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CASE REPORT

Frameless Stereotactic Deep Brain Stimulation for Parkinson's Disease: A Case Report and Technical Note

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Because deep brain stimulation (DBS) implantations and other stereotactic and functional surgical procedures require accurate, precise, and safe targeting of the brain structure, the technical aids for preoperative planning, intervention, and postoperative follow-up have become increasingly important. In this paper, we introduce a case of advanced Parkinson's disease with 10 years of medical control in which the patient received subthalamic nuclei (STN) DBS therapy through frameless surgery. A preliminary outcomes analysis is also provided. The STN DBS was implanted using a frameless stereotaxy protocol. After identifying the STN by microelectrode recording (MER), the DBS electrodes were implanted and connected to an implanted programmable generator. Programming started 1 month after the operation, and the patient was followed up on regularly and 12 months of post-STN DBS unified Parkinson's disease rating scale were recorded. After 12 months of follow-up, the patient who received the frameless surgery showed a significant improvement in clinical motor functions compared with his preoperative scores. The frameless system has the advantage of providing accuracy in postoperative lead position survey and target deviation measurements with comparison to the preoperative planning image. The outcomes of frameless DBS surgery are similar to those of frame-based surgery, with the advantages being that frameless surgery can reduce the patient's discomfort, shorten the operation and MER time, and decrease the MER trajectory number.

Key words: Frameless stereotactic, deep brain stimulation, deep brain stimulation, advanced Parkinson's disease

INTRODUCTION

Parkinson's disease (PD) is a common and potentially disabling neurodegenerative disease.[1] Motor symptoms of the disease, including bradykinesia, resting tremor, rigidity, and gait and postural changes, have long been regarded as the major symptoms of PD. In addition to classical motor symptoms, nonmotor symptoms are now widely accepted as part of the clinical picture, and cognitive decline is a critical aspect of the disease, as it brings an additional significant burden to patients and caregivers.[2] Medication therapy, especially treatment with levodopa, currently remains the most effective treatment for the motor symptoms of PD, but its benefits are only sustained through a honeymoon period generally lasting several years at most. In cases of advanced PD, periods of good mobility may be limited by the presence of motor fluctuations and drug-induced dyskinesias.[3] Through controlled trials and large clinical series, the benefits and safety of deep brain stimulation (DBS) have been established, and DBS has become a standard treatment for patients at the advanced stages of PD with severe motor complications.[4-7]

The stability, reproducibility, and accuracy of frame-based stereotaxy make this procedure an attractive alternative to trajectory-based procedures, where real-time feedback is less critical, and have provided a reliable method for accurately targeting deep-brain structures.[8] Despite their utility, stereotactic frames have limitations for both the surgical team and the patient, and frames have been supplanted gradually by frameless image-guided surgical systems in most intracranial procedures.[9] The previous studies have noted impediments such as an extended procedure time, potential obstacles to the surveillance of the patient's motor and verbal responses during the operation and particularly during stimulation, and the strain of the heavy and restrictive frame on the patient during the lengthy operation.[9-11] Combining a new software version and a new hardware for navigation, frameless stereotaxy can reduce the discomfort of patients arising from frames and allow the

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neurosurgeon to set the insertion entry, trajectory, and target directly in the preoperative planning stage.

Therefore, in this paper, we describe the techniques used for frameless DBS. We also highlight critically technical surgery in a new version of navigation software support and analyze the preliminary postoperative results of patients following both frame-based with or without cross-hair intraoperative correction and frameless surgery. We outline the procedures used in frameless stereotaxy and compare the implantation procedure and steps involved in frame-based and frameless stereotaxy, as well as providing a preliminary outcome analysis. The advantages of this version may help us plan target directly and adjust the trajectory to avoid the vascular plane and ventricle by displaying fusion image angles to the midsagittal or axial plane. Furthermore, because the frameless system has less limitations, patients can provide good coordination during macrostimulation, which can shorten the procedure time.

CASE REPORT

The patient was a 67-year-old male businessman without any previous systemic disease who had suffered from a slow movement since he was 57 years old. This slowness in the patient's voluntary movements was exacerbated as time went on. Eventually, the patient found it difficult to initiate movements and to complete movements. The patient also complained of stiffness of the limbs and trunk, which were increased during movement. This rigidity also gradually resulted in muscle aches and pain, whereas the loss of fine hand movements led to cramped handwriting (micrographia) and made eating difficult. The patient visited a neurologist out-patient department (OPD) because the symptoms persisted and disturbed his daily life. The diagnosis of PD was established as a result of the symptom response to levodopa replacement.

The patient was regularly followed up on by the neurologist OPD, and his dosage of levodopa was adjusted over time due to the motor symptoms being exacerbated as the disease advanced. Tremor symptoms began occurring as of 6 years ago, with trembling in fingers, hands, arms, feet, legs, jaw, and head being noted. Tremors most often occurred while the patient was resting, but not when he was involved in the task. Furthermore, the tremors worsened when he was excited, tired, or stressed. The dosage of the levodopa was adjusted along with the symptom progression, and dopamine agonists were also prescribed after the tremors began. The tremors subsided gradually under the medication, but, unfortunately, the patient struggled as the PD progressed still further, developing a distinctive shuffling walk with a stooped position and a diminished arm swing. He suffered from difficulty in starting to walk and in making turns, sometimes freezing in mid-stride and easily falling forward while walking. Motor fluctuations were also noted as the medication dosages were increased, with the medication eventually inducing dyskinesia. The increased levodopa dosages before the surgeries were as follows: BHL 1# QID, Mirapex 0.5# OID, Requip 1# BID, Stalevo 1# QID.

The preoperative motor score of unified Parkinson's disease rating scale (UPDRS) in the "off" state was 53, whereas the score for the "on" state was 12. After detailed investigation of the relevant indications and risks, DBS was suggested, and the patient was admitted on October 23, 2013. The frameless stereotactic procedure for subthalamic nuclei (STN) DBS implantation was performed on October 27, 2013. The procedure described in the discussion was performed well, and no immediate postoperative complications occurred. Then, the pulse generators were implanted on the anterior chest wall on November 1, 2013. The pulse generator was turned on as of November 28, 2013. The patient was then regularly followed up on at the Neurological OPD section, and the 12 months postoperative motor score of UPDRS in the "off" state was 30, while the score in the "on" state was 19.

DISCUSSION

The frameless system is an array of products designed to accurately provide deep brain access for the delivery of various therapies to smaller and deeper targets within the brain. This device is designed to provide, minimally, the same accuracy as that of the frame-based systems, while allowing more flexibility in imaging and planning for the procedure and providing an enhanced clinical outcome. Features of the frameless system, compared with the frame-based system, include [Figure 1]:

1. Five small fiducial screws that are inserted into the skull, taking the place of the head frame.
2. The use of a passive head restraint, instead of a Mayfield head holder.
3. The setting of an image-guided workstation for image fusion, target selection, preoperative lead and microelectrode recording (MER) needle insertion trajectory planning; the use of a new edition of the FrameLink software (5.2.4), matching hardware, and navigation system S7. Differences between the software versions are listed in Table 1.

The procedure overview algorithm [Figure 2] and the procedure are explained below.

Preoperative surgical planning

A magnetic resonance imaging (MRI) for target and trajectory selection should be performed days or weeks prior to surgery. Then, fiducial screws should be placed 1-3 days prior to surgery. At least five fiducial screws should be inserted into the patient's skull at different quadrants. After the fiducial screws are inserted, a brain computed tomography (CT) scan should be performed at 1-3 days prior to the surgery; surgical planning for target selection and lead trajectory are usually performed 1 day prior to the surgery.

Magnetic resonance imaging

Image fusion allows MRIs to be completed without fiducials days or weeks prior to surgery. An MRI can be performed, whereas the patient is in an on-medication state. However, patients sometimes require sedation during the performance of MRIs, due to the appearance of PD symptoms or drug-related dyskinesia.

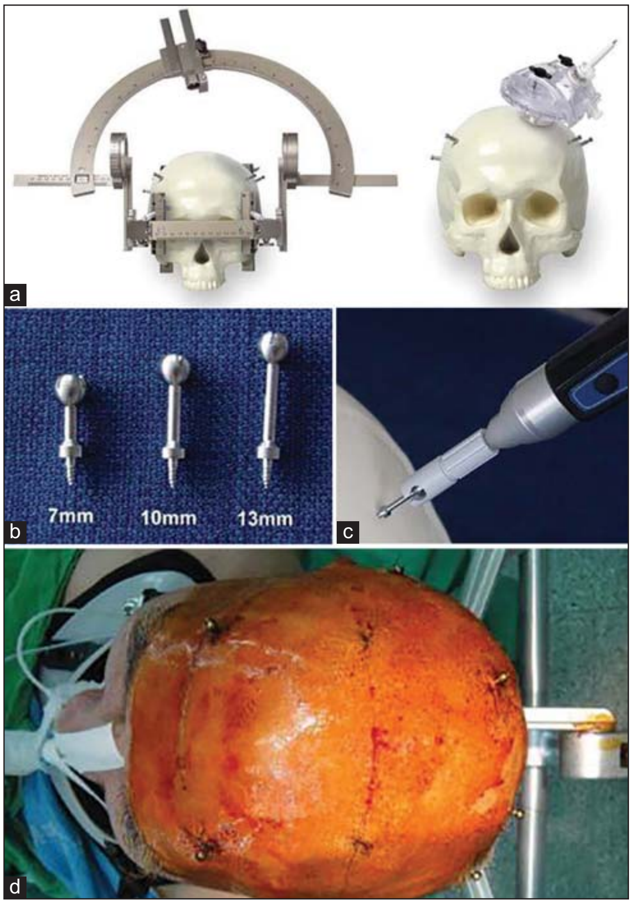

Figure 1. Photographs of patients during frame-based and frameless stereotaxic procedures for deep brain stimulation implantation. (a) Traditional frame-based stereotaxy (right panel) versus frameless stereotaxy (left panel). (b) Different sized unibody screws are available for different thicknesses of the skull bones. (c) An electric screwdriver can be used while inserting the screw, which can simplify the implant procedure. (d) The unibodies are provided after individually wrapped, under sterile micro-incision and local anesthesia, sterile pouched and screws inserted a with screwdriver guide. Then, inserted screws were protected with protective caps, and the fiducially computed tomography scan were performed. (panel a~c was adapted from Meditronic, Inc.)

Fiducial placement [Figure 1]

Fiducial placements were performed using the Nexframe Compatible fiducial systems (Medtronic IGN., Unibody). Stab incisions were performed under local anesthesia with fiducial screw insertion to the skull; five locations are recommended in different quadrants. These bone-implanted fiducial screws can provide sub-millimetric accuracy, and it can be easily tolerated by the patient, due to the minimized exposure procedure, which is comparatively to a head frame (vice grip) in the frame-based system. Fiducial screws are available in three lengths; however, 10 mm screws are typically used. The fiducial screws can be placed up to 30 days prior to surgery, but they are typically placed 1-3 days prior to surgery.

Table 1. Differences between the various editions of S7; this updated version provides greater accuracy (1 mm vs. 2 mm) during the navigation procedure and displays the angle from the mid sagittal plane and axial plane for lead entry and insertion trajectory planning

	Edition 1	Edition 2	Edition 3
Matching Navigation Hard Ware	Portable iNav Navigation	Treon Navigation	Treon Navigation/ S7 Navigation
Software Version		Frame Link 4.0	Frame Link 5.2.4 and beyond
Patient DICOM Image Manage	Not Support	Not Support	Yes
Automatically Create Entry Point	Not Support	Not Support	Yes
Display Angle from the Mid sagittal Plane and Axial Plane	Not Support	Not Support	Yes
The Safety Lead Margin Display	Not Support	Not Support	Yes
Allow Process Accuracy Value	2.0 mm	2.0 mm	1.0 mm

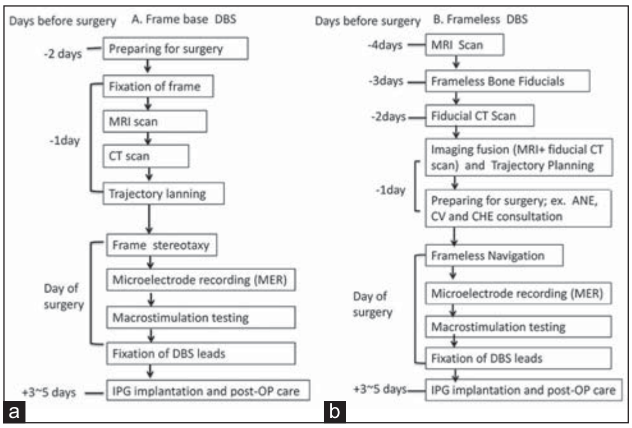

Figure 2. Differences in algorithms for stereotaxic procedures for deep brain stimulation implantation between frame-based and frameless surgery. (a) Traditional frame-based stereotaxic procedure; (b) Frameless stereotaxic procedure

Computed tomography scan procedure

After insertion of the fiducial screws, spiral or helical CT scans with no gantry tilt were performed on the immobilized heads of patients. The scans were performed with contiguous 1.0-1.5 mm-slice thicknesses and with a field of view of approximately 24-26 cm. All fiducial screws were imaged and scanned 2-3 cm above the top of the head.

Surgical planning and target selection [Figure 3]

Following the placement of the bone fiducial markers to the skull, a head CT scan was performed, and images were loaded into the FrameLink treatment planning system and combined with the MRI images to target the STN or Vim. An atlas-based system was used to target these nuclei.[12] Using FrameLink (or higher) software and matching CT and MRI with image merge [Figure 3a], we reformatted the images according to the anterior commissure-posterior commissure (AC-PC) plane [Figure 3b]. Then, we planned the target and entry points [Figure 3c]. The trajectory of lead and MER was then evaluated, and the vascular plane was avoided to prevent intraoperative bleeding. The whole tract of the planed trajectory (white arrow) was checked using fusion MRI to avoid the vascular plane and through the ventricle [Figure 3d]. As shown in Figure 3c, the new FrameLink version displays the angle from the midsagittal

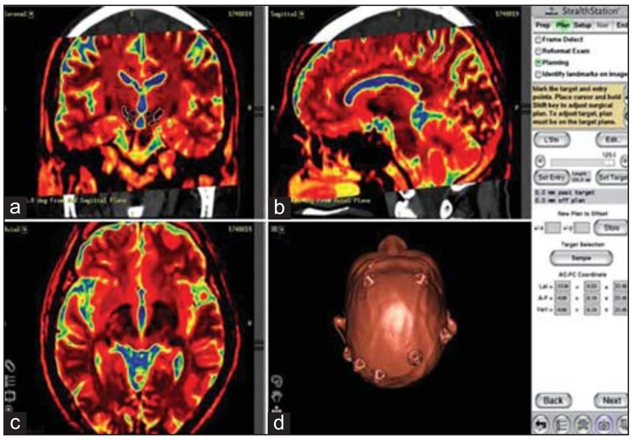

Figure 3. Pre-operation trajectory planning: After computed tomography and magnetic resonance match with image. Merge (a) we reformat images into anterior commissure-posterior commissure plane. (b) The subthalamic nuclei (STN) were shown in white dot line in (a and b) and the substantial Nigra were shown as yellow circle region (yellow dot line in a, and yellow solid line [b] below the STN while the red nuclei were shown at the medial region (blue dot line [a] and red dot line [b]. Then we planned the entry points and trajectory of lead (right side trajectory shown as yellow line and green line shown in the left [b]) after target were set. The trajectory of lead and microelectrode recording were evaluated and the vascular plane was avoided to prevent intraoperative bleeding. (c) The new version of FrameLink displays the angle from the mid sagittal plane and axial plane, which allows surgeons to evaluate the whole tract of the trajectory from entry along the trajectory to the target. After registration, the coordination of fiducial were set by the navigation system (d)

and axial planes, which allows the surgeon to evaluate the whole tract of the trajectory from the entry, along with the path of the trajectory to the target. The STN was targeted 10-12 (usually 11) mm lateral to the AC-PC line, 0 to −3.5 mm vertical to the AC-PC plane, and 3 mm posterior to the midpoint of AC-PC, and Vim was targeted 11 mm lateral to the third ventricle wall, 0 mm vertical to the AC-PC plane, and 6 mm anterior to the PC. Final targeting of the nuclei and delivery of the quadrupolar DBS electrode were fine-tuned using MER in a fashion similar to the one discussed by D'Haese *et al*.[12]

FrameLink-Fiducial selection (preoperative planning)

Magnetic resonance imaging was turned off to identify fiducial centroids using CT images and then storing images of the fiducial locations.

Equipment/room layout [Figure 4]

The procedure on the day of surgery

Non-sterile registration steps

We attached Xomed FESS Frame to the head of the patient [Figure 5a], who was fixed with a passive headrest attached to a Mayfield adaptor [Figure 5b]. A small passive frame was attached as reference [Figure 5c]. Then, we registered the patient and let navigate find the selected entries. When the selected entries were found, a skull marker was made under sterile local anesthesia using a stamen pin, which penetrated the cutaneous layer of each frontal region.

Draping-fluoro scheme

The sterile surgical file was prepared and 3M #6617 "Ortho Drape" was applied to the field and attached to the inverted C-Arm.

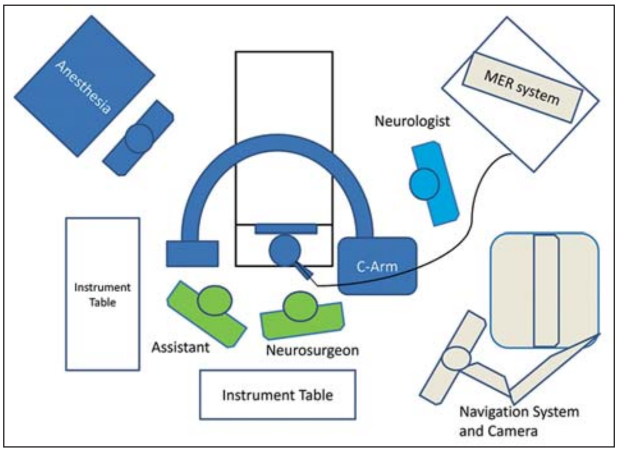

Figure 4. Equipment/room layout

Sterile registration

After non-sterile registration of the entry location, routine surgical preparation and drape were performed, followed by a bicoronal incision. The incision was then extended with enough space to accept the base of the platform (Nexframe #DB-1040, Image-guided Neurologics, Melbourne, FL, USA). Then, we created a burr hole on each side of the frontal bone, based on the entry location marked by the stamen pin. After a 14 mm burr hole was centered over the previously drilled entry point made by the stamen pin, the lead anchor or Stimloc base was mounted over the burr hole. The NeXframe with reference [Sm. Passive Frame, Figure 6b] attachment was then positioned over the StimLoc base attached to the skull bone with three self-tapping screws [Figure 6a]. The Nexframe base was then positioned over the Stimloc base and attached to the skull using three self-tapping screws. It is critical that there be no movement between the platform and the skull [Figure 6a]. Then, sterile fiducial registration was performed. Fiducial locations were registered through the drape and then prepare actively align NeXframe to target.

Verify registration

The reference arc (passive spinal reference frame) was attached to the reference bracket. Registration was performed with the reference probe (passive planar probe) [Figure 6c]. After registration, the system's accuracy was checked again by pointing each fiducial screw with a registration probe. The guidance probe (guideframe-DT) was verified prior to the next step [Figure 7]. The two-passive planar probe pointed back to fiducial locations to verify the accuracy. The dura was then opened, and a cortical incision was made. Gelfoam was placed, and fibrin glue was used to prevent CSF leakage and to minimize brain shift.

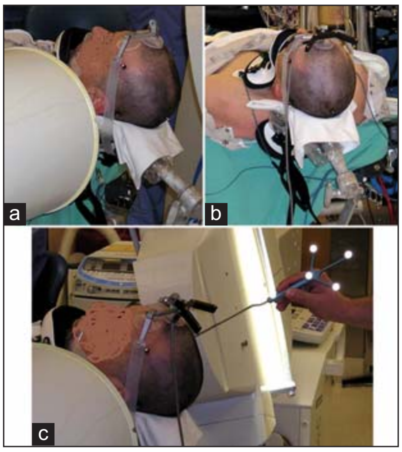

Figure 5. Non-sterile registration steps: Xomed FESS Frame was attached to the head (a), and the patient was fixed with a passive headrest attached to the Mayfield adaptor (b). Then, a small passive frame was attached as a reference (c). We registered the patient and let navigate to find the selected entry

Nexdrive alignment adaptor positioning

The Nexdrive alignment adapter is attached to the Nexframe tower. The guideframe-DT is then attached to the alignment adapter.

Steps of obtain alignment the insertion trajectory to target by using rotate and sweep of guidance probe [Figure 8].

The guidance probe (Nexprobe, Meditronic Inc.) was adjusted to align to the target by sweeping and rotating the tower, while the surgeon observes through the computer screen until alignment to the target is achieved, after which the locking screws are locked. Nexprobe was used as the guidance probe, since it is a disposable registration and alignment tool that can replace all reusable stealth probes and eliminate the user calibration step of GFDT. It also improves the line-of-site to the camera and allows the procedure to proceed with MER, macro-stimulation, and implant as if it were a framed procedure. After the depth to the target was obtained by the image-guided system, the guidance probe was removed. A 3-mm offset alignment is normally used to avoid cortical vessels.

Microelectrode drive attachment to NexDrive adaptor [Figures 9a and b]

When the Nexdrive in conjunction with the Nexframe 1-Microdrive, 2-Multi-lumen adapter was placed, the Nexdrive alignment adapter was removed, and the Nexdrive multilumen adapter was replaced. The Z-stage on the microdrive (Nexdrive

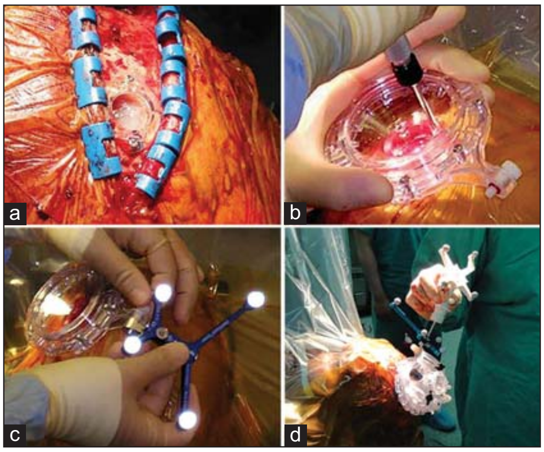

Figure 6. After a 14 mm burr-hole was centered over the previous drilled entry point made by the stamen pin, the lead anchor or Stimloc base was mounted over the burr hole. The NeXframe with reference (Sm. Passive Frame, [a]) attachment was then positioned over the StimLoc base that was attached to the skull bone with three slef-tapping screws (b). The Nexframe base was then positioned over the Stimloc base and attached to the skull using three self-tapping screws. It is crucial that there be no movement between the platform and the skull (c). The reference arc (passive spinal reference frame) was attached to the reference bracket. The registration was performed with the reference probe (passive planar probe) (d)

#MI-1000) was set to the desired depth based on the image guided system and mounted on the adapter [Figure 7]. Gelfoam was removed and the guide tube with stylet was inserted. The stylet was removed and the microelectrode spacer tube was inserted. The microelectrode collet was attached to the microdrive, and the microelectrode inserted then tightens the microelectrode collet screws.

Microelectrode recording

Microelectrode recording steps

The micro-drive starting point was calculated, the IGN NeXdrive (or FHC microTargeting drive for frame-based surgery) was assembled, and the cannulae were inserted. Then, the microelectrode and additional tracks were inserted to perform a parallel track, or the offset positioner can be used. The microelectrode was introduced automatically through the MER knob. The position of the microelectrode could be determined from the MER scale (1 mm increments) and the MER index scale (10 micron increments) or from the digital display unit [Figure 10].

Lead placement

After the MER study for physical localization [Figure 10] of the appropriate target, we initiated the process of placing

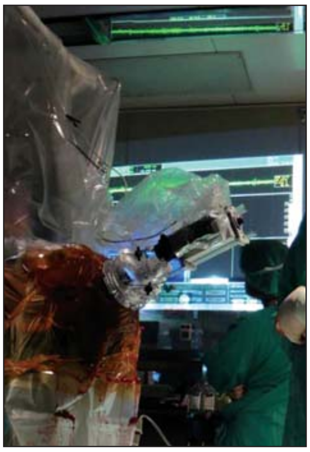

Figure 7. The NexDrive alignment adapter was removed and the NexDrive multi-lumen adapter was replaced. The Z-stage on the microdrive (Nexdrive #MI-1000) was set to the desired depth, based on the image guided system and mounted on the adapter

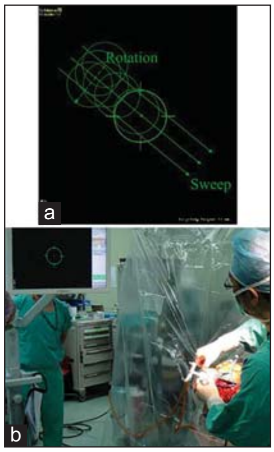

Figure 8. Steps for aligning the insertion trajectory to the target using rotate and sweep for the guidance probe. The guidance probe (Nexprobe, Meditronic, Inc.) was adjusted to align to the target by sweeping and rotating the tower (a), while the surgeon observed the computer screen until the alignment to the target was achieved; then, the locking screws were locked (b)

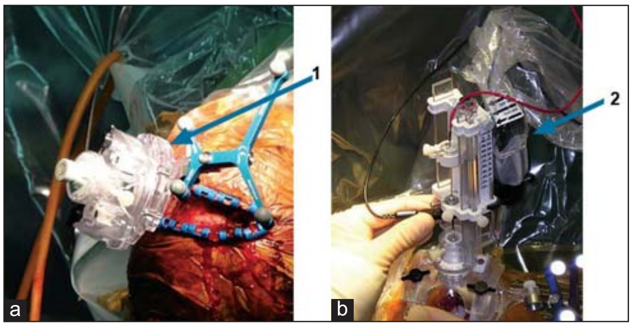

Figure 9. The multi-lumen adaptor was applied to the NexFrame (a) and then the microelectrode drive was attached to the NexDrive adaptor for the microelectrode recording. (b) NexDrive in conjunction with Nexframe. 1 - Microdrive, 2 - Multi-lumen adapter

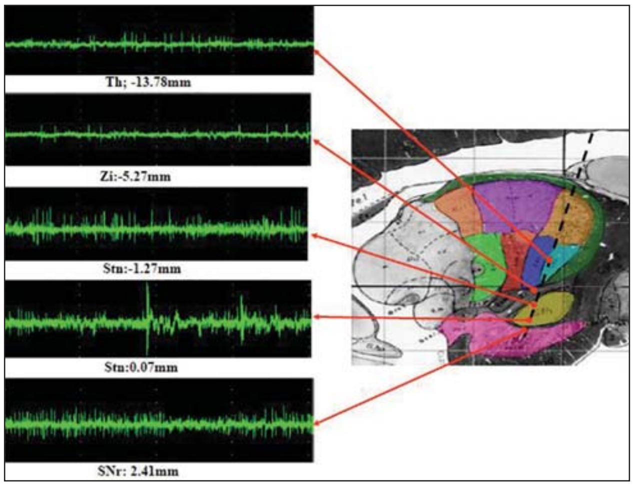

Figure 10. Micro-recording result: The microelectrode was introduced through the microelectrode recording (MER) knob manually. The position of the microelectrode can be obtained from the MER scale (1 mm increments) and the MER index scale (10 μ increments) or from the digital display unit. The cellular firing frequency of different anatomic area that recording electrode lead insertion would be recorded while the left upper panel to lower panel showing that representative firing pattern of microrecordings of each anatomical area were different along the insertion corridor (black dot line); and the right panel is the sagittal section of the brain through the thalamus. (Th: Thalamus, Zi: Zona inserta, Stn: Subthalamic nuclei, SNr: Substantial nigra pars reticulate; the number revealed the distance to the target)

the DBS lead. The drive was set to desired target depth [Figure 11a]. The microelectrode and spacer cannula were removed, and the stimulation lead was extracted from plastic canula [Figure 11b]. DBS lead length was calibrated with the measuring tube. Then, the calibration tube was removed, and the lead inserted.

Inset StimLoc Cam

StimLoc Cam was inserted to close around the lead. The lead at cam was marked using a marking pen.

Lead fixation

The lead stylet was removed, and the cannula inserted. The lead was pulled down into NEXFRAME. Disassemble for access to StimLoc. Then, the lead was placed in the StimLoc exit slot, and the final cap was placed over the base [Figure 12]. The procedure was then completed, and the fiducials removed. After the final target had been defined by MER, the microelectrode and spacer cannula were removed. The DBS lead was inserted into the DBS bracket/measured tube, and the depth was adjusted with the desired electrode at the end of the measuring tube. Then, the electrode was secured with a thumbscrew. The measuring tube was removed from the DBS bracket. The electrode was then inserted into the outer cannula. After determining the final target by macrostimulation, we then retracted the outer cannula. The DBS lead was captured by StimLoc cam and locked in place. The cannula, DBS stylet, Nexdrive, and Nexframe tower were removed. The remainder of the procedure was performed following the traditional procedures for DBS surgery.

Postoperative follow-up [Figure 13]

Testing and DBS electrode programming was performed 1 month after surgery, and patient follow-ups took place every 1-2 months for the first 6 months and every 3-4 months thereafter. The testing was performed in the off-medication and on-DBS conditions, and assessment was executed using the UPDRS. At each follow-up, stimulation parameters were adjusted to achieve optimal symptom relief and to diminish side effects.

Implantable neurostimulation devices used during stereotactic surgery have become important tools for neurosurgery. Technological advances have made it possible for these devices to treat a wide range of neurological symptoms as well as for patients to receive relief by means of cochlear implants, cortical and deep brain stimulators, and systems for spinal cord, vagus, and gastric nerve stimulation.[13] Differences in the preoperative procedures can especially be found in the stereotactic system, the imaging modality, the moment of image acquisition and the targeting technique.[14] In

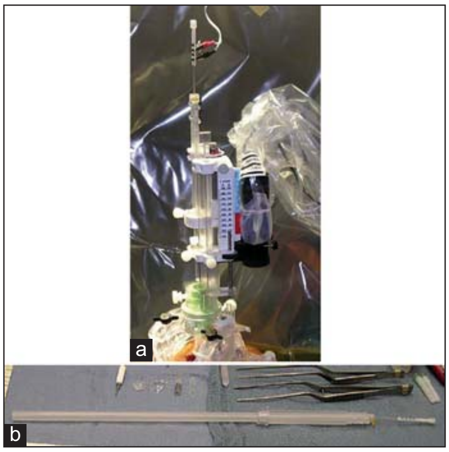

Figure 11. Stimulation lead placement: After performing the microelectrode recording study to locate the target, we initiated the process of placing the deep brain stimulation (DBS) lead. The drive was set to the desired target depth (a). The microelectrode and spacer cannula were removed, and the stimulation lead was extracted from the plastic protector (b). The DBS lead length was calibrated with the measuring tube; the calibration tube was removed and the lead inserted

Figure 12. Lead fixation: The StimLoc Cam was inserted onto the lead. The lead at cam was marked with marking pen. The lead stylet was removed and the cannula inserted. The lead was pulled down into NEXFRAME. Disassemble for access to StimLoc. The lead was placed in the StimLoc exit slot, and the final cap was placed over the base

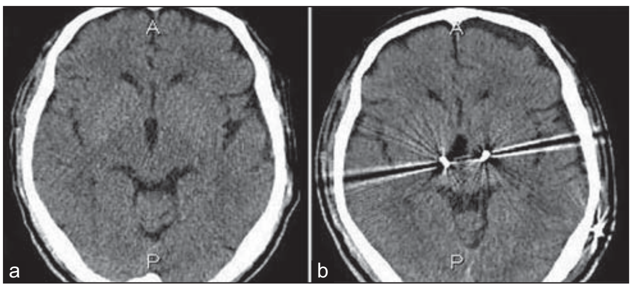

Figure 13. Post operation lead position rechecks. (a) The preoperative computed tomography scan and (b) postoperative image show the position of the tip of the lead

this paper, we highlighted the techniques related to frameless DBS surgery that uses a new version of navigation software support. We focused on the procedures involved in frameless stereotaxy compared the implantation procedures as well as the differences in steps between frame-based and frameless stereotaxy, and preliminary outcomes analysis. The advantage of this version allows us to plan the target directly and adjust the trajectory so as to avoid the vascular plane and ventricle by displaying fusion image angles to the mid sagittal or axial plane.

The new aspect of stereotactic surgery made possible by the new version of FrameLink software and S7 navigation and the advantages of this version of equipment for frameless surgery include:

1. Direct targeting in preoperative planning;
2. Detailed MER, and
3. Less discomfort for patients during the preoperative planning and perioperative stages with good coordination to mascrostimulation and shorten the surgery.

At the initial stage of surgery, the primary challenge faced by the neurosurgeon and the patient is preoperative planning, where a specific target in the brain and the trajectory for reaching this target be planned on preoperative anatomical images. In traditional frame-based stereotactic surgery, the patients must tolerate frame fixation during the perioperative stage. In the case of frameless surgery, however, only small-sized unibody fiducials are affixed to the patient's skull, which does not limit the patient's performance of daily activities. Then, the fusion image with a fiducial marker at the patient's skull is load into the stereotactic system to introduce a reference system to the images. The accuracy of the planning target via the different frameless fiducial systems for DBS implantation have been described and compared with frame-based systems.[15-18]

Because the placement of electrodes for DBS is a challenging neurosurgical procedure that demands a high degree of precision, accurate positioning of the electrodes is crucial for obtaining optimal results, and it requires an anatomically reliable preoperative target planning and physiologically intraoperative MER. Accurate positioning of electrodes is mandatory to obtain optimal results. Most centers use the same 2-step procedure: First, a target is chosen preoperatively based on anatomical landmarks identified on MRIs. Next, this point is used as an initial position that is refined intraoperatively using both MERs and macrostimulation then.

Concerning the imaging modalities, the AC-PC were used as references for atlas-based targeting, and this AC-PC line was previously identified by ventriculography, which has now been replaced by CT and MRI.[19] MRI is the imaging modality of choice. The sequence used depends on the chosen target structure: T1[20] or proton density imaging[21] is used especially for targeting the *Globus pallidus* (GPi); T2 imaging is used for STN targeting;[19,22,23] inversion recovery images are also beneficial for the direct targeting of Gpi and STN.[24] Furthermore, direct targeting techniques are now available in the new version of navigation software, as shown in Figure 3a.

There were wealth papers discussed the method for setting the target in STN. Amount of these studies, the coordination of indirect method for target selection were controversial while most of reported coordinates of the STN target are 9-12 mm lateral, 1-3 mm posterior, and 3-5 mm inferior to the midcommissural (mid-AC-PC) point;[25,26] and 12.12 mm lateral, 2.41 mm posterior, and 2.39 mm inferior relative to the midcommissural point.[27] However, some authors report targets 4 mm anterior, 4 mm deep, and 12 mm lateral to the midcommissural point.[28] In a cohort study, by using a statistical correlation of the coordinate values of active electrode contacts with the amplitude of residual clinical symptoms and side-effects, the result indicated that the optimal target is located 12-12.3 mm lateral to the ACPC line and 3.1-3.3 mm under the AC-PC line; but no preferred y-coordinate location (distance in front or behind the midcommissural point) could be found with this method.[29] MRI can safely be used for stereotactic targeting in DBS surgery, and it does not negatively affect the accuracy of the electrode implantation.[30] The distortions that are produced in each specific MRI unit to use the stereotactic coordinates clinically should be noted;[31] but it is possible to obtain excellent precision with MRI stereotactic data with higher quality assurance.[32]

In current frameless stereotactic procedure that was also used in our patient, by using MRI/CT fusion for anatomic localization could provide same accuracy as those from using direct targeting with MRI in stereotactic conditions.[31] With this technique, CT is performed by using stereotactic techniques, while the stereotactic coordinates and the outlines of the targeted nucleus are obtained with nonstereotactic MRI, and then the two datasets are fused. The use frameless stereotaxy with a skull mounted trajectory guide and an image-guided workstation for DBS surgery became popular.[10]

By using open 0.2T operative MRI real-time high field interventional MRI, could be performed DBS implants in some patients.[33,34] A system consisting of a deformable computerized atlas of optimal target points, an electrophysiologic atlas, and an intraoperative graphic interface has been developed,[35] allowing preoperative selection of target points and intraoperative optimization of the targets.

Therefore, many authors use direct MRI targeting of the STN currently and we also set the target of STN according to the previous report that indicated the STNs were visible as biconvex hypointense structures located in the upper mesencephalon by using of coronal T2-weighted images [Figure 3a and b].[36] The anterior border of the red nucleus as an internal reference for the anteroposterior location of the STN target was also used for imporatant land mark. Furthermore, an anatomic MRI study[37] has defined the spatial distribution of the STN, showing that the hypointense signal intensity located lateral to the red nucleus and dorsolateral to the substantia nigra was correlated with the presence of iron and corresponded anatomically to the STN. This study also showed that at 1.5T, the MRI T2 hypointensity predominated in the rostral two-thirds of the STN and that the posterior part of the nucleus was not hypointense and thus not visible in most cases.[38]

To use the stereotactic coordinates clinically, it is necessary to note the distortions that are produced in each specific MRI unit[39] to avoid negatively affect the accuracy of the electrode implantation.[40] With proper quality assurance, it has been shown that high precision can be obtained with MRI stereotactic data.[38,39]

Moreover, the surgical procedure time, including MER and macrostimulation, can be shortened due to the patient's high level of coordination under frameless stereotaxy. The second main issue of the procedure is the intervention itself. It can be performed under local or general anesthesia, depending on whether the patient's feedback is needed for specific testing. For various reasons, including individual variability regarding brain anatomy, several problems may arise during a DBS implantation. One of the most significant problems is the ''brain shift,'' which may occur during the incision of the dura and cause a deviation from the pre-planned target coordinates, resulting in suboptimal anatomical location with side effects or even.[41,42] In addition to varying brain anatomy, brain shifts are a reason why intraoperative measurements are often performed. Such complementary intraoperative data acquisition methods can be, for example, impedance measurements while creating the trajectory for the DBS electrode, proving the situation of the surrounding structures passed as shown in Figures 7 and 10.[43]

Another issue concerns the physiological target of the stimulation lead. The method that is used most often is MER, which is based on registering neuronal activity.[44,45] Registration is recorded along 1-5 trajectories in the volume of interest to identify the different structure boundaries. In general, these measurements are performed in millimeter steps (usually 19-20 mm) before reaching the target, and the measurements often go beyond (usually 5 mm deeper) the target structure. That is why the multi-lumen adaptor should be placed during this stage [Figure 10a].

Finally, most centers using MER also perform intraoperative stimulation along the trajectory using microelectrodes stimulating in the microampere range[35,46,47] or in the miliampere range, using, for example, RF- or DBS stimulation electrodes.[16,48] In general, this is performed at the same measurement points as for MER to evaluate the clinical effects with increasing stimulation current and to determine symptom reduction, the clinical therapeutic and side effect thresholds at each measurement point. Intraoperative correction can also be provided by cross-hairs in frame-based surgery, and the functional improvement is significant after cross-hairs were applied in the initial development stage at our center [Figures 13b and c]. The physiological localization executed by MER in our frameless procedure also improved significantly so far.

CONCLUSION

Deep brain stimulation surgery using frameless stereotaxy as a treatment for advanced PD can result in positive clinical outcomes for motor symptoms as evidenced by the significant improvements in UPDRS at mean follow-up. The clinical results are similar between the frameless and frame-based groups (except for the non-cross-hair frame-based group), however, frameless DBS can reduce the patient's discomfort, decrease operation time, and enhance the surgical team's ability to interact with the patient during the operation.

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DISCLOSURE

The authors declare this study has no conflict of interest.

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