

Intrafascicular Injection: Can AI, Ultrasound, Pressure Monitoring, and Echogenic Needles Prevent It?

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Abstract

Intrafascicular injection represents one of the most serious complications in regional anaesthesia, potentially resulting in irreversible neurological injury. Despite the advances in ultrasound-guided techniques, inadvertent intraneural and intrafascicular injections still occur. This review synthesizes the current understanding of nerve microanatomy, mechanisms of nerve injury, and the diagnostic and preventive strategies aimed at avoiding this catastrophic event. It highlights the role of ultrasound technology, echogenic needle innovations, injection pressure monitoring, neurostimulation, and emerging applications of artificial intelligence in enhancing procedural safety. The integration of these multimodal safety tools can significantly reduce operator dependency and improve real-time feedback during nerve block procedures. With continued technological refinement, structured training, and incorporation of AI-assisted imaging and robotics, the risk of intrafascicular injection can be minimized, thereby improving patient safety and outcomes in regional anaesthesia.

Keywords: Intrafascicular injection, Regional anaesthesia safety, Ultrasound guidance, Echogenic needles, Pressure monitoring, Artificial intelligence.

Introduction

Last three decades have seen a renaissance in the field of regional anaesthesia (RA), as a result of better understanding of anatomy related to nerve blocks, and availability of good resolution ultrasound (US) machines. All this has led to an increase in the number of RA procedures worldwide. Every technique in the field of medicine carries risks of complications and field of RA is not different. Intrafascicular injection, type of intraneural injection represents one of the most serious complications in RA [1], occurring when local anaesthetic (LA) is inadvertently deposited within nerve fascicles rather than in the intended perineural space. This devastating complication, involving direct drug deposition within the fascicles of peripheral nerves, can result in immediate, severe pain followed by

potentially permanent neurological deficits that may include sensory loss, motor weakness, and in extreme cases, complete limb dysfunction [2]. The clinical significance of this issue extends far beyond individual patient outcomes, encompassing medicolegal implications, healthcare costs, and the fundamental practice of RA techniques worldwide. The objective of this review article is to examine the existing literature on intraneural injections and synthesize current advancements and identify effective strategies that enhance the safety and precision of RA procedures.

Anatomy of Nerve

Understanding the aetiopathogenesis of intrafascicular injection begins with appreciating the delicate architecture of peripheral nerves [3]. The peripheral

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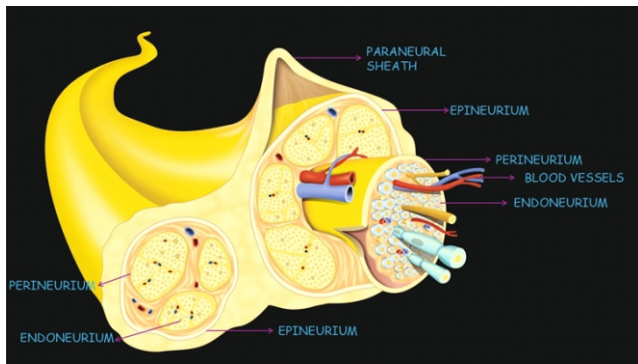


Figure 1: Structure of Nerve

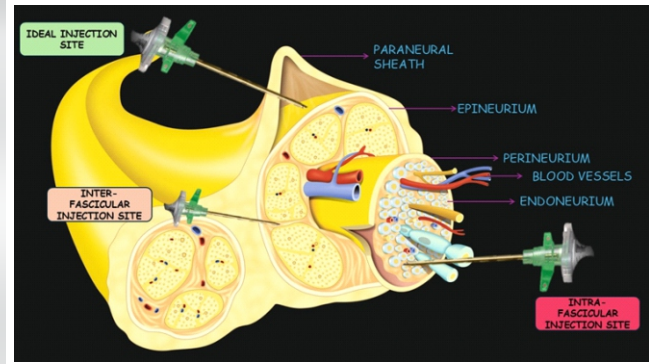


Figure 2: Injection Sites

nervous system comprises neurons bundled together in a carefully organized manner, with each nerve fibre surrounded by connective tissue layers [4]. The epineurium forms the outermost protective sheath, containing blood vessels and loose connective tissue. Beneath this lies the perineurium, a dense connective tissue layer that encircles fascicles – collections of individual nerve fibers. Within each fascicle lies the endoneurium, the delicate connective tissue surrounding individual nerve axons along with their associated schwann cells and blood supply (Fig. 1).

Classification of Intraneural Injections

In order for a successful RA block, the right drug has to be deposited at the right place. The right place in RA literature has been termed as the sweet spot of the nerve [5]. The sweet spot of the nerve is the space between epineurium-the outermost layer of the nerve and the paraneurium or circumneurium the mixed connective tissue layer which encircles the nerve outside the epineurium [6]. Breach in the

epineurium is called as intraneural injection [7]. If the needle tip lies in between fascicles it is termed as intraneural-extrafascicular injection (Table 1). If the needle tip lies inside the fascicles it is termed as intraneural-intrafascicular injection (Fig.2).

Pathophysiology of Nerve Injury from Intrafascicular Injection

The nerve injury resulting from intrafascicular injection arises through a multifactorial cascade involving mechanical, chemical, inflammatory, and vascular mechanisms [8]. Recognition of these interrelated processes is fundamental to both prevention and timely clinical intervention. Mechanical injury is initiated immediately upon deposition of injectate within the fascicular compartment, which has limited compliance [1]. Even small injection volumes can markedly increase intrafascicular pressure. Pressures exceeding 30–40 mmHg consistently produce conduction block, whereas pressures between 15–30 mmHg cause partial conduction impairment. The resulting compression compromises both axons and intrafascicular microvasculature, precipitating ischemia and conduction failure [9].

Chemical toxicity constitutes the second major component. LA deposited intrafascicularly achieve concentrations far beyond therapeutic levels. Within this restricted space, they diffuse directly into axonal membranes, disrupting ionic gradients and impairing sodium channel function. At supratherapeutic concentrations, additional cytotoxic mechanisms emerge, including mitochondrial dysfunction within 30–60 minutes, disruption of axonal transport, and direct Schwann cell injury, all of which hinder neuronal survival and regenerative capacity [10-12].

Parameter	Intraneural – Extrafascicular (Interfascicular)	Intraneural – Intrafascicular
Needle tip position	Within the epineurium but outside fascicles (between fascicles)	Inside a fascicle, breaching the perineurium
Injectate location	Interfascicular connective tissue	Endoneurial compartment surrounding axons
Tissue compliance	Relatively compliant → lower injection pressure	Non-compliant → markedly elevated injection pressure
Ultrasound features	Slight nerve swelling; preserved fascicular pattern	Marked focal swelling; loss of fascicular definition
Clinical symptoms	Usually painless, normal / fast block onset and normal or prolonged duration	Often painful (“electric shock”), rapid dense block, possible persistent deficit
Pathophysiology	Mechanical compression	Mechanical + chemical + ischemic + inflammatory injury
Likelihood of permanent nerve injury	Very low (reversible)	High (may cause irreversible axonal damage)
Typical pressure threshold	< 15 PSI	> 15 PSI (unsafe)
Recommended action	Stop injection immediately, withdraw and reposition needle	Stop injection immediately, withdraw and reposition needle

Table 1: Classification of Intraneural Injections

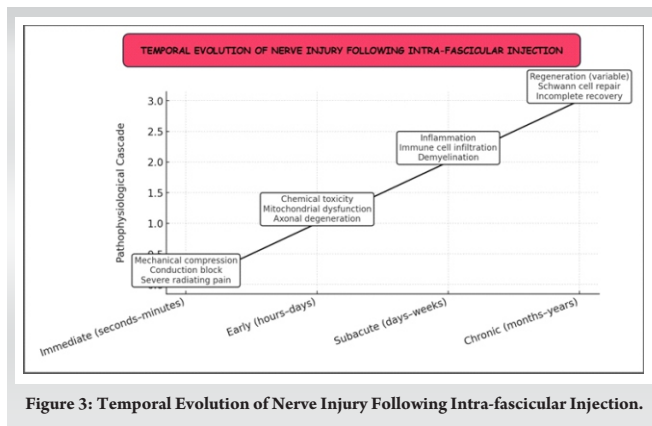


Figure 3: Temporal Evolution of Nerve Injury Following Intra-fascicular Injection.

Inflammatory responses further exacerbate tissue damage. Exposure to LA agents stimulates the release of pro-inflammatory mediators from resident macrophages and endothelial cells. Tissue factor expression activates the coagulation cascade, aggravating vascular compromise. Infiltration of neutrophils and macrophages over ensuing hours to days amplifies the inflammatory milieu, promoting demyelination and extension of the injury zone [13, 14].

Vascular compromise is an especially critical determinant of irreversible damage. Peripheral nerves depend on a delicate intraneural vascular network formed by longitudinal arterial plexuses and capillary beds. Intrafascicular injection produces both direct compression of these vessels and potential pharmacological vasoconstriction, particularly when vasoconstrictors such as epinephrine are present. The combined effect of elevated compartmental pressure and reduced perfusion culminates in ischemia, thereby compounding the chemical and inflammatory injury mechanisms [15, 16].

The temporal evolution of intrafascicular injury progresses in distinct, overlapping phases (Fig. 3). In the immediate phase (seconds to minutes), conduction block occurs due to abrupt mechanical compression, often accompanied by severe pain or “electric shock-like” sensations. In the early phase (hours to days), chemical toxicity drives axonal membrane disruption, mitochondrial dysfunction, and wallerian degeneration. The subacute phase (days to weeks) is dominated by inflammation and demyelination. Finally, in the chronic phase (months to years), regeneration—when possible—is mediated by surviving schwann cells, although recovery remains incomplete and highly variable depending on the extent of the initial injury [17, 18].

Recognition of Intraneural Injections

The modern debate about the safety of intraneural injections began with the landmark work of Bigeleisen (2006), who observed that apparent intraneural injections during ultrasound-guided axillary blocks did not invariably result in neurological injury [40]. This provocative finding

challenged the traditional belief that any penetration of the nerve would inevitably cause damage and prompted further exploration of intraneural anatomy and injection mechanics. Subsequent experimental and clinical studies, however, clarified that not all intraneural injections are equivalent—while extrafascicular (interfascicular) spread may sometimes occur without immediate neurological sequelae, true intrafascicular injection remains highly injurious and must be strictly avoided) [2, 4, 29]. Importantly, deliberate intraneural injection—regardless of fascicular involvement—should never be considered acceptable clinical practice. Intraneural injections can be identified using a combination of clinical signs, ultrasound imaging, neurostimulation response, echogenic needle feedback, and increasingly, artificial intelligence (AI)–assisted interpretation. The emphasis must remain on prevention through multimodal vigilance rather than post hoc recognition.

Clinical Symptoms of Intraneural Injections

Clinical symptoms in an awake patient include pain, paraesthesia in the distribution of nerve territory stimulated. However, in patients under general anaesthesia or sedation, these may go unrecognised. Patients who have had intraneural injections have a faster onset of sensory and motor block and block duration may be similar to perineural injections or prolonged [19].

Role of Ultrasound

US has revolutionised the practice of RA and it has become an eye for the anaesthesiologist. Current US technology enables the anaesthesiologist to identify needle tip in real time depending on the operator skills [8]. US signs of intraneural injection include visualisation of needle tip inside the nerve, expansion of nerve diameter on accidental injection of LA [20]. 0.5 ml is the minimum volume which can be recognised with US guidance [21, 22]. The effectiveness of US guidance depends heavily on operator skill and experience as the operator needs to align US beam, needle and target structure in line so as to have clear cut visualisation of needle tip. Even experienced practitioners face limitations including image quality, needle visibility, and the challenge of distinguishing between perineural and intraneural injection in real-time [21]. The current US technology can recognise an intraneural injection but cannot distinguish whether the needle tip is intra fascicular or extra fascicular [23]. Overall incidence of unintentional intraneural injections with use of US technology ranges between 16-17% and is not associated with postoperative neurological symptoms [24, 25].

While US-guided techniques have greatly enhanced the

safety of peripheral nerve blocks by enabling real-time visualization of needle trajectory and LA distribution, further progress is still needed. Emerging high-resolution US technologies, such as 40 MHz systems, offer anatomical detail with resolutions as fine as 75 micrometres. These systems can accurately localize the needle tip, whether positioned within or outside the fascicles; however, they remain largely experimental and limited to research settings [4]. Complementary advancements such as compound imaging, harmonic imaging, and speckle reduction further enhance tissue–needle contrast. Integrating these improvements with echogenic needle designs, injection pressure monitoring, and artificial intelligence–based image analysis may ultimately provide multimodal, operator-independent safety in regional anaesthesia.

Role of Echogenic Needles

Use of traditional stainless-steel needles with US technology leads to reflection of US waves primarily at the proximal shaft while the needle tip may remain poorly visualized, creating potential scenarios for undetected intraneural placement. Echogenic needle technology addresses fundamental limitations in US-guided needle visualization, particularly when needles approach neural structures at angles that reduce the acoustic reflection creating needle visibility. Modern echogenic needle innovations employ multiple strategies to enhance US visibility, primarily through surface modifications such as micro-grooving, roughening, or the incorporation of reflective materials within the coating, which increase acoustic reflection back to the transducer regardless of needle angle [26, 27]. Enhanced visualization allows more accurate needle–nerve alignment and may reduce the risk of inadvertent intraneural injection [28].

Evidence from preclinical (animal, cadaveric, and bench) studies has consistently shown the optical and acoustic superiority of echogenic needles over conventional ones. Hovgesen et al. [26] in a systematic review demonstrated that micro-textured or coated needles produced higher echogenicity and tip detectability across diverse experimental setups. Cadaveric models [29] illustrated that intraperineural but not endoneural spread could occur even with deliberate intraneural injections, emphasizing the importance of anatomic barriers. Nakagawa et al. [28] demonstrated improved tip visibility with echogenic needles at steeper insertion angles in phantom models. High-resolution US studies demonstrate that standard 22-gauge needles (0.7 mm diameter) are approximately three times larger than average nerve fascicles. Fascicular bundles tend to deflect away from approaching needles, making direct puncture technically difficult but not impossible [29]. However, in proximal locations at the level of roots in

interscalene area, fascicles are large, and nerve injury is possible with standard 22-gauge needle [2]. Clinical and volunteer studies corroborate these findings. Hebard and Hocking [27] reported superior visibility of echogenic designs compared to standard needles in clinical settings. Collectively, these studies support that echogenic technology enhances real-time ultrasound visualization, facilitating precise needle placement adjacent to neural structures and potentially lowering—but not eliminating—the risk of inadvertent intraneural injection.

Role of Injection Pressure Monitoring Devices

Numerous studies and expert reviews have confirmed that subjective tactile feedback—simply feeling whether you’ve entered a nerve—is an unreliable indicator [23]. This makes the practice inherently error-prone and potentially dangerous. Injection pressure monitoring represents a complementary approach to visual confirmation of needle placement, providing real-time physiological feedback about the site of injection [30]. The physiological rationale for injection pressure monitoring is based on the differing compliance characteristics of peri-neural tissues. Injection into perineural compartment containing loose connective tissue (relatively compliant) typically produces low opening pressures, whereas injection into the tightly constrained intrafascicular compartment generates substantially higher pressures due to limited tissue compliance [32]. Preclinical studies have provided foundational evidence for the diagnostic value of injection pressure monitoring. Vučković et al. [31] first demonstrated in a rat model that intraneural injection produced significantly higher opening pressures than extraneural injections, correlating with histological nerve injury. Similarly, Vermeylen et al. [32] performed fresh cadaveric limb experiments confirming that intraneural injections required markedly greater opening pressures compared to perineural ones. Clinical studies have translated these preclinical findings into practice. Gadsden et al. [30] evaluated opening pressure monitoring during ultrasound-guided interscalene blocks in patients and demonstrated that pressures exceeding 15 psi were consistently associated with needle–nerve contact. Paśnicki et al. [34] emphasized the importance of triple monitoring (ultrasound, pressure, and neurostimulation) to enhance procedural safety and reduce neural injury risk in clinical settings. For clinical translation, most investigators and professional guidelines describe injection pressure thresholds in pounds per square inch (PSI) with an opening pressure greater than 15 PSI generally considered unsafe and suggestive of potential intrafascicular needle placement [23]. Although elevated opening pressure should prompt immediate needle repositioning, clinical studies caution that pressure monitoring alone is

insufficiently reliable, and its diagnostic sensitivity and specificity for intrafascicular injection remain variable across studies [23]. Consequently, pressure monitoring is best employed as an adjunct alongside US guidance and peripheral nerve stimulation to enhance procedural safety rather than as a stand-alone safeguard [23].

Role of Neurostimulation

Peripheral nerve stimulation (PNS) has historically been one of the earliest adjuncts to improve the safety of RA. The principle is based on delivering low-intensity electrical currents through an insulated needle to elicit a motor response, thereby confirming proximity to the target nerve without direct intraneural placement. When combined with US, neurostimulation continues to offer complementary safety benefits by providing physiological confirmation of needle–nerve interaction. The absence of a motor response at currents ≤ 0.2 mA suggests that the needle tip is not in direct contact with a motor fascicle, whereas elicitation of a response at very low currents (< 0.2 mA) is strongly predictive of intraneural or intrafascicular needle tip location [23]. Experimental work by Steinfeldt et al. demonstrated that needle–nerve contact sufficient to generate a motor response was associated with histological evidence of axonal and perineurial trauma, reinforcing the utility of stimulation thresholds as a surrogate warning sign for possible intraneural penetration [17].

Clinical studies confirm that the presence of a motor response at low thresholds (e.g., 0.2–0.4 mA) should prompt immediate needle withdrawal and repositioning to avoid intrafascicular injection [33]. Conversely, absence of a motor response does not fully exclude intraneural placement, especially in patients with pre-existing neuropathies, diabetes, or under general anesthesia, highlighting the need to combine neurostimulation with other modalities such as US and injection pressure monitoring [23].

Recent consensus statements emphasize that neurostimulation should not be abandoned in the era of US but rather integrated into a multimodal safety framework. Used alongside US visualization and pressure monitoring, neurostimulation provides a unique layer of functional, real-time feedback about needle–nerve interaction, thereby reducing the risk of catastrophic intraneural injection [23, 34].

Role of Artificial Intelligence

Artificial intelligence (AI) is emerging as a transformative adjunct in RA, particularly for the prevention of intraneural injections. The primary strength of AI lies in its ability to process and analyse large volumes of real-time US data,

thereby reducing the dependency on operator skill and minimizing human error [35]. Deep learning algorithms, increasingly adopted since 2016, have demonstrated high accuracy in nerve detection, with overlays and real-time feedback assisting even novice practitioners in distinguishing critical structures [36, 37]. Such augmentation not only reduces operator variability but also decreases the likelihood of needle misplacement, paraesthesia, and nerve injury [38]. Beyond image recognition, AI-powered decision support systems integrate multimodal patient data, offering real-time alerts when aberrant injection patterns or resistance profiles suggest a high probability of intraneural spread [39]. Furthermore, AI-enabled robotic systems and closed-loop platforms are being explored for controlled needle trajectory and automated drug delivery, adding an additional safety layer. Early clinical evaluations of assistive AI for US-guided nerve blocks report reductions in needle passes, procedure time, and complications [38]. While these developments are promising, AI-assisted evaluation for intraneural injections should be interpreted with caution. Current algorithms are largely experimental, trained on limited and often institution-specific image datasets that may not generalize across different ultrasound systems, needle designs, patient anatomies, or block sites. False negatives may lead to missed detection of intrafascicular injection, whereas false positives can trigger unnecessary needle repositioning. Furthermore, most models lack prospective multicentre validation and have not yet been subjected to regulatory scrutiny or safety outcome assessment. Therefore, AI should presently be regarded as a supportive adjunct—complementing, but not replacing—real-time ultrasound visualization, injection pressure monitoring, neurostimulation, and clinical judgment until robust external validation and standardization are achieved.

Conclusion

Prevention of intraneural injection in regional anaesthesia requires a multimodal safety strategy integrating real-time ultrasound guidance, echogenic needles, injection-pressure monitoring, neurostimulation, and emerging artificial intelligence (AI)–based tools. No single safeguard is adequate on its own; their combined and systematic use, supported by proper training, significantly enhances procedural safety and reduces complications. Structured education, credentialing, and quality assurance programs remain central to improving patient outcomes and practitioner confidence. Intraneural injection should continue to be regarded as an avoidable event, not an acceptable one. Ongoing research should focus on high-resolution ultrasound, smarter echogenic needle designs, AI-

assisted image interpretation, and robotic precision systems. With progressive innovation and evidence-based integration of these technologies, the risk of intrafascicular injury can be

minimized—bringing us closer to the goal of eliminating injection-related nerve injury in regional anaesthesia.

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