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Topical Review Article: Nerve localization techniques for peripheral nerve block and possible future directions

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Abstract

Ultrasound guidance is now a standard nerve localization technique for peripheral nerve block (PNB). Ultrasonography allows simultaneous visualization of the target nerve, needle, local anesthetic injectate and surrounding anatomical structures. Accurate deposition of local anesthetic next to the nerve is essential to the success of the nerve block procedure. Unfortunately, due to limitations in the visibility of both needle tip and nerve surface, the precise relationship between needle tip and target nerve is unknown at the moment of injection. Importantly, nerve injury may result both from an inappropriately placed needle tip and inappropriately placed local anesthetic. The relationship between the block needle tip and target nerve is of paramount importance to the safe conduct of peripheral nerve block. This review summarizes the evolution of nerve localization in regional anesthesia, characterizes a problem faced by clinicians in performing ultrasound guided nerve block and explores the potential technological solutions to this problem.

Background

Peripheral nerve block (PNB) procedures involve the placement of a needle and local anesthetic next to target nerves. The success of PNB is determined principally by the location of the needle tip and the subsequent location of administered drug(s). 'Regional anesthesia always works—provided you put the right dose of the right drug in the right place'[1]. In determining the 'right place' to deposit local anesthetic, reliable nerve localization techniques are required which permit accurate and safe needle placement in the immediate vicinity of the peripheral nerve. Injection too far from the nerve risks block failure[2], injection within the nerve risks nerve injury[3].

Perioperative nerve injury may occur following anesthesia and surgery[4,5], with contemporaneous estimates of nerve injury following PNB of 4-6 per 10,000 blocks[6-8]. Although rare, iatrogenic nerve injury can result in permanent sensory and motor dysfunction with neuropathic pain. These devastating complications can have catastrophic physical, psychological, social and economic consequences for the injured party.

The peripheral nerve is a complex highly heterogeneous structure with variable micro anatomical architecture from root to terminal branch. Figure 1 illustrates the key components of a peripheral nerve. Nerve injury may occur via a number of mechanisms, some of which relate to the block procedure and others relate to the perioperative environment. Procedure-related nerve injury involves three interrelated mechanisms[9]. Firstly, if placed within the nerve, the block needle itself may cause direct trauma with disruption of nerve fascicles and intraneural blood vessels[10]. Even without direct fascicle or vessel injury, intraneural needle placement has been shown to cause inflammation within the nerve, with subsequent demyelination and impairment of nerve function[11,12]. Secondly, local anesthetic injection may cause harm. Injection of local anesthetic within a nerve may cause a spike in intraneural pressure, which can impair neural blood flow resulting in hypoxia and cell death (intraneural, extrafascicular injection)[13]. Should the needle tip pierce the perineurium, as little as 0.5 ml of injectate may be sufficient to rupture the fascicle (intraneural, intrafascicular injection)[14]. Finally, local anesthetic agents are known to be directly

neurotoxic via mechanisms which are as of yet poorly understood. Local anesthetic related neurotoxicity is known to be concentration dependent, with higher concentrations being more injurious[15,16]. Interestingly, observational models of intraneural needle placement and local anesthetic injection have demonstrated that not all intraneural injections result in clinically apparent nerve injury[17,18].

Although there is no universal consensus on the 'right place' to inject local anesthetic, it is intuitive that the avoidance of intraneural needle placement is desirable, and that this strategy might result in safer regional anesthesia. Innovative technologies are required to assist clinicians in avoidance of needle nerve contact and intraneural needle placement during the performance of PNB. The following paragraphs outline the evolution of nerve localization techniques used during PNB, describe the current limitations of these techniques in detecting accidental nerve puncture and investigate possible future directions for nerve localization.

The Evolution of Nerve Localization

The first reports of regional anesthesia appeared in the 1880s[19,20]. Nerve localization techniques were based upon anatomical landmarks and formal surgical dissection. Percutaneous techniques using hollow needles subsequently developed, relying on needle-to-nerve contact and paresthesia to confirm needle location at or within a target nerve. Proponents of this technique claimed high success rates without adverse sequelae, even suggesting that the absence of paresthesia was an indicator of likely failed block: 'No paresthesia, no anesthesia'[21]. By the mid-20th Century tactile cues of fascial clicks and pops became important with reports of successful block without deliberately seeking paresthesia[22]. Blind needle placement guided by clicks, pops and paresthesia are however poor markers of needle tip location and the presence of paresthesia infers needle to nerve contact (if not needle into nerve puncture). Neither paresthesia nor tactile feedback reliably defines the relationship between needle tip and target nerve during blind PNB techniques.

Electrical Nerve Stimulation

Stanley J. and L. Charlotte Sarnoff reported the use of prolonged peripheral nerve block for the treatment of hiccups in 1950[23]. In 1962 Greenblatt and Denson used a small portable transistorized nerve stimulator to perform PNB heralding the entry of electrical nerve stimulation (NS) into regional anesthesia[24]. By 1969 nerve stimulators for delivery of nerve block were readily available and in widespread use[25].

Nerve localization with NS requires an electrical circuit between a constant current generator, the block needle (the cathode) and the patient (the anode is a conductive electrode placed on the skin surface)[26,27]. Short electrical pulses result in nerve cell depolarization causing either paresthesia or muscle contraction[28]. According to Ohm's law (Equation 1), the current required to cause nerve depolarization is inversely proportional to the distance between needle and nerve[26]. This, it was thought, allowed indication of needle position relative to the nerve being stimulated.

$$Current\ (I) = \frac{Voltage\ (V)}{Resistance\ (R)}$$

Equation 1: Ohm's Law

Paresthesia or muscle contraction using a current of between 0.30 and 0.50 mA is taken to indicate the desired nerve location for drug administration[28]. Responses at stimulation currents of <0.2mA are thought to indicate intraneural needle placement. Recent data have questioned the validity of a simple interpretation of Ohm's law in living tissue. Significant inter-individual variation exists as to the minimum stimulation threshold of peripheral nerves[29]. Intraneural needle placement does not always lead to nerve stimulation[30]. Individual electrophysiological sensitivities, nerve structural diversity and varying properties of perineural tissues may account for these observations[31-33], each suggesting that NS is a somewhat insensitive tool in the detection of needle nerve contact[32,34,35].

Using a conceptual framework, based upon the physics of electricity, assumptions were made as to proximity relationship between the needle tip and the target nerve. Unfortunately the sensitivity of this technology in identifying needle nerve contact is poor.

Ultrasound Guidance

Ultrasonography permits visualization of block needle, target nerve(s) and local anesthetic injectate[36,37]. This allows accurate paraneural needle placement, which in turn facilitates rapid onset PNB and high block success rates using small volumes of local anesthetic[38]. Ultrasound (US), as a nerve localization technique, permits a detailed and person specific examination of the anatomy involved in PNB.

Medical US utilizes sound waves in the frequency range of 3 to 15 MHz. Nerve visualization requires the use of probes with the capability of producing US at 10-15MHz. Ultrasound at these frequencies provides excellent spatial resolution, allowing the discrimination of nerve architecture. The ultrasonographic appearance of nerves varies with anatomical location and the quantity of connective tissue within the nerve. Nerve roots are usually circular and have a bright hyperechoic surface a dark hypoechoic center (Fig. 2), while nerves further in the periphery (median nerve in the forearm) have a more honeycomb appearance (Fig. 3). Knowledge of the unique appearance of nerves at specific locations permits the anesthesiologist to readily identify and target the correct nerve(s) for specific procedures. Due to its watery consistency the injected local anesthetic behaves like a contrast medium enabling visualization of its distribution around the nerve[36]. A thorough understanding of how the US image is constructed is required to appropriately interpret images to guide needles during PNB. A description of the challenges in image interpretation and common image-related anomalies has been published[39,40].

Ultrasound Guidance versus Nerve Stimulation: Nerve Injury and Needle Nerve Contact

When compared with NS, US-guidance is superior from the perspective of success rates, onset times, number of needle passes and limiting local anesthetic dose[41-48]. It is not known whether this superiority translates into improved patient safety. The definition of what constitutes a nerve injury is somewhat

ambiguous, ranging from transient paresthesia lasting less than 12 hours to motor deficit extending beyond 48 hours. Multiple factors including patient co-morbidities, surgery type and duration and circumferential limb tourniquets make the interpretation of published literature on adverse outcomes following PNB difficult. Data comparing the frequency of complications during PNB performed with either US or NS is sparse[49].

International regional anesthesia registries collecting prospective outcome data have reported the frequency of transient nerve injury as 4-6 per 10,000 blocks[6-8,50,51]. The Dartmouth registry[51] provides some insight into the relationship between block location, dose and injury. More than half of the injuries reported arose following interscalene block, and high volume injectate (30ml) was used in all reported injuries. Fredrickson and Kilfoyle reported prospective data on neurological symptoms in 1000 patients following ultrasound guided peripheral nerve block (USGPNB) at10 days, 1 and 6 months. Neurological symptoms were identified in 8%, 4% and 0.6% at each time point respectively, although symptoms were minor and deemed to be unrelated to USGPNB[52]. Liu and colleagues, reported prospective data from patients undergoing shoulder surgery under USGPNB and identified 0.4% with neurological symptoms at 1 week post procedure[53]. Liu also identified the frequency of unintentional intraneural injection during USGPNB as 42/257 (17%) without reported postoperative neurological symptoms[54].

Detecting needle-to-nerve contact is problematic. Macfarlane, Bhatia and Brull examined several animal models for needle-to-nerve contact and intraneural injection. They concluded that neither NS nor US are sensitive enough to be reliable[32]. Vassiliou and co-workers studied whether combining US and NS achieved a higher rate of “close needle tip placements” than either modality alone, concluding better needle placement with the combined approach[55]. Steinfeldt explored the relationship between needle nerve contact and needle type[11,12]. Needle nerve contact, with or without nerve puncture, results in an inflammatory response which may contribute to impaired nerve function. In determining the relationship between intraneural needle placement, ultrasound and NS currents (0.2-0.5 mA), Robards at al concluded that the absence of a motor response to NS does not exclude intraneural needle position[56].

The American Society of Regional Anesthesia and Pain Medicine (ASRA) practice advisory on neurologic complications states: "No nerve localization or monitoring technique has been shown to be clearly superior in terms of reducing the frequency of clinical injury" because "There are no animal or human data to support the superiority of one nerve localization technique—paresthesia, nerve stimulation, ultrasound—over another with regards to reducing the likelihood of nerve injury"[57].

Summary

Nerve localization methods have evolved from blind needle placement using endpoints such as paresthesia, nerve stimulation and ultrasound-guidance. Nerve injury can occur when PNB needles, local anesthetic or both are placed within the substance of a peripheral nerve. The relationship between needle and nerve immediately prior to injection is therefore of critical importance. The following paragraphs discuss methods that may be used in the future to achieve more accurate information on needle tip location.

Future Directions for Nerve Localization Techniques and Extraneural Needle Placement

Inline Pressure Monitoring

The injection of solution into a non-distensible space will cause pressure within that space to rise. This might be appreciated by the operator as relative ease or difficulty with injection, and can be measured using the compressed air injection technique[58] and commercially available inline pressure manometers like B-smart (Concert Medical, Needham, MA). Compressed air techniques rely on subjective feedback from the syringe and are subject to significant inter-individual variability. The use of automated injection pressure monitoring might limit inter individual variability and improve the objectivity of this strategy to limit needle to nerve contact[59]. Hadzic et al. studied the relationship between injection pressure and neurological outcome of subgluteal sciatic block in an animal model. High injection pressures (> 20 psi) irrespective of needle tip location cause both clinically and histologically evident nerve injuries[14]. In humans undergoing interscalene block, Gadsden et al studied the relationship between opening injection

pressure and needle-to-nerve contact. In this study, high opening pressure (≥15 psi) consistently detected needle-to-nerve contact[60]. Thus the use of in-line pressure monitoring might alert the clinician to intraneural and intrafascicular needle placement, potentially preventing nerve injury. High opening pressure may be caused by factors other than intraneural needle placement - needle obstruction, tissue compression and injection into a tendon, not just needle to nerve contact. Such non-specificity might negatively influence operator behavior and impact block performance. Further clinical validation is required to define the true utility of this inline injectate manometry during PNB.

Advances in Ultrasound Imaging

Marhofer et al. published a two part review on "Fifteen years of ultrasound guidance in regional anesthesia". Part 1 of the review concluded "if experience in other technological fields is to be used as a yardstick of the pace of development, the next 15 years will see an exponential increase in the quality of both 2D images and 3D ultrasound images"[61]. In using conventional B-mode US, the clinician is provided with a narrow two dimensional representation of underlying anatomy. To guide a needle this 2-D image must be cognitively processed and appropriate visuospatial interpretations made. A three dimensional image might permit better nerve surface identification, and assist identification of appropriate needle path and endpoint. Real-time 3D US imaging (also known as 4D where 3D alone refers to static 3D images that can be collected and manipulated at a later stage[62]) has been used for: (1) continuous sciatic block at the popliteal fossa[63]; (2) axillary brachial plexus block; and (3) radial nerve block[64]. Future progression of 3D ultrasonography is likely to bring a wider image volume and thus more information to the clinician. The absolute advantage of this technology is the ability to manipulate imaging planes without moving the probe[65]. Although it is believed that 3D US imaging will further enhance the use of US for PNB procedures, this imaging modality requires a new image interpretation skill set. Currently clinicians learn two dimensional cross sectional anatomies as undergraduates. The application of anatomical representation using 2D US is somewhat intuitive. Three dimensional imaging in real-time is as of yet an unknown entity, as are the skills required to safely perform PNB using such a modality[61]. A recent

publication on 3D US imaging to evaluate local anesthetic spread and perineural catheter placement, suggests that the complexity of the technique coupled with an increased amount of information, could limit the practicality and cost effectiveness in daily clinical practice[66]. Further studies are required to determine the true role of 3D/4D US imaging in peripheral nerve block.

Multiplaner Magnetic & Robotic Needle Guidance

Magnetic needle guidance permits needle tracking and prediction of needle trajectory. Using a magnetic field and sensors on the needle and ultrasound probe, real-time overlay of needle trajectory and needle tip location on the 2D ultrasound image is achieved[67]. This technology may prove useful in assisting needle guidance from point A to point B, but it does not assist in determining the relationship between the needle tip and nerve. It is therefore not useful in either detecting or preventing needle to nerve contact.

Robotic devices have been developed to assist with the performance of complex skills during surgery. Robotic assistance in bench models of regional anesthesia has been reported in which robots advanced the needle toward a target[68,69]. This may prove useful limiting needling errors associated with PNB performance[70]. There are, however, no data to validate the use of robotics within the context of clinical PNB performance, and none to suggest better definition of needle nerve relationship.

Optical Reflectance Spectroscopy

Optical reflectance spectroscopy has been used to differentiate tissue types at needle tip. This technique uses optical fibers to carry visible and near-infrared light to the tissue in contact with the needle tip. Tissues absorb and reflect light differently depending on their composition. Sensing fibers in the device detect reflected and scattered light over a set spectrum of wavelengths. The quantity of light absorption and scatter by natural chromophores such as hemoglobin, water and lipids in a tissue at particular wavelengths is dependent on cell size and molecular structure. It is these characteristics that define the optical properties of a tissue[71]. After some calculation the absolute optical properties of tissues are quantified and subsequently absolute absorber concentrations can be determined i.e. concentration of

deoxygenated hemoglobin, oxygenated hemoglobin and water[72]. Based on the quantities of different chromophores in a specimen the tissue type can be identified. Differences in chromophore volume fractions are determined using diffusion reflectance spectroscopy[73].

Non-invasive detection of breast cancer using clinical optical tomography and near-infrared spectroscopy has been investigated[74]. Invasive applications of this technology include tissue diagnostics to allow disease states to be detected in vivo with a long term view to replace biopsies and histological analysis but more urgently to provide additional guidance in locating the optimum sites for biopsy [75]. Prostate[76] and ovarian[77] cancers have been identified by invasive use of optical reflectance spectroscopy. This technique has also provided stereotactic guidance during neurosurgery[78]. In 1985, a fiber optic needle stylet was used to identify biological fluids such as blood, bile, water, and the reflective intima of a blood or bile vessel at the needle tip allowing for its location to be known during percutaneous diagnostic and therapeutic procedures[79]. More recent studies have demonstrated the ability to identify transitions from subcutaneous fat to skeletal muscle and from the muscle to the nerve target region in vivo on swine and humans using optical impedance spectroscopy. The novel optical needle stylet has also identified vascular needle penetration which would prevent accidental intravascular anesthetic release during the USGPNB procedure[80]. Optical reflectance spectroscopy can differentiate tissue type and detect target nerves accurately. If integrated with USGPNB, procedural short comings, as characterized, might be eliminated and procedural safety improved[81,82].

Bioimpedance

All objects will impede electrical current to some degree. When AC is applied to biological material impedance is referred to as bioimpedance. The measurement of tissue bioimpedance could provide valuable information about both tissue type and physiological events of interest[83]. Several electrodes are used for impedance measurement: a small current is applied to one or more electrode while other electrodes pick up the resulting voltage. As the conductivity in biological materials is electrolytic and

based on Na^+ and Cl^- ions, changes in the content of liquid or the ion-concentration lead to changes in bioimpedance. Furthermore, cell membranes have low conductivity; hence the concentration of cells also influences bioimpedance[84,85]. The cell membrane separates two electrolytic systems i.e. intracellular fluid from extracellular fluid, which gives cells capacitor (energy storing) characteristics[83,86]. The resistive and capacitive components of biological tissues therefore are well described by the concept of complex impedance[87]. Cell size, orientation and membrane thickness also influence bioimpedance thus increasing its ability to discriminate between tissues[88].

Bioimpedance analysis has long been considered a potential tool for medical diagnostics in many different ways as it offers easy to apply techniques with low costs[89]. Current and potential medical applications for bioimpedance primarily exploit the principle that the content of liquid and the concentration of ions in the sample give different tissue types different and characteristic bioimpedances. Some tissues are very good conductors of electricity, while others are poor conductors. For example bone is a poor conductor with a typical resistivity of >40 Ω at 10 kHz while muscle is a relativity good conductor of electric charge demonstrating resistivity of 2-4 Ω at 10 kHz[90]. Bioimpedance, the inverse of conductance, can therefore be employed by the same token by measuring the tissue resistance under AC[90]. Investigations and current uses of this technology for medical diagnostics are divided into two categories: (1) invasive applications; and (2) non- invasive applications.

Non-invasive applications include Electrical Impedance Tomography (EIT), a form of real-time bedside imaging[90,91] which has been used in the diagnosis of breast cancer[92-94], epilepsy, acute stroke[91,95] and measurement of gastric emptying during continuous infusion of liquid feed[96-99]. EIT imaging is low cost and non-hazardous which permits its use for surveillance over protracted time intervals. Bioelectrical Impedance Analysis (BIA) allows measurement of human body composition mainly to estimate total body water and fat free mass in clinical settings[100,101]. Skin impedance is used to detect and to classify skin cancer[102-107] and to diagnose or analyze allergic reactions[108,109], diabetes mellitus[110], skin irritations[111,112] and skin moisture[113]. Impedance cardiography offers a continuous, non-invasive, operator-

independent method of monitoring cardiac output and stroke volume offering a potential tool in diagnosis, treatment and observation of patients[114,115].

Invasive applications of bioimpedance using needle-type probes may have more relevance to regional anesthesia than non-invasive applications. Many studies relating to invasive bioimpedance measurement suggest that the use of a bespoke probe/needle might aid tissue identification and potentially detect needle-to-nerve contact in regional anesthesia. This concept is been exploited for many medical applications to date. In 1969, impedance measurement was used for detection neural structures during percutaneous cordotomy. Penetration of spinal cord was confirmed by a rise in bioimpedance from that of the surrounding cerebrospinal fluid[116]. Kalvøy's group during several in vivo investigations determined the position of a needle within different kinds of tissue like muscle, liver, spleen, fat etc.[117] Various bioimpedance biopsy probes have been trialed for biopsies of brain tumors[118,119], pulmonary masses[120], prostate cancer[121,122] and renal biopsies[123]. In 2008 Tsui et al. evaluated the role of impedance measurement in an experimental model of USGPNB. They found a significant difference in bioimpedance between extraneural and intraneural tissue. Consequently the group postulated that bioimpedance measurement could be a useful warning signal to avoid intraneural injection in the future[124]. With this technology's ability to differentiate tissue type with a high degree of accuracy and resolution, the current procedural inability to objectively detect optimum needle tip location for PNB delivery may be resolved by using bioimpedance.

Conclusion

This review has summarized the major advances in PNB nerve localization techniques and how PNB has progressed from landmark based blind procedures to sighted guidance using ultrasound. As PNB techniques have evolved, so have the challenges facing regional anesthesiologists. A reliable method of characterizing the relationship between needle and target nerve immediately prior to injection during PNB is required. The integration of any such solution into PNB procedural skills must (1) solve the problem as

characterized; (2) lessen the cognitive burden of the anesthesiologist; (3) improve procedure related outcomes; and (4) not adversely affect patient outcome. To date, technology newly applied to PNB includes real time 3D imaging, multi-planar magnetic needle guidance and inline injection pressure monitoring. This review identified the relationship between needle tip and target nerve as a high priority deficit in PNB techniques, and postulates that optical reflectance spectroscopy and bioimpedance may hold the solution to accurately address this challenge. Until it is known how best define the relationship between needle and nerve at the moment of injection some common sense principles might be appropriate: (1) the desired location for local anesthetic solution is around the nerve and not in it (the paraneural space); (2) use a needle in-plane guidance technique; (3) only advance the needle when visible on ultrasound; (4) target the fascia at the periphery of the nerve, not the center of the nerve; (5) always aspirate the needle before injection; (6) inject small quantities of local anesthetic 0.5-1ml; (7) inspect the target nerve for signs of intraneural injection, and reposition to ensure injection outside the nerve; (8) do not persist to inject if there is resistance to injection; (8) maintain verbal contact with and seek feedback from the patient.

In conclusion, the novel application of existing and modifiable technology may assist physicians in overcoming the procedural limitations inherent within ultrasound guided peripheral nerve block. Characterization of these challenges and matching innovative technology may in time improve procedural safety and efficacy.

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Conflicts of Interest

The authors have no conflicts of interest

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Figure Legends

Figure 1: Nerve structure

Figure 2: Interscalene Brachial Plexus: ASM = Anterior Scalene Muscle; MSM = Middle Scalene Muscle; SCM = Sternocleidomastoid Muscle; C5 = fifth cervical nerve root in interscalene groove; C6 = sixth cervical nerve root in interscalene groove.

Figure 3: Median Nerve in the forearm: FDS = Flexor Digitorum Superficialis Muscles; FDP = Flexor Digitorum Profundus Muscles