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REVIEW ARTICLE

Is there still a place for the use of nerve stimulation?

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Summary

The introduction of nerve stimulation as a method of nerve localization sparked a new beginning in regional anesthesia. It was an epochal development akin to the utilization of ultrasound in more recent times. Many experts now consider ultrasound-guided peripheral nerve blockade to be more efficient, less painful, and more successful than landmark and nerve stimulation techniques. However, inadvertent intraneural injection continues to occur despite the widespread use of ultrasound and nerve stimulation. Both of these technologies allow for only limited elucidation of needle position relative to the target nerve and are unable to reliably identify intraneural position of the needle. This article will review the role of nerve stimulation in modern regional anesthesia techniques in light of the introduction of ultrasound technology.

Introduction

Almost half a century ago, the portable transistorized nerve stimulator was first introduced by Greenblatt and Denson (1). A reduction in volume and dose of local anesthetic agents, a greatly increased percentage of successful blocks, and the ability to block nerves that are difficult to locate were listed among the benefits of this emerging technology. Its acceptance in clinical practice was not without resistance. Proponents of paresthesia-based regional anesthesia advocated that block failure occurred more frequently with nerve stimulation, perhaps best captured by Moore's dictum 'no paresthesia, no anesthesia' (2). Paresthesia techniques were associated with an increased risk of nerve trauma as reported by Gentili and Wargnier in their riposte 'no paresthesia, no dysasthenia' (3). Perhaps this interaction best encapsulates what all nerve localization techniques strive for, accurate localization leading to successful anesthesia without nerve damage.

Over the past decade, the advent of ultrasound guidance has been revolutionary. After years in the exclusive realm of the seasoned expert, regional anesthesia techniques are now performed by an increasing number of anesthesiologists in their daily practice. As a localization device, it has the potential to negate the limitations of landmark, paresthesia, and nerve stimulation techniques. Now for the first time, it is possible to visualize the anatomy of the neural target, nearby structures to be avoided, the needle trajectory, and spread of local anesthetic. This is of particular relevance for pediatric regional anesthesia, where the performance of blocks in anesthetized or heavily sedated patients precludes subjective feedback.

There has been a growing body of randomized, controlled trials over the past decade comparing ultrasound-guided regional anesthesia (UGRA) with other forms of nerve localization techniques. In particular, many investigators have attempted to demonstrate the superiority of UGRA over nerve stimulation (NS). In light of these developments, the role of electrical NS must be reassessed. In the following review, we question whether it has been superannuated by a safer and more effective technique.

A preponderance of evidence suggests that the pendulum of favor is swinging toward UGRA. This is provided by a heterogeneous collection of randomized controlled trials with modest numbers and disparate endpoints (4–7). In a meta-analysis of randomized controlled trials of UGRA compared with NS, Abrahams *et al.* (8) concluded that ultrasound-guided blocks were associated with higher success rates, shorter procedure

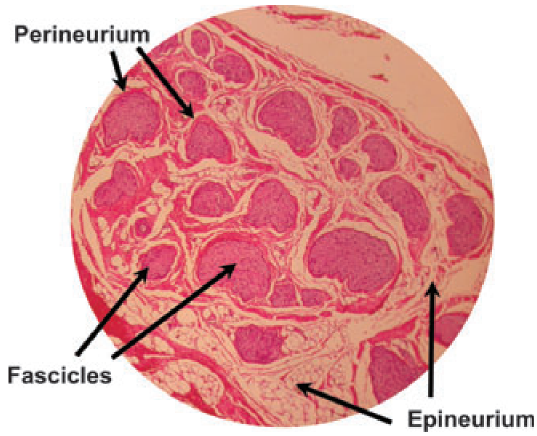

Figure 1 Histological detail from nerve cross section at × 25 magnification demonstrating fascicles with surrounding perineurium and epineurium.

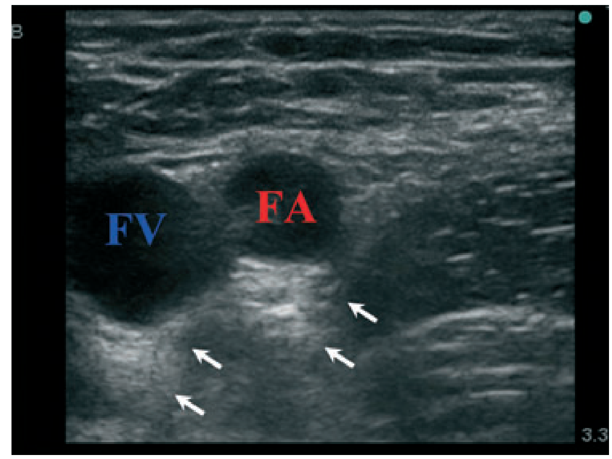

Figure 2 Ultrasound image of the structures in short axis as seen when performing a femoral nerve block. Ultrasound artifacts may lead to image interpretation error. For instance, an acoustic enhancement artifact of the tissue posterior to the blood vessels (arrows) may resemble nerve structures. FA, femoral artery; FV, femoral vein.

and onset times and longer block duration. Owing to the infrequent occurrence of complications associated with regional anesthesia, there was not enough evidence to confer any superiority of safety on UGRA over NS. This largely concurs with the American Society of Regional Anesthesia Evidence-Based Medicine Assessment that found UGRA to be superior or equal to NS in most studies and also found no evidence to suggest that UGRA reduces complications (9).

We intend to approach the current body of literature with two specific questions. Does NS confer any additional benefit when used in conjunction with UGRA, and can the use of NS be injurious to the patient?

The role of nerve stimulation for detecting intraneural injection

If the use of NS consistently leads to prolonged block times (5,6,10,11) and less successful outcomes (4,7,12–14), can we not justify its disavowal? This might be entirely appropriate if ultrasound imaging becomes an unfailing and dependable indicator of intraneural injection of local anesthetic. This phenomenon has traditionally been associated with the development of neurologic injury (15). The most recent large-scale audit of more than 7000 peripheral nerve blocks found an overall incidence of late neurologic deficit of 0.4 per 1000 nerve blocks, defined as persistence of symptoms for longer than 6 months after onset (16). This potentially catastrophic occurrence is such a rarity that it precludes statistical substantiation by comparative randomized controlled trials.

Nerve stimulation, and latterly, ultrasound guidance provide a margin of safety through elucidation of nerve–needle proximity. A number of recent studies suggest that intraneural injection of local anesthetic may occur with a greater frequency than previously thought, without inevitably leading to neurologic complications (17–20). Paradoxically, ultrasound imaging, while having enhanced our understanding of the needle–nerve relationship, has created ambivalence regarding the principles of NS. Robards *et al.* (17) investigated the frequency of intraneural needle placement using combined NS and ultrasound localization of the sciatic nerve at the popliteal fossa. A motor response was not obtained until the needle tip was advanced into an intraneural location in 20/24 patients (83.3%). The minimum stimulating current ranged from 0.35 to 1.2 mA. In 4/24 patients (16.7%), a stimulating current of 1.5 mA did not produce a motor response when the needle tip was located in the intraneural space. Intraneural injection occurred in all patients with a mean nerve expansion of 45 ± 14%. There were no reports of neurologic dysfunction after 48 h.

Bigeleisen *et al.* (18) revisited the relationship between minimum stimulating current and intraneural needle placement in a clinical investigation comparing intraneural and extraneural stimulation thresholds in ultrasound-guided supraclavicular block. Intraneural stimulation thresholds in excess of 0.2 and ≤0.5 mA were observed in 54% of patients. In 10% of patients, the stimulating threshold exceeded 0.5 mA when the needle was in an intraneural location. The minimum stimulating current was never 0.2 mA or less when the

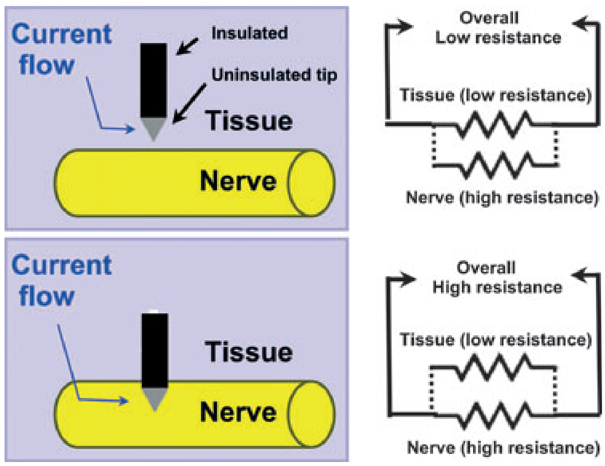

Figure 3 Schematic diagram of electrical impedance (EI) in the tissue (extraneural) and nerve (intraneural) compartments. (Left) Needle placement. (Right) Simplified equivalent circuit diagrams. The extraneural tissue, with low EI, provides a path through which most of the stimulating current will conduct. As the needle tip punctures the nerve, the low-resistance path is no longer available and a substantial increase in the EI of the circuit occurs. [Adapted from Tsui *et al.* (51)].

needle was placed extraneurally. This controverts conventionally held beliefs and suggests that a minimum stimulating current of 0.2 mA or less may be predictive of intraneural needle placement during supraclavicular brachial plexus block. However, a threshold current >0.2 mA does not preclude an intraneural location. There were no reports of neurologic deficit at 6 months.

A number of recent animal studies substantiate the insensitivity of NS as an indicator of needle–nerve proximity. In a porcine model of sciatic nerve blockade, Tsai *et al.* (21) demonstrated that with the needle tip in an intraneural position, the mean minimum stimulating current was 0.56 mA, while 12.5% of cases required a current intensity between 0.8 and 1.8 mA. A minimum stimulating threshold of <0.2 mA was obtained only when the needle was positioned intraneurally. Voelckel *et al.* (22) similarly demonstrated in a pig model that evidence of histologic nerve injury was present in 50% of nerves studied when the minimum stimulating current was 0.2 mA or less. No histologic changes were seen at a threshold current between 0.3 and 0.5 mA.

The distillation of human and animal studies into clinically useful guidelines suggests that NS has higher specificity than sensitivity for detecting intraneural needle placement. With an intraneural needle tip location, a high stimulating current may be required to generate a motor response. Current evidence suggests that a minimum stimulating current of 0.2 mA always signifies an intraneural position.

Ultrasonographic detection of intraneural injection

The eclipse of NS by ultrasound as a means of detecting intraneural injection is dependent upon current limitations of ultrasound technology in addition to the practitioner's skill in obtaining and interpreting an image. Most relevant studies have been performed by ultrasound experts, and generalization of results to less practiced physicians may be inappropriate. In the studies outlined earlier (17,18), ultrasonographic detection of nerve expansion upon injection required consensus between two independent expert sonographers. To this end, Altermatt *et al.* (23) demonstrated in a porcine model that ultrasonographic nerve expansion during injection was consistent with intraneural injection as confirmed by histologic analysis. Lupu *et al.* (24) demonstrated an association between ultrasonographically visible nerve expansion after injection of clinically relevant volumes and inflammatory changes of nerve injury in a pig model.

Recent cadaveric studies corroborate the described clinical findings regarding intraneural injection. The risk and extent of nerve injury after intentional intraneural needle placement were investigated by Sala-Blanch *et al.* (19). Impalement of a cryopreserved cadaveric sciatic nerve resulted in structural damage to only 3.2% of fascicles in the immediate vicinity of the needle trajectory. Peripheral nerves are composed of groups of fascicles surrounded by the epineurium which is comprised of collagen and adipose tissue. Each nerve fascicle is surrounded by the perineurium, a tough and mechanically resistant connective tissue sheath (Figure 1). This study suggests that the path of least resistance for an intraneurally placed needle may be through the more compliant adipose tissue of the interfascicular epineurium rather than through the fascicles.

The ratio of fasicular to epineurial tissue varies between 30% and 70% of the total nerve area (19), a relationship that deviates not only between different nerves but also within individual nerves. The ratio of neural to nonneural tissue in the sciatic nerve changes from 2 : 1 at mid-gluteal and subgluteal locations to 1 : 1 at mid-femoral and popliteal locations (25). The greater density of neural tissue in the proximal sciatic nerve may explain the almost twofold reported difference in the rate of neuropathy between proximal (0.41%) and distal sciatic nerve blockade (0.24%) (26).

The neural architecture of the brachial plexus was found to be similarly proportioned. The ratio of neural to nonneural tissue increased from 1 : 1 at interscalene and supraclavicular locations to 1 : 2 at an infraclavicular location (27).

While ultrasound guidance may permit a rudimentary assessment of nerve diameter as a surrogate of intraneural injection, the prohibitive resolution of available ultrasound technology precludes consistent differentiation between intrafascicular and extrafascicular injections. Intrafasicular injection with resultant axonal degeneration has been associated with functional nerve injury (15). A 15-MHz transducer, in the high end of most practitioner's armamentarium, only permits visualization of one-third of sciatic nerve fascicles as compared with light microscopy (28). There is also no evidence to suggest that NS is any better at detecting intrafascicular needle placement than ultrasound guidance. However, the two modalities may be complimentary and serve to compensate for their respective deficits.

Two recently published case studies in the adult literature illustrate the challenge associated with identification of intraneural injection during ultrasound-guided nerve block. Cohen and Gray (29) describe a profound transient sensory and motor deficit in the distribution of the fifth and sixth cervical nerve roots following an ultrasound-guided interscalene brachial plexus block for shoulder surgery. Although appearing uneventful during the procedure, a posthoc review of stored video images revealed an intraneural injection into a component of the brachial plexus. There was no neurologic deficit detectable 6 weeks after block placement. Reiss *et al.* (30) report on a severe brachial plexus injury following dual nerve stimulator and ultrasound-guided supraclavicular brachial plexus block. The minimum stimulating current in this instance was recorded as 0.4 mA, and ultrasound images were not recorded. A disabling motor deficit was still present at 8 months. Such case reports serve to remind us that ultrasound guidance, even in expert hands, does not prevent neurologic complications.

Mechanisms of nerve injury

In addition to mechanical injury, neurologic complications have been associated with direct local anesthetic toxicity and neural ischemia. Local anesthetics can produce a range of cytotoxic effects in cell culture at clinically relevant concentrations (31). These effects are greater as the concentrations increase. In an isolated sensory neuron model, Williams *et al.* (32) showed that neuronal viability was halved at 24 h after exposure to ropivacaine at 2.5 $mg{\cdot}ml^{-1}$ concentration. Direct neuronal toxicity has been associated more with intrathecal use compared with peripheral nerve blockade and appears to be related to the concentration of the agent, time of exposure, site of action, and the specific agent used (33). Neuronal ischemia has been induced *in vitro* by the presence of vasoconstricting agents, for example, epinephrine. In a rat sciatic nerve model, Myers and Heckman (34) demonstrated a reduction in neural blood flow of 77.8% with a solution of 2% lidocaine with 1 : 200 000 epinephrine. Even though these concerns are of a theoretic nature, a prudent choice of local anesthetic concentration with judicious use of vasoconstrictor additives may help minimize those complications that neither NS nor ultrasound can prevent.

Nerve stimulation for epidural anesthesia

Although there is general consensus regarding the safety of performing regional anesthesia in anesthetized children, there remains some inherent risk associated with performing blocks where there is minimal feedback pertaining to the warning signs of neural damage (35). This is particularly relevant for neuraxial blockade where the anatomic structures are tightly positioned leading to a reduced margin of safety for needle placement. The epidural space can be as narrow as 2 mm, and puncture depth to the subarachnoid and epidural space may be difficult to predict because of the large variation in body habitus in the pediatric population (36). The use of preprocedural or real-time ultrasound guidance appears promising in this regard. The mostly cartilaginous posterior vertebral column affords adequate beam penetration to view spinal structures, needle tip trajectory, and spread of fluid during injection. There is an increasing body of literature describing ultrasound-guided neuraxial techniques, but there is insufficient evidence to demonstrate any benefit based on relatively small studies (36).

Electrical stimulation may be used during epidural needle and catheter placement (37). It utilizes principles of electrophysiology similar to those of peripheral nerve blockade. The test has shown 80–100% positive prediction for epidural catheter placement and is effective for guidance to within two segmental levels. It allows detection of intrathecal, intravascular, or subdural catheter placement. The test may also be used during either single injection or continuous caudal anesthesia with cephalad catheter advancement (38).

Use of nerve stimulation for training of novices

Successful ultrasound-guided nerve blockade is predicated upon consistent, clear views of the entire needle, neural target with surrounding tissue, and circumferential spread of local anesthetic. In practice, while expertise in recognition and location of the relevant sonoanatomy may be acquired with time, haptic perception and consistent hand–eye coordination are more challenging skills to acquire. Indeed, failure to maintain needle tip visualization was the most common error observed in residents learning UGRA (39).

Concomitant use of NS may serve to increase the confidence of the learner at this early stage while lessening the anxiety of the attending preceptor. Other common sources of error during novice practice and beyond include failure to distinguish between adjacent isoechoic structures, for example, tendon and nerve, and failure to appreciate the nuances between acoustic artifact and nerve (40) (Figure 2). The use of a dual NS – ultrasound may improve block efficiency and efficacy while preventing injection of local anesthetic at a nonneural location. Finally, the experienced practitioner may benefit from the reassurance provided by NS when challenged with an obese patient where target neural structures may be difficult to identify with precision, particularly at a deep location.

Is the use of nerve stimulation injurious?

Over the past decade, there has been a profusion of randomized controlled trials comparing ultrasound with peripheral NS. These have largely demonstrated the superiority of ultrasound guidance using a variety of outcomes including block performance time (5,10,11,41), reduced volume of local anesthetic (13,42–44), and block efficacy (5,7,13,14).

Although there is no evidence that reduced doses of local anesthetic will decrease the incidence of systemic toxicity, it would still seem prudent to use the lowest possible dose (45). Ultrasound technology allows the provider to use these lower doses. Oberndorfer *et al.* (46) demonstrated a successful outcome with approximately two-thirds of a conventional volume of levobupivacaine for ultrasound-guided sciatic and femoral nerve blockade in children. Using highly accurate ultrasound-guided deposition of local anesthetic for adult interscalene brachial plexus blockade, McNaught *et al.* (43) report a minimum effective local anesthetic volume of 0.9 ml ropivacaine 0.5% compared with 5.4 ml in the nerve stimulator group.

Fewer studies compare a dual NS – ultrasound guidance approach with ultrasound guidance alone. Dingemans *et al.* found that the addition of NS to ultrasound guidance lengthened block performance time and reduced the success rate (47). Chan *et al.* (48) found no difference in the success rate of ultrasound-guided axillary brachial plexus blockade irrespective of the use of NS. However, a combined NS – ultrasound approach took significantly longer to perform than ultrasound alone. In a comparison of ultrasound vs ultrasound and NS for femoral nerve block, Sites *et al.* (49) found no difference in efficacy between the two approaches. Block performance time was longer, and more needle redirections were required when NS was also used. Gurkan *et al.* (6) demonstrated that block performance time was significantly shorter when ultrasound was used alone for a lateral sagittal infraclavicular nerve block compared with ultrasound and NS. However, success rates were identical regardless of the technique employed.

A longer block performance time may be required when NS is used with ultrasound guidance if anatomic and neurophysiologic endpoints are desired. However, it is possible that the procedure time may be shortened by using NS for the sole purpose of excluding intraneural needle placement rather than fastidiously seeking a nerve-specific motor response.

The role of impedance during nerve stimulation

The unpredictable response to electrical stimulation coupled with its low sensitivity for detecting intraneural needle placement has inspired renewed investigation into these incongruities. Electrical impedance is a calculated measurement that is accessible in commercially available nerve stimulators. It is highly sensitive to tissue composition and has been shown to vary greatly between tissues of different water content (50). The disparity between extraneural and intraneural impedance, resultant from the difference in physical composition of the tissue components was explored by Tsui *et al.* (51). A significant difference in electrical impedance measured between the extraneural and intraneural compartments was demonstrated in porcine sciatic nerve. This difference in electrical impedance may be explained by the variation in water and lipid content between the intraneural and extraneural space (Figure 3). The intraneural compartment contains much greater amounts of nonconducting lipid and lower water content (5–20% by weight) than the surrounding muscle (73–78% water by weight).

The highly variable response to NS as observed during UGRA may be explained in part by the significant difference between intraneural and extraneural tissue impedance at different sites along the same nerve. An inverse relationship between electrical impedance and current threshold has been reported for the median nerve (52). Stimulation of the median nerve in the axilla required significantly higher current thresholds than at the elbow. The lower impedance of muscle tissue in the axilla may have lead to a highly conductive tissue around the needle tip dispersing current away from the nerve. Higher current settings may be required when a stimulating needle is advanced through low-impedance muscle tissue. Conversely, lower current settings may be warranted for nerves located in high-impedance fat or connective tissue.

Conclusion

The introduction of ultrasound guidance is an epochal development in the evolution of regional anesthesia. It has advanced our understanding of the needle–nerve relationship and inspired further investigation into the incongruities thereby revealed. Ultrasound-guided peripheral nerve blockade is more efficient, less painful, and more successful than landmark and NS techniques. However, ultrasound guidance does not lessen the possibility of block-related nerve injury. Occasional calls for the dispatch of NS have come with alarming alacrity. Minimum stimulating threshold and electrical impedance may provide valuable information regarding the needle–nerve relationship. When combined with the superior nerve-locating qualities of ultrasound guidance, peripheral nerve blockade may be more prolonged but more successful and safer.

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Conflict of interest

No conflicts of interest declared.

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