



Case Report

Cryoneurotomy as a Percutaneous Mini-invasive Therapy for the Treatment of the Spastic Limb: Case Presentation, Review of the Literature, and Proposed Approach for Use



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KEYWORDS

Cryosurgery;
Denervation;
Hemiplegia;
Muscle spasticity;
Nerve block;
Rehabilitation

Abstract *Objective:* To provide a proof-of-concept study demonstrating that the decades old procedure of cryoneurotomy, used traditionally for analgesia, is a safe adjunctive and effective treatment for limb spasticity.

Design: Case series.

Setting: Publicly funded outpatient hospital spasticity clinic and community interventional anesthesia clinic.

Participants: Patients (N=3) who had plateaued with standard of care spasticity treatments including botulinum toxin. Two hemiplegic stroke patients with elbow spasticity and 1 pregnant patient with multiple sclerosis and a spastic equinovarus foot for whom botulinum toxin was now contraindicated.

Interventions: Selective anesthetic diagnostic motor nerve blocks with ultrasound and e-stimulation with 1cc of 1% lidocaine to the motor nerve to the targeted spastic muscle were performed to either the musculocutaneous nerve to brachialis, radial nerve to the brachioradialis or the tibial nerve. If the benefits included improved active and passive range motion and or decreased clonus, a percutaneous cryoneurotomy was performed.

List of abbreviations: AROM, active range of motion; BoNT, botulinum toxin; e-stim, electrical stimulation; DNB, diagnostic nerve block; MAS, Modified Ashworth Scale; MSCN, musculocutaneous nerve; PROM, passive range of motion; ROM, range of motion; US, ultrasound.

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Main Outcome Measures: Active and passive range of motion were measured using the Modified Tardieu Scale. The change in resistance to passive stretch was measured using the Modified Ashworth Scale (MAS). Videos of the before and after treatment were collected.

Results: Both elbows' treatments resulted in MAS improving from a 3 to a 1+. Greatly improved active range of motion was noted at 94 and 64 degrees, respectively, as well as improvements in passive range on the Modified Tardieu Scale. The tibial nerve cryoneurotomy resulted in improvements in all parameters with a much improved gait. Results were maintained up to 17 months of follow-up.

Conclusion: Cryoneurotomy as a treatment for spasticity is a novel safe adjuvant treatment. Our initial results suggest patients can achieve significantly increased active and passive range of motion in the upper extremity and decreased clonus, and improved gait after tibial nerve cryoneurotomy.

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Spasticity is a potentially debilitating condition that arises from injury to the central nervous system, manifesting as intermittent or sustained involuntary muscle contractions.¹ Spasticity may negatively affect health status, function, and quality of life despite current multimodal management strategies.²

A diagnostic anesthetic nerve block (DNB) with electrical stimulation (e-stim) for nerve localization may identify the contribution of an individual muscle in spasticity patterns and the presence or severity of underlying joint contraction.³⁻⁷ The addition of ultrasound (US) for nerve localization in DNB has recently been reported.³ An accurate DNB allows for identification of the primary muscle contributors to problematic spasticity and provides a temporary demonstration of the effects of *disabling* the associated nerve(s). The DNB thus informs whether the use of more permanent treatment options such as neurotomy is a potential treatment without the loss of existing function due to unmasking of underlying weakness or overactive antagonist muscles that become unopposed.

The management of spasticity by selective neurolysis is well established, including surgical partial neurotomy for the elbow,^{8,9} the spastic equinus foot,^{6,10} and hip adduction¹¹; alcohol or phenol chemodenervation^{12,13}; and sparse case studies of neuroablation by percutaneous radiofrequency¹⁴ or cryoanalgesia.¹⁵ Cryoanalgesia is performed using a cryoprobe that is percutaneously inserted to target sensory peripheral nerves for long lasting pain relief from months to years, with outcomes that are well established in the pain literature.¹⁶⁻¹⁹ The tip of the cryoprobe creates an ice ball or oval between 3.5 and 9.4 mm²⁰ at approximately -60° C, which causes a limited zone of axon and myelin disruption (cryoneurotomy) and subsequent Wallerian degeneration of the targeted nerve. The procedure is proposed to be safer than alcohol chemodenervation due to decreased risk of damage to surrounding structures.^{19,20} Neurotrophin, implicated in the formation of painful neuromas, is proposed to uniquely not be released from nerve endings during cryoneurolysis procedures.²¹ More than 50 years of evidence of *inherent safety* of cryoneurotomy is available.^{16,20,22}

We propose that the cryoprobe can be safely used in a novel manner to perform a selective cryoneurotomy of peripheral motor nerve branches for the management of limb spasticity. Published data on cryoneurotomy in spasticity are scarce, and more research is needed to determine whether cryoneurotomy may improve outcomes. The primary objective of this proof of concept study is to explore the hypothesis that cryoneurotomy has potential as an adjunct treatment to improve the management of limb spasticity by reporting results of several initial cases and a review of the literature. The secondary objective is to leverage our collective experience and propose an approach to the use of cryoneurotomy in limb spasticity management so as to optimize outcomes, minimize risks, and create a standardized approach for future research.

Case studies

Patients with limb spasticity including stroke and multiple sclerosis were assessed for candidacy of cryoneurotomy procedure in a publicly funded outpatient spasticity clinic. Patients were first assessed by a specialist in Physical Medicine and Rehabilitation (P.W.). The assessment included the Modified Ashworth Scale (MAS), the Modified Tardieu Scale, and the first DNB. DNB was performed with e-stim and US for nerve localization and 1 cc of 2% lidocaine. The musculocutaneous nerve (MSCN) was localized using the approach described by Genet et al⁷ and recently published describing US guidance by Matsumoto et al¹² (fig 1). The radial nerve branch to the brachioradialis muscle was localized using the approach described by orthopedic surgeon Keenan.²³ Motor branches of the tibial nerve were localized using the approach described by Deltombe et al⁴ which coincide with the recently published US landmarks by Picelli et al.³ A successful candidate demonstrated no loss of function or other adverse outcomes with DNB as well as greater range of motion (ROM), decreased MAS, and improvements on the Modified Tardieu Scale. The patients were referred to the interventional anesthesiologist (author D.V., >20 years' experience in e-

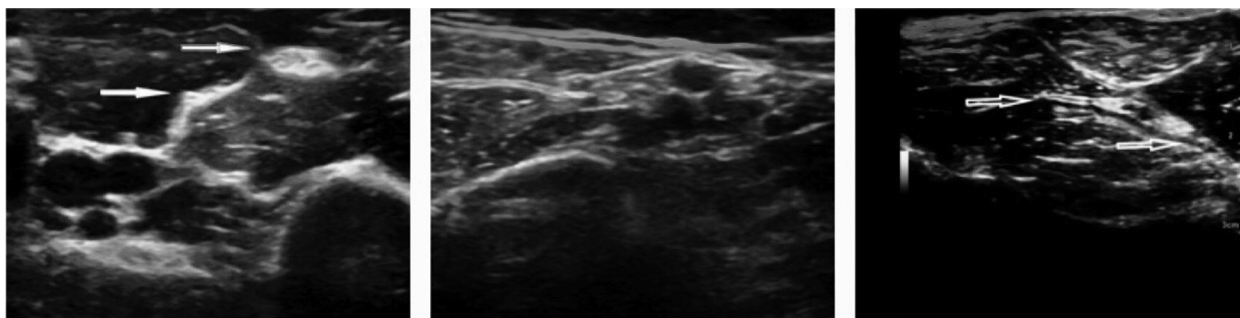


Fig 1 Left, high to low. US of musculoskeletal nerve, branch to brachialis in a nonspastic limb. Top arrow indicates the musculoskeletal nerve trunk, the lower arrow indicates the nerve branch to the brachialis muscle. Right case 2, appearance after BoNT chemodenervation. Right, the tip of the needle contacting the tibial nerve. The arrow points to the tibial nerve branches to the medial (left) and lateral (right) gastrocnemius muscles.

stim and US-guided DNB and cryoanalgesia) who performed a repeat DNB for reproducibility. If consistent, the patient was offered the option of cryoneurotomy of the same targeted peripheral motor nerve(s) (Westco Lloyd SL Neurostat^a). Postprocedure physical examinations were performed and documented by P.W. Videos were taken before and after DNB and cryoneurotomy procedures.

Case 1

A 54-year-old man with a left middle cerebral artery stroke underwent 5 rounds of US-guided botulinum toxin (BoNT chemodenervation, with incobotulinumtoxinA beginning 4mo poststroke, to the right spastic elbow flexors [biceps muscle 75 U, brachialis muscle 75 U, brachioradialis muscle 50 U]) at 3-month intervals. BoNT with intensive outpatient physiotherapy improved elbow active and passive range of motion (AROM and PROM). At 16 months post stroke, he remained with a high elbow flexor MAS of 3 and limited AROM of 72° (table 1) (status pre-DNB). A DNB was performed to the brachialis motor branch of the MSCN. Post-DNB his elbow AROM showed a decrease in MAS (see table 1). The second DNB demonstrated similar results. At 24 months poststroke, a percutaneous cryoneurotomy of the same brachialis motor branch (fig 2) was performed. Three weeks postprocedure there was an increase in AROM and PROM to full extension (see table 1). His elbow AROM postcryoneurotomy matched, then over time, exceeded his maximal PROM precryoneurotomy, resulting in a significantly improved angle of paresis on the Modified Tardieu Scale (angle of paresis=initial V1 [as slow as possible PROM] minus AROM).²⁴ The MAS reduced from 3 to 1+. No postprocedure adverse events were noted. The results of the cryoneurotomy permitted the redistribution of the BoNT used in previous injections to the brachioradialis muscle and the finger flexor muscles. Postcryoneurotomy, PROM remained at full extension with gains continued to be made in elbow AROM with a gain of 94° at 1-year follow-up and maintained at 17 months (see fig 2).

Case 2

A 48-year-old woman with a pontine stroke underwent chemodenervation with onabotulinumtoxinA 200 U each

to both the spastic left leg and arm at 3-month intervals for 8 years. With adjuvant periodic physiotherapy and daily stretching, she continued to have limited PROM, AROM, and a high MAS (table 2). The elbow was held in tight flexion with ambulation. A DNB to the brachialis muscle motor branch resulted in improved PROM and AROM. A brachialis muscle motor branch cryoneurotomy was performed. At 1-month postcryoneurotomy her elbow AROM improved by 52°. The paresis angle dropped from 78° to 33°. A subsequent DNB of the radial nerve branch to the brachioradialis muscle resulted in increased elbow AROM and a drop in the MAS to 1+ (see table 2). The 75 units of BoNT from the brachialis muscle were redistributed to the brachioradialis muscle and long finger flexor muscles for the subsequent injection sessions. Partial gains in AROM were achieved, but less than that temporarily gained by the radial DNB. Percutaneous cryoneurotomy was next performed to the radial nerve motor branch to the brachioradialis muscle 8 months after the first cryoneurotomy. Two months later (10 months post first cryoneurotomy), her elbow AROM had further improved by 64° (see table 2) (fig 3).

Case 3

A 28-year-old woman with multiple sclerosis received 4 injection series at 3-months interval of 400 U of onabotulinumtoxinA into the left tibialis posterior muscle and triceps surae muscles for ankle spasticity. On patient notifying the intention to conceive a child, BoNT was stopped. As her gestation progressed, her gait deteriorated because spasticity increased and she was unable to wear her ankle foot orthosis. Video observation demonstrated a step to gait with equinovarus posturing during swing phase, stance phase characterized by initial contact with forefoot, toe clawing, and poor tibial progression. A DNB to the tibial nerve motor branches to the gastrocnemius and soleus muscles was performed. Ankle clonus ceased, with an improvement in initial contact during stance phase. At 28 weeks of gestation, she underwent a left tibial nerve cryoneurotomy of the motor branches to the same motor branches. At 4 weeks post-cryoneurotomy, she had no ankle clonus and improved active and passive ankle dorsiflexion, with a faster step

Table 1 Results for the 2 elbow spasticity cases treated with cryoneurotomy

Time	Event	V3*	V1*	AROM*	Paresis Angle*	MAS*
Case 1						
Baseline	Pre-/postlidocaine nerve block	97/110	142/142	72/96	70/46	3/2
2 wk	Post-CryoN	112	177	151	-9	1+
6 mo	Post-CryoN	120	177	161	-19	1+
9 mo	Post-CryoN	130	177	165	-23	1+
12 mo	Post-CryoN	Undetected	180	166	-24	1+
17 mo	Post-CryoN	Undetected	180	166	-24	1+
Case 2						
Baseline	Pre-/postlidocaine nerve block	87/112	150/153	72/110	78/40	3/2
9 d	Post-CryoN	115	157	114	36	2
1 mo	Post-CryoN	115	155	124	26	2
4 mo	Post-CryoN	119	157	123	27	1+
10 mo, 2 mo post second CryoN	Post-CryoN MSCN and radial	Undetected	177	136	14	1+

NOTE. V1=as slow as possible passive ROM. V3=catch passively as fast as possible. Paresis angle=initial V1-current AROM. Abbreviation: CryoN, cryoneurotomy.

* Modified Tardieu Scale.

through gait. She noted decreased calf cramping and less pain at night. She subsequently had a healthy delivery of her child. At her 9 months of follow-up, her gait had continued to improve, clonus was absent, and active ankle ROM was better.

Literature review

A systematic search strategy, developed by the College of Physicians and Surgeons of British Columbia librarians, identified relevant studies published between 1980 and



Fig 2 Case 1. Top row: left V3 before cryoneurotomy. Right 2 weeks after cryoneurotomy. Middle row: V1 before cryoneurotomy, and right 2 weeks after. Bottom row: active range of motion. Left, 2 weeks after cryoneurotomy, middle 3 months, right at 1 year. NOTE: Active range of motion was 72° prior to cryoneurotomy.

Table 2 Recommended initial nerve branches to target for cryoneurotomy

Nerve	Muscle	Reference
Musculocutaneous	Brachialis or biceps	Genet et al ⁷ and Matsumoto et al ¹²
Radial	Brachioradialis	Keenan et al ²⁴
Tibial	Gastrocnemius, soleus, tibialis posterior	Picelli et al ³ and Deltombe et al ⁴
Obturator	Adductors	Kanoplat et al ¹⁴ and Kim and Ferrante ¹⁵
Pectoral nerves	Pectoral major	Creze et al ²⁵
Femoral nerve	Rectus femoris	Trescott ²¹

March 2019 using electronic databases MEDLINE, EMBASE, CINAHL, and Cochrane Central Register of Controlled Trials. Reference lists of systematic reviews and included articles were manually scanned to expand the data set. The search strategy was based on 3 key concepts: spasticity, cryoneurotomy, and cryoanalgesia (see [supplemental appendix S1](#) for MEDLINE search strategy, available online only at <http://www.archives-pmr.org/>). Inclusion criteria was any study reporting the use of cryoneurotomy for spasticity management in humans, English language. Two studies were found that documented the use of cryoneurotomy in spasticity a case study published in 1998¹⁵ and a proof of concept abstract.²⁶ The 1998 article described a 72-year-old woman with multiple sclerosis who had failed oral medications, and a baclofen pump. Bilateral obturator nerve cryoneurotomies were performed after successful DNB with 0.25% bupivacaine. Her MAS dropped from 3 to 1 in the adductor muscles. The proof-of-concept abstract assessed 19 patients with spasticity who underwent MSCN cryoneurotomy with the iovera system handheld cryoneurotomy device.^b At 4 weeks postcryoneurotomy, there were 15 responders (79%), 3 (20%) had 1-point reduction, 4 (27%) a 2-point reduction, 7 (47%) a 3-point, and 1 (7%) a 4-point reduction on the MAS. There were significant improvements on the MAS and Modified Tardieu Scale V1 and V2 at all post-treatment time points. The minimal side effects were noted to be transient.

In the animal literature, successful motor cryoneurotomy with regeneration has been seen in rats.²⁷

Methods of our proposed approach

Reflecting on 18 months using cryoneurotomy in >30 patients in the management of limb spasticity, the systematic review and the collective spasticity management clinical experience of this article's authors, we propose the following approach to the use of cryoneurotomy of motor branches for spasticity management: (1) Knowledge of the motor peripheral nerves anatomy is required to understand where they can be targeted without affecting sensory peripheral nerves, thus minimizing the risk of dysesthesia. Numerous references describe optimal locations.^{5,6,10,21,28} Table 2 outlines the nerves that can be initially safely targeted due to identifiable motor branches. (2) Motor branches to be targeted should be confirmed with DNB on 2 separate occasions precryoneurotomy to demonstrate expected clinical benefits and minimize potential of adverse events such as loss of function or sensory impairment. (3) There are different devices available on the market, which if used, should be capable of delivering similar e-stim.²¹ Procedural details include (a) a thermal insulating catheter (#16 angiocatheter) that serves as a guide and thermocutaneous

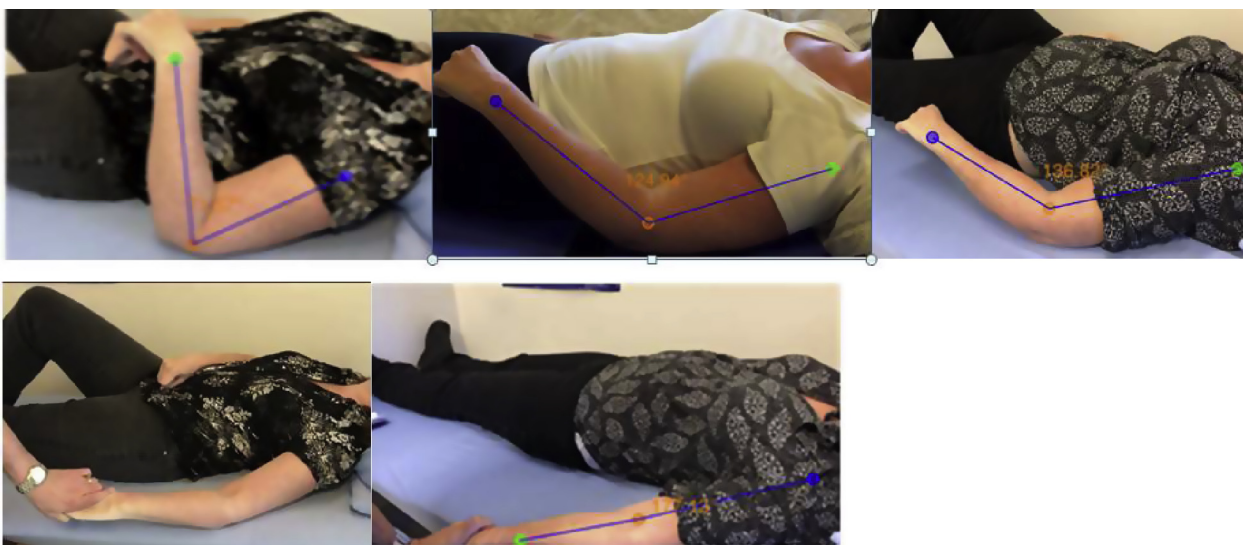


Fig 3 Case 2. Upper row demonstrates active range of motion. Left: before cryoneurotomy, middle: 1 month post-cryoneurotomy to MSCN, right: 2 months postcryoneurotomy to MSCN and radial nerve. Bottom row: passive as slow as possible range of motion is shown by V1. Left: before cryoneurotomy and right: after cryoneurotomy to MSCN and radial nerves.

protection from cutaneous frostbite.²¹ The catheter also serves as an insulator to provide optimal e-stim. (b) Small dose of local anesthesia for cutaneous and subcutaneous anesthesia; <1 mL of 1% lidocaine to avoid diffusion. (c) Cryoneurotomy lesions are performed juxtapositioned to the motor nerve branch using an in-plane US technique to optimally view and guide the cryoprobe tip. (d) Two lesions are performed, either superior/inferior or medial/lateral to the motor nerve at a temperature of -60° for 3.5 minutes per lesion for a total of 7 minutes as per standard cryoneurotomy protocols.²¹ (e) Should the patient experience a painful sensation, then the probe tip is readjusted immediately, and the cryoneurotomy resumed. (f) Care is taken to avoid any vascular structures; therefore, color Doppler setting on the US is essential. (g) Postprocedure, the percutaneous entry point is stabilized with pressure and sealed with skin glue and occlusive dressing applied. No specific activity restrictions are required. (4) Standardized outcome measures should be used to capture outcomes and adverse events. We recommend using the Modified Tardieu Scale²⁴ and MAS, as well as video capture to compare before and after. (5) Reassessment of the patient postprocedure to readjust the spasticity management strategy and goals. Redistribution of BoNT will likely occur. Ongoing follow-up as of the patient as needed, because there is a potential for nerve regrowth and repeat procedures.

Discussion

This is the first article in the literature that we are aware of to report results of cryoneurotomy of peripheral motor nerve branches in patients with chronic spasticity who had plateaued in their spasticity management. The use of cryoneurotomy is relatively new to this spasticity clinic. These preliminary results suggest that not only does cryoneurotomy have the potential to result in additional gains in this difficult to treat population, these gains were clinically significant. Our first case (Case 1) achieved an elbow AROM greater than the maximal passive ROM that he had prior to treatment.

There is the potential for nerve regeneration as the basal lamina, as well as the epineurium and perineurium of the targeted nerve remain intact; this could result in a return of spasticity.^{16,17,26} However, in Case 1, there was the ongoing improvement in movement over time with ongoing gains documented at the 17-month final follow-up.

Not all muscles can be safely targeted with cryoneurotomy, with the main limitation being whether sensory nerves can be avoided. When using BoNT for problematic spasticity, there is a limitation in how many muscles can be selected so as to respect the upper limits of BoNT doses. However, when used in combination, it is ideal that those muscles that are amenable to cryoneurotomy be targeted, thus allowing the BoNT to be used for the remaining problematic muscles. This approach is demonstrated in Cases 1 and 2 where both patients had received large doses of BoNT. After cryoneurotomy, BoNT was redistributed into the other muscles of the forearm or hand, further improving gains. Cryoneurotomy has the additional advantage as a mini-invasive intervention with no recovery time.

We propose that our approach of using both US and e-stim to perform the DNB presents the possibility of improved accuracy of the DNB^{3,12} to support safe²² improvements in spasticity outcomes. Systematic reviews have noted nerve localization with US guidance increased the rate of successful peripheral blockade compared with e-stim alone and reduced the rate of vascular puncture.^{29,30} Andrea Trescot, pioneer in cryoanalgesia, wrote in 2003, "An accurate diagnosis with specific diagnostic injections of small volumes of local anesthetic and meticulous localization of the nerve is critical for successful outcome."^{16(p358)} In 2019, Picelli proclaimed, "In daily practice, US should be coupled with needle electrical stimulation in order to maximize precise identification."^{3(p383)}

Study limitations

Longer-term follow-up and outcomes of additional peripheral nerve cryoneurotomies are required.

Conclusions

Cryoneurotomy has the potential to be an effective and minimally invasive procedure for reducing limb spasticity. This is a novel application of a procedure that has a decades-long history of reproducible, effective, and safe use in thousands of patients in the cryoanalgesic literature. A standardized methodology should be used in research on the effects of cryoneurotomy of motor nerves in the spastic limb to allow comparisons of future studies. There is a need for additional high-quality research in this promising field which is at its infancy, but has the potential to significantly improve the experience of individuals suffering from spasticity.

Suppliers

- a. Westco Lloyd SL Neurostat; Westco.
- b. Cryoneurotomy device; MyoScience.

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