

# **Development of Innovative minimally invasive interventional pain technology for whiplash-associated disorder**

## **PhD thesis**

ÁGNES STOGICZA, MD, FIPP, CIPS

Szentágotthai János Faculty of Neurological Sciences

Program: Clinical Neurological Research



Supervisor: med. habil. Loránd György Erőss, MD, Ph.D, FIPP

Official reviewers:

Opponent 1: Prof. Béla Fülesdi, MD

Opponent 2: László Entz, MD, PhD, FIPP

Head of the Complex Examination Committee: Prof. Réthelyi Miklós, MD

Members of the Complex Examination Committee: Prof. Alán Alpár, MD

Prof. Emília Madarász, MD

Budapest, 2024

## 1. Introduction

Management of Whiplash Associated Disorders (WAD) have been the author's interest over the last 15 years. The complexity and diversity of WAD manifestations, that range from cervicgia, headaches to fatigue and cognitive disturbances necessitate a thorough understanding of their pathophysiology in order to develop optimal, individualized treatment approaches. The work presented here synthesizes the author's studies, incorporating various minimally invasive methods to treat WAD, as supported by retrospective and prospective data analyses.

### Whiplash Associated Disorders (WAD) Overview

The U.S. incidence of WAD, primarily resulting from motor vehicle collisions (MVCs) is 4 per 1,000 people (1–5). Approximately 83% of individuals involved in MVCs experience some form of WAD, making it the most common injury in these accidents. Financially, WAD is a significant burden, with annual costs of \$3.9 billion due to sick leave, medical expenses, and disability, escalating to over \$29 billion when litigation is included. The cervical spine allows significant range of motion and may be divided into lower cervical (C3-7) and craniocervical (C0-2) motion segments. The specialized C1 and C2 vertebrae are highly mobile and responsible for 50% of neck flexion and rotation, which makes it uniquely susceptible to whiplash injuries. Stability and motion are controlled by intervertebral discs, facet joints, and various ligaments (e.g., alar, transverse, anterior, and posterior longitudinal ligaments), emphasizing the cervical spine's delicate balance between mobility and stability (6–8).

### Clinical Presentation of WAD

The Quebec Task Force defines WAD as injuries arising from acceleration-deceleration forces transferred to the neck, typically from MVCs or other traumas. Clinical symptoms can vary widely, including neck stiffness, muscle spasm, paresthesia, headaches, cognitive issues (e.g., brain fog, memory problems), psychological distress, dizziness, and even gastrointestinal symptoms (1,9). Acute whiplash often presents with sudden neck pain, arm pain, and neck stiffness, which may arise immediately or days after the incident. Chronic WAD, affecting 40% of those with MVC-related injuries, is defined by persistent symptoms lasting over three months, with 2-4.5% experiencing permanent disability.

Markers for delayed recovery include age, gender (higher risk in females), pre-existing neck pain, legal involvement, lower educational attainment, and lower back pain. Chronic WAD often coexists with mood disorders, depression, and anxiety. Central sensitization and dorsal horn neuron sensitization may occur, causing hyperalgesia beyond the initial injury site. This imbalance in pain modulation underscores the complexity of WAD-related chronic pain and disability (10–13).

WAD classification ranges from Grade 0 (no symptoms) to Grade IV (fracture or dislocation), per the Quebec Task Force guidelines. Grades I-III involve increasing severity of symptoms, from neck pain and tenderness (Grade I) to neurological deficits (Grade III). (14–18).

### Pathophysiology of WAD

Cervical ligament laxity, caused by acute macrotrauma or chronic microtrauma (e.g., poor posture, repetitive movements), leads to instability and excess motion in cervical segments. This instability triggers muscle spasms, chronic myofascial pain, and nerve entrapment, eventually resulting in degeneration of cervical structures and discs. Genetic predispositions (e.g., Marfan's syndrome, Ehlers-Danlos disease) and autoimmune conditions like rheumatoid arthritis can further exacerbate instability. Cranial nerves IX, X, XI, XII run immediately anterior to the C0-1-2 zygapophyseal joints, so entrapment of these may explain symptoms like GI disturbances, swallowing difficulties and tongue deviation observed in severe cases. The altered CSF flow has been shown in WAD patients and may also contribute to the clinical picture.

Rear-end collisions, even at low speeds, pose significant risk, as the neck hyperextends and recoils forward during impact. Factors like low-neck rest car seats and female gender, particularly women with thinner necks, heighten susceptibility. Research indicates that 60% of WAD-related pain originates from zygapophysial facet joints, predominantly at C2-3 and C5-6 (12).

### Diagnosis of Whiplash Injury

The diagnosis of WAD depends on a thorough clinical evaluation, history taking, and imaging. Symptoms may be delayed, emerging hours to weeks after trauma, and can include neck pain, headache, muscle tightness, cognitive issues, and neurological deficits. Psychological factors, such as depression and anxiety, often complicate diagnosis and recovery. Conventional imaging (e.g., X-rays, MRIs) may appear normal in acute Grade I-III WAD, but flexion-extension films and

dynamic imaging techniques like Dynamic Motion X-ray (DMX) can reveal instability by capturing neck movements. Flexion-extension X-rays may show increased displacement (>3.5 mm or 20% translation) or angulation, suggesting ligamentous insufficiency (19–25).

#### Treatment Options for Whiplash-Associated Disorders

WAD treatment is challenging due to the interplay of physical, psychosocial, and legal factors, and there is also a significant gap in research data for WAD grade I-III. These patients often circulate and utilize healthcare extensively looking for appropriate diagnosis and treatment. Initial management often involves conservative measures, such as maintaining activity, exercise, analgesics, and short-term opioids. Physical therapy and other treatments like Pilates, Feldenkrais, traction, massage, manual therapies, cervical manipulations, kinesio taping may offer relief, but evidence remains insufficient for these (26,27).

#### Minimally Invasive Treatment Approaches

Invasive options include corticosteroid injections, trigger point injections, selective nerve root blocks, and radiofrequency neurotomy targeting medial branch nerves for zygapophyseal joint denervation. Relief from these treatments typically lasts 8-12 months, though efficacy may diminish with repeated procedures (15,28–30). Ultrasound-guided cervical medial branch blocks (CMBB) are gaining popularity for their benefits (e.g., soft tissue visualization, accessibility, ease of use, low cost), but fluoroscopy guidance remains the gold standard (31–43). Surgical interventions, such as spinal fusion or occipital nerve decompression, are reserved for severe, refractory cases (46–48).

#### Cryoanalgesia for Pain Management

Cryoablation is a percutaneous minimally invasive procedure, during which a cryoablation probe is placed onto target peripheral nerves and the myelin and axon is destroyed via Wallerian degeneration, preserving the nerve's structural integrity (endoneurium, perineurium and epineurium) allowing for eventual regeneration within 6-12 months. It has proven effective for conditions like neuralgias, joint denervations and phantom limb pain (49,50).

#### Orthobiologics in Pain Management

Orthobiologics, like PRP (Platelet-Rich Plasma) and prolotherapy rely on the inflammatory cascade to induce tissue healing similar to the body's natural processes and promotes collagen deposition and tissue regeneration. (34–58). Prolotherapy triggers the inflammatory cascade by injecting irritant solutions (e.g., hypertonic dextrose) to create a hyperosmolar environment causing cell disruption while PRP relies on concentrated platelet injections for healing and tissue regeneration. There is ample level 1 study supporting PRP and prolotherapy use for various conditions, however literature is scarce when it comes to treatment of cervical spine and craniocervical junction (44,45).

## 2. Objectives

This work aimed at describing and synthesizing various new minimally invasive treatment options developed and /or studied by the author for relieving pain and dysfunction associated with WAD:

1. Review retrospective data of prolotherapy for WAD related instability, headache and neck pain.
2. Review prospective data collection of PRP used to address WAD related instability, headache and neck pain, particularly for the craniocervical junction.
3. Describe new technique of cryoablation of the proximal greater occipital nerve.
4. Assess and compare the precision and safety of the commonly performed US-guided cervical medial branch injection techniques (as published by Finlayson and Eichenberger-Siegenthaler) using fresh cadavers.

## Study Design

Retrospective data analysis, prospective data analysis, technical description and cadaveric study

### 3. Methods

The treatment of ligamentous instability may be achieved with regenerative interventions that address underlying biomechanical dysfunction, yielding long-term pain relief and functional improvement. In cases where regenerative therapies are either not feasible or ineffective, alternative options like radiofrequency or cryodenervation may be utilized to manage persistent pain.

#### Regenerative Medicine - Prolotherapy

A retrospective analysis was conducted at the Center for Pain Relief, University of Washington, focusing on patients who underwent cervical prolotherapy for chronic headaches and neck pain unresponsive to conservative and standard interventional therapies. The review included 27 patients who had received a minimum of four prolotherapy sessions, utilizing hyperosmolar proliferative injections targeting cervical facet joints and accessory spinal ligaments. The follow-up period ranged from 4 to 14 months, with outcomes measured using a five-question questionnaire that assessed pain perception and functional improvements.

#### Regenerative Medicine - PRP Treatment

From 2018 to 2024, 502 PRP treatments were performed, including 56 cervical procedures aimed at reducing cervicogenic headaches and cervicalgia. Once online data collection became available in 2022 seven patients with trauma-induced WAD were treated and evaluated over an 18-month follow-up period, using the Neck Disability Index to track functional outcomes and VAS scores for pain assessment. PRP treatments targeted similar sites to prolotherapy, but included additional injections for the medial atlantoaxial joint, alar, apical, cruciate and anterior longitudinal ligaments in order to improve craniocervical junction stability.

#### Cryoablation for Greater Occipital Nerve entrapment and neuralgia

Cryoablation is used in patients whose WAD or cervicogenic headaches are dominated by GON entrapment. The author described the technique and performed 50 cryoablation procedures at

University of Washington from 2010 to 2016, confirming its safety through retrospective data analysis. Cryoneurolysis temporarily ablates peripheral nerves by applying cold temperatures between -70 and -80 Celcius, leading to Wallerian degeneration while preserving the nerve structure for eventual regeneration. Diagnostic blocks were performed beforehand to confirm treatment suitability and predict outcomes.

### Cryoablation Procedure

The procedure involved patient positioning in a prone state with maximum neck flexion for optimal GON visualization via ultrasound at the level of the inferior oblique capitis muscle. A small volume of local anesthetic was used for diagnostic blocks to confirm pain relief. Successful diagnostic results warranted cryoablation using two 2-minute freezing cycles at -70°C, performed under ultrasound guidance to ensure precise targeting and safety. Structures like the vertebral artery and spinal cord were carefully visualized to minimize risks.

### Ultrasound-Guided Cervical Medial Branch Blocks (CMBB)

The study compared three ultrasound-guided techniques for needle placement at the third occipital nerve (TON) and C3-C6 medial branches using cadavers. Experienced proceduralists conducted the placements, anteroposterior and lateral fluoroscopy images were saved and were later evaluated by independent experts for precision and safety. Accurate needle placement was determined by assessing location within specified zone on the articular pillar and ensuring no compromise to spinal or vascular structures.

### Approaches compared

Three ultrasound-guided needle placement approaches were examined:

1. **Approach #1 (ES):** This involved using a coronal plane ultrasound probe to visualize cervical articular pillars and inserting needles from anterior to posterior, out-of-plane technique.
2. **Approach #2 (Fi):** Using a transverse ultrasound probe in a slight caudal rotation, needles were placed from posterior to anterior, targeting specific levels (C3-C6 and TON), in-plane technique.

3. **Approach #3 (FiM):** This combined the Fi approach with adjustments based on coronal ultrasound visualization for added precision, in-plane needle placement, out of plane needle position verification.

### **Procedure Description**

Cadavers were positioned in a lateral decubitus for optimal imaging. Practitioners placed needles at the specified medial branches using each of the three approaches, resulting in 165 needle placements. No feedback was given during the procedures. Images of needle placement were independently reviewed by blinded evaluators for precision and safety using standard fluoroscopy views.

### **Evaluation Criteria**

Specific questions assessed included:

1. Whether the needle was at the correct level or missed entirely.
2. Needle position relative to joint line or articular pillar for TON and C3-C6.
3. Needle precision within a predefined "green zone," based on a 5 mm rhombus for accurate placement, as derived from previous studies.
4. Safety of needle placement, focusing on potential compromise of spinal contents, nerve roots, or the vertebral artery.

## **4. Results**

### **Prolotherapy Results**

Twenty-six patients with neck and/or headache pain received prolotherapy during the study. Twenty-four completed the follow-up questionnaire. On average, patients underwent 4.5 prolotherapy sessions (range: 4 to 8). The mean VAS (Visual Analog Scale) pain scores decreased significantly, from 6.5 to 2.9. Regarding functional improvement, 50% reported “a lot” of improvement, 42% reported “a little,” and 8% reported “no” improvement. Overall, 38% of patients reported more than 80% improvement, 21% experienced 50-79% improvement, 33% showed 25-50% improvement, and 8% reported less than 25% improvement.

An illustrative case featured a 62-year-old female patient who showed marked improvement across self-reported and exam-based outcomes by 18 months. ROM improved early, while pain and disability scores on the Oswestry Disability Index dropped from 52% to 22%. Depression, anxiety,



sleep, and quality-of-life metrics also improved significantly. All improvements were maintained for 18 months. The patient discontinued prescription medications and reduced pain-related healthcare utilization during the follow-up period.

### PRP Results

Seven patients undergoing PRP (Platelet-Rich Plasma) treatment for the cervical spine, including the medial C1-2 (PICL) procedure, reported an average 39-point improvement on the Neck Disability Index (NDI) and a 5.2-point reduction on VAS scores. Data from five patients followed for 12 months indicated sustained improvement beyond one year, while two patients showed sustained improvement at the three-month mark. Data collection is still ongoing.

A representative case involved a 33-year-old WAD patient who experienced an 80% pain reduction after the first PRP treatment and over 90% relief following the second. Her NDI score dropped from 72% to 4% two years post-treatment. She returned to full functionality, caring for her family and pursuing medical studies, with only occasional non-disabling headaches.

### Statistical Analysis

Given the small sample size, a nonparametric permutation test (5,000 iterations) was applied to create a Gaussian distribution. One-way ANOVA showed a significant reduction in neck disability scores over one year ( $F=5.0631$ ,  $p<0.01$ ). Posthoc Bonferroni correction indicated significant changes at one-year follow-up ( $p<0.0026$ , Effect size: 2.46). Similarly, VAS scores demonstrated a significant reduction ( $F=8.4902$ ,  $p<6e-04$ ), with substantial improvements at six months and one year ( $p<0.003799$  and  $p<0.0002$ , respectively).

### GON Cryoneurolysis Results

With the above-described technique, we have performed cryoneurolysis of the GON more than 50 times at University of Washington and further 6 in Hungary, treating both unilateral and bilateral occipital neuralgia. There have been no major complications. Minor complications were rare, consisting only of post-procedure soreness, which resolved spontaneously in 1 to 3 weeks. Slight

numbness was confirmed at the GON distribution are that also spontaneously decreased within 1-2 months.

### CMBB Injection Results

Five cadavers were used for third occipital nerve (TON), C3, C4, C5, and C6 cervical CMBB procedures, totaling 165 needle placements. Ten placements were excluded due to missing AP fluoroscopic views, leaving 155 for assessment. The cadaver characteristics were described using means, standard deviations, and percentages, and Fleiss' Kappa coefficient assessed interobserver agreement for needle placement. When disagreements occurred, the most frequent score was used. The methods were evaluated for correct needle placement on the target, placements within the green zone, dangerous placements, and missed levels using generalized linear mixed-effects regression.

### Interobserver Agreement and Precision

Interobserver agreement was high, with a Fleiss' Kappa value of 0.923. No significant differences were found among approaches (ES, Fi, FiM) in crude target placements (77.6% for ES, 79.5% for Fi, and 75.6% for FiM;  $P=0.911$ ). However, ES resulted in more placements within the center of the articular pillar (42.9%) compared to Fi (22.7%) and FiM (24.4%), with  $P=0.032$ .

### Potentially Dangerous Placements

Three potentially dangerous placements occurred with the ES approach, compromising the exiting nerve root and vertebral artery. None were reported with Fi and FiM, making ES significantly more dangerous (5.5% vs. 0%;  $P=0.042$ ).

### Target Level Missed

Missed levels occurred with similar frequencies across methods (ES: 10.9%, Fi: 12.0%, FiM: 10.0%), though differences were not statistically significant. Occasionally, operators misplaced needles caudad from the intended level due to reference errors, resulting in a potential total of 24.4%, 12.0%, and 10.0% missed levels for ES, Fi, and FiM, respectively.

## 5. Discussion

Whiplash-Associated Disorders (WAD) present a multifaceted challenge in diagnosis and treatment due to the wide range of symptoms they manifest. Cervical injury from WAD, as well as genetic predispositions and postural abnormalities, can lead to a host of issues, including headaches, neck and shoulder pain, cognitive impairment, visual disturbances and fatigue. This symptom constellation often complicates the diagnostic process, resulting in numerous medical consultations and increased healthcare expenditures. Recognizing that these symptoms often stem from cervical instability is crucial. Such instability can cause alterations in cervical alignment, leading to secondary myofascial pain and overloading of facet joints, disc degeneration, and in severe cases, nerve root or spinal cord compromise.

WAD that is resistant to conservative therapy poses a significant therapeutic challenge. Common interventions, including cervical medial branch blocks, third occipital nerve blocks, and greater occipital nerve blocks, tend to offer only short-term relief, typically lasting around three months. While steroid injections may provide initial pain reduction, their repeated use often results in diminishing returns and shorter relief periods. Moreover, steroids have shown no disease-modifying effects in non-autoimmune musculoskeletal conditions and may even exacerbate outcomes in the long run (72, 73). Moderate evidence supports radiofrequency neurotomy for WAD-related pain, though its effects are temporary. Other treatments, such as botulinum toxin injections and surgical options like cervical discectomy and fusion, lack consistent evidence to substantiate their efficacy. Among invasive treatments for chronic WAD, radiofrequency neurotomy is currently the most robustly supported intervention (48).

This study explored novel regenerative approaches, including prolotherapy and PRP for headaches and neckpain, cryoanalgesia for managing headaches associated with whiplash injuries. A review of minimally invasive treatment options for WAD was conducted, alongside a comparison of two ultrasound-guided medial branch injection techniques in terms of precision and safety.

#### Understanding WAD as a Biomechanical Condition

A key innovation in this thesis is the conceptualization of the cervical spine as a biomechanical unit, rather than an addition of separate pain generators. Flexion-extension injuries, especially those classified as WAD Grades 2 and 3, can result in cervical instability (or microinstability) due

to ligamentous and zygapophyseal capsular damage. This instability can lead to chronic muscle tightness, myofascial pain, nerve entrapment, and accelerated degeneration of the spine and shoulder joints. Routine emergency room evaluations and imaging often fail to detect these underlying instabilities, leaving patients with chronic symptoms and limited treatment options, despite extensive use of healthcare resources.

With this concept of the cervical spine being a biomechanical unit, craniocervical instability can be diagnosed and treated using regenerative medicine. The present study highlighted 24 cases of WAD-associated cervicogenic headache treated successfully with prolotherapy. These patients, who were unresponsive to standard treatments, experienced significant symptom relief through regenerative therapy, with sustained long-term benefits.

#### Prolotherapy for Chronic WAD

Prolotherapy became a routine treatment option at the University of Washington for cervicalgia and cervicogenic headaches that did not respond to conventional therapies, such as facet joint steroid injections, medial branch blocks, and radiofrequency denervation. Over a seven-year period, more than 200 cases were treated with prolotherapy at the UW Center for Pain Relief. A 2014 retrospective review assessed 24 patients, with 59% reporting greater than 50% pain improvement. The online data collection tool (PainTracker) (63) became available later. In this thesis a single representative case was discussed beyond the above data. This case demonstrated significant long-term improvements in all outcome measures, like pain intensity, mood, quality of life, sleep and daily functioning. Fluoroscopy-guided P2G prolotherapy injections targeted specific cervical structures, providing lasting relief that was otherwise unattainable through conventional treatments. Importantly, patients reported no further use of healthcare services during the follow-up period, highlighting the potential of prolotherapy as a sustainable treatment for chronic WAD.

#### PRP for Cervical Spine Treatment

Platelet-Rich Plasma (PRP) therapy offers another regenerative approach, operating on similar principles to prolotherapy but using concentrated platelet injections to stimulate tissue repair and healing. Seven WAD patients treated with cervical PRP at the craniocervical junction and cervical spine experienced significant improvements, with NDI scores dropping from an average of 64.7%

to 25.7%. A notable case involved a female patient who returned to full functionality after years of failed treatments. PRP injections targeted cervical facets, ligaments, and craniocervical junctions, emphasizing the need for accurate identification of treatable causes before assigning psychological diagnoses.

Regenerative medicine, encompassing prolotherapy, PRP, and stem cell injections, is supported by an expanding body of literature. By 2024, over 17600 peer-reviewed publications, including 1150 randomized controlled trials and 959 systematic reviews, had been documented on platelet rich plasma (75). The majority of high-quality clinical evidence for prolotherapy comes from studies of peripheral joint disorders including knee OA prolotherapy (1–4) and tendinopathies including lateral epicondylitis (5) showing improved pain, function and patient satisfaction. A recently published systematic review of 14 randomized controlled trials, one case control and 18 case series showed dextrose prolotherapy to have benefits in tendinopathies, knee and finger joint OA, and spinal/pelvic pain due to ligament dysfunction (6). Similarly, for PRP the most studies with highest quality have been assessing PRP use for knee OA and tennis elbow, probably owing to its high prevalence and relatively low risk in treatment. PRP provides good, sustained improved function and pain reduction for knee OA as demonstrated by multiple RCTs and metanalysis and systematic reviews of the available literature (7–9). Furthermore, a wealth of compelling evidence supports the application of LR-PRP injection in addressing lateral epicondylitis and LP-PRP for managing knee osteoarthritis. There is also substantial and reliable evidence indicating the effectiveness of LR-PRP injection in treating patellar tendinopathy, as well as the use of PRP injection for alleviating symptoms of plantar fasciitis.

Evidence supporting prolotherapy or PRP for neck and cervical pain remains limited to case series and case reports describing non validated self-reported outcomes. One study followed 98 patients with unresolved neck pain treated with 15% dextrose and 0.2% lidocaine for 18 months, reporting that 89% of patients experienced over 50% pain relief, 72% discontinued pain medications and 97% with increased quality of life (10). Another study followed 147 patients with chronic cervical, thoracic or lumbar pain and joint laxity demonstrated on stress test – given weekly injections of dextrose 20% for up to 3 weeks. Results showed 90% of patients with symptom and functional improvement, 76% with improved ability to work and 82% with decreased medication use (11). Hooper treated patients with intraarticular prolotherapy by placing 0.5 – 1mL of 20% in

a retrospective case series of 18 patients and shown similar improvements in pain, function, ROM and overall satisfaction (12). Finally, Centeno demonstrated a reduction in cervical flexion and extension translation and VAS after facet joint intraarticular prolotherapy injection (13). A recent study showed no difference at 6 month treatment between steroid and PRP in the cervical facet joint (14), however they admittedly used low platelet count, which is already known to have lesser to no effects (15). 44 people underwent cervical facet PRP injections in the prospective case series by Smith et al and demonstrated significant (>50%) and sustained improvement in NDI and VAS (16). Sustained relief is crucial, as the life span of these patients does not differ from normal populations, and previous treatments like steroids had no long-term benefit. Repeated steroid use provides shorter and shorter pain relief, yet the obvious side effects cumulate.

These minimally invasive injections stimulate the body's natural healing mechanisms, improving joint stability and reducing pain. Prolotherapy typically involves injecting a dextrose solution (15% dextrose with 0.25% lidocaine) into ligaments, tendons, and joint spaces. Treatment intervals vary from two weeks to six weeks, with a minimum of three sessions recommended. PRP, prepared with centrifugation, often requires fewer sessions for comparable results.

The mechanism of action for prolotherapy is thought to involve an inflammatory response triggered by cell injury and hyperosmolar volume expansion, leading to tissue regeneration and improved stability. PRP enhances healing by delivering growth factors, including vascular endothelial growth factor, fibroblast growth factor, and platelet-derived growth factor, which modulate the pericellular environment and again, promote tissue repair (81).

#### Cryoanalgesia for Greater Occipital Neuralgia (GON)

In cases where regenerative treatments are unsuitable, cryodenervation after a positive diagnostic block can reduce pain and improve function. Conditions such as headache, occipital neuralgia—often stemming from trauma or degenerative conditions related microinstability of the spine leading to myofascial pain and nerve entrapment—are common in WAD. Minimally invasive treatments include steroid injections, radiofrequency ablation show varied success. Gille et al. found success with GON neurolysis. Classical approaches, such as injections near the nuchal ridge with large volumes, are less target-specific, and have reduced diagnostic benefit. Also the entrapment site is proximal, as the GON pierces through the cervical musculature. Greher et al.'s

proximal ultrasound-guided method between C1 and C2 offers precise needle placement and selective diagnostic blocking. This technique captures most nerve branches before splitting, improving effectiveness. We described a new proximal cryoneuroablation method, that similarly offers better visualization of the GON compared to distal approaches, while targeting it proximal from the entrapment sites.

### Cervical Medial Branch Blocks (CMBB)

Cervical medial branch injections (CMBB) are used to treat headaches, neck, and shoulder pain, with precise needle placement crucial for effectiveness and safety due to the cervical spine's complex anatomy. Two significant groups have contributed to CMBB approaches: the European Eichenberger-Siegenthaler (ES) and the Canadian Finlayson (Fi) groups, but the techniques have not been compared or assessed for safety. The ES technique, initially tested on 14 healthy volunteers, demonstrated 90% accuracy and shortened radiofrequency procedure times with sonographic localization. Subsequent studies by Siegenthaler achieved a 77% needle placement accuracy (in the centroid of the articular pillar) for healthy volunteers, though limitations included a young and less arthritic population, potentially affecting generalizability.

Finlayson introduced a posterior-to-anterior in-plane approach to target C3-C7 medial branches and TON, achieving high placement success rates in his studies. The technique's effectiveness in achieving adequate contrast spread was demonstrated, although variability in precise needle positioning, especially at C5 and C6, was noted due to degenerative changes. The development of the biplanar (FiM) technique was later developed and abandoned. A serious limitation of these articles is that the procedures were performed by only one proceduralist, Finlayson, who is an expert in cervical spine procedures, so his results may not be reproducible by broader pain physician populations.

### Safety Considerations

The cervical spine contains vital structures, and any needle misplacement can lead to severe outcomes, including stroke or spinal cord damage. ES proved more dangerous, with three cases of nerve root and vertebral artery compromise, while Fi and FiM had no such instances. ES's anterior-posterior trajectory risked targeting the neuroforamen and spinal canal, especially with challenging

patient anatomy like higher BMI or arthritis. Conversely, Fi's posterior-to-anterior approach offers a safer trajectory with no critical structures in the needle path.

### Precision and Technique Comparisons

Precision of needle placement was assessed by crude and precise targeting. All three approaches demonstrated similar success rates for crude targeting (placing the needle onto the articular pillar), but ES showed a higher percentage of needles placed in the centroid of the articular pillar. However, anatomical variability of the medial branches may reduce the relevance of such precise targeting. Fi's approach, though slightly more challenging to learn, offered safer needle placement with better in-plane visualization, making it suitable for radiofrequency procedures. FiM, despite combining elements of ES and Fi, did not consistently improve precision, reflecting challenges in maintaining accurate needle positioning.

In conclusion, while the ES technique offers strong visualization cues, its safety risks make it less favorable compared to Fi, which balances precision and safety. Understanding the detailed cervical anatomy and refining needle placement techniques are critical for minimizing risks and optimizing outcomes in CMBB procedures (34, 36, 37).

### Strengths and Limitations of the Study

The study reviewed WAD and discussed a new potential paradigm to understand whiplash associated complex symptomatology. This understanding may open new therapeutic approaches to WAD and chronic cervicogenic headaches. Peripheral nerve ablation is well established, and the study added a novel ablative technique to the literature to aid GON cryoablation. Regenerative approaches are well established for various chronic pain indications, however there is only limited low quality evidence to support its use in WAD. This work is the first to describe the use of orthobiologics in the craniocervical junction and is the first to provide long term data collection.

Main weakness is the heterogeneity of the treatment approaches, small patient number, inconsistent data collection. The study design and the limited number of study participants prevents the study authors to establish causality of the presenting complaints and generalize the study results for the entire population.



## Key findings

- Regenerative medicine may provide a solution to treatment resistant WAD, cervicogenic headache.
- Regenerative medicine may improve stability of the cervical spine by improving biomechanics.
- Injection of the median C1-2 joint has been safely performed and led to clinical improvements in severe WAD (novel technique).
- Cryoablation of the GON at the level of the IOCM appears safe with precise ultrasonographic guidance (novel technique).
- Cryoablation of the GON improves treatment resistant cervicogenic headaches, occipital neuralgia.
- Medial branch block performed according to Eichenberger-Siegenthaler are potentially more dangerous than that described by Finlayson, as danger zones (vertebral artery and exiting nerve root) are in the needle trajectory with the first approach. They seem equal in their precision in getting the local anesthetic spread to the appropriate site.

## 6. Conclusion

Whiplash associated disorders, and related headache and neck pain create a pathophysiologic and diagnostic challenge, which also lead to a therapeutic challenge. Here we discussed the biomechanics of WAD and some new therapeutic options.

Regenerative medicine (PRP, prolotherapy) treatment options may address the underlying instability and therefore provide long-term solutions as shown in our retrospective review and prospective data collection.

In cases where regenerative medicine may not be available cryoablation of the GON decreases occipital headaches and is safely performed at the level of the IOCM.

The use of PRP and hypertonic dextrose at the craniocervical junction, the GON cryoablation at the proximal location posterior to the IOCM was first reported in the literature.

Cervical procedures are dangerous, high-risk procedures even in experienced hands, and they may compromise patient safety if anatomy is challenging because of, for example, advanced arthrosis. The currently taught and practiced CMBB methods both in-plane and out-of-plane (ES, Fi, and FiM) should yield a similarly successful block. However, the ES approach seems more helpful in placing the needle precisely on the centroid of the articular pillar, but it also leads to a greater number of dangerously placed needle tips. The 3 approaches are equally inadequate in identifying cervical vertebral levels, so the aid of fluoroscopy is still recommended to prevent those errors.

Further high-quality studies, randomized controlled trials are needed to establish these procedures, prove their safety and benefit to WAD.

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