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Radiofrequency thermocoagulation of Gasserian ganglion in trigeminal neuralgia

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Abstract

Introduction: Trigeminal neuralgia (TN) is a form of neuropathic pain that targets the fifth cranial nerve, leading to intense facial pain that can significantly impact one's quality of life. This condition typically manifests as recurring episodes of sharp, unilateral pain along one or more branches of the trigeminal nerve.The exact mechanism of trigeminal neuralgia remains largely unknown. Most pain attacks are triggered by certain stimuli in the areas served by the trigeminal nerve. One possible treatment approach for trigeminal neuralgia is radiofrequency thermocoagulation.

Aim: The aim of this article is to explore the underlying mechanisms of trigeminal neuralgia and assess the effectiveness of treating it through radiofrequency thermocoagulation of the Gasserian ganglion.

Review methods: A comprehensive analysis of research papers available on PubMed and Google Scholar was undertaken using the searchterms encompassing the following keywords: trigeminal neuralgia / Gasserian ganglion radiofrequency thermal therapy/ radiofrequency thermal coagulation/ radiofrequency trigeminal rhizotomy/ trigeminal neuralgia mechanism.

Conclusion: The exact mechanisms behind trigeminal neuralgia are still unclear, but several theories suggest that factors such as inflammation, ion channel dysfunction, neuroinflammatory conditions, or bioresonance issues may be involved. Radiofrequency

Thermocoagulation (RFT) has proven to be an effective option for easing pain in individuals suffering from Trigeminal Neuralgia. Research indicates that RFT not only significantly reduces pain initially but also provides a prolonged period of relief post-procedure. The temperature achieved during radiofrequency treatments is a key factor in determining the effectiveness of RFT.

Keywords
trigeminal neuralgia; Gasserian ganglion radiofrequency thermal therapy; radiofrequency thermal coagulation; radiofrequency trigeminal rhizotomy; trigeminal neuralgia mechanism

Introduction
Trigeminal neuralgia (TN), a form of neuropathic pain affecting the fifth cranial nerve, is a debilitating form of facial pain that causes severe discomfort and reduces quality of life. Trigeminal neuralgia is a recurrent episode of unilateral and lancinating facial pain along one or more branches of the trigeminal nerve [1]. Pain is usually described as being paroxysmal, stabbing, reminiscent of electric shock or burning. This condition has an annual incidence of approximately 4.5 per 100,000, with a female to male ratio of 2.3 [2,3]. Trigeminal neuralgia can occur either sporadically or within families, but the causes behind both types remain unclear [4]. Age is a risk factor for the development of trigeminal neuralgia, which is most common in patients over the age of 50 [4,5]. Pain attacks are usually caused by stimulation of trigger points, usually in the area innervated by the trigeminal nerve.

Materials and methods
A comprehensive analysis of research papers available on PubMed and Google Scholar was undertaken using the searchterms encompassing the following keywords: trigeminal neuralgia / Gasserian ganglion radiofrequency thermal therapy/ radiofrequency thermal coagulation/ radiofrequency trigeminal rhizotomy/ trigeminal neuralgia mechanism.

Pathophysiology of Trigeminal Neuralgia
According to the beta version of the 3rd edition of the International Classification of Headache Disorders (ICHD-3 Beta), trigeminal neuralgia (TN) is characterized by recurrent, unilateral episodes of sharp, electric shock-like pain that start and stop suddenly. This pain is localized to one or more divisions of the trigeminal nerve and can be triggered by seemingly harmless sensory stimuli. TN is categorized into two types: classical trigeminal neuralgia (CTN) and secondary trigeminal neuralgia (STN), the latter of which can occur due to conditions such as multiple sclerosis or the presence of a mass, such as a tumor or cerebral aneurysm [6]. Classical trigeminal neuralgia is typically caused by neurovascular compression,

often involving small, tortuous branches of the basilar artery, primarily the superior cerebellar artery and, occasionally, the anterior inferior cerebellar artery pressing against the trigeminal nerve roots as they enter the pons [7-10]. Many molecular mechanisms linked to TN have been discovered, especially involving changes to sodium and potassium channels in trigeminal ganglion neurons. Emerging studies suggest a strong association between neurovascular conflicts, characterized by changes in the trigeminal nerve-such as distortion, dislocation, distension, indentation, flattening, or atrophy- and classical trigeminal neuralgia (TN). Approximately half of TN patients exhibit these morphological alterations [11,12]. The exact causes of trigeminal neuralgia (TN) remain uncertain, but a wealth of neurophysiological, neuroimaging, and histological research suggests that focal demyelination of the primary trigeminal afferents at the point where the trigeminal root enters the pons may underlie its pathophysiology [13]. The effects of demyelination remain somewhat unclear, but it is suggested that when demyelination occurs to a certain extent, the primary afferent fibers become hyperexcitable. This happens when ions can flow in and out of the axon beyond the areas around the Ranvier nodes, leaving the axons with insufficient energy to quickly restore their resting potential. As a result, these axons hover at a depolarized state, increasing their excitability. Ectopic impulses may arise either spontaneously from the sensory afferents or in response to direct mechanical stimuli, such as those produced by arterial pulsations, likely contributing to this heightened state of excitability. Furthermore, findings from animal studies on localized demyelination of the trigeminal root indicate that ephaptic transmission—essentially communication between nearby healthy nerve fibers—and the production of high-frequency discharges may also play a role in fostering this hyperexcitable condition in trigeminal neuralgia [14,15].

While the idea that microvascular compression is the primary cause of trigeminal neuralgia (TN) has gained broad acceptance, and many patients have benefitted from microvascular decompression (MVD) procedures, there remains significant debate regarding the origins and underlying mechanisms of the condition. Several clinical observations still lack clear explanations. In literature, studies indicate that between 3.3% and 28.5% of patients with trigeminal neuralgia (TN) do not exhibit any signs of trigeminal vascular compression during surgical evaluations. Interestingly, around 25% of individuals without TN show signs of trigeminal vascular compression, which does not contribute to their condition [17,18]. Additionally, while some patients may experience bilateral trigeminal vascular compression, most present with symptoms affecting only one side. Different diameters of blood vessels that compress the trigeminal nerve exert varying levels of pressure. Interestingly the intensity of pain is not directly related to the extent of vascular compression. While vascular compression is a constant presence, trigeminal neuralgia (TN) tends to manifest intermittently. In fact, some patients experience sudden relief from facial pain, which can last for years.

Bioresonance Disorder

Therefore, Jia and Li [19] put forward the bioresonance hypothesis which states that as long as the vibrational frequency of a blood vessel aligns with the natural frequency of the trigeminal nerve, pain will manifest, irrespective of any compression on the trigeminal vascular network. Conversely, the pain subsides once the frequency drops below the

trigeminal nerve's natural resonance frequency, which remains unaffected by the blood vessel's thickness or pressure.

Neuroinflammatory Disorder

Orofacial pain in TN can also be influenced by pathways related to inflammation. In secondary trigeminal neuralgia (TN), the underlying mechanism is likely similar to that of classical TN. However, the cause is related to specific structural issues, most commonly involving an MS plaque affecting the trigeminal root or a space-occupying lesion in the cerebellopontine cistern. These lesions may include epidermoid tumors, meningiomas, neurinomas, arteriovenous malformations, or aneurysms [14,16]. Multiple sclerosis (MS) is a well-recognized autoimmune disorder characterized by central demyelination and the formation of plaques, leading to various motor and sensory neurological impairments. Notably, a small but distinct percentage of patients with trigeminal neuralgia (TN), estimated between 2.4% and 8%, also have MS [16,20]. Research has shown that TN associated with MS is linked to demyelinating plaques situated in the pontine area where the primary afferents of the trigeminal nerve connect, specifically between the root entry zone and the trigeminal nucleus [21,22]. The role of these central MS-associated plaques in TN remains unclear. It's uncertain whether demyelination leads to harmful activity directly, like abnormal nerve firing instead of ephaptic coupling, or if it occurs through indirect inflammatory mechanisms. Dong et al. [23] show that neuroinflammation may play a role in trigeminal neuralgia. They analyzed the studies and showed elevated levels of inflammatory biomarkers in the CSF including substance P (SP), vasoactive intestinal peptide (VIP) and calcitonin gene–related peptide (CGRP) as well as endogenous regulators of inflammation like inflammatory cytokine interleukin-6 (IL-6) and tumor necrosis factor–α (TNFα) [23-28].

Oxidative Stress Disorder

TN has been assessed as a malfunction in cell signaling and transduction networks. Oxidative stress occurs when there is an imbalance of reactive oxygen species (ROS) - which are oxygen derivatives with oxidizing capabilities, including superoxide, hydroxyl radicals, and hydrogen peroxide. An excess of ROS can result in the oxidation of proteins, nucleic acids, and lipids, which disrupts normal cellular functions. Oxidative stress has been linked to neurodegenerative diseases [23,29]. Vasavda et al. [30] found that patients with TN have elevated levels of 4-hydroxynonenal (4-HNE) in their cerebrospinal fluid (CSF). These compounds are reactive oxygen species (ROS) resulting from lipid peroxidation, which interact with the TRP ankyrin 1 (TRPA1) channel. This interaction leads to pain by inducing depolarization. Research suggests that TRPA1 could serve as a promising therapeutic agent for TN by targeting aberrant oxidative stress signaling.

Ionotropic Channelopathy

Recent studies have pointed to possible irregularities in how cation channels are expressed or function, which may be linked to TN and various other pain syndromes. Structural mutations in the γ-aminobutyric acid (GABA)–gated chloride channel GABA type A receptor (GABAAR) and the T-type low voltage–gated calcium channel Cav3.2 have been identified

as potential pathological channels associated with TN in humans and have also been confirmed through mouse model research [23,31,32].

Gasserian Ganglion

The trigeminal ganglion, also known as the Semilunar or Gasserian Ganglion, is located in a cavity called the cavum Meckelii, which is situated in the dura mater. This ganglion can be found near the apex of the petrous part of the temporal bone, and it has a crescent shape with the convex side facing forward. Medially, it is related to the internal carotid artery and the back part of the cavernous sinus. The motor root of the trigeminal nerve runs in front of and toward the middle of the sensory root, passing beneath the ganglion. It exits the skull through the foramen ovale and quickly joins the mandibular nerve just below this opening. Additionally, the greater superficial petrosal nerve is positioned beneath the ganglion as well. On its medial side, the ganglion receives filaments from the carotid plexus of the sympathetic nervous system. It sends out small branches to the tentorium cerebelli and the dura mater in the middle cranial fossa. From its forward and outwardly directed convex border, three major nerves emerge: the ophthalmic, maxillary, and mandibular nerves. The ophthalmic and maxillary nerves are composed entirely of sensory fibers, whereas the mandibular nerve receives the motor root outside the cranium.

Radiofrequency thermal coagulation - surgical course

The patient is positioned supine on the operating table. The fluoroscopy settings are adjusted to visualize the cella turcica, clivus, and petrous apex in the lateral view. Confirmation of the optimal position is achieved by ensuring the alignment of the orbital roofs and anterior clinoid processes. For the percutaneous procedures targeting the Gasserian Ganglion, Härtel's anatomical landmarks are utilized. The entry point is identified 2.5 cm lateral to the mouth’s angle. An 18-gauge needle cannula is carefully inserted along the medial side of the coronoid process of the mandible, directed towards a plane that intersects at a point 30 mm anterior to the external acoustic meatus, extending along the zygomatic arch and toward the medial aspect of the pupil. A free-hand technique guides the needle towards the foramen ovale, with a finger placed inside the oral cavity to prevent the puncture of the ipsilateral buccal mucosa and to ensure the needle remains medial to the mandible. The needle positioning is monitored using lateral image fluoroscopy throughout the procedure.

Once the foramen ovale is successfully penetrated, cerebrospinal fluid is visible at the proximal end of the needle. This observation, while indicative of entry into Meckel Cave, necessitates further verification of proper electrode placement through motor and sensory stimulations. The RF device is then switched to stimulus mode, applying a low-frequency stimulus. If a masticatory response is noted, the stimulus frequency is gradually increased. During re-stimulation, pain resembling neuralgia is anticipated. Final needle localization is confirmed based on the character and location of the pain elicited by the radiofrequency generator’s stimulation. An ineffective response may indicate a misplaced electrode, prompting a repositioning based on the patient’s feedback. Additionally, if stimulation results in pain around the eye, it further suggests that the needle may have strayed into the V1 zone, which carries an increased risk of keratitis. Upon confirming proper localization, three

radiofrequency lesions are created, each at about 70°C, with sizes between 3–5 mm. After each repositioning of the electrode, the accuracy of placement is reassessed through stimulation. Corneal reflex checks are conducted at each phase of the intervention.

Radiofrequency thermal coagulation in trigeminal neuralgia

In a retrospective study involving 280 patients who underwent 464 radiofrequency rhizotomy procedures, Mulford et al. [33] found that 59.7% of participants reported complete pain relief by their first follow-up appointment. For those who did experience pain recurrence, the median time until recurrence was found to be 8 weeks. The findings also indicated an interesting correlation: as the lesion temperature increases, the time until recurrence decreases. Specifically, for every 1°C rise in temperature, there is a 5% greater chance of pain returning at any point after the procedure. When looking at temperatures between 65°C and 75°C, this results in an increase of just over 50% in recurrence risk [33]. The radiofrequency temperature plays a significant role in the success of Radiofrequency Thermoablation (RFT), yet there is no established standard for determining the optimal CRF temperature for treating TN. Yao et al. [37,38] found that 68˚C to be the most effective temperature for addressing both maxillary (V2) and mandibular (V3) idiopathic TN, as well as for bilateral cases. In contrast, Zhao et al. [39] proposed that 70˚C is ideal for RFT, while Tang et al. [40] recommended a slightly higher temperature of 75˚C for idiopathic TN. Wu et al. [41] observed that patient satisfaction improved when temperatures ranged from 68 to 70˚C, although efficiency peaked within a broader range of 66 to 80˚C. Other research suggested using a temperature range of 60 to 65˚C for the V1 division, and 72˚C and 75˚C for the V2 and V2/V3 divisions, respectively, both of which yielded excellent patient satisfaction [43]. For Pulsed Radiofrequency (PRF), a temperature range of 45 to 50˚C is advised, particularly for elderly patients [39]. A research study conducted by Neerja Bharti et al. [42] investigated the effectiveness of radiofrequency therapy (RFT) on the peripheral branches of the trigeminal nerve, comparing it to RFT of the Gasserian ganglion for treating idiopathic trigeminal neuralgia (ITGN). They assessed both the quality and duration of pain relief achieved. The results showed a marked decrease in pain scores, with the control group experiencing a 95% pain relief rate, while the study group reported 90%—results consistent with earlier findings [34,35,44,45]. Similarly, Kanpolat et al. [35] analyzed the effectiveness of percutaneous radiofrequency trigeminal rhizotomy in a large cohort of 1,600 ITGN patients, revealing that 92% of those treated, whether through a single or multiple RFT procedures over five years, experienced significant pain relief. Moreover, a study by Huibin et al. [34] compared RFT on the first division branches of the trigeminal nerve to RFT on the Gasserian ganglion. They noted immediate efficacy rates of 93% and 95% for the peripheral and central groups, respectively, without any notable difference upon follow-up. Additionally, the recurrence rates of pain without medication after three and five years were not statistically different between the groups. A retrospective analysis by Kosugi et al. [36] looked at the long-term outcomes of RFT on the Gasserian ganglion for multiple trigeminal nerve divisions in comparison to isolated second and third divisions. They found that while immediate outcomes were similar, the duration of pain relief was longer in patients with isolated third division TGN compared to those with multiple divisions ($P = 0.012$).

Conclusion

The precise causes of trigeminal neuralgia remain somewhat mysterious. However, various theories propose that things like inflammation, problems with ion channels, neuroinflammatory conditions, or issues related to bioresonance could play a role.

In conclusion, this systematic review looked into how effective Radiofrequency Thermocoagulation (RFT) is for alleviating pain in patients with Trigeminal Neuralgia (TN). The results showed that RFT led to a substantial reduction in pain initially and offered an extended period of relief after the procedure. Furthermore, RFT can be readily reapplied if the pain recurs. The temperature achieved during radiofrequency applications is crucial for the effectiveness of Radiofrequency Thermoablation (RFT). However, there currently isn't a standardized guideline for identifying the best CRF temperature when addressing TN.

Author's contribution

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References

1. Cruccu G, Bonamico LH, Zakrzewska JM. Cranial neuralgias. Handb Clin Neurol. 2010;97:663-78. doi: 10.1016/S0072-9752(10)97056-5. PMID: 20816462.
2. Grasso G, Landi A, Alafaci C. A Novel Pathophysiological Mechanism Contributing to Trigeminal Neuralgia. Mol Med. 2016 Oct;22:452-454. doi: 10.2119/molmed.2016.00172. Epub 2016 Aug 11. PMID: 27533070; PMCID: PMC5072416.
3. Katusic S, Williams DB, Beard CM, Bergstralh EJ, Kurland LT. Epidemiology and clinical features of idiopathic trigeminal neuralgia and glossopharyngeal neuralgia: similarities and differences, Rochester, Minnesota, 1945-1984. Neuroepidemiology. 1991;10(5-6):276-81. doi: 10.1159/000110284. PMID: 1798430.
4. Gambeta E, Chichorro JG, Zamponi GW. Trigeminal neuralgia: An overview from pathophysiology to pharmacological treatments. Mol Pain. 2020 Jan-Dec;16:1744806920901890. doi: 10.1177/1744806920901890. PMID: 31908187; PMCID: PMC6985973.
5. Montano N, Conforti G, Di Bonaventura R, Meglio M, Fernandez E, Papacci F. Advances in diagnosis and treatment of trigeminal neuralgia. Ther Clin Risk Manag. 2015 Feb 24;11:289-99. doi: 10.2147/TCRM.S37592. PMID: 25750533; PMCID: PMC4348120.
6. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013 Jul;33(9):629-808. doi: 10.1177/0333102413485658. PMID: 23771276.
7. Jones MR, Urits I, Ehrhardt KP, Cefalu JN, Kendrick JB, Park DJ, Cornett EM, Kaye AD, Viswanath O. A Comprehensive Review of Trigeminal Neuralgia. Curr Pain Headache Rep. 2019 Aug 6;23(10):74. doi: 10.1007/s11916-019-0810-0. PMID: 31388843.
8. Arnold M. Headache Classification Committee of the International Headache Society (IHS) the international classification of headache disorders, 3rd edition. *Cephalalgia* 2018; 38: 1–211.
9. Kim HK, Chung KM, Xing J, Kim HY, Youn DH. The Trigeminal Sensory System and Orofacial Pain. Int J Mol Sci. 2024 Oct 21;25(20):11306. doi: 10.3390/ijms252011306. PMID: 39457088; PMCID: PMC11508441.
10. Gerwin, R. Chronic Facial Pain: Trigeminal Neuralgia, Persistent Idiopathic Facial Pain, and Myofascial Pain Syndrome-An Evidence-Based Narrative Review and Etiological Hypothesis. *Int. J. Environ. Res. Public Health.* **2020**, *17*, 7012.
11. Antonini G, Di Pasquale A, Cruccu G, Truini A, Morino S, Saltelli G, Romano A, Trasimeni G, Vanacore N, Bozzao A. Magnetic resonance imaging contribution for diagnosing symptomatic neurovascular contact in classical trigeminal neuralgia: a blinded case-control study and meta-analysis. Pain. 2014 Aug;155(8):1464-1471. doi: 10.1016/j.pain.2014.04.020. Epub 2014 Apr 28. PMID: 24785270.

12. Maarbjerg S, Wolfram F, Gozalov A, Olesen J, Bendtsen L. Significance of neurovascular contact in classical trigeminal neuralgia. Brain. 2015 Feb;138(Pt 2):311-9. doi: 10.1093/brain/awu349. Epub 2014 Dec 24. PMID: 25541189.
13. Lutz J, Thon N, Stahl R, Lummel N, Tonn JC, Linn J, Mehrkens JH. Microstructural alterations in trigeminal neuralgia determined by diffusion tensor imaging are independent of symptom duration, severity, and type of neurovascular conflict. J Neurosurg. 2016 Mar;124(3):823-30. doi: 10.3171/2015.2.JNS142587. Epub 2015 Sep 25. PMID: 26406792.
14. Maarbjerg S, Di Stefano G, Bendtsen L, Cruccu G. Trigeminal neuralgia - diagnosis and treatment. Cephalalgia. 2017 Jun;37(7):648-657. doi: 10.1177/0333102416687280. Epub 2017 Jan 11. PMID: 28076964.
15. Devor M, Amir R, Rappaport ZH. Pathophysiology of trigeminal neuralgia: the ignition hypothesis. Clin J Pain. 2002 Jan-Feb;18(1):4-13. doi: 10.1097/00002508-200201000-00002. PMID: 11803297.
16. Jensen TS, Rasmussen P, Reske-Nielsen E. Association of trigeminal neuralgia with multiple sclerosis: clinical and pathological features. Acta Neurol Scand. 1982 Mar;65(3):182-9. doi: 10.1111/j.1600-0404.1982.tb03076.x. PMID: 7080803.
17. Ishikawa M, Nishi S, Aoki T, Takase T, Wada E, Ohwaki H, Katsuki T, Fukuda H. Operative findings in cases of trigeminal neuralgia without vascular compression: proposal of a different mechanism. J Clin Neurosci. 2002 Mar;9(2):200-4. doi: 10.1054/jocn.2001.0922. PMID: 11922717.
18. Sindou M, Howeidy T, Acevedo G. Anatomical observations during microvascular decompression for idiopathic trigeminal neuralgia (with correlations between topography of pain and site of the neurovascular conflict). Prospective study in a series of 579 patients. Acta Neurochir (Wien). 2002 Jan;144(1):1-12; discussion 12-3. doi: 10.1007/s701-002-8269-4. PMID: 11807642.
19. Jia DZ, Li G. Bioresonance hypothesis: a new mechanism on the pathogenesis of trigeminal neuralgia. Med Hypotheses. 2010 Mar;74(3):505-7. doi: 10.1016/j.mehy.2009.09.056. Epub 2009 Nov 8. PMID: 19900765.
20. Ferraro D, Annovazzi P, Moccia M, et al. Characteristics and treatment of Multiple Sclerosis-related trigeminal neuralgia: An Italian multi-centre study. Mult Scler Relat Disord. 2020 Jan;37:101461. doi: 10.1016/j.msard.2019.101461. Epub 2019 Oct 19. PMID: 31678859.
21. Gass A, Kitchen N, MacManus DG, Moseley IF, Hennerici MG, Miller DH. Trigeminal neuralgia in patients with multiple sclerosis: lesion localization with magnetic resonance imaging. Neurology. 1997 Oct;49(4):1142-4. doi: 10.1212/wnl.49.4.1142. PMID: 9339705.
22. Cruccu G, Biasiotta A, Di Rezze S, Fiorelli M, Galeotti F, Innocenti P, Mameli S, Millefiorini E, Truini A. Trigeminal neuralgia and pain related to multiple sclerosis. Pain. 2009 Jun;143(3):186-191. doi: 10.1016/j.pain.2008.12.026. Epub 2009 Jan 25. PMID: 19171430.
23. Dong B, Xu R, Lim M. The pathophysiology of trigeminal neuralgia: a molecular review. J Neurosurg. 2023 Mar 31;139(5):1471-1479. doi: 10.3171/2023.2.JNS23274. PMID: 37922556.

24. Strittmatter M, Grauer M, Isenberg E, Hamann G, Fischer C, Hoffmann KH, Blaes F, Schimrigk K. Cerebrospinal fluid neuropeptides and monoaminergic transmitters in patients with trigeminal neuralgia. Headache. 1997 Apr;37(4):211-6. doi: 10.1046/j.1526-4610.1997.3704211.x. PMID: 9150615.
25. Qin ZL, Yang LQ, Li N, Yue JN, Wu BS, Tang YZ, Guo YN, Lai GH, Ni JX. Clinical study of cerebrospinal fluid neuropeptides in patients with primary trigeminal neuralgia. Clin Neurol Neurosurg. 2016 Apr;143:111-5. doi: 10.1016/j.clineuro.2016.02.012. Epub 2016 Feb 10. PMID: 26918582.
26. Strittmatter M, Grauer M, Isenberg E, Hamann G, Fischer C, Hoffmann KH, Blaes F, Schimrigk K. Substance P, somatostatin and monoaminergic transmitters in the cerebrospinal fluid of patients with chronic idiopathic trigeminal neuralgia. Schmerz. 1996 Oct 28;10(5):261-8. German. doi: 10.1007/s004829600026. PMID: 12799848.
27. Ericson H, Abu Hamdeh S, Freyhult E, Stiger F, Bäckryd E, Svenningsson A, Gordh T, Kultima K. Cerebrospinal fluid biomarkers of inflammation in trigeminal neuralgia patients operated with microvascular decompression. Pain. 2019 Nov;160(11):2603-2611. doi: 10.1097/j.pain.0000000000001649. PMID: 31373951.
28. Liu MX, Zhong J, Xia L, Dou NN, Li ST. A correlative analysis between inflammatory cytokines and trigeminal neuralgia or hemifacial spasm. Neurol Res. 2019 Apr;41(4):335-340. doi: 10.1080/01616412.2018.1564188. Epub 2019 Jan 5. PMID: 30612530.
29. Pizzino G, Irrera N, Cucinotta M, Pallio G, Mannino F, Arcoraci V, Squadrito F, Altavilla D, Bitto A. Oxidative Stress: Harms and Benefits for Human Health. Oxid Med Cell Longev. 2017;2017:8416763. doi: 10.1155/2017/8416763. Epub 2017 Jul 27. PMID: 28819546; PMCID: PMC5551541.
30. Vasavda C, Xu R, Liew J, Kothari R, Dhindsa RS, Semenza ER, Paul BD, Green DP, Sabbagh MF, Shin JY, Yang W, Snowman AM, Albacarys LK, Moghekar A, Pardo-Villamizar CA, Luciano M, Huang J, Bettegowda C, Kwatra SG, Dong X, Lim M, Snyder SH. Identification of the NRF2 transcriptional network as a therapeutic target for trigeminal neuropathic pain. Sci Adv. 2022 Aug 5;8(31):eabo5633. doi: 10.1126/sciadv.abo5633. Epub 2022 Aug 3. PMID: 35921423; PMCID: PMC9348805.
31. Gambeta E, Gandini MA, Souza IA, Zamponi GW. Ca V 3.2 calcium channels contribute to trigeminal neuralgia. Pain. 2022 Dec 1;163(12):2315-2325. doi: 10.1097/j.pain.0000000000002651. Epub 2022 Apr 20. PMID: 35467587.
32. Dong W, Jin SC, Kahle KT et al. Exome Sequencing Implicates Impaired GABA Signaling and Neuronal Ion Transport in Trigeminal Neuralgia. iScience. 2020 Sep 11;23(10):101552. doi: 10.1016/j.isci.2020.101552. PMID: 33083721; PMCID: PMC7554653.
33. Mulford KL, Darrow DP, Dharnipragada R, Woolums M, Nixdorf DR, Haines SJ, Grande AW. Effect of lesion temperature on the durability of percutaneous radiofrequency rhizotomies to treat trigeminal neuralgia. J Neurosurg. 2023 Feb 24;139(3):625-632. doi: 10.3171/2023.1.JNS222441. PMID: 36840736.
34. Huibin Q, Jianxing L, Guangyu H, Dianen F. The treatment of first division idiopathic trigeminal neuralgia with radiofrequency thermocoagulation of the peripheral branches compared to conventional radiofrequency. J Clin Neurosci. 2009

Nov;16(11):1425-9. doi: 10.1016/j.jocn.2009.01.021. Epub 2009 Aug 15. PMID: 19683927.

35. Kanpolat Y, Savas A, Bekar A, Berk C. Percutaneous controlled radiofrequency trigeminal rhizotomy for the treatment of idiopathic trigeminal neuralgia: 25-year experience with 1,600 patients. Neurosurgery. 2001 Mar;48(3):524-32; discussion 532-4. doi: 10.1097/00006123-200103000-00013. PMID: 11270542.
36. Kosugi S, Shiotani M, Otsuka Y, Suzuki T, Katori N, Hashiguchi S, Morisaki H. Long-term outcomes of percutaneous radiofrequency thermocoagulation of gasserian ganglion for 2nd- and multiple-division trigeminal neuralgia. Pain Pract. 2015 Mar;15(3):223-8. doi: 10.1111/papr.12163. Epub 2014 Jan 17. PMID: 24433261.
37. Yao P, Hong T, Wang ZB, Ma JM, Zhu YQ, Li HX, Ding YY, Jiang CL, Pan SN. Treatment of bilateral idiopathic trigeminal neuralgia by radiofrequency thermocoagulation at different temperatures. Medicine (Baltimore). 2016 Jul;95(29):e4274. doi: 10.1097/MD.0000000000004274. PMID: 27442662; PMCID: PMC5265779.
38. Yao P, Deng YY, Hong T, Wang ZB, Ma JM, Zhu YQ, Li HX, Ding YY, Pan SN. Radiofrequency thermocoagulation for V2/V3 idiopathic trigeminal neuralgia: effect of treatment temperatures on long-term clinical outcomes: A Cohort Study. Medicine (Baltimore). 2016 Jun;95(26):e4019. doi: 10.1097/MD.0000000000004019. PMID: 27368021; PMCID: PMC4937935.
39. Zhao WX, Wang Q, He MW, Yang LQ, Wu BS, Ni JX. Radiofrequency thermocoagulation combined with pulsed radiofrequency helps relieve postoperative complications of trigeminal neuralgia. Genet Mol Res. 2015 Jul 13;14(3):7616-23. doi: 10.4238/2015.July.13.5. PMID: 26214440.
40. Tang YZ, Yang LQ, Yue JN, Wang XP, He LL, Ni JX. The optimal radiofrequency temperature in radiofrequency thermocoagulation for idiopathic trigeminal neuralgia: A cohort study. Medicine (Baltimore). 2016 Jul;95(28):e4103. doi: 10.1097/MD.0000000000004103. PMID: 27428194; PMCID: PMC4956788.
41. Wu H, Zhou J, Chen J, Gu Y, Shi L, Ni H. Therapeutic efficacy and safety of radiofrequency ablation for the treatment of trigeminal neuralgia: a systematic review and meta-analysis. J Pain Res. 2019 Jan 18;12:423-441. doi: 10.2147/JPR.S176960. PMID: 30697063; PMCID: PMC6342144.
42. Bharti N, Sujith J, Singla N, Panda NB, Bala I. Radiofrequency Thermoablation of the Gasserian Ganglion Versus the Peripheral Branches of the Trigeminal Nerve for Treatment of Trigeminal Neuralgia: A Randomized, Control Trial. Pain Physician. 2019 Mar;22(2):147-154. PMID: 30921978.
43. Guo Z, Wu B, Du C, Cheng M, Tian Y. Stereotactic Approach Combined with 3D CT Reconstruction for Difficult-to-Access Foramen Ovale on Radiofrequency Thermocoagulation of the Gasserian Ganglion for Trigeminal Neuralgia. Pain Med. 2016 Sep;17(9):1704-16. doi: 10.1093/pm/pnv108. Epub 2016 Feb 13. PMID: 26874883.
44. Onofrio BM. Radiofrequency percutaneous Gasserian ganglion lesions. Results in 140 patients with trigeminal pain. J Neurosurg. 1975 Feb;42(2):132-9. doi: 10.3171/jns.1975.42.2.0132. PMID: 1113146.

45. Erdine S, Ozyalcin NS, Cimen A, Celik M, Talu GK, Disci R. Comparison of pulsed radiofrequency with conventional radiofrequency in the treatment of idiopathic trigeminal neuralgia. Eur J Pain. 2007 Apr;11(3):309-13. doi: 10.1016/j.ejpain.2006.04.001. Epub 2006 Jun 9. PMID: 16762570.