Trigeminal Neuralgia: Treatments

Aetna considers the following surgical procedures for the treatment of trigeminal neuralgia medically necessary when the condition has persisted for at least 6 months despite conservative treatment with pharmacotherapies (carbamazepine, phenytoin, and baclofen) or the member is unable to tolerate the side effects of the medications.

- Balloon compression
- CyberKnife (see CPB 0083 - Stereotactic Radiosurgery (../1_99/0083.html))
- Gamma knife (see CPB 0083 - Stereotactic Radiosurgery (../1_99/0083.html))
- Microvascular decompression
- Percutaneous glycerol rhizotomy (or injections)*
- Percutaneous radiofrequency rhizolysis/rhizotomy*

Aetna considers surgery for trigeminal neuralgia not meeting the aforementioned criteria experimental and investigational.

Aetna considers trigeminal nerve blocks medically necessary for refractory cases of trigeminal neuralgia.
Aetna considers the following interventions experimental and investigational for the treatment of trigeminal neuralgia because their effectiveness has not been established (not an all-inclusive list):

- Acupuncture
- Adipose-derived stem cells
- Botulinum toxin
- CT-guided percutaneous pulsed radiofrequency of the Gasserian ganglion
- Combination of pulsed radiofrequency (PRF) with continuous RF thermocoagulation
- Deep brain stimulation
- Electrical stimulation of the occipital nerve or trigeminal nerve
- Intra-arterial modulation (e.g., intra-arterial lidocaine) of the trigeminal nerve ganglion
- Intravenous lidocaine (alone or in combination with magnesium)
- Intravenous magnesium (alone or in combination with lidocaine)
- Motor cortex stimulation (see CPB 0755 - Motor Cortex Stimulation (../700_799/0755.html)).
- Percutaneous ozone injection
- Percutaneous neuroablation
- Peripheral neurectomy (e.g., transection of the auriculo-temporal nerve, zygomatico-temporal nerve, and/or other branches of the mandibular nerve or trigeminal nerve)
- Peripheral / subcutaneous nerve field stimulation
- Pulsed radiofrequency (see CPB 0735 - Pulsed Radiofrequency (../700_799/0735.html))
- Radial extracorporeal shock wave therapy
- Spheno-palatine ganglion block / stimulation
- Spinal cord stimulation
- Topical ambroxol
- Topical lidocaine (e.g., lidocaine medicated plaster)
- Transcranial direct current stimulation
- Trigeminal tractotomy.

*Note: These peripheral procedures refer to techniques that target portions of the trigeminal nerve distal to the Gasserian ganglion or techniques that target the Gasserian ganglion itself.
Trigeminal neuralgia (TN), also known as tic douloureux, is a neuropathic pain syndrome characterized by paroxysmal, triggered, trigeminally distributed pain. It affects more women than men (3:1 ratio), and is more common in the elderly. The anti-epileptic drug carbamazepine (Tegretol) is the drug of choice for the management of TN. Tegretol, at a dose of 600 to 1,200 mg per day, has been demonstrated to inhibit or shorten the duration of attacks. Phenytoin (Dilantin), is also effective in treating TN, but less so than carbamazepine. For patients who cannot tolerate carbamazepine because of its adverse side effects (poor liver function, confusion, ataxia, drowsiness, and allergic responses), baclofen and other anti-convulsant drugs such as clonazepam (Klonopin) may be useful. If pharmacotherapy fails, surgical intervention may be necessary.

Surgical treatment can be divided into 2 categories: (i) percutaneous, and (ii) open. The former approaches include radiofrequency rhizolysis, glycerol injection, and balloon compression techniques. The principal open approach is microvascular decompression, which entails posterior fossa craniotomy and has a small incidence of serious neurological morbidity. In general, elderly or medically debilitated patients, patients with multiple sclerosis, or individuals who have failed to attain pain relief from the open approach are encouraged to use the percutaneous approaches, while the open approach is recommended for younger and healthier subjects.

The gamma knife, one type of stereotactic radiosurgery, is also used as a means of treating patients with TN. It was developed in the 1950's by Larsson and Leksell, and is primarily used as a non-invasive alternative treatment for certain types of brain lesions such as intra-cranial arteriovenous malformations and brain tumors. When the gamma knife is used to treat TN, the beams are focused on the root of the trigeminal nerve. The stereotactic coordinates of the target site are often
determined by computed tomography and/or magnetic resonance imaging. Patients undergoing gamma knife radiosurgery are usually given local anesthesia with a mild sedative.

Pulsed radiofrequency (PRF) treatment entails the application of short bursts of RF energy to nervous tissue. It is a minimally destructive procedure that may serve as an alternative to traditional RF heat lesion. In a review on PRF treatment, Gallagher (2006) stated that "we should cautiously prescribe this promising intervention following clinical algorithms that are based upon the best clinical evidence available. However, it is critically important to avoid the mistake of creating a "carte blanche" environment for those practitioners who would abuse the privilege and opportunity presented by this new technology, besmirching our credibility and ultimately impeding the opportunity to use this treatment to the benefit of the public. Ultimately, evidence, not reimbursement, should determine whether PRF finds a place in our clinical toolbox".

Cahana et al (2006) stated that PRF, a non- or minimally-neurodestructive technique, has been used as alternative to radiofrequency heat lesions. Clinical advantages and mechanisms of PRF remain unclear. These investigators reviewed current clinical and laboratory data on PRF. The final analysis yielded 58 reports on the clinical use of PRF in different applications: 33 full publications and 25 abstracts. They also retrieved 6 basic science reports, 5 full publications, and 1 abstract. The authors concluded that the accumulation of these data showed that the use of PRF generates an increasing interest of pain physicians for the management of a variety of pain syndromes. Although the mechanism of action has not been completely elucidated, laboratory reports suggested a genuine neurobiological phenomenon altering the pain signaling, which some researchers have described as neuromodulatory. No side effects related to PRF were reported to date. They stated that further research in the clinical and biological effects of this technique is justified.

In the only controlled clinical trial of PRF for TN published to date, Erdine et al (2007) concluded that PRF is not an effective treatment for TN. Erdine et al (2007) reported on a prospective, randomized, double-blinded study to compare PRF to conventional radiofrequency (CRF) in the treatment of idiopathic TN. A total of 40 patients with idiopathic TN
were randomly assigned to PRF or CRF. Visual Analog Scale (VAS) scores decreased significantly \( (p < 0.001) \) and Patient Satisfaction Scale (PSS) scores improved significantly \( (p < 0.001) \) after the procedure in subjects assigned to CRF. The VAS score decreased in only 2 of 20 patients from the PRF group and pain recurred 3 months after the procedure. The investigators reported that, at the end of 3 months, they performed CRF in patients assigned to PRF, because all patients in this group still had intractable pain.

Cheshire (2007) stated that many treatments have been developed for TN. Anti-epileptic drugs are superior to traditional analgesics with carbamazepine being the drug of first choice. Additional drugs for which there is evidence of efficacy include oxcarbazepine, baclofen, gabapentin, lamotrigine and phenytoin. However, many patients eventually experience tachyphylaxis or may not tolerate effective doses. Surgical interventions include microvascular decompression; balloon compression; RF thermocoagulation or glycerol rhizotomies; and subcutaneous alcohol branch blockade. Stereotactic gamma knife radiosurgery is a further option. Motor cortex stimulation and transcranial magnetic stimulation, although having shown initial promise for trigeminal neuropathic pain, seem to be ineffective for classical TN.

The Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies' practice parameter on the diagnostic evaluation and treatment of TN (Gronseth et al, 2008) stated that for patients with TN refractory to medical therapy, Gasserian ganglion percutaneous techniques, gamma knife, and microvascular decompression may be considered.

Adler et al (2009) stated that although stereotactic radiosurgery is an established procedure for treating TN, the likelihood of a prompt and durable complete response is not assured. Moreover, the incidence of facial numbness remains a challenge. To address these limitations, a new, more anatomic radiosurgical procedure was developed that uses the CyberKnife (Accuray, Inc., Sunnyvale, CA) to lesion an elongated segment of the retro-Gasserian cisternal portion of the trigeminal sensory root. Because the initial experience with this approach resulted in an unacceptably high incidence of facial numbness, a gradual dose and volume de-escalation was performed over several years. In this single-
institution prospective study, these researchers assessed clinical outcomes in a group of TN patients who underwent lesioning with seemingly optimized non-isocentric radiosurgical parameters. A total of 46 patients with intractable idiopathic TN were treated between January 2005 and June 2007. Eligible patients were either poor surgical candidates or had failed previous microvascular decompression or destructive procedures. During a single radiosurgical session, a 6-mm segment of the affected nerve was treated with a mean marginal prescription dose of 58.3 Gy and a mean maximal dose of 73.5 Gy. Monthly neurosurgical follow-up was performed until the patient became pain-free. Longer-term follow-up was performed both in the clinic and over the telephone. Outcomes were graded as excellent (pain-free and off medication), good (greater than 90 % improvement while still on medication), fair (50 to 90 % improvement), or poor (no change or worse). Facial numbness was assessed using the Barrow Neurological Institute Facial Numbness Scale score. Symptoms disappeared completely in 39 patients (85 %) after a mean latency of 5.2 weeks. In most of these patients, pain relief began within the first week. Trigeminal neuralgia recurred in a single patient after a pain-free interval of 7 months; all symptoms abated after a second radiosurgical procedure. Four additional patients underwent a repeat rhizotomy after failing to respond adequately to the first operation. After a mean follow-up period of 14.7 months, patient-reported outcomes were excellent in 33 patients (72 %), good in 11 patients (24 %), and poor/no improvement in 2 patients (4 %). Significant ipsilateral facial numbness (Grade III on the Barrow Neurological Institute Scale) was reported in 7 patients (15 %). The authors concluded that optimized non-isocentric CyberKnife parameters for TN treatment resulted in high rates of pain relief and a more acceptable incidence of facial numbness than reported previously. Moreover, they stated that longer follow-up periods will be needed to establish whether or not the durability of symptom relief after lesioning an elongated segment of the trigeminal root is superior to isocentric radiosurgical rhizotomy.

Fariselli et al (2009) reported the safety and effectiveness and safety of CyberKnife robotic radiosurgery as a first-line treatment against pharmacologically refractory TN. These investigators treated 33 patients with the frameless CyberKnife system as a monotherapy. The retro-Gasserian portion of the trigeminal nerve (a length of 4 mm, 2 to 3 mm
anterior to the root entry zone) was targeted. Doses of 55 to 75 Gy were prescribed to the 100 % isodose line, according to a dose escalation protocol. Patients were evaluated for the level of pain control, time to pain relief, hypesthesia, and time to pain recurrence. The median age was 74 years. All but 2 patients (94 %) achieved a successful treatment outcome. The follow-up period was 9 to 37 months (mean of 23 months). The Barrow Neurological Institute Pain Intensity Scale (BPS) score before radiosurgery was III in 2 patients (6 %), IV in 8 patients (24 %), and V in 23 patients (70 %). The time to pain relief was 1 to 180 days (median of 30 days). No facial numbness was observed. Only 1 patient developed a transitory dysesthesia of the tongue. After treatment, the BPS score was I, II, or III in 31 patients (97 %). Pain recurred in 33 % (11 patients) at a mean of 9 months (range of 1 to 43 months). Three patients with recurrences had low pain control by medication (BPS score, IV), and 1 patient (BPS score, V) needed a RF lesioning (BPS score, I at 12 months). The authors concluded that CyberKnife radiosurgery for TN allows pain relief at safe doses and is suggested for pharmacologically refractory TN. It should be noted that the rate of pain recurrence is rather high in this study (33 %).

Kouzounias et al (2010) compared percutaneous balloon compression (PBC) and percutaneous retrogasserian glycerol rhizotomy (PRGR) for the treatment of TN in terms of effectiveness, complications, and technical aspects. A total of 66 consecutive PBC procedures were performed in 45 patients between January 2004 and December 2008, and 120 PRGR attempts were performed in 101 patients between January 2006 and December 2008. The PRGR procedures were not completed due to technical reasons in 19 cases. Five patients in the PBC group and 9 patients in the PRGR group were lost to follow-up and were excluded from the study. The medical records as well as the intra-operative fluoroscopic images from the remaining cases were retrospectively examined, and the follow-up was completed with telephone contact, when necessary. The 2 groups were compared in terms of initial effect, duration of effect, and rates of complications as well as severity and type of complications. The rates for immediate pain relief were 87 % for patients treated with glycerol injection and 85 % for patients treated with balloon compression. The Kaplan-Meier plots for the 2 treatment modalities were similar. The 50 % recurrence time was 21 months for the balloon procedure and 16 months for the glycerol
procedure. When the groups were broken down by the "previous operations" criterion, the 50% recurrence time was 24 months for the Glycerol First Procedure Group, 6 months for the Balloon First Procedure Group, 8 months for the Glycerol Previous Procedures Group, and 21 months for the Balloon Previous Procedures Group. The rates of complications (excluding numbness) were 11% for PRGR and 23% for PBC, and this difference was statistically significant (chi-square test, p = 0.04). The authors concluded that both PRGR and PBC are effective techniques for the treatment of TN, with PRGR presenting some advantages in terms of milder and fewer complications and allowing lighter anesthesia without compromise of analgesia. For these reasons the authors consider PRGR as the first option for the treatment of TN in patients who are not suitable candidates or are not willing to undergo microvascular decompression, while PBC is reserved for patients in whom the effect of PRGR has proven to be short or difficult to repeat due to cisternal fibrosis.

A Cochrane review on “Neurosurgical interventions for the treatment of classical trigeminal neuralgia” (Zakrzewska and Akram, 2011) noted that surgical treatments for refractory trigeminal neuralgia are divided into 2 main categories: (i) ablative (destructive) and (ii) non-ablative. These treatments can be done at 3 different sites: (i) peripherally, (ii) at the Gasserian ganglion level, and (iii) within the posterior fossa of the skull. The authors concluded that “There is very low quality evidence for the effectiveness of most neurosurgical procedures for trigeminal neuralgia because of the poor quality of the trials. All procedures produced variable pain relief, but many resulted in sensory side effects …. Well-designed studies are urgently needed”.

An UpToDate review on "Trigeminal neuralgia" (Bajwa et al, 2013) states that “Peripheral neurectomy can be performed on the branches of the trigeminal nerve, which are the supraorbital, infraorbital, alveolar, and lingual nerves. Neurectomy is accomplished by incision, alcohol injection, radiofrequency lesioning, or cryotherapy. Cryotherapy involves freezing of the nerve using special probes, in theory to selectively destroy the pain fibers. The AAN/EFNS practice parameter noted that the evidence regarding peripheral techniques for the treatment of TN is either negative or inconclusive".
Collet et al (2013) stated that the etiology of TN remains unclear and several theories have been proposed. Many medical and surgical methods have been applied with only partial effectiveness and several side effects. New hypotheses and therapeutic methods are urgently needed. Using evidence presented in a literature review and in the authors’ case report, these researchers hypothesized that pain resulting from TN can be caused by demyelinating lesions in the trigger zone; and that these lesions can be repaired through the injection of fat containing adipose-derived stem cells.

Parmar et al (2013) stated that pharmacotherapy still remains the first line therapy for the management of TN. However, often the patients become refractory to the pharmacotherapy and need surgical interventions. There is a wide array of surgical treatment modalities available for TN. These investigators evaluated the various surgical modalities by employing a comparative analysis with respect to patient selection, success rate, complications and cost-effectiveness. For the evaluation, a critical review of literature was done with pre-defined search terms to obtain the details of individual procedures, which were then compared, under similar parameters. The results suggested that microvascular decompression seem to be the most effective treatment in terms of patient satisfaction and long term cost-effectiveness. However, if patient factors do not permit, then the peripheral procedures may be employed as a substitute, though they have higher recurrence rate and complications and have relatively lower long-term cost effectiveness. The authors noted that newer modalities like stereotactic radiosurgery and botulinum toxin have promising results and further refinement in these procedures will provide additional options for the patients suffering from TN.

Hu and colleagues (2013) systematically reviewed the therapeutic safety and effectiveness of botulinum toxin type A (BTX-A) in the treatment of TN. PubMed, EMBASE, Cochrane Library Clinical Trials and Web of Science from January 1966 to March 2013 were searched with the terms of "botulinum toxin" and "trigeminal neuralgia", and references of related articles were traced. Data on the safety and effectiveness of BTX-A in this disorder were extracted and analyzed by at least 2 reviewers. Data for individual studies were reported, and pooled data were analyzed if appropriate. A total of 5 prospective studies and 1 double-blind, randomized, placebo-controlled study were identified. Response was
achieved in approximately 70 to 100% of patients, and the mean pain intensity and frequency were reduced by approximately 60 to 100% at 4 weeks after treatment in most studies. Major adverse events were not reported. Available studies showed BTX-A may be effective in treatment of TN. However, the authors concluded that well-designed randomized, controlled, double-blinded trial is still lacking. They stated that future BTX-A treatment studies on optimal dose, duration of the therapeutic effectiveness, common adverse events, and the time and indications for repeat injection would be promising.

Fontaine et al (2014) stated that although most patients suffering from TN respond to medical or surgical treatment, non-responders remain in very severe painful condition. These researchers described for the first time a case of severe refractory classical TN treated successfully (follow-up 1 year) by chronic bilateral occipital nerve stimulation (ONS), because other classic medical and surgical options failed or could not be performed. The authors concluded that this single case suggested that ONS might be offered to TN patients who are refractory both to standard drugs and interventions, with a favorable risk/benefit ratio, although its long-term effectiveness remains unknown. This preliminary finding needs to be validated by well-designed studies.

Tamburin et al (2014) reported on 2 patients with classical TN in whom conventional drugs for TN were not tolerated. In these patients, treatment with 5% lidocaine medicated plaster (LMP) resulted in reduction of pain intensity and the number of pain paroxysms. Lidocaine medicated plaster is known to block the sodium channels on peripheral nerves and may cause a selective and partial block of Aδ and C fibers. According to the TN ignition hypothesis, blockage of peripheral afferents by LMP may reduce pain paroxysms. The effect of LMP may outlast the pharmacokinetics of the drug by reducing pain amplification mechanisms in the central nervous system; LMP has limited or no systemic side effects. The authors concluded that LMP may be an effective and well-tolerated treatment option for TN in those patients who do not tolerate or who refuse other therapies. They stated that future randomized controlled studies should better address this issue.
Stavropoulou et al (2014) stated that intravenous lidocaine infusions are gaining acceptance in a variety of pain-management settings. These researchers stated that future clinical research should focus on identifying the effective dosage of lidocaine alone, magnesium alone, and lidocaine-magnesium combination to be used in the treatment of TN.

An UpToDate review on “Trigeminal neuralgia” (Bajwa et al, 2015) states that “Several other drugs have shown some evidence of efficacy for TN in small, generally lower-quality controlled trials …. Topical lidocaine given by intra-oral application was more effective than placebo for pain reduction in a two-week, randomized cross-over trial of 24 subjects with TN whose pain was most severe in the mouth. However, blinding may have been compromised because of the bitter taste or numbness perceived by some patients when treated with lidocaine …. There is only limited evidence to support treatment alternatives for patients with TN who are refractory to first-line medical therapy …. Intravenous infusion of phenytoin, fosphenytoin or lidocaine may provide analgesia while oral medications are titrated …. Nevertheless, there are no randomized controlled trials comparing monotherapy with combination therapy for TN”. Moreover, magnesium is not mentioned as a therapeutic option.

Tuleasca et al (2014) examined the safety and effectiveness of repeat Gamma Knife surgery (GKS) for recurrent TN. Using the prospective database of TN patients treated with GKS in Timone University Hospital (Marseille, France), data were analyzed for 737 patients undergoing GKS for TN Type 1 from July 1992 to November 2010. Among the 497 patients with initial pain cessation, 34.4 % (157/456 with greater than or equal to 1-year follow-up) experienced at least 1 recurrence. Thirteen patients (1.8 %) were considered for a second GKS, proposed only if the patients had good and prolonged initial pain cessation after the first GKS, with no other treatment alternative at the moment of recurrence. As for the first GKS, a single 4-mm isocenter was positioned in the cisternal portion of the trigeminal nerve at a median distance of 7.6 mm (range of 4 to 14 mm) anterior to the emergence of the nerve (retrogasserian target). A median maximum dose of 90 Gy (range of 70 to 90 Gy) was delivered. Data for 9 patients with at least 1-year follow-up were analyzed. A systematic review of literature was also performed, and results are compared with those of the Marseille study. The median time to re-treatment in the Marseille study was 72 months (range of 12 to 125
months) and in the literature it was 17 months (range of 3 to 146 months). In the Marseille study, the median follow-up period was 33.9 months (range of 12 to 96 months), and 8 of 9 patients (88.9%) had initial pain cessation with a median of 6.5 days (range of 1 to 180 days). The actuarial rate for new hypesthesia was 33.3% at 6 months and 50% at 1 year, which remained stable for 7 years. The actuarial probabilities of maintaining pain relief without medication at 6 months and 1 year were 100% and 75%, respectively, and remained stable for 7 years. The systematic review analyzed 20 peer-reviewed studies reporting outcomes for repeat GKS for recurrent TN, with a total of 626 patients. Both the selection of the cases for re-treatment and the way of reporting outcomes vary widely among studies, with a median rate for initial pain cessation of 88% (range of 60% to 100%) and for new hypesthesia of 33% (range of 11% to 80%). The authors concluded that results from the Marseille study raised the question of surgical alternatives after failed GKS for TN. The rates of initial pain cessation and recurrence seem comparable to, or even better than, those of the first GKS, according to different studies, but toxicity is much higher, both in the Marseille study and in the published data. Neither the Marseille study data, nor the literature data, answered the 3 cardinal questions regarding repeat radiosurgery in recurrent TN: which patients to re-treat, which target is optimal, and which dose to use.

Tempel et al (2015) reviewed pain outcomes and complications in TN patients who required 3 radiosurgical procedures for recurrent or persistent pain. These researchers performed a retrospective review of all patients who underwent 3 Gamma Knife radiosurgery (GKRS) procedures for TN at 4 participating centers of the North American Gamma Knife Consortium from 1995 to 2012 was performed. The Barrow Neurological Institute (BNI) pain score was used to evaluate pain outcomes. A total of 17 patients were identified; 7 were males and 10 were females. The mean age at the time of last GKRS was 79.6 years (range of 51.2 to 95.6 years). The TN was Type I in 16 patients and Type II in 1 patient. No patient suffered from multiple sclerosis. Eight patients (47.1%) reported initial complete pain relief (BNI Score I) following their third GKRS and 8 others (47.1%) experienced at least partial relief (BNI Scores II-IIIb). The average time to initial response was 2.9 months following the third GKRS. Although 3 patients (17.6%) developed new facial sensory dysfunction following primary GKRS and 2 patients (11.8%) experienced new or worsening sensory disturbance following the
second GKRS, no patient sustained additional sensory disturbances after the third procedure. At a mean follow-up of 22.9 months following the third GKRS, 6 patients (35.3 %) reported continued Score I complete pain relief, while 7 others (41.2 %) reported pain improvement (BNI Scores II-IIlb). Four patients (23.5 %) suffered recurrent TN following the third procedure at a mean interval of 19.1 months. The authors concluded that a third GKRS resulted in pain reduction with a low risk of additional complications in most patients with medically refractory and recurrent, intractable TN. In patients unsuitable for other microsurgical or percutaneous strategies, especially those receiving long-term oral anti-coagulation or anti-platelet agents, GKRS repeated for a third time was a satisfactory, low risk option.

Combination of Pharmacotherapy and Lidocaine Block

In a pilot study, Stani et al (2015) evaluated the therapeutic effect of combination of pharmacotherapy and lidocaine block in the treatment of classical TN (CTN). A total of 13 patients with CTN managed with pharmacotherapy were recruited and assigned either to no additional treatment (Group I) or to additional analgesic block (Group II). The primary end-point was the reduction in the frequency of pain episodes in a month assessed at 30 and 90 days. Comparisons of measurements of pain, general health and depression scales were secondary end-points. The results from the follow-up visits at 30 and 90 days showed the Group II to have larger reduction in the frequency of pain and exhibited a bigger improvement in the scores of the pain, general health and depression scales. The authors concluded that the findings of this study suggested a clinical benefit of the combination of pharmacotherapy and lidocaine block. These preliminary findings need to be validated in well-designed studies.

Peripheral/Subcutaneous Trigeminal Nerve Field Stimulation

Klein et al (2016) stated that peripheral nerve field stimulation (PNFS) is a promising modality for treatment of intractable facial pain. However, evidence is sparse. These researchers presented their experience with this technique in a small patient cohort. Records of 10 patients (5 men, 5 women) with intractable facial pain who underwent implantation of one or several subcutaneous electrodes for trigeminal nerve field stimulation
were retrospectively analyzed. Patients' data, including pain location, etiology, duration, previous treatments, long-term effects and complications, were evaluated. Four patients suffered from recurrent classical TN, 1 had classical TN and was medically unfit for microvascular decompression. Two patients suffered from trigeminal neuropathy attributed to multiple sclerosis, 1 from post-herpetic neuropathy, 1 from trigeminal neuropathy following radiation therapy and 1 from persistent idiopathic facial pain. Average patient age was 74.2 years (range of 57 to 87), and average symptom duration was 10.6 years (range of 2 to 17).

Eight patients proceeded to implantation after successful trial. Average follow-up after implantation was 11.3 months (range of 5 to 28). Using the VAS, average pain intensity was 9.3 (range of 7 to 10) pre-operatively and 0.75 (range of 0 to 3) post-operatively; 6 patients reported absence of pain with stimulation; 2 had only slight constant pain without attacks. The authors concluded that PNFS may be an effective treatment for refractory facial pain and yields high patient satisfaction. These preliminary findings need to be validated by well-designed studies.

William et al (2016) retrospectively reviewed their early experience with stimulation involving the trigeminal and sphenopalatine ganglion (SPG) stimulation for trigeminal neuropathic pain (TNP), anesthesia dolorosa, and persistent idiopathic facial pain (PIFP) between 2010 and 2014 to evaluate the feasibility of implanting at these ganglionic sites. A total of 7 patients received either trigeminal and/or SPG stimulation with or without peripheral nerve stimulation, having failed multiple alternative modalities of treatment. The treatments were tailored on the physical location of pain to ensure regional coverage with the stimulation. Fluoroscopy or frameless stereotaxy was utilized to place the SPG and/or trigeminal ganglion stimulator. All patients were initially trialed before implantation. Trial leads implanted in the pterygopalatine fossa near the SPG were implanted via transpterygoid (lateral-medial, infra-zygomatic) approach. Trial leads were implanted in the trigeminal ganglion via percutaneous Hartel approach, all of which resulted in masseter contraction. Patients who developed clinically significant pain improvement underwent implantation. The trigeminal ganglion stimulation permanent implants involved placing a grid electrode over Meckel's cave via sub-temporal craniotomy, which offered a greater ability to stimulate subdivisions of the trigeminal nerve, without muscular (V3) side effects; 2 of the 7 overall patients did not respond well to the trial and were not implanted; 5
patients reported pain relief with up to 24-month follow-up. Several of the SPG stimulation patients had pain relief without any paresthesias. There were no electrode migrations or post-surgical complications. The authors concluded that refractory facial pain may respond positively to ganglionic forms of stimulation. It appeared safe and durable to implant electrodes in the pterygopalatine fossa via a lateral transpterygoid approach. Also, implantation of an electrode grid overlying Meckel's cave appeared to be a feasible alternative to the Hartel approach. They stated that further investigation is needed to evaluate the usefulness of these approaches for various facial pain conditions.

Maniam et al (2016) stated that craniofacial pain, including TN, TNP, and PIFP, is difficult to treat and can have severe implications for suffering in patients afflicted with these conditions. In recent years, clinicians have moved beyond treating solely with pharmacological therapies, which are generally not very effective, and focused on new interventional pain procedures. These procedures have evolved as technology has advanced, and thus far, early results have demonstrated effectiveness in small patient cohorts with a variety of craniofacial pain states. Some of the most promising interventional pain procedures include deep brain stimulation, high-frequency spinal cord stimulation, PNFS, and SPG stimulation. These researchers focused on a better understanding of craniofacial pain and emerging interventional pain therapies. With the advent of newer miniature wireless devices and less invasive implantation techniques, this should allow for more widespread use of neurostimulation as a therapeutic modality for treating craniofacial pain. The authors concluded that larger studies would aid in best practice strategies vis-à-vis traditional pharmacological therapies and emerging interventional pain techniques.

Jakobs and colleagues (2016) stated that neurosurgical pain management of drug-resistant TN is highly challenging. Microvascular decompression is a first-line neurosurgical approach for classical TN with neurovascular conflict, but can show clinical relapse despite proper decompression. Second-line destructive techniques like RF thermocoagulation have become reluctantly used due to their potential for irreversible side effects. Subcutaneous PNFS (sPNFS) is a minimally invasive neuro-modulatory technique which has been shown to be effective for chronic localized pain conditions. Reports on sPNFS for the
treatment of trigeminal pain are still sparse and primarily focused on pain intensity as outcome measure. Detailed data on the impact of sPNFS on attack frequency are currently not available. Patients were classified according to the International Headache Society classification (ICHD-3-beta); 3 patients had classical TN without (n = 3) and another 3 TN with concomitant persistent facial pain (n = 3); 2 patients suffered from post-herpetic trigeminal neuropathy (n = 2). All 8 patients underwent a trial stimulation of at least 7 days with subcutaneous leads in the affected trigeminal area connected to an external neurostimulator. Of those, 6 patients received permanent implantation of a neurostimulator. During the follow-up (6 to 29 months, mean of 15.2), VAS-scores, attack frequencies, oral drug intake, complications and side effects were documented; 7 of 8 patients responded to sPNFS (i.e., greater than or equal to 50 % pain reduction) during the test trial. The pain intensity (according to VAS) was reduced by 83 ± 16 % (mean ± SD) and the number of attacks decreased by 73 ± 26 % (mean ± SD); 5 of 6 patients were able to reduce or stop pain medication; 1 patient developed device infection; 2 patients developed stimulation-related side effects that could be resolved by re-programming. The authors concluded that treatment by sPNFS is a beneficial option for patients with refractory trigeminal pain. Moreover, they stated that prospective randomized trials are needed to systematically evaluate the safety and effectiveness of this low-invasive neurosurgical technique.

Trigeminal Tractotomy

Cetas et al (2008) stated that non-malignant pain has been treated in the past century with ablative, or more appropriately, destructive procedures. Although individual outcomes for these procedures have previously been described in the literature, to the authors’ knowledge this was the first comprehensive and systematic review on this topic. A US National Library of Medicine PubMed search was conducted for the following ablative procedures: cingulotomy, cordotomy, DREZ (also input as dorsal root entry zone), ganglionectomy, mesencephalotomy, myelotomy, neurotomy, rhizotomy, sympathectomy, thalamotomy, and tractotomy. Articles related to pain resulting from malignancy and those not in peer-reviewed journals were excluded. In reviewing pertinent articles, focus was placed on patient number, outcome, and follow-up. A total of 146 articles was included in the review. The large majority of studies
constituted Class III evidence; 11 Class I and 4 Class II studies were found, of which nearly all (13 of 15) evaluated radiofrequency rhizotomies for different pain origins, including lumbar facet syndrome, cervical facet pain, and type I or typical trigeminal neuralgia. Overall, support for ablative procedures for non-malignant pain is derived almost entirely from Class III evidence; despite a long history of use in neurosurgery, the evidence supporting destructive procedures for benign pain conditions remains limited. The authors concluded that newly designed prospective standardized studies are needed to define surgical indications and outcomes for these procedures, to provide more systematic review, and to advance the field.

Kahilogullari et al (2010) stated that TN pain secondary to bee sting has not been reported previously in the literature. These investigators reported the case of a 52-year old male patient with right-sided trigeminal neuropathic pain that began a month earlier, following a honeybee sting to the right forehead. The patient was successfully treated by computed tomography (CT)-guided percutaneous trigeminal tractotomy. The present report showed that a honeybee sting may result in trigeminal neuropathic pain and CT-guided percutaneous trigeminal tractotomy is effective in the treatment of such cases.

Jiang et al (2010) examined the feasibility of surface tractotomy of trigeminal nerve sensory root (STS) for the treatment of TN. A total of 7 patients with TN were operated on using the STS; 6 patients were followed-up for 4.8 to 9.8 years. In addition, these researchers performed micro-anatomical studies using paraffin embedding and hematoxylin-eosin staining technique on the trigeminal nerve root (TNR) obtained from 30 cadavers. Clinically, patients' symptoms (e.g., face ache) disappeared after the surface nerve fiber bundles of trigeminal nerve sensory root (TNSR) were severed. Only 1 patient died of brainstem bleeding on post-operative day 18. Histological examination: The common type of sensory root fibers were arranged parallel for 3 to 6 mm at its exit of brainstem, and then the glial myelin transformed to Schwann cells. The axon bifurcated from outer layer to middle region, and gradually formed the tiny nerve fiber bundles in the surface layer and the giant nerve fiber bundles in the center of the root. The authors concluded that TN can be cured by STS without impairing nerve functions. They stated that this new approach is an effective, advanced surgical technique for TN treatment.
Ibrahim et al (2015) presented a novel technique, ventral pontine trigeminal tractotomy via retrosigmoid craniectomy, as an adjunct treatment in TN when there is no significant neurovascular compression. These researchers presented a non-randomized, retrospective comparison between 50 patients who lacked clear or impressive arterial neurovascular compression of the trigeminal nerve as judged by preoperative magnetic resonance imaging and intra-operative observations. These patients had intractable TN unresponsive to previous treatment. Trigeminal tractotomy was performed either alone or in conjunction with microvascular decompression. Stereotactic neuro-navigation was used during surgery to localize the descending tract via a ventral pontine approach for descending tractotomy; follow-up was a mean of 44 months. At first follow-up, 80 % of patients experienced complete relief of their pain, and 18 % had partial relief. At the most recent follow-up, 74 % of patients were considered a successful outcome; only 1 (2 %) patient had no relief after trigeminal tractotomy. Of those with multiple sclerosis-related TN, 87.5 % experienced successful relief of pain at their latest follow-up. The authors concluded that while patient selection is a significant challenge, this procedure represents an option for patients with TN who have absent or equivocal neurovascular compression, multiple sclerosis-related TN, or recurrent TN.

Furthermore, an UpToDate review on "Trigeminal neuralgia" (Bajwa et al, 2016) does not mention trigeminal tractotomy as a therapeutic option.

The current evidence supporting the use of trigeminal tractotomy for the treatment of TN is mainly based on case-series studies. Well-designed studies are need to validate the effectiveness of this approach.

**Intra-Arterial Modulation of the Trigeminal Nerve Ganglion**

Qureshi and colleagues (2018) stated that nerves and nerve gangliaons are supplied by segmental arteries and the vasa nervorum, but the intra-arterial route has not been used for diagnostic or therapeutic purposes. These investigators presented the results of intra-arterial delivery of medication for modulating trigeminal nerve ganglion function in patients with refractory TN. They administered intra-arterial lidocaine in doses up to 50 mg in the middle meningeal artery territory adjacent to the arterial branch that supplies the trigeminal nerve ganglion. These researchers
performed electrophysiologic monitoring to serially assess the latency and amplitude of R1 and R2 responses in the blink reflex before and concurrent with each incremental dose of lidocaine. Clinical outcome assessment included a 10-point numeric rating, 4-point severity grading, and the pain-free time interval pre- and post-treatment. Intra-arterial lidocaine was administered to 3 patients with TN (35-year old woman, 57-year old man, and 34-year old woman). In all patients, there was a latency prolongation and amplitude reduction of R1 or R2 responses or both that was evident after 5 to 10 mg of lidocaine administration; a more pronounced effect was seen with increasing doses. The 2nd and 3rd patients reported improvement in pain severity on all scales with pain-free intervals of 5 and 3 days, respectively. There was improvement in facial hyperalgesia in all 3 patients in all dermatomes. All 3 patients’ symptoms had returned to baseline severity 1 month later. The authors found that modulation of trigeminal nerve activity via the intra-arterial route is possible based on consistent intra-procedural electrophysiologic suppression and short-term clinical improvement in patients with refractory TN. Moreover, they stated that this procedure needs more investigation and should only be considered for patients with therapy-refractory TN, due to the risk profile of the procedure and the short duration of pain relief.

The authors also acknowledged that the lack of electrophysiologic data limited their ability to define the duration of R1 and R2 response alterations after lidocaine administration. They stated that further studies would be necessary to determine if intra-arterial injection of longer acting anesthetic agents or chemotherapeutic agents in the middle meningeal artery has any value in either the diagnosis or treatment of TN.

Percutaneous Ozone Injection

In a retrospective study, An and colleagues (2018) evaluated the therapeutic effect of CT-guided percutaneous ozone injection for the treatment of refractory TN. A total of 29 patients with a diagnosis of refractory TN were enrolled. All patients were treated with a percutaneous ozone injection and 1 patient was excluded. There were 21 patients with classical TN (group A) and 7 patients with painful trigeminal neuropathy caused by post-herpetic neuralgia (group B). The percutaneous injection was an oxygen-ozone mixture at an ozone
concentration of 30 μg/ml into the Gasserian ganglion performed under CT guidance. The number of procedures performed varied from 1 to as many as 16. Outcomes were evaluated using VAS pain scores. The combined VAS scores were \( 7.11 \pm 1.23 \) pre-treatment, \( 2.86 \pm 1.69 \) post-treatment (\( p < 0.05 \)) and \( 3.25 \pm 2.01 \) after 6-month follow-up (\( p < 0.05 \)). In group A, the VAS scores were \( 7.10 \pm 1.04 \) pre-treatment and \( 2.90 \pm 1.84 \) post-treatment (\( p < 0.05 \)). In group B, the VAS scores were \( 7.14 \pm 1.77 \) pre-treatment and \( 2.71 \pm 1.25 \) post-treatment (\( p < 0.05 \)). After 6-months follow-up, the VAS score was \( 3.38 \pm 2.18 \) in group A and \( 2.86 \pm 1.46 \) in group B, a decrease compared to pre-treatment (\( p < 0.05 \)); VAS of Group A and B showed no difference not only in pre-treatment, but also in post-treatment and follow-up. The authors concluded that percutaneous ozone injection is a safe and effective treatment for patients with refractory TN.

The authors stated that this study had several drawbacks. First, this study was retrospective in design. Out of 28 charts reviewed, clinical records were incomplete with data missing in 1 case (3.57 %) during therapy and follow-up period. Second, a large-scale longitudinal prospective study would confirm the validity of these findings. Third, follow-up time was limited to 6 months and was relatively short. Moreover, researchers could not control for other treatments such as transcutaneous electrical nerve stimulation (TENS) and physical therapy (PT) during follow-up. These treatments might have influenced the results of this study. Finally, contrast medium injected at the site of the procedure might have provided further validation of correct needle placement, but it may also have interfered with the therapy itself.

Radial Extracorporeal Shock Wave Therapy

Zhang and co-workers (2018) reported on the case of a patient with primary TN who exhibited pain relief without medication after radial extracorporeal shock wave therapy (ESWT). The 52-year old woman had a 3-year history of primary TN, involving the right maxillary division (V2) and the mandibular division (V3). She became refractory to carbamazepine and exhibited hepatic dysfunction. She hence received 3,000 to 6,000 impulses of craniofacial radial ESWT to the region centered on the surface projection of the trigeminal ganglion and pain areas at 10 Hz; the intensity ranged from 1.4 to 4.5 bars twice-weekly for
8 weeks. At baseline, and 1, 2, and 5 months after treatment, the Barrow Neurological Institute scores were IV, IIIa, II, and II, and the VAS were 8, 3, 1, and 1, respectively. No complications or adverse effects were observed. The hepatic function returned to normal after the discontinuation of carbamazepine. The authors concluded that this case report demonstrated the feasibility of radial EWT for primary TN without complications or adverse effects with careful regulation of the therapy intensity. These findings need to be validated by well-designed studies.

CT-Guided Percutaneous Pulsed Radiofrequency of the Gasserian Ganglion

Lan and colleagues (2018) stated that there is a lack of prospective studies for the long-term results of percutaneous PRF of the Gasserian ganglion in the treatment of patients with medically refractory TN. These researchers prospectively examined the outcomes of 28 idiopathic TN patients who received CT-guided percutaneous PRF of the Gasserian ganglion. All of the patients had stopped responding to drug therapy before PRF treatment. The effective treatment standard was a reduction in the pain numeric rating scale (NRS) by greater than or equal to 50 % after the procedure. The post-operative NRS score decreased gradually from pre-operative 7.6 ± 0.8 months to 1.5 ± 2.4, 0.2 ± 0.4, 0.2 ± 0.4, 0.1 ± 0.4, and 0.1 ± 0.4 at 1, 3, and 6 months, 1 and 2 years after the PRF treatment. The response rates at 1, 3, and 6 months were 85.7 %, and the rates at 12 months and 2 years were maintained at 78.6 %. No serious side effects were observed. The authors concluded that CT-guided PRF invention was a safe, effective, and non-destructive technique for medically intractable idiopathic TN patients; this minimally invasive alternative treatment has the potential as a 1st-line therapy for TN. Whether PRF treatment is effective cannot currently be determined pre-operatively. Age, gender, illness course, co-morbidities, and other risk factors for ineffective treatment should be assessed in the future to aid pain physicians in developing individualized treatment plans for TN patients.

The authors stated that this study had several drawbacks. These researchers merely included 28 patients and examined the efficacy of PRF for only 2 years after treatment. Larger number of cases and longer follow-ups would provide more significant results with regard to the
effectiveness of PRF treatment in TN. This single-center prospective cohort study revealed that PRF invention was effective in idiopathic TN who had not responded to medication; however, the evidence base was weak. More high-quality clinical trials, such as multi-center, randomized, controlled studies, are needed to examine the safety and effectiveness of the PRF technique. For example, further researches comparing the efficacy of repeated nerve block or other contemporary options (such as MVD) and PRF in TN patients refractory to drugs are needed. The median duration of idiopathic TN disease in this study was 3 (1.375 to 4.375) years. There was a very large range for disease duration. The correlation between length of disease duration and curative effect is worth further study. Furthermore, studies of a larger sample size are needed to compare the differences in patients who did respond to PRF treatment versus who did not respond. Pain is just a subjective experience; for example, quality of life (QOL) by the Short Form-12 (SF-12) and distress by the Hospital Anxiety and Depression Scale should be evaluated in these patients. Other than subjective indicators, such as pain relief, objective evaluation methods, such as electrophysiological examination, warrant further study to obtain additional information with respect to changes in the trigeminal nerve. Other parameters, such as treatment duration of PRF, waveform, pulse-width, frequency, and combined PRF and CRF treatment of the Gasserian ganglion at 60 °C or 65° C, which have been reported to be effective in idiopathic TN patients should also be examined in the future.

Combination of Pulsed Radiofrequency with Continuous Radiofrequency Thermocoagulation

Ding and colleagues (2018) noted that primary TN is a common clinical refractory neuralgia. Severe pain is experienced during episodes, severely impacting the patient's QOL. Long-term suffering from the disease can lead to anxiety, depression, and even suicide. The pathological processes involved in TN are complex, the mechanisms of pathogenesis are unknown, and effective treatment is lacking. In a retrospective comparative study, these researchers examined the safety and efficacy of computed tomography (CT)-guided PRF combined with low-temperature continuous radiofrequency (CRF) thermos-coagulation in V2/V3 primary TN. A total of 80 hospitalized patients with TN were selected and randomly assigned to 2 groups differentiated by therapeutic
method: CRF (CRF group, n = 40) and PRF + CRF (PCRF group, n = 40). Radiofrequency therapy was performed under the guidance of CT. Follow-up measures assessed pre-operative conditions, pain remission, complications and side effects, recovery time, and recurrence rate over the 2 years following the surgery. The VAS scores decreased in both groups after surgery. After 1 month, the decrease in the VAS score in the PCRF group was more apparent, and this difference was maintained for 2 years. The total efficiency rates in the CRF and PCRF groups were 85 % and 97.5 %, respectively, at 6 months, 1 year, and 2 years post-surgery. The differences in total efficiency rate of pain between the 2 groups at 6 months, 1 year, and 2 years were statistically significant. Recovery times in the PCRF group were shorter than those in the CRF group. Specifically, recovery times for facial numbness in the CRF and PCRF groups were 3.12 ± 1.21 months and 2.23 ± 1.02 months, respectively. Recovery times for masticatory muscle weakness were 4.33 ± 1.54 months and 3.42 ± 0.98 months, respectively. The authors concluded that CT-guided PRF combined with low-temperature CRF thermocoagulation for treating V2/V3 primary TN effectively relieved pain, increased late-stage pain remission rate, reduced complications, and reduced the rate of recurrence. These researchers stated that this study was limited by being a retrospective study, and by having a relatively small sample size (n = 40 for each of the 2 groups) from a single center.

Peripheral Neurectomy

Yuvaraj and colleagues (2019) stated that of the many chronic painful conditions, TN affecting the oro-facial region needs the particular attention of physicians and surgeons, especially those specializing in the maxilla-facial region. Therapeutic protocols for the management of classic TN include pharmacology and surgical intervention. Oral and maxilla-facial surgeons have traditionally employed the peripheral neurectomy in the surgical management of TN. These researchers examined the efficacy of peripheral neurectomy in the management of TN with regard to the relief of symptoms in comparison with standard neurosurgical procedures, and the duration of pain relief and complications observed compared to standard neurosurgical procedures. The review of the literature was performed according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines and included randomized controlled trials (RCTs), reviews and
prospective clinical studies involving surgical procedures for the management of TN. The primary outcomes evaluated were initial relief of pain, duration of relief of pain, complications observed with ablative procedures and recurrence of symptoms. A total of 43 studies met the inclusion criteria. A total of 7,913 patients from the 43 studies, central procedures were found to have best results for both quality and duration of pain relief. Percutaneous and peripheral procedures were associated with increased recurrence rates. The consolidated rates of complication for peripheral, percutaneous and central procedures were 39.46 %, 65.42%, and 10.41 %, respectively. The use of peripheral neurectomy alone in the management of classic TN was observed in 10 studies. The authors concluded that peripheral neurectomy in TN was associated with lesser quality of pain relief in comparison with central neurosurgical procedures. It also provided only short- to medium-term pain relief. Most studies with the use of peripheral neurectomy involved only a small group of patients with short follow-up periods. These investigators stated that oral and maxilla-facial surgeons must not consider the peripheral neurectomy as the 1st surgical option in the management of classic TN. Long-term results could be better-achieved with appropriate central neurosurgical procedures and pharmacotherapy.

Furthermore, an UpToDate review on “Trigeminal neuralgia” (Bajwa et al, 2019) states that “Peripheral neurectomy can be performed on the branches of the trigeminal nerve, which are the supraorbital, infraorbital, alveolar, and lingual nerves. Neurectomy is accomplished by incision, alcohol injection, radiofrequency lesioning, or cryotherapy. Cryotherapy involves freezing of the nerve using special probes, in theory to selectively destroy the pain fibers. The AAN/EFNS practice parameter noted that the evidence regarding peripheral techniques for the treatment of TN is either negative or inconclusive”.

Repeat Gamma Knife Radiosurgery (GKRS)

Patra and colleagues (2019) noted that GKRS has emerged as a promising treatment modality for patients with classical TN; however, considering that almost 50 % of the patients experience post-GKRS failure or lesion recurrence, a repeat treatment is typically necessary. The existing literature does not offer clear evidence to establish which treatment modality, repeat GKRS or microvascular decompression
(MVD), is superior. These researchers compared the overall outcome of patients who have undergone either repeat GKRS or MVD after failure of their primary GKRS; they did so by conducting a systematic review and meta-analysis of the literature and analysis of data from their own institution. These investigators conducted a systematic review and meta-analysis of the PubMed, Cochrane Library, Web of Science, and CINAHL databases to identify studies describing patients who underwent either repeat GKRS or MVD after initial failed GKRS for TN. The primary outcomes were complete pain relief (CPR) and adequate pain relief (APR) at 1 year. The secondary outcomes were rate of post-operative facial numbness and the re-treatment rate. The pooled data were analyzed with R software. Bias and heterogeneity were assessed using funnel plots and I² tests, respectively. A retrospective analysis of a series of patients treated by the authors who underwent repeat GKRS or MVD after post-GKRS failure or relapse was presented. A total of 22 studies met the selection criteria and were included for final data retrieval and meta-analysis. The search did not identify any study that had directly compared outcomes between patients who had undergone repeat GKRS versus those who had undergone MVD. Thus, the authors’ final analysis included 2 groups: studies describing outcome after repeat GKRS (n = 17) and studies describing outcome after MVD (n = 5). The authors’ institutional study was the only study with direct comparison of the 2 cohorts. The pooled estimates of primary outcomes were APR in 83 % of patients who underwent repeat GKRS and 88 % of those who underwent MVD (p = 0.49), and CPR in 46 % of patients who underwent repeat GKRS and 72 % of those who underwent MVD (p = 0.02). The pooled estimates of secondary outcomes were facial numbness in 32 % of patients who underwent repeat GKRS and 22 % of those who underwent MVD (p = 0.11); the re-treatment rate was 19 % in patients who underwent repeat GKRS and 13 % in those who underwent MVD (p = 0.74). The authors’ institutional study included 42 patients (repeat GKRS in 15 and MVD in 27), and the outcomes 1 year after re-treatment were APR in 80 % of those who underwent repeat GKRS and 81 % in those who underwent MVD (p = 1.0); CPR was achieved in 47 % of those who underwent repeat GKRS and 44 % in those who underwent MVD (p = 1.0). There was no difference in the rate of post-operative facial numbness or re-treatment. The authors concluded that the current meta-analysis failed to identify any superiority of one treatment over the other.
with comparable outcomes in terms of APR, post-operative facial numbness, and re-treatment rates. However, MVD was shown to provide a better chance of CPR compared with repeat GKRS.

**Radiofrequency Ablation**

In a systematic review and meta-analysis, Wu and colleagues (2019) examined the safety and effectiveness and safety of TN treatment via different RF approaches such as continuous RF (CRF), PRF, and combined CRF and PRF (CCPRF) treatments, thus providing high-quality clinical evidence for TN treatment. A series of databases were searched for relevant articles published between January 1998 and April 2018. The modified Jadad scale was referred to evaluate the methodological quality of the included studies. Data were extracted independently, and the outcome and safety of different routes, temperatures, and guidance used in CRF, PRF, and CCPRF were compared. Meta-analysis and publication bias were calculated using Review Manager software. A total of 34 studies involving 3,558 participants were included. With regard to TN treatment, PRF had no difference in cured rate in comparison with CRF, while CRF was more effective than CCPRF (p < 0.05). The comparison of complication rates showed that PRF and CCPRF were safer. For puncture guidance via CRF, 3D-printed template was more accurate in success rate at 1st puncture than computed tomography guidance (p < 0.05). For puncture route, foramen rotundum (FR) or pterygopalatine fossa (PPF) route had no significance in efficiency rate via CRF in comparison with foramen oval (FO) route, but PPF and FR routes were safer. For CRF treatment, low temperature (68° C to 70° C) compared with high temperature (71° C to 75° C) had no effect. Moreover, higher temperature (66° C to 80°C) had a greater effect compared with lower temperature (55° C to 65° C) on TN treatment (p < 0.05), while the safety of which was decreasing. The authors concluded that CCPRF could achieve a greater effect and safety on TN treatment; FR and FO routes in TN puncture treatment via CRF were safer. Medium temperature range was better for CRF therapy, and higher temperature was recommended in PRF, especially for the elders. Moreover, these researchers stated that further international, multi-center studies are needed to confirm these findings.

**Spheno-Palatine Ganglion (SPG) Block**
Peterson and colleagues (1995) stated that SPG block is a safe, easy method for the control of acute or chronic pain in any pain management office. It takes only a few moments to implement, and the patient can be safely taught to effectively perform this pain control procedure at home with good expectations and results. Indications for the SPG blocks include pain of musculo-skeletal origin, vascular origin and neurogenic origin. It has been used effectively in the management of temporo-mandibular joint (TMJ) pain, cluster headaches, tic douloureux, dysmenorrhea, TN, bronchospasm and chronic hiccups.

Manahan (1996) reported the case of a 56-year old woman with a diagnosis of TN, unresponsive to medical therapy, received a SPG block using bupivacaine 0.5 %. A total of 10 treatments were given. The patient remained pain-free as of 30 months after initial treatment. The authors concluded that this treatment appeared to be effective and deserved further study.

Kanai and associates (2006) noted that trigeminal nerve block has been widely used for TN. This may induce paresthesia. The 2nd division of the trigeminal nerve passes through the SPG, which is located posterior to the middle turbinate and is covered by a mucous membrane. These investigators examined the effectiveness of intra-nasal lidocaine 8 % spray on paroxysmal pain in 2nd-division trigeminal neuralgia. A total of 25 patients with 2nd-division TN were randomized to receive 2 sprays (0.2 ml) of either lidocaine 8 % or saline placebo in the affected nostril using a metered-dose spray. After a 7-day period, patients were crossed-over to receive the alternative treatment. The paroxysmal pain triggered by touching or moving face was assessed with a 10-cm VAS before and 15 mins after treatment. Patients used a descriptive scale to grade pain outcome, and were asked to note whether the pain returned and how long after therapy it recurred. Intra-nasal lidocaine 8 % spray significantly decreased VAS [baseline: 8.0 (2.0) cm, 15 mins post-spray: 1.5 (1.9) cm, mean (SD)], whereas the placebo spray did not [7.9 (2.0) cm, 7.6 (2.0) cm]. Moreover, pain was described as moderate or better by 23 patients of the lidocaine spray and 1 of the placebo group. The effect of treatment persisted for 4.3 hours (range of 0.5 to 24 hours). The authors concluded that intra-nasal lidocaine 8 % administered by a metered-dose spray produced prompt but temporary analgesia without serious adverse events (AEs) in patients with 2nd-division TN.
Nguyen and Wilkes (2010) stated that TN is a chronic condition affecting the 5th cranial nerve and resulting in sporadic intense burning and shock-like pain lasting for seconds to minutes that can be incapacitating to patients. Atypical TN includes additional features such as continuous pain and sensory disturbances in the area innervated by one or more branches of the trigeminal nerve. Documented cases of TN have dated back to the 18th century. Today, there are roughly 140,000 people suffering with this condition in the USA. Conventional treatments for this disorder include medical management with non-convulsants such as carbamazepine, which decrease the nerves response to peripheral stimulation. These agents have good initial pain relief, but relief rates fall off dramatically over the long-term. Recently, methadone has shown promise as a pharmacologic adjunct to patients with intractable neuropathic non-cancer pain, including patients suffering from TN. Cases refractory to medical management can be treated with surgical micro-decompression or minimally invasive procedures such as RF treatment; PRF is a method gaining interest as it is delivered in pulses, allowing adequate time for dissipation of heat and energy resulting in less damage to surrounding structures. This case report described the successful treatment of atypical V2 TN refractive to medical management requiring PRF treatment, a SPG block series, and low-dose methadone.

Malec-Milewska and co-workers (2015) presented the outcomes of trigeminal neuropathy management with the application of neurolytic block of SPG. This type of procedure is used in cases where pain is not well-controlled with medical treatment. A total of 20 patients were treated with SPG neurolysis after their response to pharmacological management was unsatisfactory. Significant pain relief was experienced by all but 1 patient and they were able to reduce or stop their pain medication. The time of pain relief was between a few months and 9 years during the study period. Number of procedures implemented varied as some of the patients had been under the care of the authors’ pain clinic for as long as 18 years, satisfied with this type of management and willing to have the procedure repeated if necessary. The authors concluded that it appeared that neurolytic block of SPG is effective enough and may be an option worth further consideration in battling the pain associated with trigeminal neuropathy.
Ho and colleagues (2017) noted that SPG is the largest collection of neurons in the calvarium outside of the brain. Over the past 100 years, it has been a target for interventional treatment of head and facial pain due to its ease of access. Block, RF ablation (RFA), and neuro-stimulation have all been applied to treat a myriad of painful syndromes. Despite the routine use of these interventions, the literature supporting their use has not been systematically summarized. These investigators summarized the level of evidence supporting the use of SPG block, radiofrequency ablation and neuro-stimulation. Medline, Google Scholar, and the Cochrane Central Register of Controlled Trials (CENTRAL) databases were reviewed for studies on SPG block, RFA and neuro-stimulation. Studies included in this review were compiled and analyzed for their treated medical conditions, study design, outcomes and procedural details. Studies were graded using Oxford Center for Evidence-Based Medicine for level of evidence. Based on the level of evidence, grades of recommendations were provided for each intervention and its associated medical conditions. A total of 83 publications were included in this review, of which 60 were studies on SPG block, 15 were on RFA, and 8 were on neuro-stimulation. Of all the studies, 23 have evidence level above case series. Of the 23 studies, 19 were on SPG block, 1 study on RFA, and 3 studies on neuro-stimulation. The rest of the available literature was case reports and case series. The strongest evidence lied in using SPG block, RFA and neuro-stimulation for cluster headache; SPG block also has evidence in treating TN, migraines, reducing the needs of analgesics after endoscopic sinus surgery and reducing pain associated with nasal packing removal after nasal operations. The authors concluded that SPG is a promising target for treating cluster headache using blocks, RFA and neuro-stimulation; SPG block also has some evidence supporting its use in a few other conditions. However, most of the controlled studies were small and without replications. They stated that further controlled studies are needed to replicate and expand on these previous findings.

Furthermore, an UpToDate review on “Trigeminal neuralgia” (Bajwa et al, 2019) does not mention sphenopalatine ganglion block as a therapeutic option.

**Topical Ambroxol**
Kern and colleagues (2019) noted that TN is difficult to treat and shows up-regulation of sodium channels. The expectorant ambroxol acts as a strong local anesthetic, about 40 times stronger than lidocaine. It preferentially inhibits the channel subtype Nav 1.8, expressed especially in nociceptive C-fibers. It appeared reasonable to try ambroxol for the treatment with neuropathic facial pain unresponsive to other standard options. Medical records of patients suffering from classical TN (n = 5) and successful pain reduction following topical ambroxol 20 % cream in addition to standard treatment were reported. All patients reported pain attacks with pain intensity between 4 and 10 NRS (numeric pain scale). In all cases they could be triggered, 3 patients reported additional spontaneous pain. Attacks were reduced in all 5 patients. Pain reduction achieved following ambroxol 20 % cream was 2 to 8 points (NRS) earliest within 15 to 30 mins and lasted for 4 to 6 hours mostly. This was reproducible in all cases; in 1 case pain was eliminated after 1 week. No patient reported side effects or skin changes; oral medication was reduced in 2 patients. The authors concluded that for the first time, a clinically significant pain relief following topical ambroxol 20 % cream in patients with TN was reported. In view of the positive side effect profile, topical ambroxol for patients with such a highly impaired quality of life (QOL) should be further investigated.

Transcranial Direct Current Stimulation

In a pre-clinical trial, Callai and colleagues (2019) evaluated the effect of transcranial direct current stimulation (tDCS) on facial allodynia induced by chronic constriction of the infra-orbital nerve (CCI-ION) and on the brain-stem levels of tumor necrosis factor-alpha (TNF-α), nerve growth factor (NGF), interleukin (IL)-10, and serum lactate dehydrogenase (LDH) in rats. Rats were exposed to the CCI-ION model. Facial allodynia was assessed by von Frey filaments test at baseline, 3, 7, 10, and 14 days post-surgery and 24 hours and 7 days after the bi-modal tDCS sessions for 20 min/day/8 days. Chronic constriction of the infra-orbital nerve induced a significant decrease in the mechanical threshold 14 days after surgery. This effect was reversed by tDCS treatment, with the mechanical threshold returning to basal levels at 24 hours after the end of the treatment and it persisted for 7 days after the end of the treatment; tDCS also decreased LDH serum levels compared to those in the control group. There was an interaction between pain and treatment with respect
to brain-stem levels of NGF, TNF-α, and IL-10. The authors concluded that chronic constriction of the infra-orbital nerve model was effective in establishing trigeminal neuropathic pain on 14 days after surgery, and tDCS reduced allodynia and LDH serum levels and promoted alterations in NGF, TNF-α, and IL-10 brain-stem levels. The authors concluded that these findings suggested that tDCS may be a potential therapy in the treatment of trigeminal pain. Trigeminal neuralgia was one of the key words in this study.

Acupuncture

Hu and colleagues (2019) noted that acupuncture is increasingly used by patients with primary TN (PTN). These researchers examined the safety and efficacy of acupuncture for PTN. A total of 7 databases were searched. Risk of bias was assessed and meta-analyses were conducted. The evidence level was assessed using Grading of Recommendations, Assessment, Development and Evaluation (GRADE). A total of 33 RCTs were included. Meta-analysis results demonstrated that the effect of both manual acupuncture (MA) and electro-acupuncture (EA) for improving response rate and recurrence rate was more significant than carbamazepine. Besides, MA achieved more significant effect on alleviating pain intensity. Moreover, acupuncture combined with carbamazepine had a more positive effect on response rate than carbamazepine alone. The authors concluded that acupuncture might have some positive effects for PTN. Nevertheless, the level of all evidence was low or very low. These investigators stated that this was the first PRISMA-compliant meta-analysis to examine the efficacy of acupuncture for PTN; however, they could not yet draw a firm conclusion on the efficacy of acupuncture for PTN.

Liu and associates (2019) provided the methods / protocols of a systematic review protocol for examining the safety and effectiveness of acupuncture on the treatment of idiopathic TN (ITN). These investigators will search for RCTs on this subject in 8 electronic databases and they are Cochrane Central Register of Controlled Trials (CENTRAL), Medline, Embase, Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), the Wan-Fang Database, and Chinese Scientific Journal Database (VIP database). Other relevant literatures will be manually searched as a complement. Only RCTs related to
acupuncture for ITN in English or Chinese will be included, without limitation of publication types. The risk of bias and trial quality will be assessed by the Cochrane collaboration’s tool. All data will be analyzed by RevMan V.5.3.3 statistical software. Ethical approval is not necessary as this paper does not involve patient data. This protocol will be disseminated by a peer-review journal or conference presentation.

**Radiofrequency Thermoablation / Thermocoagulation of the Gasserian Ganglion**

In a prospective, randomized, observer-blinded, clinical trial, Bharti and colleagues (2019) compared the safety and efficacy of radiofrequency thermoablation (RFT) of the peripheral branches of the trigeminal nerve with RFT of the Gasserian ganglion for the management of ITN. A total of 40 adult patients of ITN were randomly allocated into 2 groups. The control group received RFT of the Gasserian ganglion while the study group received RFT of the peripheral branches of trigeminal nerve. The procedures were performed in the operation room under all aseptic precautions with fluoroscopic guidance. Post-procedure, the patients were assessed for loss of sensation along the nerve distribution and the adequacy of pain relief on the NRS. The patients were followed-up for 3 month to evaluate the quality of pain relief by the NRS and the Barrow Neurological Institute (BNI) pain intensity scale. Improvement in pain was considered excellent if patients had complete pain relief without any medication, good if there was significant reduction in pain (greater than 50 %) with or without medication, and poor if there was less than 50 % reduction in pain with medications. Patients were also assessed for numbness and any other side effects. Patients' satisfaction with the procedure was recorded. A total of 19 patients in the control group and 18 in study group had effective pain relief of up to 3 months. Their pain scores were comparable at all time-intervals, though the number of patients receiving supplementary medications was more in study group at 2 months (p = 0.015). The patients showed overall satisfaction score of 8.5 (8 to 9) and 8 (7 to 9) in control and study groups, respectively. The average procedure duration was 30 (30 to 38) mins in the control group and 28 (25 to 40) mins in the study group. Most of the patients in both groups had mild numbness after the procedure; 1 patient in the control group had lower eyelid swelling and another had mild weakness of the masseter muscle, which resolved few days later. No major complication
was reported in the study group except for 1 patient who reported local ecchymosis. The authors found that RFT of the peripheral branches of the trigeminal nerve was a safe and effective procedure for the management of ITN. Moreover, these researchers stated that further multi-centric studies with long-term follow-up are needed to establish the efficacy of the peripheral branches RFT for the management of ITN.

The authors stated that the main drawback of this study was that the patients and the investigator performing the procedure were not blinded, although the person who assessed the patient during follow-up was blinded to the group assignment. Another drawback was that these researchers could not follow-up with the patients after 3 months due to time constraints.

In a prospective, randomized, double-blinded study, Wan and associates (2019) examined the safety and efficacy of high-voltage, long-duration pulsed radiofrequency (PRF) on the Gasserian ganglion in patients with acute/subacute zoster-related TN. A total of 96 patients with acute/subacute zoster-related TN were equally randomly assigned into 2 groups. The electrode needle punctured the Gasserian ganglion guided by CT in every patient. High-voltage, long-duration PRF at 42°C for 900 seconds was applied in the PRF group (n = 48). It was also applied in the sham group (n = 48) without RF energy output. The therapeutic effects were evaluated using a VAS and the 36-Item Short Form Health Survey (SF-36) at different time-points. The average dosage of pregabalin (mg/day) administrated within the 1st month following treatment was also recorded. The post-procedure VAS scores in the PRF group were significantly lower than those in the sham group at different time-points after treatment (p < 0.01). The SF-36 scores, which included physical functioning, physical role, bodily pain, general health perceptions, vitality, social function, emotional role, and the mental health index, were significantly improved at the 6th month after treatment in the PRF group compared with the sham group (p < 0.01). The average dosage of pregabalin administered (mg/day) within the 1st month after treatment was also significantly reduced in the PRF group compared with the sham group (p < 0.01). There were no bleeding, infection, or other severe side effects in both groups. The authors concluded that high-voltage, long-duration PRF on the Gasserian ganglion was a safe and effective therapeutic alternative for patients with acute/subacute zoster-related TN.
The authors stated that this study design had several limitations that should be addressed in future trials. First, the patients were recruited from a single center, and the sample size was relatively small. Second, the patients were only followed for 6 months after treatment. These researchers stated that future studies should include a large, prospective study across multiple sites and a longer length of follow-up. However, the current findings provided strong preliminary evidence that PRF is an effective pain relief method for acute/subacute zoster-related TN.

**CyberKnife**

In a systematic review, Tuleasca et al (2018) provided an objective summary of the published literature specific to the treatment of classical trigeminal neuralgia (TN) with stereotactic radiosurgery (SRS) and developed consensus guideline recommendations for the use of SRS, as endorsed by the International Society of Stereotactic Radiosurgery (ISRS). These investigators carried out a systematic review of the English-language literature from 1951 up to December 2015 using the Embase, PubMed, and Medline databases. The following MeSH terms were used in a title and abstract screening: "radiosurgery" AND "trigeminal". Of the 585 initial results obtained, these researchers performed a full text screening of 185 studies and ultimately found 65 eligible studies. Guideline recommendations were based on level of evidence and level of consensus, the latter pre-defined as at least 85 % agreement among the ISRS guideline committee members. The results for 65 studies (6461 patients) were reported: 45 Gamma Knife RS (GKS) studies (5,687 patients [88 %]), 11 linear accelerator (LINAC) RS studies (511 patients [8 %]), and 9 CyberKnife RS (CKR) studies (263 patients [4 %]). With the exception of 1 prospective study, all studies were retrospective. The mean maximal doses were 71.1 to 90.1 Gy (prescribed at the 100 % isodose line) for GKS, 83.3 Gy for LINAC, and 64.3 to 80.5 Gy for CKR (the latter 2 prescribed at the 80 % or 90 % isodose lines, respectively). The ranges of maximal doses were as follows: 60 to 97 Gy for GKS, 50 to 90 Gy for LINAC, and 66 to 90 Gy for CKR. Actuarial initial freedom from pain (FFP) without medication ranged from 28.6 % to 100 % (mean of 53.1 %, median of 52.1 %) for GKS, from 17.3 % to 76 % (mean of 49.3 %, median of 43.2 %) for LINAC, and from 40 % to 72 % (mean of 56.3 %, median of 58 %) for CKR. Specific to
hypesthesia, the crude rates (all Barrow Neurological Institute Pain Intensity Scale scores included) ranged from 0 % to 68.8 % (mean of 21.7 %, median of 19 %) for GKS, from 11.4 % to 49.7 % (mean of 27.6 %, median of 28.5 %) for LINAC, and from 11.8 % to 51.2 % (mean of 29.1 %, median of 18.7 %) for CKR. Other complications included dysesthesias, paresthesias, dry eye, deafferentation pain, and keratitis. Hypesthesia and paresthesia occurred as complications only when the anterior retrogasserian portion of the trigeminal nerve was targeted, whereas the other listed complications occurred when the root entry zone was targeted. Recurrence rates ranged from 0 % to 52.2 % (mean of 24.6 %, median of 23 %) for GKS, from 19 % to 63 % (mean of 32.2 %, median of 29%) for LINAC, and from 15.8 % to 33 % (mean of 25.8 %, median of 27.2 %) for CKR. Two GKS series reported 30 % and 45.3 % of patients who were pain-free without medication at 10 years. The authors concluded that the literature is limited in its level of evidence, with only 1 comparative randomized trial (1 versus 2 isocenters) reported to-date. At present, one could conclude that SRS is a safe and effective therapy for drug-resistant TN. A number of consensus statements have been made and endorsed by the ISRS.

Romanelli et al (2019) stated that image-guided robotic radiosurgery is an emerging minimally-invasive therapeutic option for TN. These investigators had treated 560 cases to-date, and reported the clinical outcomes of 387 treatments with 3 years follow-up. This study represented the largest single-center experience on CyberKnife radiosurgery for the treatment of TN so far reported. CyberKnife radiosurgery treatment was offered to patients with drug-resistant TN, after the failure of other treatments or refusal of invasive procedures. A second treatment was offered to patients with a poor response after the 1st treatment or with recurrent pain. Treatment protocol required the non-isocentric delivery of 60 Gy prescribed to the 80 % isodose to a 6-mm retrogasserian segment of the affected trigeminal nerve. Re-treatments typically received 45 Gy, again prescribed to the 80 % isodose. The final plan was developed accordingly to individual anatomy and dose distribution over the trigeminal nerve, gasserian ganglion, and brainstem. Clinical outcomes such as pain control and hypesthesia/numbness have been evaluated after 6, 12, 24, and 36 months. This research group has treated 527 patients with Cyber Knife radiosurgery at Centro Diagnostico Italiano (CDI), Milan, Italy, during the past 10 years. A minimum follow-up
of 6 months was available on 496 patients. These patients received 560 treatments: 435 patients (87.7 %) had a single treatment, 60 patients (12.1 %) had 2 treatments, and 1 patient (0.2 %) had 5 treatments (2 on the right side, 3 on the left side); 24 patients had multiple sclerosis (MS; 4.8 %). A total of 443 patients (84 %) received the treatment without previous procedures, while 84 patients (16 %) underwent radiosurgery after the failure of other treatments. A neurovascular conflict was identified in 59 % of the patients; 343 patients (receiving a total of 387 treatments) had a minimum of 36 months follow-up. Pain relief rate at 6, 12, 18, 24, 30 and 36 months was respectively 92, 87, 87, 82, 78 and 76 %; 44 patients out of 343 (12.8 %) required a 2nd treatment during the observed period. At 36 months post-treatment, 21 patients (6.1 %) reported the presence of bothering facial hypoesthesia; 18 patients out of 21 (85.7 %) developed this complication after a repeated treatment. The authors concluded that frameless image-guided robotic radiosurgery in experienced hands was a safe and effective procedure for the treatment of TN, providing excellent pain control rates in the absence of major neurological complications. Repeated treatments due to recurrent pain were associated with restored pain control but at the price of a higher rate of sensory complications.

Conti et al (2020) noted that SRS is an effective treatment for TN. Nevertheless, a proportion of patients will experience recurrence and treatment-related sensory disturbances. In order to evaluate the predictors of safety and efficacy of image-guided non-isocentric radiosurgery, these researchers analyzed the impact of trigeminal nerve volume and the nerve dose/volume relationship, together with relevant clinical characteristics. A total of 296 procedures were performed on 262 patients at 3 centers. In 17 patients the TN was secondary to MS. Trigeminal pain and sensory disturbances were classified according to the Barrow Neurological Institute (BNI) scale. Pain-free-intervals were examined using Kaplan Meier analyses. Univariate and multivariate Cox regression analyses were carried out to identify predictors. The median follow-up period was 38 months, median maximal dose 72.4 Gy, median target nerve volume 25 mm3, and median prescription dose 60 Gy. Pain control rate (BNI I to III) at 6, 12, 24, 36, 48, and 60 months were 96.8, 90.9, 84.2, 81.4, 74.2, and 71.2 %, respectively. Overall, 18 % of patients developed sensory disturbances. Patients with volume greater than or equal to 30 mm3 were more likely to maintain pain relief (p = 0.031), and
low integral dose (less than 1.4 mJ) tended to be associated with more pain recurrence than intermediate (1.4 to 2.7 mJ) or high integral dose (greater than 2.7 mJ; low versus intermediate: log-rank test, χ² = 5.02, p = 0.019; low versus high: log-rank test, χ² = 6.026, p = 0.014). MS, integral dose, and mean dose were the factors associated with pain recurrence, while re-irradiation and MS were predictors for sensory disturbance in the multivariate analysis. The authors concluded that the dose-to-nerve volume ratio was predictive of pain recurrence in TN, and re-irradiation has a major impact on the development of sensory disturbances after non-isocentric SRS. Interestingly, the integral dose may differ significantly in treatments using apparently similar dose and volume constraints.

Bal et al (2020) noted that TN is one of the most common cranial neuropathies. Pathologies located alongside the long nerve can also cause its mechanical compression or secondary involvement in the inflammatory process, and thus cause pain. TN is characterized by severe paroxysmal unilateral facial pain in the innervation area of branches I to III of the nerve V when provoked by light touch or slight movement. Multiple therapeutic methods are available, but most of them yield unsatisfactory results. According to guidelines (AAN and EFNS) the 1st-line therapy in TN is carbamazepine/oxcarbazepine, and if there is a poor response - surgical treatment. The array of surgical options includes percutaneous retrogasserian glycerol injection, radiofrequency (RF) thermocoagulation, balloon decompression, thermal rhizotomy, and SRS. These investigators presented their own experiences with CyberKnife (CK), a new type of radio-surgical (RS) treatment of 64 TN patients. The authors concluded that CyberKnife radiotherapy is characterized by high efficacy in 80 % of patients with TN, minimal invasiveness, and subsiding mild side effects. Radio-ablation of nerve V root in patients with neuralgia allowed these investigators to entirely stop anti-epileptic therapy or reduce its doses, which in turn reduces the risk of potential side effects. These researchers stated that CyberKnife can be a therapeutic option in those patients who have been offered ineffective therapies, or treatments with limited efficacy, and/or in older patients with co-morbidities.

Furthermore, an UpToDate review on “Trigeminal neuralgia” (Ho et al, 2021) states that “For patients with TN refractory to medical therapy, it is reasonable to discuss options for surgical therapy using microvascular
decompression (for TN caused by compression of the trigeminal nerve root), various types of rhizotomy, or gamma knife radiosurgery. The decision to have surgery and the choice among surgical options will be influenced by individual circumstances including patient preference, adverse effect profile of the available techniques, and expertise of the local center."

**CPT Codes / HCPCS Codes / ICD-10 Codes**

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "x".

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>61450</td>
<td>Craniectomy, subtemporal, for section, compression, or decompression of sensory root of gasserian ganglion</td>
</tr>
<tr>
<td>61458</td>
<td>Craniectomy, suboccipital; for exploration or decompression of cranial nerves</td>
</tr>
<tr>
<td>61460</td>
<td>for section of one or more cranial nerves</td>
</tr>
<tr>
<td>61796</td>
<td>Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 simple cranial lesion</td>
</tr>
<tr>
<td>+ 61797</td>
<td>each additional cranial lesion, simple (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>61798</td>
<td>1 complex cranial lesion</td>
</tr>
<tr>
<td>+ 61799</td>
<td>each additional cranial lesion, complex (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>64400</td>
<td>Injection, anesthetic agent; trigeminal nerve, any division or branch</td>
</tr>
<tr>
<td>64600</td>
<td>Destruction by neurolytic agent; trigeminal nerve; supraorbital, infraorbital, mental, or inferior alveolar branch</td>
</tr>
<tr>
<td>64605</td>
<td>second and third division branches at foramen ovale</td>
</tr>
<tr>
<td>64610</td>
<td>second and third division branches at foramen ovale under radiologic monitoring</td>
</tr>
<tr>
<td>64612</td>
<td>Chemodenervation of muscle(s); muscle(s) innervated by facial nerve, unilateral (eg., for blepharospasm, hemifacial spasm)</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>64716</td>
<td>Neuroplasty and/or transposition; cranial nerve (specify)</td>
</tr>
<tr>
<td>64732</td>
<td>Transection or avulsion of; supraorbital nerve</td>
</tr>
<tr>
<td>64734</td>
<td>Transection or avulsion of; infraorbital nerve</td>
</tr>
</tbody>
</table>

**CPT codes not covered for indications listed in the CPB**

*Trigeminal Tractotomy, CT-guided percutaneous pulsed radiofrequency, Pulsed radiofrequency with continuous radiofrequency thermocoagulation, Transcranial direct current stimulation.*

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>15769</td>
<td>Grafting of autologous soft tissue, other, harvested by direct excision (eg, fat, dermis, fascia)</td>
</tr>
<tr>
<td>15773</td>
<td>Grafting of autologous fat harvested by liposuction technique to face, eyelids, mouth, neck, ears, orbits, genitalia, hands, and/or feet; 25 cc or less injectate</td>
</tr>
<tr>
<td>+15774</td>
<td>each additional 25 cc injectate, or part thereof (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>20926</td>
<td>Tissue grafts, other (eg, paratenon, fat, dermis)</td>
</tr>
<tr>
<td>61850</td>
<td>Twist drill or burr hole(s) for implantation of neurostimulator electrodes, cortical</td>
</tr>
<tr>
<td>61860</td>
<td>Craniectomy or craniotomy for implantation of neurostimulator electrodes, cerebral, cortical</td>
</tr>
<tr>
<td>61885</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array</td>
</tr>
<tr>
<td>61886</td>
<td>with connection to two or more electrode arrays</td>
</tr>
<tr>
<td>64640</td>
<td>Destruction by neurolytic agent; other peripheral nerve or branch</td>
</tr>
<tr>
<td>64505</td>
<td>Injection, anesthetic agent; sphenopalatine ganglion</td>
</tr>
<tr>
<td>64553</td>
<td>Percutaneous Implantation of neuromuscular electrode; cranial nerve</td>
</tr>
<tr>
<td>95961</td>
<td>Functional cortical and subcortical mapping by stimulation and/or recording of electrodes on brain surface, or of depth electrodes, to provoke seizures or identify vital brain structures; initial hour of attendance by a physician or other qualified health care professional</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>+95962</td>
<td>each additional hour of attendance by a physician or other qualified health care professional (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>95970</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, autonomic nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
</tr>
<tr>
<td>97810</td>
<td>Acupuncture, 1 or more needles; without electrical stimulation, initial 15 minutes of personal one-on-one contact with the patient</td>
</tr>
<tr>
<td>+97811</td>
<td>without electrical stimulation, each additional 15 minutes of personal one-on-one contact with the patient, with re-insertion of needle(s) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>97813</td>
<td>with electrical stimulation, initial 15 minutes</td>
</tr>
<tr>
<td>+97814</td>
<td>with electrical stimulation, each additional 15 minutes of personal one-on-one contact with the patient, with re-insertion of needle(s) (List separately in addition to code for primary procedure)</td>
</tr>
</tbody>
</table>

Other CPT codes related to the CPE

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>96365 - 96368</td>
<td>Intravenous infusion, for therapy, prophylaxis, or diagnosis  (specify substance or drug)</td>
</tr>
<tr>
<td>96373</td>
<td>Therapeutic, prophylactic, or diagnostic injection; intra-arterial [intra-arterial modulation]</td>
</tr>
</tbody>
</table>

HCPCS codes covered if selection criteria are met

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G0173</td>
<td>Linear accelerator based stereotactic radiosurgery, complete course of therapy in one session</td>
</tr>
<tr>
<td>G0251</td>
<td>Linear accelerator based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, maximum 5 sessions per course of treatment</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>---------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>G0339</td>
<td>Image guided robotic linear accelerator-based stereotactic radiosurgery, complete course of therapy in one session, or first session of fractionated treatment</td>
</tr>
<tr>
<td>G0340</td>
<td>Image guided robotic linear accelerator-based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, second through fifth sessions, maximum 5 sessions per course of treatment</td>
</tr>
</tbody>
</table>

HCPCS codes not covered for indications listed in the CPE

*Topical ambroxol - no specific code*

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1767</td>
<td>Generator, neurostimulator (implantable), nonrechargeable</td>
</tr>
<tr>
<td>C1770</td>
<td>Imaging coil, magnetic resonance (insertable)</td>
</tr>
<tr>
<td>C1778</td>
<td>Lead, neurostimulator (implantable)</td>
</tr>
<tr>
<td>C1787</td>
<td>Patient programmer, neurostimulator</td>
</tr>
<tr>
<td>C1816</td>
<td>Receiver and/or transmitter, neurostimulator (implantable)</td>
</tr>
<tr>
<td>C1820</td>
<td>Generator, neurostimulator (implantable), non high-frequency with rechargeable battery and charging system</td>
</tr>
<tr>
<td>C1883</td>
<td>Adaptor/extension, pacing lead or neurostimulator lead (implantable)</td>
</tr>
<tr>
<td>C1897</td>
<td>Lead, neurostimulator test kit (implantable)</td>
</tr>
<tr>
<td>E0745</td>
<td>Neuromuscular stimulator, electronic shock unit</td>
</tr>
<tr>
<td>J0585</td>
<td>Injection, onabotulinumtoxinA, 1 unit</td>
</tr>
<tr>
<td>J0586</td>
<td>Injection, abobotulinumtoxinA, 5 units</td>
</tr>
<tr>
<td>J0587</td>
<td>Injection, rimabotulinumtoxinB, 100 units</td>
</tr>
<tr>
<td>J0588</td>
<td>Injection, incobotulinumtoxinA, 1 unit</td>
</tr>
<tr>
<td>J2001</td>
<td>Injection, lidocaine HCl for intravenous infusion, 10 mg</td>
</tr>
<tr>
<td>J3475</td>
<td>Injection, magnesium sulfate, per 500 mg</td>
</tr>
<tr>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td>L8681</td>
<td>Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only</td>
</tr>
<tr>
<td>L8682</td>
<td>Implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>---------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>L8683</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td>L8685</td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8686</td>
<td>Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td>L8689</td>
<td>External recharging system for battery (internal) for use with implantable neurostimulator, replacement only</td>
</tr>
<tr>
<td>L8695</td>
<td>External recharging system for battery (external) for use with implantable neurostimulator, replacement only</td>
</tr>
</tbody>
</table>

Other HCPCS codes related to the CPB

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0475</td>
<td>Injection baclofen, 10 mg</td>
</tr>
<tr>
<td>J1165</td>
<td>Injection, phenytoin sodium, per 50 mg</td>
</tr>
</tbody>
</table>

CD-10 codes covered if selection criteria are met

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G50.0</td>
<td>Trigeminal neuralgia</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


7. Bajwa ZH, Ho CC, Khan SA. Trigeminal neuralgia. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed February 2013; February, 2015; February 2016; February 2019.


36. Ho CC, Khan SA, Whealy MA. Trigeminal neuralgia. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed February 2021.


38. Hu H, Chen L, Ma R, et al. Acupuncture for primary trigeminal neuralgia: A systematic review and PRISMA-


85. Tatli M, Satci O, Kanpolat Y, Sindou M. Various surgical modalities for trigeminal neuralgia: Literature study of


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0374 Trigeminal Neuralgia: Treatments

There are no amendments for Medicaid.