Stereotactic Ablative Procedures for Pain Relief

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ABSTRACT

Intracranial stereotactic procedures in the central nervous system for the treatment of medically refractory chronic pain have evolved over the years. Neuroablative lesions have become a rare treatment for chronic pain, primarily because of the advent of more effective pharmacotherapy and intrathecal drug delivery. Lesion generation has the advantage of being less costly and having none of the hardware-related side effects of deep brain stimulation but the disadvantage of not being modifiable or reversible when the lesion has been generated. Although neuroablative procedures typically result in short-lived pain relief and the possibility of deafferentation pain, these procedures are still useful in certain clinical settings. The indications, methods employed, and outcome for these procedures are covered in this article.

KEYWORDS: Thalamotomy, mesencephalic tractotomy, chronic pain

Objectives: Upon completion of this article, the reader should be able to: (1) list the neuroablative central nervous system procedures still in use today for the treatment of medically refractory chronic pain; and (2) list the indications, methods, and outcomes for these procedures.

This article describes certain intracranial stereotactic ablative procedures in the central nervous system (CNS) for the treatment of medically refractory, chronic pain. Cingulotomies, trigeminal nucleus caudalis lesions, dorsal root entry zone lesions, deep brain stimulation, and motor cortex stimulation are reviewed elsewhere in this issue.

It should be noted at the outset of this discussion that destructive CNS lesions for the treatment of chronic pain have virtually been replaced by electrical stimulation and the advent of new types of pharmacotherapy. In the small population of patients in whom these procedures may be indicated, ablative procedures should be considered only after more conservative measures have been ruled out or failed.

ANATOMY OF PAIN PATHWAYS

The anatomy and physiology of pain pathways are covered in greater detail elsewhere in this issue. Briefly, peripheral nociceptors generate impulses that are transmitted along thinly myelinated A-δ and unmyelinated C fibers to cell bodies in the spinal ganglia, along the posterior roots to enter the spinal cord, where they synapse primarily on the cells of lamina I but also on the cells of lamina II and III of the dorsal horn and on cells of lamina VII (ventral horn). The two main ascending pathways that carry painful sensation from the dorsal horn are the lateral or neospinothalamic pathway and the medial or paleospinothalamic pathway. The lateral pathway has been implicated in the sensory and discriminatory aspects of pain. This pathway is composed of fibers...
that deccussate in the spinal cord to run in the contralateral spinothalamic tract. The rostral (medullary) continuation of the dorsal horn is the trigeminal spinal nucleus, which mediates pain sensation in the face. Relay neurons of the trigeminal spinal nucleus project to nucleus ventralis posteromedialis (Vpm) of the thalamus, the posterior thalamic region, the intralaminar nuclei, and the brain stem reticular formation. The primary termination of the spinothalamic (STT) and trigeminothalamic (TTT) tracts in humans is in the ventrocaudal nucleus (Vc, also known as nucleus ventralis posterolateralis/medialis, or Vpl/Vpm) and in the region ventroposterior to Vc in the lateral thalamus. Evidence in monkeys7 of STT terminations has also been found in VMpo (ventromedian pars oralis), which is located posteromedial to the ventral posterior lateral (VPL) and ventral posterior medial (VPM) nuclei, ventral to the anterior pulvinar and centromedian nuclei, lateral to the parafascicular nuclei, and dorsal to the medial geniculate nucleus.7–9 In the human, recordings in Vmop have demonstrated cells that respond to cooling of the skin, and stimulation of this region has evoked cold sensations in a circumscribed region of the skin.10 The lateral thalamic nuclei involved in pain processing include the posterior thalamic region, the intralaminar nuclei, the medial thalamic nuclei (e.g., the parafascicular [PF] and centrolateral [CL] nuclei), and ultimately to limbic brain stem, the periaqueductal gray, the hypothalamus, the amygdala, the pineal gland, and the hypothalamic (TH) tracts in humans is in the ventrocaudal nucleus (Vc, also known as nucleus ventralis posterolateralis/medialis, or Vpl/Vpm).8,9 The region posterior to Vc has been found to cause pain accompanied by a strong affective component in patients who have previously experienced pain with a strong affective component.16,18 This affective component is thought to be related to the fact that ventralis caudalis portae (Vcpor), the region posterior to Vc, projects to nociceptive cortical areas that project to limbic structures within the medial temporal lobe.18 Specifically, Vcpor projects to the inferior parietal lobule, including the parietal operculum and the secondary somatosensory cortex (SII), located within the parietal operculum on the upper bank of the sylvian fissure.12 In addition, Vcpc projects to the anterior insular cortex.19 Both SII and the anterior insular cortex are involved in pain processing,20,21 and SII projects to insular areas that then project to the amygdala.

**Table 1** Primarily Historical Central Nervous System Targets for the Ablative Treatment of Chronic Pain

<table>
<thead>
<tr>
<th>TARGET</th>
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<tr>
<td>Trigeminal spinal tract (medullary tractotomy)</td>
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<tr>
<td>Pontine tractotomy</td>
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<tr>
<td>Prefrontal white matter</td>
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<tr>
<td>Lateral spinothalamic and trigeminothalamic tract (mesencephalic tractotomy)</td>
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<td>Pulvinar</td>
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<td>Posteromedial hypothalamus</td>
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<tr>
<td>Hypophysis</td>
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<td>CM-Pf</td>
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<td>Vpm</td>
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CM-Pf, centrum medianum–parafascicularis; Vpm, nucleus ventralis posteromedialis.
supplanted by other modalities including indwelling pump delivery systems and chronic nervous system stimulation.25

CURRENT PROCEDURES
Ablative lesions have become a very rare treatment for chronic pain, primarily because of the advent of more effective pharmacotherapy and the widespread use of deep brain stimulation,25 which affords reversibility coupled with the ability to modulate the amount, character, and location of stimulation. Of the stereotactic ablative procedures still in use for the treatment of pain, medial thalamotomy and cingulotomy are the most commonly employed, although mesencephalic tractotomy, hypophysectomy, and trigeminal tractotomy may still performed at some centers.

INDICATIONS AND PATIENT SELECTION FOR ABLATIVE PROCEDURES
The two main types of chronic pain are that caused by direct activation of nociceptors and their afferent pathways (nociceptive pain) and that arising from injury to the nervous system.26 The latter is referred to as central pain if it results from injury to the brain or spinal cord and deafferentation pain if it results from injury to the peripheral nervous system. Pain resulting from chronic osteoarthritis is an example of nociceptive pain; pains resulting from stroke, multiple sclerosis lesions, or spinal cord injury are all examples of central pain—of which thalamic pain resulting from demonstrable damage to the thalamus is a subset27; postherpetic neuralgia, amputation-induced pain, and brachial plexus injuries are all examples of deafferentation pain.28 Neuropathic pain refers to pain that is initiated or caused by a primary lesion or dysfunction of the nervous system and therefore overlaps with the term central pain.26 It is important to note that the literature on surgical outcomes that deals with the treatment of chronic pain is confounded by the fact that many authors lump together nociceptive, central, and deafferentation pain; that they do not apply the terms in a consistent fashion; and that the terms themselves are somewhat lacking in precision.

Nociceptive pain can, in some cases, be alleviated by opiate administration and by interrupting the pathway of pain conduction, as with neurectomy, rhizotomy, or spinothalamic tractotomy, or by chronic stimulation of the periaqueductal gray matter or CM (centromedian) thalamus.

Central pain and deafferentation pain respond differently than nociceptive pain to surgical intervention.28 Allodynia, defined as pain in response to a stimulus that does not normally provoke pain,26 and hyperpathia, defined as an abnormally magnified painful reaction to a painful stimulus,26 seem to respond to the same interventions as nociceptive pain. The burning or dysesthetic element of pain that characterizes nociceptive as well as central and deafferentation pain does not seem to respond to opiates or to interruption of pain pathways but does respond to stimulation that induces paresthesias coincident with the distribution of dysesthetic pain.

Despite the caveats mentioned previously that neuroablative procedures typically result in short-lived pain relief and the possibility of deafferentation pain, these procedures may still be useful in the setting of a terminal illness, such as cancer, or in medically refractory patients in whom the implantation of hardware seems ill advised, such as brittle diabetics.

TECHNIQUE
The initial steps involved in the generation of ablative lesions for the treatment of chronic pain are similar; hence, the general stereotactic techniques are described first, followed by a discussion of the individual procedures.

Frame Application and Magnetic Resonance Imaging–Based Anatomical Target Localization
The stereotactic frame is affixed to the patient’s head on the morning of surgery, and magnetic resonance images are obtained. The center of the frame is determined on a magnetic resonance image. There are two methods of targeting: (1) directly from the patient’s magnetic resonance imaging (MRI) scan and (2) indirectly by calculating the x, y, and z coordinates based on the patient’s AC-PC (anterior commissure-posterior commissure) line.

For indirect targeting, the x, y, and z coordinates of the patient’s AC, PC, and midcommissural point (MCP) and desired anatomical target(s) are determined relative to the central point of the frame. The AC and PC coordinates are entered into a computer program that adjusts the selected sagittal template of the Schaltenbrand-Wahren atlas29 by either shrinking or lengthening the AC-PC length of the template to match the patient’s AC-PC length. Microelectrode data are then recorded on this adjusted map.

The MRI-based anatomical target coordinates are then compared with calculated coordinates based on the MRI-derived MCP coordinates and standard, atlas-derived coordinates for the particular target. The MRI- and atlas-based coordinates are then averaged to determine the coordinates of the initial target. The coordinates of the final target are determined by subsequent microelectrode recording data.

Operative Technique
Following MRI, the patient is taken to the operating room and positioned on the operating room table. The
target is then approached via a twist-drill hole or a burr hole at the level of the coronal suture, contralateral to the side of the patient’s maximal pain; the underlying dura is coagulated and opened and the pial surface pierced and coagulated.

Physiological Target Localization
In our experience, physiological localization based on microelectrode recording data is important to facilitate target identification. Reliance solely on MRI-based anatomical localization is problematic given the frequent discrepancies between the expected location based on MRI data and the actual location based on physiology. The x, y, and z coordinates of the chosen target are set on the Leksell frame and arc. A cannula is attached to the arc and lowered into the brain. A guide tube containing two microelectrodes is carefully inserted into the cannula and secured to the Leksell arc. This procedure is described in greater detail elsewhere.30

Continuous, extracellular recordings typically begin 10 to 15 mm above the target. Single-unit and multunit neuronal discharges are amplified, filtered, displayed on an oscilloscope, and fed to an audio monitor. The discharge frequency of neurons, the relative size and shape of the action potentials, and audio monitoring of firing patterns are all recorded.

Cell characteristics, such as firing patterns and the presence of bursting, as well as the presence of quiet intervals or increases in background activity are noted along the electrode trajectory.

High-frequency stimulation (0.1 to 100 μA, 1-second train, 300 Hz, 100-μsec pulse width) is performed through the same electrode. The elicitation of paresthesias at low thresholds of stimulation is useful in determining proximity to the lemniscal fibers. The elicitation of muscle contractions at low thresholds of stimulation is useful in determining proximity to the internal capsule.

Typically, two—but as many as six—electrode tracks are made for the purpose of optimal physiological localization. For patients with bilateral pain, the ablation is performed first in the medial thalamic nuclei on the side contralateral to the more severe pain. Surgery on the second side, if required, is performed after the patient has recuperated from the first surgery and has demonstrated sustained pain relief from lesioning.

Radiofrequency Electrode Placement and Lesioning
The frame and arc are adjusted to the desired target coordinates, the radiofrequency (RF) electrode is inserted, and the passage of the tip of the RF electrode to the intended target is followed by fluoroscopy. When the target has been satisfactorily localized on the basis of physiology, the RF lesioning electrode is introduced. We use an electrode of 1.1 mm diameter with a 2- or 3-mm exposed tip, equipped with a temperature-monitoring probe. The electrode is then connected to an RF generator, which monitors tip temperature and electrode impedance as current is applied.

Lesion size is tailored according to the target. Tailoring of lesion size is accomplished by varying the length of the uninsulated electrode tip, the temperature, and the duration of applied current. The patient is carefully monitored for untoward effects during the lesioning.

TECHNICAL ASPECTS OF SPECIFIC ABLATIVE PROCEDURES

Medial Thalamotomy

INDICATIONS
The evolution of thalamotomy for the treatment of chronic pain began with the use of Vc thalamotomy.31 The high incidence of sensory complications—particularly proprioceptive deficits and postoperative neuropathic pain—resulting from Vc thalamotomy and the lower rate of successful outcome32,33 led to its replacement with medial thalamotomy.28 The goal of medial thalamotomy is to destroy one or more of the medial thalamic nuclei involved in processing nociceptive information (i.e., CL, PF, and/or CM),6 thereby interrupting pain transmission in the nonspecific spino-reticulothalamic tract. Medial thalamotomy can therefore be predicted to relieve nociceptive pain but not to be very effective in the treatment of neuropathic pain.53 Of note, there is no consensus about which of the medial nuclei constitutes the optimal target.23 Medial thalamotomy has been used to treat chronic pain resulting from stroke, peripheral deafferentation,34 spinal cord injury,34 malignancy,35 arthritis,35 and neurogenic pain of Parkinson’s disease.36

LOCALIZATION
Electrode position within the medial thalamus is difficult to ascertain directly as there are no known pathognomonic electrophysiological findings or stimulation-induced responses unique to this region.37 The following coordinates have been used for targeting sites within the medial thalamus: 7 to 11 mm posterior to the midpoint of the AC-PC line, 6 to 10 mm lateral, and 1 mm below to 2 mm above the level of the AC-PC line.38,39 Alternatively, initial targeting of Vc (Vpl) can be performed by selecting a point 14 to 15 mm lateral to the midpoint (corresponding to upper limb representation) at the level of the PC. Electrode trajectories are...
made through the thalamus in a parasagittal plane. Microelectrode recording and microstimulation are used to find the appropriate body part representation in Vc by finding neuronal receptive fields that respond to sensory stimulation and by the induction of contralateral paresthesias through stimulation.\(^3\)\(^5\),\(^4\)\(^0\) The presence of cells that fire spontaneously in a bursting pattern, although not unique to the medial thalamus, can help to localize this region as the electrode is moved medial to Vc for the final target (Fig. 1).\(^4\)\(^1\)

**LESION GENERATION**

After a series of electrode trajectories (typically three) to find the optimal target site, an RF lesion is made in the medial thalamus.

**OUTCOME**

Frank and colleagues reported a 60% rate of pain relief following medial thalamotomy by targeting multiple sites within the medial thalamus (including Vcpc, CM, nucleus limitans, and lamella medialis).\(^4\)\(^2\) Tasker reported a 46% incidence of nociceptive pain relief and a 29% incidence of neuropathic pain relief.\(^4\)\(^3\) Although medial thalamotomy affords a lower efficacy rate in these two studies than that reported for stereotactic mesencephalotomy (85% for nociceptive cancer pain;\(^4\)\(^4\); see later), the indications for medial thalamotomy are broader and the potential morbidity and mortality are less.\(^4\)\(^1\) Finally, Jeanmonod and colleagues reported a higher rate (67%) of patients attaining pain relief (50 to 100%) in their series of 45 patients who underwent medial thalamotomy.\(^4\)\(^1\) The reason(s) for the better outcome in this latter study is unclear, but improvements in imaging and equipment and better patient or target selection may all have contributed to the improved results.

**MORBIDITY AND MORTALITY**

Postoperative dysesthesia and paresis are the most common complications of Vc thalamotomy.

**Mesencephalic Tractotomy**

**INDICATIONS**

First used in 1953 by Spiegel and Wycis to treat pain arising from malignant disease,\(^4\)\(^5\) mesencephalic tractotomy is most effective for nociceptive cancer pain of the head, neck, upper trunk, or upper extremities above C5. Percutaneous cordotomy is effective for pain at or below the C5 level. The goal of mesencephalic tractotomy is to interrupt the lateral spinothalamic and spinoreticular tracts at the level of the superior or inferior colliculus while preserving the medial lemniscus.\(^4\)\(^4\),\(^4\)\(^6\)

**LOCALIZATION**

At this level, the STT tracts are located 6 to 9 mm lateral to the midline and 5 mm posterior and inferior to the PC. The 9-mm sagittal brain map is generally selected for use in mapping, as this location corresponds to the greatest cross-sectional area through the STT.

Microelectrode recording can nonetheless provide useful information about structures neighboring the STT. The medial lemniscus, which lies 9 to 12 mm lateral to the midline, can be localized by micro- or macroelectrode. Stimulation of the medial lemniscus results in contralateral paresthesias. The STT lies dorsal and medial to the medial lemniscus. Stimulation of the STT results in hot, cold, or burning sensations.\(^4\)\(^7\) Stimulation of the periaqueductal gray, resulting from an electrode placement that is too medial, can result in sensations of fear or anxiety, piloerection, blushing, or ocular movements.\(^4\)\(^6\),\(^4\)\(^7\) The spinoreticulothalamic tract, which lies 4 to 7 mm lateral to the midline, is difficult to localize on the basis of physiologic characteristics, and its location is generally extrapolated from the physiologic information about the location of STT. Macrostimulation begins at 10 mm rostral to the target and continues along the electrode trajectory to a point 10 mm caudal to the target location (Fig. 2).

**LESION GENERATION**

Following physiologic localization of the STT and medial lemniscus, lesioning of the STT and the more medial spinoreticulothalamic tract begins. Lesioning of the STT results in a contralateral dissociated sensory loss, with loss of pinprick sensation resulting in analgesia and hence pain relief. A transient deficit in light touch perception may also result.
OUTCOME
Stereotactic mesencephalic tractotomy has been reported to provide satisfactory pain relief in 57% to 85% of patients with nociceptive cancer pain localized to the face, head, neck, or upper body. The results are far less satisfactory for other types of pain, such as deafferentation pain.44

MORBIDITY AND MORTALITY
The morbidity of mesencephalic tractotomy includes dysesthesias (due to medial lemniscus damage; 5–20%), anesthesia dolorosa (1%48), and oculomotor disturbances (5–20%), with a combined complication rate of 37% reported.49 Although usually transient, oculomotor disturbances occur to some degree in nearly all patients. Ocular disturbances are more common with lesions placed closer to the superior colliculus. Reported mortality rates range from 0.5% to 7%.49

Pontine and Trigeminal Tractotomy

INDICATIONS
Described by Hitchcock in 1973,50 lesioning of the spinothalamic tract at the level of the pons has been limited by an estimated 50% morbidity and the tendency for a loss of efficacy over time. Deafferentation pain of the face, upper shoulder, and neck can be treated by pontine and trigeminal tractotomy. It is difficult to obtain sufficiently high levels of analgesia in these upper regions using percutaneous cordotomy without incurring autonomic complications—specifically, respiratory and micturition disorders.51 The goal of trigeminal nucleus caudalis lesioning is to interrupt intranuclear trigeminal connections in the caudal trigeminal nucleus. It is therefore recommended primarily for facial deafferentation pain. This procedure is described in greater detail elsewhere in this issue.

Gamma Knife
Gamma knife radiosurgery has been used to target both the thalamus and the trigeminal nerve root entry zone in the treatment of chronic pain.52 The use of gamma knife for the treatment of trigeminal neuralgia is reviewed elsewhere in this issue. The virtue of the gamma knife is that it is noninvasive, eliminating the risk of infection and intracranial hemorrhage in the treatment of pain. However, the noninvasive nature of radiosurgery also prevents the surgeon from obtaining electrophysiological
data, as well as macrostimulation data, in the determination of the optimal placement of lesions.

SHORT-TERM AND LONG-TERM OUTCOME

Outcomes analyses of ablative procedures targeting pain at the various sites just described are confounded by the absence of blinded, prospective studies that evaluate the relative merits of the various procedures, by the frequent lumping together of patients with chronic pain of various etiologies and character, by the lack of reference to standardized outcomes measures, and by the variability in length of follow-up within and across series. With respect to the last point, it has been noted that pain gradually recurs following surgical intervention; hence, the length of follow-up in any given study can have profound implications for the outcome reported.

MORBIDITY, MORTALITY, AND SIDE EFFECTS

The generation of lesions in the CNS for the treatment of medically refractory chronic pain has the advantage of being less costly and having none of the hardware-related side effects of deep brain stimulation—including erosion through skin, infection, and malfunction of hardware. The disadvantage of lesioning versus deep brain stimulation is that the effect of the former cannot be modulated or reversed when the lesion has been generated.

CONCLUSIONS

Stereotactic ablative procedures for chronic pain have, by and large, been replaced by improvements in pharmacotherapy, the advent of intrathecal delivery systems, and the widespread use of deep brain stimulation. However, in certain patients whose underlying medical condition(s) poses relative contraindications to the implantation of hardware, the generation of ablative lesions remains an option for the treatment of chronic, refractory pain.

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