CHAPTER xx: ABLATIVE PROCEDURES FOR MOVEMENT DISORDERS

Introduction

Although deep brain stimulation (DBS) has dominated functional neurosurgery since its introduction in the late 1990's, there is still a role for lesional techniques in the treatment of some patients with Parkinson's disease (PD), dystonia, tremor, or hemiballismus. Okun[1], Hariz[2], Gross[3], Bulluss[4] and Hooper[5] have reviewed the evidence and potential advantages of lesioning compared to DBS, and emphasized the importance for a functional neurosurgeon to be skilled in the techniques of lesioning in addition to DBS to best treat the various symptoms of adequately selected patients with movement disorders. The most recent evidence-based medicine review by the Movement Disorder Society[6] concluded that unilateral pallidotomy is efficacious as a symptomatic adjunct to levodopa (L-Dopa) for motor fluctuations and dyskinesia, and unilateral thalamotomy is likely efficacious as well for PD patients. Unilateral pallidotomy is considerably better for patients with advanced PD than best medical therapy alone[7], and better than pallidal DBS at least for dyskinesias[8, 9]. The main advantage of DBS is that it can be done bilaterally with greater safety than pallidotomy or thalamotomy. Pallidotomy, however, has been used effectively following failures of DBS[4]. The standard technique of lesioning has involved the use of a radiofrequency generator; although newer techniques currently under development include magnetic resonance imaging (MRI) guided focused ultrasound lesioning[10] and MRI-guided laser ablations.

Pallidotomy:

Patient Selection

The selection of PD patients for surgery is best done by a multi-disciplinary team (movement disorder neurologist, neuropsychologist, psychiatrist, and neurosurgeon). The best candidates for pallidotomy have asymmetric idiopathic PD responsive to dopaminergic therapy but with moderate to severe motor fluctuations, dyskinesias, or tremor despite optimal medical therapy. Speech, balance, or gait problems not responsive to levodopa are not primary indications for surgery. Relative contraindications for surgery include dementia (Mini-Mental status examination (MMSE) ≤ 24/30, or Mattis Dementia Rating Scale (MDRS) ≤ 130/144), depression (Montgomery and Åsberg Depression Rating Scale – MADRS score ≥ 19 points), uncontrolled psychiatric disorders, severe postural instability, and patients with secondary Parkinsonism and Parkinson's plus syndromes. Unilateral pallidotomy is an effective and safe procedure yielding 20-30% decreases in "off" motor scores with excellent effects on contralateral dyskinesias and dystonia, good benefits on tremor, akinesia, and rigidity, but with minimal benefits on axial symptoms[3]. Patient selection for pallidotomy rather than DBS might include: 1. Logistical issues related to DBS (i.e. programming), 2. Patient choice against implanted hardware and hardware-related complications, 3. Medical co-morbidities prohibiting the use of general anesthesia (pallidotomy can be entirely performed under local anesthesia), 4. Immunosuppression increasing the risk of infection with implanted hardware, 5. Patients with a previous DBS procedure who sustained a postoperative infectious complication requiring explantation of the DBS system, and 6. DBS is not available due to reasons of geography or expense. Patients with PD are evaluated by the movement disorder neurology team in both the off medication condition (defined as 8 hours without medication) and in the on medication condition (defined as 1 hour after taking medication). Objective measures of disability are documented using standard scales

for assessment of PD (Hoehn and Yahr stages, the Schwab and English disability scale, and the Unified Parkinson's Disease Rating Scale). Neuropsychological evaluation and psychiatric screening are performed for all patients.

The selection of dystonia patients for surgery requires a multi-disciplinary team (movement disorder neurologist, neuropsychologist, psychiatrist, neuroradiologist, and neurosurgeon). The best candidates are younger patients with primary dystonia (particularly those with DYPT-1 gen mutations) and/or tardive dystonia who have failed medical therapy and are fairly disabled. The severity of dystonia and disability must be assessed by appropriate rating scales (including the Burke-Fahn-Marsden Dystonia Rating Scale and the Toronto Western Spasmodic Torticollis Rating Scale), and cognitive and psychiatric assessments are required as baseline measures. Pallidotomy is an option for patients who are not candidates for DBS[11,12].

Preoperative Preparation

When possible, surgery is performed after withholding medications overnight and without sedation to facilitate the clinical assessment of the effects of incremental lesions. An MRI scan is obtained which includes a 3 dimensional SPGR volumetric sequence with 1mm slice thickness allowing reconstruction in the sagittal, coronal, and axial planes, and a SWI sequence (TR: 49 ms, TE: 40 ms, slice thickness: 3.0 mm, resolution: 256x192) that sharply delineates the globus pallidus nuclei from the internal capsule (Figure 1).

Operative Technique

Anesthesia preparation

Ipsilateral intravenous access is established to permit freedom of movement of the extremity of interest. Oxygen is supplied via a nasal cannula and EKG, pulse oximetry, and BP is monitored. Arterial line placement and bladder catheterization are not routinely performed. Pallidotomy is facilitated by the full cooperation of the patient and is performed under local anesthetic. The blood pressure should be well controlled intraoperatively and postoperatively to reduce the risk of hemorrhage.

Headframe placement

The patient is sedated with a short acting anesthetic such as propofol, and after infiltration of the pin insertion sites a COMPASS stereotactic frame (Rochester, MN)[13] is secured to the outer table of the skull. Following application of the head frame a CT scan is obtained (1mm contiguous slices, 512 x 512 matrix, no gantry tilt).

Target and Trajectory Planning

CT and MRI images are analyzed using the COMPASS software which is compatible with either a COMPASS or Leksell stereotactic systems, and the CT fiducials are selected[13]. The stereotactic CT is then merged with the preoperative MRI14. GPi targeting is performed both indirectly in relationship to the midcommisural point (2-3 mm anterior, 3-5 mm inferior, 19-22

mm lateral) and by direct visualization of the GPi on axial and coronal MRI images. The direct target is selected using the slice at the level of the AC-PC and drawing a line along the pallidocapsular border (the border of the GPi and the internal capsule). This line is typically about 18-20 mm in length. This line is divided into thirds and the target is placed 1/3 the distance from the posterior end of the line and 3 mm lateral along a line drawn from the pallidocapsular border. After selecting this target, the final target is chosen along the trajectory using the probe's eye view to the bottom of the GPi at a point usually just lateral and 2 mm above the optic tract[15]. The GPi target can be visualized on a stereotactic atlas that has been proportionally adjusted to the individual patient[16] Once an appropriate target has been selected, a trajectory is chosen along as near a parasagittal plane as possible that avoids the lateral ventricle and any sulci (Figure 2). The GPi target coordinates are placed into the center of the COMPASS stereotactic frame.

Surgical Technique – Stereotactic Pallidotomy

The patient is positioned with the head secured in the stereotactic headholder in the semi-siting position. Every effort should be made to make the patient as comfortable as possible. We have found that foam padding behind the neck is particularly helpful. Appropriate prophylactic antibiotics and a single dose of 8 mg of dexamethasone are administered intravenously, and a grounding pad is applied for stimulation and lesioning. The entry site (chosen in the preoperative simulation) and linear incision in the coronal direction are marked and the hair is parted along the incision line. The wound is prepped and draped keeping the draping to a minimum, usually with an Ioban drape (3M, St Paul, MN) and a single craniotomy drape attached to IV poles on both sides in a tent-like manner so that the patient's face and body are free for assessment by the movement disorder neurology team (movement disorder neurologist who assesses the patient's function and a nurse who records the finding).

The scalp is infiltrated with local anesthetic (1% Ropivacaine), the incision is made, and a burr hole placed using a high speed drill. The dura is coagulated with bipolar cautery and incised, and the pia is coagulated and incised to assure atraumatic insertion of the electrode. The stereotactic frame is positioned and the guide tube inserted into the burr hole. Gelfoam is used to fill the burr hole around the guide tube and bone wax is used to seal the opening to minimize the loss of CSF.

Physiologic Confirmation of the Target

The next step is physiologic confirmation of the target. The two options are microelectrode recording/microstimulation and macrostimulation. The role of microelectrode recording in pallidotomy is actively debated. Microelectrode recordings have been used by many centers in an effort to identify the optimal target and minimize injury to the internal capsule and optic tract with reports of clear benefit from those centers that use this technique[17-20]. However, pallidotomy without microelectrode recordings can achieve similar results[21-23]. The issue of the potential benefits of microelectrode recordings compared to the increased risks of hemorrhage and prolonged surgery remains unresolved and will likely remain so, as it is unlikely that a large randomized study to definitively answer such a question will ever be completed. Suffice it to say that expertise in the surgical treatment of movement disorders demands familiarity and competence in both of these techniques.

The techniques for microelectrode recording have been well described by Lozano et al[24] and Starr et al[25]. The principles are that transitions between gray and white matter can be identified, and that the basal ganglia nuclei have characteristic patterns of spontaneous discharge that can be identified[24,26]. Additionally, motor subterritories of a region can be distinguished from nonmotor regions by identifying neurons whose discharge frequency can be modulated by movement, and somatotopic organization of a nucleus can be determined. GPe neurons have two distinct patterns of activity. Some units have a 10-20 Hz discharge frequency punctuated by rapid bursts while others have an irregular firing pattern at 36-60 Hz with intervening periods of low activity. Neurons of the GPi in patients with PD have a higher and more continuous baseline firing rate (80Hz) than GPe neurons, and respond to contralateral movements with an increase in firing rate. As the microelectrode exists the inferior border of the GPi and enters the white matter of the ansa lenticularis the neuronal activity decreases. A few millimeters beyond the inferior border of the GPi is the optic tract that is best identified by microstimulation (1-2 sec trains of 1-2 msec square waves at 100-300 Hz) that elicits visual phenomena of flashing lights reported by the patient, although sometimes spontaneous neuronal activity can be evoked with the use of photic stimulation. A lateral x-ray or c-arm is obtained to confirm the target site.

At our institution pallidotomy is now more commonly performed without microelectrode recordings with physiologic target confirmation confirmed by macrostimulation using an RF generator (Cosman G4). A1.1 mm macroelectrode with a 3mm exposed tip (Radionics, Burlington, MA) is inserted through the guide tube under impedance monitoring[27] (impedance decreases in the gray matter of the basal ganglia) and advanced to a point 4 mm above the target site. Macrostimulation is then performed using high frequency stimulation (100Hz) to assess for proximity to the optic tract, speech dysfunction, and amelioration of symptoms, while low frequency stimulation (5 Hz) is performed to assess for motor thresholds and proximity to the internal capsule. The threshold for any visual phenomenon such as flashing lights or phosphenes in the contralateral hemifield should be a minimum of 2 volts and preferably 3-4 volts. A threshold < 2volts means the electrode is too close to the optic tract and should be withdrawn until the visual threshold meets this criteria. Motor thresholds are assessed by slowly increasing the low frequency stimulation until contractions are observed in the contralateral hand, face, or tongue. The motor thresholds should be a minimum of 2 volts and preferably 3-4 volts. A motor threshold < 2 volts implies the electrode is too close to the internal capsule and should be moved laterally or anteriorly. Macrostimulation at low and high frequency is performed at 4 mm and 2 mm above the target and at the target. High frequency stimulation usually produces improvements in contralateral rigidity and bradykinesia assessed during surgery by finger and toe tapping, and pronation/supination of the forearm. In some cases high frequency stimulation elicits dyskinesias, a finding the generally portends a good outcome. Speech is assessed during high frequency stimulation for any dysfunction.

Once the electrode is advanced to the target, a lateral skull x-ray or c-arm image (fixed lateral x-ray in our operating room (Figure 3) is obtained to verify the position of the electrode at the center of the stereotactic bomb sites confirming the electrode is at the chosen target site positioned at the center of the stereotactic frame. If necessary, the electrode is repositioned based upon the macrostimulation and x-ray findings by using a parallel trajectory 2mm in the appropriate direction from the initial trajectory.

Lesioning

After the target site has been confirmed, a test lesion is first made at 46 degrees for 60 seconds and the patient assessed for any evidence of motor, speech or visual impairment. If the test lesion is tolerated without any side effects, a therapeutic lesion is made using 80 degrees for 60 seconds. The electrode is then withdrawn 2mm and subsequently 4 mm above the target and a lesion made at each site using the same parameters (80 degrees for 60 seconds). After each lesion the patient is assessed for therapeutic effects on rigidity, bradykinesia, and tremor as well as for any motor or visual side effects. After these lesions are completed, if further therapeutic benefit is needed, one can consider using a parallel trajectory using the same technique and expanding the lesion. When the results of the pallidotomy are considered satisfactory the electrode is withdrawn. The wound is irrigated, the burr hole closed with Gelfoam, and the wound closed in layers. The head frame is removed.

Surgical Technique – Intraoperative MRI Laser Pallidotomy

The mainstays for successful pallidotomy or thalamotomy have always been proper surgical placement of the lesion probe and reliable neurological examination of the patient during the lesioning process itself. In rare circumstances, it may be challenging to perform neurological assessments, which can compromise the surgeon's ability to accurately assess the size of the lesion during surgery. For example, patients with severe anxiety, difficulty focusing or significant speech disturbance (such as hypophonia or festination) can be difficult to examine quickly and reliably.

In recent years, interventional MRI has been used to perform deep brain stimulator placement with patients under general anesthesia. This technique allows devices to be placed in the basal ganglia using real-time MR guidance with a high degree of accuracy and clinical outcomes that are comparable to awake, physiologically guided surgery[28-30]. More recently, the use of temperature sensitive MR sequences and the development of optical fiber laser delivery systems now make it possible to create thermal lesions in the CNS and monitor their progress in real-time using interventional MRI[28].

MRI-guided lesioning under general anesthesia is now a consideration for patients that are felt to be good motoric candidates for surgery but would not tolerate an awake procedure. In this technique, proper lesion size is determined not by physical exam but by direct visualization of the volume of tissue destruction on thermal-sensitive sequences relative to adjacent structures such as the internal capsule.

Planning is performed on MR sequences that allow direct visualization of the GPi and the internal capsule (such as inversion recovery). The software specific to the laser system being used allows the surgical team to set thermal safety limits on specific structures, such as the internal capsule; if the temperature exceeds these pre-set limits as the lesion is expanding, the laser will shut off automatically. This is important because the

thermal-sensitive images are by necessity acquired rapidly (every 6 seconds) to monitor lesion growth, which means they are relatively low resolution and do not provide the tissue discrimination of a scan that is acquired over 8 or 10 minutes. For this reason, the surgeon should target and plan their lesion size on high resolution images that show the relevant anatomy and then set sub-lesional thermal limits on structures they wish to protect.

For pallidotomy, the structures to protect are the internal capsule and the optic tract, both of which can be seen clearly on appropriate imaging. Target selection is determined based on direct visualization of the GPi and surrounding anatomy, and is done in the same manner as described above for awake patients.

Once the laser fiber is placed and the position is confirmed, the process of lesioning can begin. The laser software shows a so-called "damage map"; this is the predicted size of the lesion based on the temperature sensitive MR sequences (Figure 4). Keep in mind that there will be a penumbra or "halo" of increased but sub-lesional temperatures larger than the actual lesion size. For this reason, one should pay attention to the damage map and use thermal limits to monitor progress, as the lesion process itself happens very quickly. Once the laser is either turned off by the surgeon or automatically shut off by a thermal limit, one can obtain a diffusion-weighted image set to assess the true lesion size. Be wary of relying on T2 sequences at this stage, as they frequently show high signal that is significantly larger than the actual lesion.

The relative merits of this technique over awake surgery must be considered on a case-by-case basis, and decision-making must be based on clinical factors, not convenience.

Postoperative Management and Results

All patients are monitored overnight in the hospital with careful attention to the blood pressure to avoid hypertension, and most all (87%) returned home the day following surgery. Preoperative Parkinson's medications are resumed, and the rapidity of action, magnitude, and duration of motor response to levodopa therapy is maintained after pallidotomy[31]. In more than 360 patients undergoing lesioning procedures at our center, none have experienced a visual field deficit, no patient has required a craniotomy for evacuation of an acute intracerebral hematoma, and there have been no infections. The most common side effects are transient confusion, and mild transient weakness particularly in the face which resolve within 7-10 days after surgery. Patients who had transient weakness tended to have excellent outcomes from pallidotomy, an observation made many previous stereotactic surgeons. On patient was mute for 2 weeks following a left-sided pallidotomy but regained normal speech by 6 weeks. In general, the risks of complications following pallidotomy ranges from 2-5%[32, 33, 39].

A primary benefit of pallidotomy is reduction of contralateral dyskinesias during the ON state, as 90-100% of patients with well-placed lesions have significant reduction or elimination of contralateral dyskinesias[33-37]. Rigidity and tremor also respond well to pallidotomy, with UPDRS scores in the OFF state improving 25-30%[34,37,38] (Figure 5). Gait

disorders, balance, and freezing have a less predictable response. Nonresponsive symptoms include autonomic dysfunction, incontinence, drooling and swallowing difficulties, and cognitive impairment[39]. Benefits from surgery are durable, with one report demonstrating improvements for 4 years following surgery[40]. Studies of neuropsychological outcomes following pallidotomy have found that cognitive abilities generally remain stable following surgery; however, performance of measures of letter fluency and semantic fluency may decline with left-sided pallidotomy. The speech decline was modest and mild when it did occur[37]. Additionally, unilateral pallidotomy is safe and associated with improved motor functioning in elderly as well as younger PD patients experiencing significant disability despite optimal medical therapy[20]. However, changes in semantic fluency were more likely to develop in older patients[41].

Postoperative MRI imaging reveals acute lesion ranging in size from 75-200 mm^3 which decrease in size over time (Figure 6). Overall, lesion volume has not correlated with motor or neuropsychological outcome[41,42]. Analysis of outcome to lesion location[43,44] (Figure 7) reveals a spacial relationship for both left and right-sided pallidotomies. Anteromedial lesions tended to be more effective for contralateral rigidity and "on" medication motor UPDRS scores (Figure 8). Posterolateral lesions were more effective for contralateral and ipsilateral akinesia, "off" medication motor UPDRS scores, "on-time" improvement and activities of daily living scores (Figure 9). Improvements in tremor were weakly correlated with lesion location, being greater with posterolateral lesions (Figure 10A) while improvements in gait disorder and postural instability were greatest with more centrally located lesions (Figure 10B). These findings are thought to correlate with the segregated but parallel organization of specific motor circuits in the basal ganglia and may help explain variability in clinical outcome after pallidotomy.

Conclusions

Unilateral pallidotomy can be a safe and effective treatment for carefully selected patients with Parkinson's disease and dystonia. There are no large randomized studies of lesion therapy and DBS for PD, although one small study showed no difference between GPi stimulation and GPi lesioning[45]. DBS is safer when performed bilaterally, but is clearly more expensive, particularly given the problems with lead fractures, battery replacements, skin erosions, and infection that vary from 25-55% in experienced centers[46, 47]. The significantly fewer complications reported for lesion surgery and the reduced costs associated with the procedure may reopen the debate regarding the proper balance of lesion versus stimulation therpy[1]. It is therefore important for a functional neurosurgeon to be skilled in the techniques of lesioning in addition to DBS to best treat the various symptoms of adequately selected patients with movement disorders.

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Figure Legends

Figure 1 - MRI planning sequences: T1 (A) and SWI (B) revealing a right pallidotomy in an optimal location

Figure 2 – Merging of Stereotactic CT and preoperative MRI with point verification (A) blended registration (B) and trajectory planning (C)

Figure 3 – Radiologic confirmation of the target using a fixed lateral x-ray

Figure 4 - Laser software demonstrating a so-called "damage map" which is the predicted size of the lesion based on the temperature sensitive MR sequences during a laser thermal ablation asleep pallidotomy

Figure 5 – UPDRS total scores in the "off " state) following pallidotomy (a) and UPDRS motor scores in the "off" and "on" states following pallidotomy for patients with PD

Figure 6 – Immediate triplanar postoperative MRI image of a right pallidotomy

Figure 7 – Postoperative MRI with segmented pallidotomy lesion after reformatting along the AC-PC level

Figure 8 – Correlation of outcome using a quartile threshold (0-25% = red; 25-50% = yellow; 50-75% = yellow-green; 75-100 % = green) to pallidotomy lesion. Anteromedial lesions tended to be more effective for contralateral rigidity (A) and "on" medication motor UPDRS scores (B)

Figure 9 - Correlation of outcome using a quartile threshold (0-25% = red; 25-50% = yellow; 50-75% = yellow-green; 75-100 % = green) to pallidotomy lesion. Posterolateral lesions were more effective for contralateral (A) and ipsilateral akinesia (B), "off" medication motor UPDRS scores (C), "on-time" improvement (D) and activities of daily living scores (E)

Figure 10 - Correlation of outcome using a quartile threshold (0-25% = red; 25-50% = yellow; 50-75% = yellow-green; 75-100 % = green) to pallidotomy lesion. Improvements in tremor were weakly correlated with lesion location, being greater with posterolateral lesions (A) while improvements in gait disorder and postural instability were greatest with more centrally located lesions (B)

Authors:

Robert E Wharen, Jr MD
Professor of Neurosurgery
Mayo Clinic Florida

Sanjeet Grewal, MD
Mayo Clinic Florida

Bruce A Kall
Mayo Clinic, Rochester, MN

Ryan J. Uitti, MD
Professor of Neurology
Mayo Clinic Florida

Paul Larson, MD
Professor of Neurosurgery
UCSF School of Medicine
San Francisco, CA