ELSEVIER
SAUNDERS

Neurosurg Clin N Am 15 (2004) 335–342

NEUROSURGERY CLINICS OF NORTH AMERICA

Ablative procedures for chronic pain

Pantaleo Romanelli, MD[a,b,c,*], Vincenzo Esposito, MD[a,b], John Adler, MD[c]

[a]*Epilepsy Surgery Unit, Neuromed IRCCS, Via Atinense 18, 86077 Pozzilli (IS), Italy*
[b]*Department of Neurosurgery, University "La Sapienza," Rome, Italy*
[c]*Department of Neurosurgery, Stanford University, 300 Pasteur Drive, Room 200, Stanford, CA 94305, USA*

Ablative surgery has played an important role in the management of chronic pain during the twentieth century. Recently, there has been a steady trend toward the application of non-destructive techniques, such as spinal cord, deep brain, and motor cortex stimulation, which have progressively replaced such procedures as cordotomies, dorsal root entry zone (DREZ) lesions, sympathectomies, and neurectomies. Although neuroaugmentation is now the preferred strategy for the management of neuropathic pain of functional origin, the use of ablative techniques remains quite established for the management of medically refractory pain related to malignancies, especially in terminally ill patients. Ablative techniques can produce fast and satisfactory pain relief, but their effect is usually limited in time, restricting their use mostly to terminal patients suffering from cancer pain. These procedures obviously need to be performed by neurosurgeons specializing in pain management because of the complexity of medical, surgical, and ethical considerations involving the treatment of terminal patients plagued by excruciating pain (not to mention the technical demands of the procedure). Recent improvements in imaging technologies (especially functional imaging) and radiosurgical technologies could make radiosurgery an important player in the treatment of refractory pain in the near future. Current applications of radiosurgery for the treatment of pain are briefly reviewed.

* Corresponding author.
E-mail address: leoromanelli@neuromed.it (P. Romanelli).

Ablative procedures involving spinal targets

The aim of spinal cord ablative procedures is to interrupt the nociceptive pathways running through specific sectors of the spinal cord itself, namely, the DREZ, the spinothalamic pathway, and the midline posterior column visceral pathway. DREZ lesions can be used to destroy the superficial laminae of the dorsal horn, where the central processing of pain begins. Anterolateral cordotomy targets the spinothalamic pathway that carries somatic pain. The destruction of the spinothalamic pathway within the anterolateral quadrant of the cord is usually followed by abolition of pain and temperature sensation below the level of the lesion. The main difference between cordotomies and DREZ lesions is that the latter can produce analgesia over a restricted area in a segmental fashion, whereas the former produces analgesia covering the whole hemibody below the level of the section. Visceral pain has its own pathway located in the deep and medial region of the dorsal columns. Midline myelotomy is a recently described technique to relieve visceral pain by lesioning this pathway.

Dorsal root entry zone lesion

Ablative surgery of the DREZ in the spinal cord is considered a good surgical option in patients with segmental paroxysmal and allodynic pain related to peripheral nerve, root, and spinal cord lesions. This operation aims to destroy the superficial layers of the dorsal horn, thus interrupting the afferent pain pathway. The success of a DREZ operation depends essentially on the ability to select the proper level at which to place

1042-3680/04/$ - see front matter
doi:10.1016/j.nec.2004.02.009

the lesion. DREZ lesions can be particularly useful to manage segmental pain that can be traced back to specific levels of the spinal cord and can be viewed as a sort of ablative equivalent of spinal cord stimulation (SCS). It has been reported that the rate of segmental pain relief after DREZ lesioning can be as high as 90% [1]. In cases of poorly localized pain, a DREZ lesion is contraindicated because of inherent difficulties in identifying the level at which the lesion should be placed, with consequent poor outcomes [1]. In these cases, an anterolateral cordotomy may be a better option. Pain caused by cervical root avulsions as well as brachial plexus injuries in general, which are usually poorly responsive to SCS, can be effectively treated with DREZ lesions [2]. DREZ surgery is also effective in cases of spinal cord injuries with segmental pain at the transitional level [3].

Cordotomy

Anterolateral cordotomy was first described by Spiller and Martin [4] in 1912. An important role in the conceptual development of this procedure was played by the identification of the physiologic properties of the anterolateral cord and its relation to pain transmission, based on clinical studies in patients affected by restricted spinal cord damage [5–7].

Anterolateral cordotomy was practiced originally through an open approach, but the percutaneous cervical approach became quite popular after its introduction in the early 1960s [8]. Since the introduction of (SCS), cordotomy has been less and less frequently used but remains an important option for intractable malignant pain [9].

Cordotomy can produce immediate pain relief with quite substantial or complete abolition of pain below the level of the transection. The main disadvantages are the short life of pain relief (rarely lasting more than 1 year) and the fact that only the homolateral hemibody is affected, which can cause unmasking of pain on the contralateral side. Cordotomy is especially effective in relieving neuropathic pain poorly managed by opioids in terminally ill cancer patients. Recent series [10,11] have shown that the percutaneous microelectrode-guided approach can produce excellent pain relief in up to 85% of carefully selected patients. In some cases, painful dysesthesias have been reported after the procedure. Described complications after unilateral cordotomy are urinary retention (6%), hemiparesis (8%), and unmasking of contralateral pain (6%) [11]. The complication rate becomes substantially higher (approximately 28% overall) after bilateral cordotomies, suggesting that this procedure is best used for unilateral intractable pain [11]. A thorough investigation of pain complaints is thus required to assess whether the pain is truly unilateral or just predominant on one side because the possible unmasking effect on contralateral pain, can strongly reduce the therapeutic gain.

Midline myelotomy

Midline myelotomy is a recently described procedure aimed at destroying visceral pain fibers located close to the midline in the deep region of the dorsal columns [12]. Visceral pain is usually poorly sensitive to SCS or traditional ablative procedures, such as cordotomies or DREZ operations. Nauta et al [12] report that the interruption of a midline posterior column pathway by performing a punctate midline myelotomy provides significant pain relief without causing adverse neurologic sequelae in cancer patients with visceral pain located in the pelvic and abdominal areas that is refractory to other therapies. This procedure has been employed to treat visceral pain related to residual, progressive, or recurrent local cancer and can provide an alternative treatment modality for cancer-related pain in patients in whom adequate pain control with narcotics cannot be achieved or narcotic side effects cannot be tolerated [12].

Ablative procedures involving intracranial targets

Intracranial ablative procedures have been used to treat cranial neuropathies causing facial pain as well as cancer and noncancer-related pain originating from the head and neck or other parts of the body. Some of these procedures have by now only historical value (eg, parietal corticectomy, hypophysectomy, pulvinarotomy) or are rarely used, especially as far as neurosurgeons specialized in pain treatment are concerned (eg, trigeminal neurectomies). Nevertheless, it is intriguing to note how old targets may become fashionable again using improved or less invasive techniques. For example, the destruction of the pituitary gland, a procedure used in the 1970s and 1980s for the treatment of cancer-related pain, has been recently employed again in the form of radiosurgical hypophysectomy [13]. The main shortcomings of intracranial ablative procedures for pain share a common ground with those related to spinal ablative procedures and are mainly related to the nonpermanent nature of the pain relief (which may be lost after 1–2 years) or to the possibility of inducing deafferentation pain (if the lesion affects the nociceptive pathways). Several of these procedures have been largely replaced by neuroaugmentative techniques, including intrathecal or intraventricular administration of morphine or spinal cord, deep brain, and motor cortex stimulation, which have obvious advantages: the placement of a lesion is not required, thus reducing the risk for permanent neurologic complications; the stimulation or drug infusion can be modulated by the physician; and no instances of deafferentation pain, such as dysesthesias, are to be expected. As the target moves up along the neuraxis, the effects on nociceptive processing may differ substantially. Although a stereotactic mesencephalotomy is in essence a procedure aimed at destroying the pain pathway within the brain stem and is not conceptually different from an anterolateral cordotomy, except for the location of the target, which is intracranial, a medial thalamotomy affects pain processing in a way that is not limited to the simple interruption of fibers but involves the affective and cognitive components of pain processing. A cingulotomy affects the cognitive processing of pain even more, whereas its transmission and basic processing within the thalamus and somatosensory cortex are preserved. The advantage of performing medial thalamotomies or cingulotomies is in the fact that not affecting the pain pathways per se, these lesions are not associated with the induction of deafferentation pain.

Mesencephalic tractotomy

Mesencephalic tractotomy is a stereotactic procedure aimed at destroying fibers carrying somatic pain from the spine to higher centers, such as the thalamus and the cortex. In this respect, it not unlike a cordotomy, except for the location of the target, which is intracranial.

The dorsolateral tegmentum of the mesencephalon contains fibers originating from the superficial laminae of the dorsal horns and mostly directed to the lateral thalamus and from there to the sensory cortex. Within the mesencephalic tegmentum, an orderly mediolateral localization of the periaqueductal gray (PAG), trigeminothalamic tract, and spinothalamic tract can be found. The most common coordinates for stereotactic mesencephalotomy are 5 mm posterior to the posterior commissure (PC) (range: 0–16 mm), 5 mm inferior (range: 0–8 mm), and 7.5 mm lateral (range: 5–10 mm) (for a review, see the article by Shieff and Nashold [14]). In general, the border between the PAG and trigeminothalamic tract can be considered to be around 5 mm lateral to midline and that between the trigeminal and spinothalamic tract approximately 9 mm lateral. Intraoperative electrophysiologic confirmation of the target is mandatory. Several authors include the spinothalamic and reticulothalamic tracts in their lesion [15]. Mesencephalic tractotomy is a quite effective procedure in experienced hands, producing limited complications and effective pain relief in up to two thirds of patients [14]. Complications include transient disorders of ocular motility, perioperative dysesthesia, and motor paresis (2%). The mortality rate in a large series was less than 0.5% [16]. Conversely, this procedure requires refined stereotactic skills and should be recommended and performed only by neurosurgeons with extensive specific experience.

Medial thalamotomy

Several nuclear structures located in the medial region of the thalamus are involved in the processing of pain, including the centromedian (CM), parafascicular (Pf), centrolateral (CL), and dorsomedial (DM) nuclei. The cells of the spinothalamic tract projecting to the intralaminar nuclei of the medial thalamus originate in the deep dorsal horn and the ventral horn of the spinal cord. The axons decussate immediately and ascend in the ventral and then in the ventrolateral white matter. After passing through the brain stem, they terminate in the intralaminar nuclei, especially the CL nucleus. Some of the laterally projecting spinothalamic tract neurons send collaterals to the medial thalamus, where they end in the CL nucleus. A retrograde labeling study has recently demonstrated that the output of the medial thalamus is mainly directed to the cingulate gyrus (area 24), which receives pain-related thalamic inputs from the intralaminar nuclei [17]. Nociceptive neurons located in the medial thalamus are characterized by lack of somatotopic organization with large receptive fields [18,19].

Neural recordings from intralaminar nuclei, including the CL, CM, and Pf nuclei, in awake trained monkeys have shown that cells located there have nociceptive qualities with large and usually bilateral receptive fields, suggesting that they do not play a localizing role in sensory discrimination but are involved in the affective processing of pain [20,21]. These neurons were able to distinguish between different stimulus intensities, suggesting an involvement in the appreciation of pain intensity as well [20,21].

Sustained neuronal bursting in the medial and intralaminar thalamic nuclei has been found in patients with deafferentation pain [22]. Stereotactic lesions in the medial thalamus have been reported to induce better pain relief when colocalized with such bursting activity [23]. In terms of pain control, medial thalamotomy has been reported to produce 50% to 100% relief in 67% of all patients with peripheral as well as central neurogenic pain in all body locations, without producing neurologic deficits and without risk for the development of iatrogenic pain [24]. What seems particularly appealing about medial thalamotomy is the minimal incidence of neurologic complications (which seem to consist mostly of transient cognitive disturbances [25]) as compared with other procedures, such as mesencephalic tractotomy, which is considered more effective in producing adequate pain relief but is associated with a more severe complication pattern.

Cingulotomy

The human anterior cingulate gyrus (Brodmann's area 24) receives direct nociceptive inputs as shown by several metabolic studies. Positron emission tomography (PET) scanning studies indicate that painful thermal stimuli produce metabolic activation of the ipsilateral [26] plus contralateral anterior cingulate gyrus [26–30], primary and secondary somatosensory areas, insular cortex [27,28], and supplementary motor area. It is also known from retrograde labeling studies that nociceptive inputs reach the cingulate gyrus from the medial thalamus [17].

Stereotactic lesions of the anterior cingulate gyrus have been employed to relieve chronic pain since the early 1960s, with relief rates varying from 23% [31] to 75% [32]. These lesions are centered in the cingulate gyrus 1 to 3 cm posterior to the genu of the corpus callosum [31,32]. Such lesions do not abolish nociception but modify the affective response to pain in such a way that the patient does not report being bothered by pain anymore, a phenomenon already reported in the first published series [32].

The most common technique used recently to perform a stereotactic cingulotomy is based on MR targeting. The aim is to place a radiofrequency lesion in the center of the cingulate gyrus [33], which has been reported to produce excellent results for cancer-related pain and nociceptive pain. Bilateral cingulotomy has also been shown to be quite effective in patients with noncancer-related pain. In a cohort of 28 patients described by Wilkinson et al [34], 13 patients had pain caused by lumbar adhesive arachnoiditis, or "failed back," and the remainder had venous occlusive disease, ischemic bilateral leg pain, phantom leg pain, postoperative neck pain, or atypical facial pain. A 12-gauge stereotactic electrode with a 10-mm bare tip was inserted into the cingulum bundle, with the tip 5 mm above the roof of the ventricle and 5 mm lateral to the midline. The authors of this study report that 72% of patients reported improvement in their pain, 55% were no longer taking narcotics, 67% noted improvement in their family life, and 72% noted improvement in their social interactions. Fifty-six percent of patients reported that the cingulotomy was beneficial, and 28% returned to their usual activities or work. Thirty-nine percent of patients developed seizures, however, and some of these patients required antiepileptic medications. More than half of all respondents thought that they had a positive outcome and that cingulotomy was beneficial to them. There were no deaths related to the procedure. The cognitive effects of cingulotomies (even bilateral) are relatively mild. Recent neuropsychologic studies on the effects of bilateral anterior cingulate cortex lesions have shown a lack of major side effects on cognitive and behavioral performance in patients with noncancer pain [35,36]. Cingulotomy patients were intact across most cognitive domains, but they showed deficits of focused and sustained attention as well as mild executive dysfunction. Self-initiated responding was most impaired. Results indicate that the greatest impact of cingulotomy lesions is on response intention and self-initiated behavior, with reduced behavioral spontaneity.

Overall, it seems that cingulotomy can be beneficial on cancer and noncancer pain but can induce seizures requiring medication and produces some degree of executive dysfunction.

Radiosurgery and pain

The use of radiosurgical techniques to perform ablative procedures for chronic pain is tempting because of easy application and lack of major complications. The obvious limit is the lack of electrophysiologic confirmation, which makes this procedure virtually blind. If there is a clear anatomic target, however, such as the cisternal portion of the trigeminal nerve when treating patients with trigeminal neuralgia (TN), precise targeting can be obtained with excellent clinical outcomes. In our view, the future of functional radiosurgery lies in the ability to guide the creation of the lesion through functional imaging. Improvement in functional MRI (fMRI) and coregistration software could allow the functional neurosurgeon to select a specific target within the basal ganglia, thalamus, or cortex (eg, cingulus), replacing microelectrode recording guidance with fMRI guidance. It has recently been shown that patients with chronic pain may present with acute foci on PET scanning, which are useful for guiding deep brain stimulation (DBS) procedures [37]. It is conceivable that PET or fMRI guidance may help to guide the radiosurgical lesioning of targets within the medial thalamus or the cingulus to relieve chronic pain.

Radiosurgical thalamotomy

Because the procedure is noninvasive, the notion of a radiosurgical thalamotomy is an attractive concept. More specifically, the thalamic nuclei that would seem to be good targets for pain relief include the CM, Pf, CL, and DM. Based on an analogous experience with radiofrequency thalamotomy, one would expect that between one half and two thirds of the patients undergoing radiosurgical ablation procedures would experience good pain relief in association with a modest complication rate. The first reports on gamma-knife thalamotomy for the treatment of refractory pain were published by Leksell [38] and Forster et al [39]. Later on, Steiner et al [40] published an extended report reviewing the Karolinska University experience up to 1974. This article reported about 52 patients with cancer pain and short life expectancy who underwent radiosurgical lesioning of the ventromedial thalamus using the Leksell stereotaxic system and the Co60 Gamma Unit [41]. The prescribed radiosurgical doses were in the range of 160 to 180 Gy. The treatment was unilateral in 24 patients (performed on the thalamus contralateral to the pain) and bilateral in 26.There was no outcome difference between these two groups. Two thirds of the patients developed immediate relief, but the relapse rate was quite high; overall, only 8 patients experienced a good outcome. In 18 patients, the pain relief was scored as moderate, whereas in 24, the procedure was deemed ineffective. A second operation after recurrence of pain was rarely of value. There was a tendency toward more efficient relief of pain located in the face, arm, or shoulder than of pain located in the lower part of the body. Although contralateral lesions seemed to be most effective, ipsilateral operations produced some relief of pain. The best results were obtained when the lesions were placed close to the wall of the third ventricle and at the level of the PC, focusing on ablation of the CM-Pf complex. Severe complications were found in 2 patients who developed weakness of upward gaze, hemianesthesia, and hemiparesis. A postmortem examination was performed on 21 of the brains treated in this first study and disclosed that the mean error in the placement of the radiosurgical lesion was about 1 mm. A subsequent report from Young et al [42] is characterized by better outcomes, with approximately 60% of the patients developing excellent or good pain relief after MR-based gamma-knife thalamotomy. The prescribed doses were comparable to those originally reported by the Karolinska University group (140–180 Gy versus 160–180 Gy), and the target location was a little more anterior, including the DM and CL nuclei as well as the CM-Pf complex. No permanent neurologic complications were identified, but there was one death as a result of radiation necrosis 14 months after the first lesion of a bilateral thalamotomy was performed. Furthermore, 4 patients developed extensive edema surrounding their lesions approximately 6 to 12 months after irradiation, which only slowly resolved. Within the relatively short follow-up period, there were no instances of cognitive problems. Of note, these pain patients were not affected by end-stage malignancies. As a result, these cases could be followed for a longer time, which probably explains why more complications were noted than in the initial Karolinska University report. The better pain outcomes of this later report may be based on the fact that MR guidance was used and the target encompassed the intralaminar nuclei. In particular, the inclusion of the CL nucleus, which projects directly to the cingulated cortex, might be an important factor in improving the pain outcome.

Radiosurgery for trigeminal neuralgia

Radiosurgical ablation of the trigeminal nerve has become increasingly accepted as a treatment for TN. Commonly prescribed doses range from 60 to 90 Gy. Higher doses correlate with greater rates of pain relief. Although major complications are virtually nonexistent, some patients can develop facial numbness that is eventually associated with bothersome dysesthesias or corneal hypoesthesia ("dry eye"). Patients with typical TN who have not undergone previous procedures (eg, microvascular decompression [MVD], radiofrequency rhizotomy [RFR]) seem to experience rates of pain relief comparable to those of MVD or RFR. Not surprisingly, however, patients with atypical features or those who have undergone invasive procedures already tend to have less successful outcomes. Currently, radiosurgery is performed mostly on elderly patients or patients with medical conditions contraindicating invasive procedures. Most young patients with typical TN are being preferentially treated with MVD. Similar results have been published so far using the gamma-knife or linear accelerator (LINAC), both requiring the use of a stereotactic head frame [43–45]. Meanwhile, Cyberknife radiosurgical rhizotomy seems to offer comparable rates of pain relief without the need for a stereotactic frame [46].

Hypophysectomy

Gamma-knife radiosurgical ablation of the pituitary gland has recently been reported to be effective in the treatment of cancer pain that was refractory to other treatments [13].This clinical study involved nine patients with bone metastasis in whom there were no other effective treatment options for managing pain. In addition, all the patients in this study had Karnofsky Performance Scale scores greater than 40, preserved sensitivity to morphine, and no history of prior irradiation (gamma knife surgery [GKS] or conventional radiotherapy) for brain metastasis. The radiosurgical target, which included the pituitary gland and stalk, was covered with either one (8-mm collimator) or two (4-mm collimator) isocenters. The maximum treatment dose used in this study was 160 Gy. Of note, the dose to the optic nerve was kept below 8 Gy. In this small group of patients, good pain relief was obtained within several days of the procedure in every case and without complication. Importantly, after a follow up of 1 to 24 months, no recurrence of pain or hormonal dysfunction was observed. Despite the small number of patients and short follow-up in this study, the results are particularly intriguing. If replicated in a bigger trial, radiosurgical hypophysectomy could become an important option for treating cancer pain.

Radiosurgery for spinal pain caused by metastatic cancer

As we have seen, radiosurgical hypophysectomy may be a new and quite effective treatment of pain related to bone metastasis. A more targeted approach can also be used to treat pain that stems from metastatic involvement of the spine with invasion of the vertebral body, which is often associated with vertebral body collapse. Excruciating pain (axial, appendicular, or both) is commonly associated with metastatic involvement of the thoracic spine or the thoracolumbar junction. In such patients, an alternative approach to central pain modulation is the direct ablation of a symptomatic vertebral body lesion. At Stanford University Medical Center, Cyberknife radiosurgery has been employed in terminally ill cancer patients to treat severe spinal pain refractory to aggressive medical management stemming from metastatic invasion and, sometimes, collapse of one or more vertebral segments [47]. Preliminary results over several years have been encouraging. Nearly all patients experience a significant reduction in pain scores over a few days to a couple of weeks.

Summary

The advent of neuroaugmentative techniques has reduced the application of neuroablative procedures, especially as regards pain of functional origin. Although intracranial ablative procedures are now rarely performed, spinal ablative procedures, such as anterolateral cordotomies or midline myelotomies, remain important in the management of cancer pain. These procedures produce immediate and satisfactory pain relief with acceptable complication rates. An important future trend will be the application of radiosurgery guided by functional imaging (eg, fMRI, PET) to place such intracranial lesions as cingulotomies or medial thalamotomies.

References

[1] Spaic M, Markovic N, Tadic R. Microsurgical DREZotomy for pain of spinal cord and cauda equina injury origin: clinical characteristics of pain and implications for surgery in a series of 26 patients. Acta Neurochir (Wien) 2002;144(5): 453–62.

[2] Prestor B. Microsurgical junctional DREZ coagulation for treatment of deafferentation pain syndromes. Surg Neurol 2001;56(4):259–65.

[3] Sindou M, Mertens P, Wael M. Microsurgical DREZotomy for pain due to spinal cord and/or cauda equina injuries: long-term results in a series of 44 patients. Pain 2001;92(1–2):159–71.

[4] Spiller WG, Martin E. The treatment of persistent pain of organic origin in the lower part of the body by division of the anterolateral column of the spinal cord. JAMA 1912;58:1489–90.

[5] Gowers WR. A case of unilateral gunshot injury to the spinal cord. Trans Clin Lond 1878;11:24–32.

[6] Spiller WG. The occasional clinical resemblance between caries of the vertebrae and lumbothoracic syringomyelia, and the location within the spinal cord of the fibres for the sensations of pain and temperature. Univ PA Med Bull 1905; 18:147–54.

[7] Head H, Thompson T. The grouping of afferent impulses within the spinal cord. Brain 1906;29: 537–741.

[8] Mullan S, Hekmatpanah J, Dobbe G, Beckman F. Percutaneous interruption of spinal pain tracts by means of a 90 strontium needle. J Neurosurg 1963; 20:931–9.

[9] Meyerson BA. Neurosurgical approaches to pain treatment. Acta Anaesthesiol Scand 2001;45: 1108–13.

[10] Lahuerta J, Bowsher D, Lipton S, Buxton PH. Percutaneous cervical cordotomy: a review of 181 operations in 146 patients with a study on the location of "pain fibers" in the C-2 spinal cord segment of 29 cases. J Neurosurg 1994;80:975–85.

[11] Sanders M, Zuurmond W. Safety of unilateral and bilateral percutaneous cervical cordotomy in 80 terminally ill cancer patients. J Clin Oncol 1995; 13(6):1509–12.

[12] Nauta HJ, Soukup VM, Fabian RH, Lin JT, Grady JJ, Williams CG, et al. Punctate midline myelotomy for the relief of visceral cancer pain. J Neurosurg 2000;92(2 Suppl):125–30.

[13] Hayashi M, Taira T, Chernov M, Fukuoka S, Liscak R, Yu CP, et al. Gamma knife surgery for cancer pain-pituitary gland-stalk ablation: a multicenter prospective protocol since 2002. J Neurosurg 2002;97(5 Suppl):433–7.

[14] Shieff G, Nashold BS Jr. Stereotactic mesencephalotomy. Neurosurg Clin North Am 1990;1:825–39.

[15] Gybels JM, Sweet WH. Stereotactic mesencephalotomy. In: Neurosurgical treatment of persistent pain. Basel: Karger; 1989. p. 210–9.

[16] Frank F, Fabrizi AP, Gaist G. Stereotactic mesencephalic tractotomy in the treatment of chronic cancer pain. Acta Neurochir (Wien) 1989; 99(1–2):38–40.

[17] Kuroda R, Yorimae A, Yamada Y, Furuta Y, Kim A. Frontal cingulotomy reconsidered from a WGA-HRP and c-Fos study in cat. Acta Neurochir Suppl (Wien) 1995;64:69–73.

[18] Giesler GJ Jr, Yezierski RP, Gerhart KD, Willis WD. Spinothalamic tract neurons that project to medial and/or lateral thalamic nuclei: evidence for a physiologically novel population of spinal cord neurons. J Neurophysiol 1981;46: 1285–308.

[19] Ammons WS, Girardot MN, Foreman RD. T2–T5 spinothalamic neurons projecting to medial thalamus with viscerosomatic input. J Neurophysiol 1985;54:73–89.

[20] Bushnell MC, Duncan GH. Mechanical response properties of ventroposterior medial thalamic neurons in the alert monkey. Exp Brain Res 1987;67: 603–14.

[21] Bushnell MC, Duncan GH. Sensory and affective aspects of pain perception: is medial thalamus restricted to emotional issues? Exp Brain Res 1989;78:415–8.

[22] Rinaldi PC, Young RF, Albe-Fessard D, Chodakiewitz J. Spontaneous neuronal hyperactivity in the medial and intralaminar thalamic nuclei of patients with deafferentation pain. J Neurosurg 1991;74(3):415–21.

[23] Jeanmonod D, Magnin M, Morel A. Thalamus and neurogenic pain: physiological, anatomical and clinical data. Neuroreport 1993;4:475–8.

[24] Jeanmonod D, Magnin M, Morel A. Chronic neurogenic pain and the medial thalamotomy. Schweiz Rundsch Med Prax 1994;83(23):702–7.

[25] Tasker RT. Thalamotomy. Neurosurg Clin North Am 1990;1:841–64.

[26] Vogt BA, Derbyshire S, Jones AKP. Pain processing in four regions of human cingulate cortex localized with coregistered PET and MRI. Eur J Neurosci 1996;8:1461–73.

[27] Casey KL, Minoshima S, Berger KL, Koeppe RA, Morrow TJ, Frey KA. Positron emission tomographic analysis of cerebral structures activated specifically by repetitive noxious heat stimuli. J Neurophysiol 1994;71:802–7.

[28] Coghill RC, Talbot JD, Evans AC, Meyer E, Gjedde A, Bushnell MC, et al. Distributed processing of pain and vibration by the human brain. J Neurosci 1994;14:4095–108.

[29] Craig AD, Reiman EM, Evans A, Bushnell MC. Functional imaging of an illusion of pain. Nature 1996;384:258–60.

[30] Talbot JD, Marrett S, Evans AC, Meyer E, Bushnell MC, Duncan GH. Multiple representations of pain in human cerebral cortex. Science 1991;251:1355–8.

[31] Hurt RW, Ballantine HT. Stereotactic anterior cingulate lesions for persistent pain: a report of 68 cases. Clin Neurosurg 1973;21:334–51.

[32] Folz EL, White LE. Pain "relief" by frontal cingulotomy. J Neurosurg 1962;19:89–100.

[33] Pillay PK, Hassenbusch SJ. Bilateral MRI-guided stereotactic cingulotomy for intractable pain. Neurosurgery 1990;27(2):220–3.

[34] Wilkinson HA, Davidson KM, Davidson RI. Bilateral anterior cingulotomy for chronic noncancer

pain. Neurosurgery 1999;45(5):1129–34; discussion 1134–6.

[35] Cohen RA, Kaplan RF, Zuffante P, Moser DJ, Jenkins MA, Salloway S, et al. Alteration of intention and self-initiated action associated with bilateral anterior cingulotomy. J Neuropsychiatry Clin Neurosci 1999;11(4):444–53.

[36] Cohen RA, Paul R, Zawacki TM, Moser DJ, Sweet L, Wilkinson H. Emotional and personality changes following cingulotomy. Emotion 2001; 1(1):38–50.

[37] Franzini A, Ferroli P, Leone M, Broggi G. Stimulation of the posterior hypothalamus for treatment of chronic intractable cluster headaches: first reported series. Neurosurgery 2003;52: 1095–101.

[38] Leksell L. Cerebral radiosurgery, gamma-thalamotomy in two cases of intractable pain. Acta Chir Scand 1968;134:585–95.

[39] Forster DMC, Meyerson BA, Leksell L, Steiner L. Stereotaxic radiosurgery in intractable pain. In: Janzen R, editor. Pain. London: G Thieme; 1972. p. 194–8.

[40] Steiner L, Forster D, Leksell L, Meyerson BA, Boethius J. Gammathalamotomy in intractable pain. Acta Neurochir (Wien) 1980;52(3–4):173–84.

[41] Young RF, Jacques DS, Rand RW, Copcutt BG, Vermeuker SS, Posewitz AE. Technique of stereotactic medial thalamotomy with the Leksell Gamma knife for treatment of chronic pain. Neurol Res 1995;17:59–65.

[42] Leksell L. Stereotaxis and radiosurgery. Springfield: Charles C. Thomas; 1971.

[43] Goss BW, Frighetto L, De Salles AA, Smith Z, Solberg T, Selch M. Linear accelerator radiosurgery using 90 Gy for essential trigeminal neuralgia: results and dose volume histogram analysis. Neurosurgery 2003;53:823–30.

[44] Pollock BE, Phuong LK, Gorman DA, Foote RL, Stafford SL. Stereotactic radiosurgery for idiopathic trigeminal neuralgia. J Neurosurg 2002;97:347–53.

[45] Kondziolka D, Lunsford LD, Flickinger JC. Stereotactic radiosurgery for the treatment of trigeminal neuralgia. Clin J Pain 2002;18:42–7.

[46] Romanelli P, Heit G, Chang SD, Martin D, Pham C, Adler J. Cyberknife radiosurgery for trigeminal neuralgia. Stereotact Funct Neurosurg 2003;81: 105–9.

[47] Ryu SI, Chang SD, Kim DH, Murphy MJ, Le QT, Martin DP, et al. Image-guided hypo-fractionated stereotactic radiosurgery to spinal lesions. Neurosurgery 2001;49(4):838–46.