stimulation on, Intedication on). Yamada et al. also reported that UPDRS II, III, IV on and off scores were 89gM6da0dly.loReyein the GAlaendi, GA: ghoappetat/3;1200thsgcBoeberanis/elky; attributer activities off dailyliestoff (dailyliestoff (dailyli synAcKon 83. Nsstimutasionad ykomesad, attensionesiaidayidandeabaylos draytokenschappedinesidnistanakytactic anid study, a reduction and improvement of sleep and off period duration, and improvement of sleep

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In their study, not only the UPDRS II and III off score, but also the total UPDRS off scores at postoperative 1 year 91. Tsai, S.T.; Chuang, W.Y.; Kuo, C.C.; Chao, P.C.; Chen, T.Y.; Hung, H.Y.; Chen, S.Y. Dorsolateral subthalamic neuronal improved significantly, and the total UPDRS score continued to improve for up to 7 years. activity enhanced by median nerve stimulation characterizes Parkinson's disease during deep brain stimulation with general anesthesia. J Neurosurg 2015, 123, 1394-1400, doi:10.3171/2014.11.JNS141208.

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