Pain Medicine Case Reports

ISSN 2768-5152

Volume 7, Number 5, pp. 265-269

# Cryoablation of Peripheral Nerves for Treatment of Pain Secondary to Intracranial Tumors: A Case Report

Ahish Chitneni, DO[1], Richard Kim, DO[1], and Neal Rakesh, MD[2]

**Background:** Cryoablation involves destroying tissue by freezing and thawing cycles. Recent developments have led to the use of cryoablation of peripheral nerves. Despite various methods of treatment of cancer pain, intractable pain due to intracranial tumors require treatment with unconventional methods.

**Case Report:** We present a case series of 2 patients with a history of cancer presenting with head and neck pain. In these cases, the patients underwent cryoablation of head and neck nerves, such as the greater auricular nerve and greater occipital nerve. In the first patient, there was an overall decrease in daily morphine milligram equivalents from 400s to 100s at 2-month post-procedure follow-up. In the second patient, there was an overall 70% decrease in reported pain at the 2-week post-procedure follow-up.

**Conclusion:** Cryoablation of peripheral nerves may be a viable option for pain relief in patients with intracranial tumors who have failed conservative therapies.

**Key words:** Cancer pain, case report, cryoablation, head and neck pain, intracranial tumor

## BACKGROUND

Cryoablation involves destroying tissue by freezing and thawing cycles. Physiologically, cryoablation results in cellular damage, death, and necrosis of tissues due to the cold-induced injury of cells (1). The application of cryoablation for the treatment of cancer was studied in the 19th century when research groups used temperatures between -18°C to -24°C to freeze a variety of tumors (2). Indeed, a more recent phenomenon, cryoablation of peripheral nerves, also known as cryoneurolysis, involves the direct application of cold temperatures resulting in cold-induced injury of cells (3). While cryoablation are historically used to target soft tissue and has use cases in malignancies, recent developments have led to the use of cryoablation of peripheral nerves, utilizing temperatures as low as -19°6 C for tissue ablation (4).

The procedure of cryoablation involves 2 mechanisms: direct cellular injury and indirect cellular injury (1). Through direct mechanisms that result in cold-induced cell injury, as well as indirect mechanisms that alter the cellular microenvironment and reduce tissue viability, cryoablation damages, kills, and necrotizes tissues (1). The tissue cools when the cryoprobe removes heat from it, and as a result, ice crystals eventually develop in the extracellular space. Additionally, the extracellular environment becomes more tonic as a result of the ice crystals' capture of free water and results in dehydration of cells, resulting in injury (1). Aside from the cooling process of cryoablation, the thawing phase plays an important role in resulting in damage. During the thawing phase, the melting of ice in the extracellular space cre-

From: [1]Department of Rehabilitation and Regenerative Medicine, NewYork-Presbyterian Hospital - Columbia and Cornell, New York, NY; [2]Department of Anesthesiology and Critical Care Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Corresponding Author: Neal Rakesh, MD, MSE, E-mail: rakeshn@mskcc.org
Disclaimer: The author(s) were supported by the MSKCC Support Grant (P30 Core Grant) and the Memorial Sloan Kettering Department of Anesthesiology and Critical Care There was no external funding in the preparation of this manuscript.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.
Patient consent for publication: Memorial Sloan Kettering Cancer Center institutional policy exempts the need for patient consent when there are no patient identifiers.
Authors adhere to the CARE Guidelines for writing case reports and have provided the CARE Checklist to the journal editor.
Accepted: 2023-05-18, Published: 2023-09-30

ates an osmotic gradient which leads to cellular swelling and cell damage (1). As mentioned, cryoablation also functions through indirect cellular injury. In this form of cellular damage, cryoablation and the cold-induced change to the tissue is thought to result in damage to endothelial cells, thrombus formation, and ischemia which results in further cellular injury (1). Neuropraxia is thought to occur in temperatures of 10°C to -20°C with recovery within minutes to weeks (5). In temperatures of -20°C to -100°C, Wallerian degeneration/axonotmesis occurs past the lesion resulting in decreased transmission for weeks to months after insult (5). In short, one of the benefits of cryoablation is that the mechanism allows for it to cause axonotmesis which results intact endoneurium, perineurium, and epineurium that allows for axonal regrowth over time with a decreased incidence of neuroma formation (6).

Moderate to severe pain in cancer patients is known to affect almost 80% of patients with advanced stage cancer (7). In many cases, cancer pain occurs due to the primary pathology, metastasis to various regions of the body, or as a side effect of chemotherapy or radiation therapy. In addition, many patients with intracranial tumors experience moderate to severe pain post-craniotomy (8). One study revealed that pain compromised 21% of all hospital admissions in patients with intracranial tumors. Among cancer patients evaluated in inpatient neurological consultations, 15.4% reported headaches (9). Additionally, an overwhelming number of cancer patients in the United States are undertreated for their pain, with many failing conservative measures of treatment and requiring additional and/or alternative modalities (10).

## CASE REPORT

This retrospective review was approved via waiver for informed consent by Memorial Sloan Kettering Cancer Center's (MSKCC) Internal Review Board and supported by MSKCC Support Grant (P30 Core Grant) and the Department of Anesthesiology and Critical Care. A chart review of 2 patients with intracranial malignancy related pain and history of oncologic diseases was performed. We reviewed patients' pain symptomatology, relevant medical history and pre- and post-procedure pain levels.

The procedures were performed using an ultrasound device (GE P9TM 9L linear probe) and a 16-gauge cryoablation probe (Frigitronics Cooper Surgical, Trumbull, CT, USA) with supercooled liquid nitrogen gas. A series of 3 freeze-thaw cycles were used for cryoneurolysis. Each cycle was 1.5 minutes long (starting when the temperature reached below -60°C) followed by a 30-second thawing period.

### Case 1

A 20-year-old woman with a history of pilocytic astrocytoma of the posterior thalamus (status-post suboccipital craniotomy 5 years prior) and chronic migraines presented with 10/10 right occipital pain around her craniotomy scar. The pain was described as an intermittent sharp pain worsening when lying on her abdomen and worsened at nighttime. The patient reported pain radiating to the top of the scalp and toward the ears bilaterally. Additionally, she reported that current pain symptoms did not present similar to her chronic migraine symptoms. The patient had limited relief with conservative medication management involving cyclobenzaprine and acetaminophen, which eventually became refractory. Ten months prior, the patient underwent a right occipital nerve block and bilateral cervical trigger point injections with mild symptomatic relief of limited duration. A physical examination revealed a well-healed craniotomy scar without allodynia, and moderate trigger points at the bilateral trapezius muscles. A magnetic resonance image (MRI) of the brain with and without contrast demonstrated unchanged nonenhancing signal abnormality surrounding the site of the previously resected cystic pilocytic astrocytoma, determined stable compared to previous imaging. The patient underwent a right greater occipital nerve (GON) cryoablation under ultrasound, done at the C2 level between the semispinalis capitis and inferior obliquus capitis. Post-procedure, the patient reported significant lasting pain relief in the right occipital region. As a result, there was an overall decrease in daily morphine milligram equivalents (MMEs) from 400s to 100s during a 2-month post-procedure follow-up.

### Case 2

An 84-year-old woman with a history of benign leiomyoma metastatic to the brain, lungs, and bone (status-post radiation therapy to the brain and lungs 3 months prior) presented with worsening left-sided neck and head pain. The pain was described as 8/10 and worsening since completing radiation therapy. The pain originated in the left neck and radiated to the left scalp behind the ear. Tenderness and sensitivity to touch at the left neck and scalp were reported. The patient was admitted to the hospital and placed on a pain regimen involving intravenous patient-controlled analgesia with about 400 MMEs daily. The patient underwent a left superficial cervical plexus block and left greater auricular nerve (GAN) block with significant relief for 24 hours and subsequent return of severe pain. A physical examination demonstrated tenderness to palpation at the left cranium and no tenderness to palpation at the cervical spine and neck. An MRI of the brain with and without contrast revealed, compared to previous imaging, unchanged left posterior skull expansile osseous metastasis with slightly increased edema in the adjacent left occipital lobe. The patient underwent a left GAN cryoablation followed by a left GON cryoablation 8 days later with significant overall pain relief since admission. During the procedure, the target of the cryoablation under ultrasound was the superficial cervical plexus (between the posterior edge of the sternocleidomastoid (SCM) and the middle scalene) and the GAN (superficial to the posterior edge of the SCM). In this patient, there was an overall 70% decrease in pain at the 2-week post-procedure follow-up after the cryoablation.

## DISCUSSION

Our case study presents the successful use of cryoablation for pain relief in patients with intracranial tumors by targeting nerves including the GON and GAN. At post-procedure follow-up, patients reported a significant overall decrease in daily MMEs used or >70% overall pain relief, respectively.

In the first case, the target of the procedure was at the C2 level between the semispinalis capitis and the inferior obliquus capitis. As described by Stogicza et al (11), ultrasound can be used to identify the proximal GON between the C2 spinous process and the C1 transverse process over the inferior oblique capitis muscles (IOCM) where the GON can be clearly visualized. In the paper, the authors describe the position where the patient is in a prone position, the ultrasound probe is placed parallel to the IOCM, and the GON is visualized on the superior aspect of the IOCM (11). Additionally, the authors note the advancement of the cryoprobe in a medial to lateral direction to avoid any dissection of the vertebral artery and overall safety of the procedure (1). Anatomically, the GON is the sensory branch of the posterior ramus of the C2 nerve and innervates the occipital region (12). After exiting from the C2 nerve, the GON travels between the inferior capitis obliquus and semispinalis capitis muscles underneath the suboccipital triangle (12).

In the second case, the target for the procedure was the superficial cervical plexus between the deep posterior edge of the SCM and the middle scalene, and the GAN superficial to the posterior edge of the SCM. Anatomically, the SCM muscle lies anterior to the nerves of the superficial cervical plexus C2-C4 which have terminal nerve branches including the lesser occipital nerve, GAN, transverse cervical, and supraclavicular nerve (13). As noted, one of the targets for this case was the GAN, which is a major sensory branch of the cervical plexus (14). In general, the fact that the nerve is located in a superficial region and traverses anterior to the SCM allows for a possible target under ultrasound guidance (14).

In our literature search, there are sparse cases reporting the use of peripheral nerve cryoablation for treatment of pain in patients with intracranial tumors. Despite this, the use of cryoablation of peripheral nerves has been well-reported in reducing pain levels with other indications. In one case by Fiala et al (15), a patient with phantom limb pain, who had failed conservative measures, had cryoablation of the bilateral posterior tibial nerves (IceSphere, Boston Scientific) with freeze-thaw cycles involving 8 minutes of freezing, 3 minutes of passive thawing, 3 minutes of freezing, and 3 minutes of passive thawing. The patient reported immediate pain relief after the procedure with continued improvement of his phantom limb pain for up to 6-weeks post procedure (15). In another case by Wordekemper et al (16), the authors describe a 39-year-old patient with a 20-year history of chronic penile pain who underwent cryoablation of the penile nerves after failing conservative management, and had long-lasting pain relief post-procedure.

The potential for an intervention such as peripheral nerve cryoablation to reduce daily MME burden in patients is a significant impetus for further investigation into this modality. The large reduction in daily MMEs in our patient from Case 1 highlights this procedure's potential in this patient population. Indeed, reports of nerve cryoablation reducing daily opioid burden have been previously demonstrated. A study by Graves et al (17) studied the overall reduction in opioid requirement in patients undergoing intraoperative intercostal nerve cryoablation during a Nuss procedure. In the study, 20 patients undergoing the procedure were evaluated and randomized to receive either cryoanalgesia or thoracic epidural analgesia with the primary outcome measure of the study being postoperative length of stay while secondary outcome measures included total/daily opioid requirements and inpatient pain scores (17). Results showed that patients in the cryoablation group required significantly less inpatient opioid analgesia with a mean decrease of 416 mg oral morphine equivalents per patient and required 52-82% fewer milligrams on postoperative days 1-3 (17). While the aforementioned study observed non-cancer pain patients, its results, along with the findings from Case 1, demonstrate the potential of this intervention to decrease opioid requirements in patients. Furthermore, the immediate utility of cryoablation in an acute care setting is demonstrated in the Graves et al study as well with the patient in Case 2, who had the procedure performed while admitted for refractory pain. While these findings indicate the utility of peripheral nerve cryoablation across the time course of pain, better understanding its place in acute versus chronic care settings is worthwhile for further investigation.

As a theorized minimally invasive, rapid-acting, clinically effective solution for severe head and neck pain, peripheral nerve cryoablation is not alone. Nerve and plexus blocks are a staple in the treatment algorithm for this cancer pain patient population. In both our cases, patients underwent peripheral nerve blocks prior to attempting cryoablation procedures (right occipital nerve and left superficial cervical plexus/left GAN, respectively). However, both patients were eventually refractory to treatment with only short-term relief of pain symptoms and required an alternative modality. Peripheral nerve cryoablation may provide a valuable option when patients fail conservative measures and reach the end of the current treatment algorithms for pain management. Our case study provides valuable insight into where peripheral nerve cryoablation may fit in the pain management algorithm for patients with pain secondary to intracranial tumors.

Several limitations exist when discussing the outcomes from these cases. One consideration includes if peripheral nerve cryoablation presented with positive outcomes for patients because they underwent prior nerve blocks. Secondly, heterogeneity of the patients and low sample size present limitations on the generalizability of results. Furthermore, the outcome measures (daily MMEs, numeric rating scale) and follow-up intervals were not consistent between patients. As a retrospective case review, the results of this study are limited. However, this study demonstrates this intervention's potential for the head and neck cancer pain population and provides an impetus to justify further, more robust investigation.

Further research on the use of cryoablation compared to traditional nerve blocks or other forms of interventional techniques (e.g., GON block) can be conducted in a randomized-controlled setting to provide data on outcomes of the technique. When conducting large studies, other than assessments of pain relief, secondary outcomes such as Oswestry Disability Index (ODI), total daily opioid use, improvements in activities of daily living/instrumental activities of daily living, sleep quality, improvements in depression and fatigue should all be assessed to understand the effects of the procedure in improving function. Additionally, further case reports and case series on the use of peripheral nerve cryoablation for similar tumors and pain would be beneficial additions to the current literature and to observe if results can be reproducible in other patients with similar case presentations. Studies should also be conducted to assess if significant pain relief with diagnostic nerve blocks is a predictor of success with peripheral nerve cryoablation.

Understanding this association could provide valuable knowledge underpinning peripheral nerve cryoablation's mechanism of efficacy. Further investigation into the neurological etiology of the patient's pain (i.e., GON, greater auricular, occipital, etc.) and efficacy of cryoablation can also be categorized and better understood with the progression of research in this arena.

## CONCLUSION

Cryoablation of peripheral nerves may be a viable option for patients with intracranial tumors who have significant head and/or neck pain refractory to medication management, traditional nerve blocks, and other conservative measures. While the generalizability of results in this case series is limited, this study demonstrates the potential of this treatment modality in the cancer pain population and provides an impetus to investigate further. Further studies should be conducted to explore the use of the procedure compared to other conservative measures and interventional procedures. Additionally, further studies assessing outcomes when comparing the use of cryoablation ablation with other procedures and conducting studies to assess improvements in secondary outcomes, such as ODI and daily function, should be conducted.

## REFERENCES


1. Erinjeri JP, Clark TW. Cryoablation: Mechanism of action and devices. *J Vasc Interv Radiol* 2010; 21(8 Suppl):S187-191.
2. Arnott J. Practical illustrations of the remedial efficacy of a very low or anesthetic temperature in cancer. *Lancet* 1850; 56:257-259.
3. Ilfeld BM, Preciado J, Trescot AM. Novel cryoneurolysis device for the treatment of sensory and motor peripheral nerves. *Expert Rev Med Devices* 2016; 13:713-725.
4. Gage AA. History of cryosurgery. *Semin Surg Oncol* 1998; 14:99-109.
5. Zhou L, Kambin P, Casey K F, et al. Mechanism research of cryoanalgesia. *Neurol Res* 1995; 17:307-311.
6. Trescot AM. Cryoanalgesia in interventional pain management. *Pain Physician* 2003; 6:345-360.
7. Bruera E, Kim HN. Cancer pain. *JAMA* 2003; 290:2476-2479.
8. Foust Winton RE, Draucker CB, Von Ah D. Pain management experiences among hospitalized post craniotomy brain tumor patients. *Cancer Nurs* 2021; 44:E170-E180.
9. Clouston PD, DeAngelis LM, Posner JB. The spectrum of neurological disease in patients with systemic cancer. *Ann Neurol* 1992; 31:268-273.
10. Bennett M, Paice JA, Wallace M. Pain and opioids in cancer care: Benefits, risks, and alternatives. *Am Soc Clin Oncol Educ Book* 2017; 37:705-713.
11. Stogicza A, Trescot A, Rabago D. New technique for cryoneuroablation of the proximal greater occipital nerve. *Pain Pract* 2019; 19:594-601.
12. Kemp WJ, Tubbs RS, Cohen-Gadol AA. The innervation of the scalp: A comprehensive review including anatomy, pathology, and neurosurgical correlates. *Surg Neurol Int* 2011; 2:178.
13. Christ S, Kaviani R, Rindfleisch F, Friederich P. Brief report: Identification of the great auricular nerve by ultrasound imaging and transcutaneous nerve stimulation. *Anesth Analg* 2012; 114:1128-1130.
14. Thallaj A, Marhofer P, Moriggl B, Delvi BM, Kettner SC, Almajed M. Great auricular nerve blockade using high resolution ultrasound: A volunteer study. *Anaesthesia* 2010; 65:836-840.
15. Fiala M, Azariah A, Woo J, Aal AKA, Levey A. Treating phantom limb pain: Cryoablation of the posterior tibial nerve. *Radiol Case Rep* 2022; 17:3168-3171.
16. Wordekemper B, Clifton B, Deibert CM. Cryoablation of the penile nerves for chronic penile pain. *Int J Impot Res* 2022; 35:415-418.
17. Graves CE, Moyer J, Zobel MJ, et al. Intraoperative intercostal nerve cryoablation during the Nuss procedure reduces length of stay and opioid requirement: A randomized clinical trial. *J Pediatr Surg* 2019; 54:2250-2256.