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

References

1. Denny NM, Harrop-Griffiths W. Location, location, location! Ultrasound imaging in regional anaesthesia. Br J Anaesth 2005; 94: 1-3.
2. Albrecht E, Kirkham KR, Taffe P, Endersby RV, Chan VW, Tse C, Brull R. The maximum effective needle-to-nerve distance for ultrasound-guided interscalene block: An exploratory study. Reg Anesth Pain Med 2014; 39: 56-60.
3. Cohen JM, Gray AT. Functional deficits after intraneural injection during interscalene block. Reg Anesth Pain Med 2010; 35: 397-9.
4. Cheney FW, Domino KB, Caplan RA, Posner KL. Nerve injury associated with anesthesia - a closed claims analysis. Anesthesiology 1999; 90: 1062-69.
5. Kroll DA, Caplan RA, Posner K, Ward RJ, Cheney FW. Nerve injury associated with anesthesia. Anesthesiology 1990; 73: 202-07.
6. Auroy Y, Benhamou D, Bargues L, Ecoffey C, Falissard B, Mercier FJ, Bouaziz H, Samii K. Major complications of regional anesthesia in france: The sos regional anesthesia hotline service. Anesthesiology 2002; 97: 1274-80.
7. Orebaugh SL, Williams BA, Vallejo M, Kentor ML. Adverse outcomes associated with stimulator-based peripheral nerve blocks with versus without ultrasound visualization. Reg Anesth Pain Med 2009; 34: 251-5.
8. Barrington MJ, Watts SA, Gledhill SR, Thomas RD, Said SA, Snyder GL, Tay VS, Jamrozik K. Preliminary results of the australasian regional anaesthesia collaboration: A prospective audit of more than 7000 peripheral nerve and plexus blocks for neurologic and other complications. Reg Anesth Pain Med 2009; 34: 534-41.
9. Chambers WA. Peripheral-nerve damage and regional anesthesia. Br J Anaesth 1992; 69: 429-30.
10. Sala-Blanch X, Ribalta T, Rivas E, Carrera A, Gaspa A, Reina MA, Hadzic A. Structural injury to the human sciatic nerve after intraneural needle insertion. Reg Anesth Pain Med 2009; 34: 201-5.

11. Steinfeldt T, Poeschl S, Nimphius W, Graf J, Zoremba M, Mueller HH, Wulf H, Dette F. Forced needle advancement during needle-nerve contact in a porcine model: Histological outcome. Anesth Analg 2011; 113: 417-20.

12. Steinfeldt T, Werner T, Nimphius W, Wiesmann T, Kill C, Muller HH, Wulf H, Graf J. Histological analysis after peripheral nerve puncture with pencil-point or tuohy needletip. Anesth Analg 2011; 112: 465-70.

13. Kapur E, Vuckovic I, Dilberovic F, Zaciragic A, Cosovic E, Divanovic KA, Mornjakovic Z, Babic M, Borgeat A, Thys DM, Hadzic A. Neurologic and histologic outcome after intraneural injections of lidocaine in canine sciatic nerves. Acta Anaesthesiol Scand 2007; 51: 101-7.

14. Hadzic A, Dilberovic F, Shah S, Kulenovic A, Kapur E, Zaciragic A, Cosovic E, Vuckovic I, Divanovic KA, Mornjakovic Z, Thys DM, Santos AC. Combination of intraneural injection and high injection pressure leads to fascicular injury and neurologic deficits in dogs. Reg Anesth Pain Med 2004; 29: 417-23.

15. Hogan QH. Pathophysiology of peripheral nerve injury during regional anesthesia. Reg Anesth Pain Med 2008; 33: 435-41.

16. Selander D, Sjostrand J. Longitudinal spread of intraneurally injected local-anesthetics - experimental-study of initial neural distribution following intraneural injections. Acta Anaesthesiol Scand 1978; 22: 622-34.

17. Jeng CL, Rosenblatt MA. Intraneural injections and regional anesthesia: The known and the unknown. Minerva Anestesiol 2011; 77: 54-58.

18. Bigeleisen PE. Nerve puncture and apparent intraneural injection during ultrasound-guided axillary block does not invariably result in neurologic injury. Anesthesiology 2006; 105: 779-83.

19. Yentis SM, Vlassakov KV. Vassily von anrep, forgotten pioneer of regional anesthesia. Anesthesiology 1999; 90: 890-5.

20. Halsted WS. Practical comments on the use and abuse of cocaine; suggested by its invariably successful employment in more than a thousand minor surgical operations. The New York Medical Journal 1885; 42: 294-95.

21. Moore D. Supraclavicular approach for block of the brachial plexus. In: Moore D, ed. Regional anesthesia. Springfield, IL: Thomas, Charles C., 1953:221-42.

22. Burnham PJ. Regional block of the great nerves of the upper arm. Anesthesiology 1958; 19: 281-4.

23. Sarnoff SJ, Sarnoff LC. Prolonged peripheral nerve block by means of indwelling plastic catheter; treatment of hiccup; note on the electrical localization of peripheral nerve. Anesthesiology 1951; 12: 270-5.

24. Greenblatt GM, Denson JS. Needle nerve stimulatorlocator: Nerve blocks with a new instrument for locating nerves. Anesth Analg 1962; 41: 599-602.

25. Sardesai AM, Iyer U. Nerve stimulation for peripheral nerve blockade. In: Anaestologists WFoSo, ed. Anaesthesia Tutorial of the Week (149). 2009.

26. Urmey WF. Electrical stimulation and ultrasound in regional anesthesia. Eur J Pain Suppl 2010; 4: 319-22.

27. Urmey WF. Percutaneous electrode guidance of the block needle for peripheral or plexus neural blockade. Tech Reg Anesth Pain Manag 2002; 6: 145-49.

28. Tsui BCH. Electrical nerve stimulation. In: Chan VWS, Finucane BT, Grau T, Walji AH, eds. Atlas of ultrasound- and nerve stimulation-guided regional anesthesia. New York: Springer, 2007:12.

29. Chan VW, Brull R, McCartney CJ, Xu D, Abbas S, Shannon P. An ultrasonographic and histological study of intraneural injection and electrical stimulation in pigs. Anesth Analg 2007; 104: 1281-4.

30. Sinha SK, Abrams JH, Weller RS. Ultrasound-guided interscalene needle placement produces successful anesthesia regardless of motor stimulation above or below 0.5 ma. Anesth Analg 2007; 105: 848-52.

31. Gebhard R. Modalities of nerve block performance-is there a silver bullet?, in dual guidance-a multimodal approach to nerve location. In: Inc. BBM, ed. B Braun Melsungen AG. Bethlehem, Pennsylvania, 2008: 2-10.

32. Macfarlane AJ, Bhatia A, Brull R. Needle to nerve proximity: What do the animal studies tell us? Reg Anesth Pain Med 2011; 36: 290-302.

33. Ben-David B, Chelly JE. Current channeling: A theory of nerve stimulator failure. Anesth Analg 2003; 96: 1531-2.

34. Urmey WF, Stanton J. Inability to consistently elicit a motor response following sensory paresthesia during interscalene block administration. Anesthesiology 2002; 96: 552-54.

35. Choyce A, Chan VW, Middleton WJ, Knight PR, Peng P, McCartney CJ. What is the relationship between paresthesia and nerve stimulation for axillary brachial plexus block? Reg Anesth Pain Med 2001; 26: 100-4.

36. Marhofer P, Greher M, Kapral S. Ultrasound guidance in regional anaesthesia. Br J Anaesth 2005; 94: 7-17.

37. Kapral S, Marhofer P, Grau T. Ultrasound in local anaesthesia. Part i: Technical developments and background. Anaesthesist 2002; 51: 931-37.

38. McCartney CJ, Lin L, Shastri U. Evidence basis for the use of ultrasound for upper-extremity blocks. Reg Anesth Pain Med 2010; 35: S10-5.

39. Sites BD, Brull R, Chan VWS, Spence BC, Gallagher J, Beach ML, Sites VR, Hartman GS. Artifacts and pitfall errors associated with ultrasound-guided regional anesthesia. Part i: Understanding the basic principles of ultrasound physics and machine operations. Reg Anesth Pain Med 2007; 32: 412-18.

40. Sites BD, Brull R, Chan VW, Spence BC, Gallagher J, Beach ML, Sites VR, Abbas S, Hartman GS. Artifacts and pitfall errors associated with ultrasound-guided regional anesthesia. Part ii: A pictorial approach to understanding and avoidance. Reg Anesth Pain Med 2007; 32: 419-33.

41. Perlas A, Brull R, Chan VWS, McCartney CJL, Nuica A, Abbas S. Ultrasound guidance improves the success of sciatic nerve block at the popliteal fossa. Reg Anesth Pain Med 2008; 33: 259-65.

42. Chan VS, Perlas A, McCartney CL, Brull R, Xu D, Abbas S. Ultrasound guidance improves success rate of axillary brachial plexus block. Can J Anesth 2007; 54: 176-82.

43. Sites BD, Beach ML, Spence BC, Wiley CW, Shiffrin J, Hartman GS, Gallagher JD. Ultrasound guidance improves the success rate of a perivascular axillary plexus block. Acta Anaesthesiol Scand 2006; 50: 678-84.

44. Kapral S, Greher M, Huber G, Willschke H, Kettner S, Kdolsky R, Marhofer P. Ultrasonographic guidance improves the success rate of interscalene brachial plexus blockade. Reg Anesth Pain Med 2008; 33: 253-58.

45. Liu F-C, Liou J-T, Tsai Y-F, Li AH, Day Y-Y, Hui Y-L, Lui P-W. Efficacy of ultrasound-guided axillary brachial plexus block: A comparative study with nerve stimulator-guided method. Chang Gung Med J 2005; 28: 396-402.

46. Williams SR, Chouinard P, Arcand G, Harris P, Ruel M, Boudreault D, Girard F. Ultrasound guidance speeds execution and improves the quality of supraclavicular block. Anesth Analg 2003; 97: 1518-23.

47. Guerkan Y, Acar S, Solak M, Toker K. Comparison of nerve stimulation vs. Ultrasound-guided lateral sagittal infraclavicular block. Acta Anaesthesiol Scand 2008; 52: 851-55.

48. Taboada M, Rodriguez J, Amor M, Sabate S, Alvarez J, Cortes J, Atanassoff PG. Is ultrasound guidance superior to conventional nerve stimulation for coracoid infraclavicular brachial plexus block? Reg Anesth Pain Med 2009; 34: 357-60.

49. Hadzic A, Sala-Blanch X, Xu D. Ultrasound guidance may reduce but not eliminate complications of peripheral nerve blocks. Anesthesiology 2008; 108: 557-58.

50. Barrington MJ, Kluger R. Ultrasound guidance reduces the risk of local anesthetic systemic toxicity following peripheral nerve blockade. Reg Anesth Pain Med 2013; 38: 289-97.

51. Sites BD, Taenzer AH, Herrick MD, Gilloon C, Antonakakis J, Richins J, Beach ML. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: An analysis from a prospective clinical registry. Reg Anesth Pain Med 2012; 37: 478-82.

52. Fredrickson MJ, Kilfoyle DH. Neurological complication analysis of 1000 ultrasound guided peripheral nerve blocks for elective orthopaedic surgery: A prospective study. Anaesthesia 2009; 64: 836-44.

53. Liu SS, Gordon MA, Shaw PM, Wilfred S, Shetty T, Yadeau JT. A prospective clinical registry of ultrasound-guided regional anesthesia for ambulatory shoulder surgery. Anesth Analg 2010; 111: 617-23.

54. Liu SS, YaDeau JT, Shaw PM, Wilfred S, Shetty T, Gordon M. Incidence of unintentional intraneural injection and postoperative neurological complications with ultrasound-guided interscalene and supraclavicular nerve blocks. Anaesthesia 2011; 66: 168-74.

55. Vassiliou T, Eider J, Nimphius W, Wiesmann T, de Andres J, Muller HH, Wulf H, Steinfeldt T. Dual guidance improves needle tip placement for peripheral nerve blocks in a porcine model. Acta Anaesthesiol Scand 2012; 56: 1156-62.

56. Robards C, Hadzic A, Somasundaram L, Iwata T, Gadsden J, Xu D, Sala-Blanch X. Intraneural injection with low-current stimulation during popliteal sciatic nerve block. Anesth Analg 2009; 109: 673-7.

57. Neal JM, Bernards CM, Hadzic A, Hebl JR, Hogan QH, Horlocker TT, Lee LA, Rathmell JP, Sorenson EJ, Suresh S, Wedel DJ. Asra practice advisory on neurologic complications in regional anesthesia and pain medicine. Reg Anesth Pain Med 2008; 33: 404-15.

58. Tsui BC, Li LX, Pillay JJ. Compressed air injection technique to standardize block injection pressures. Can J Anaesth 2006; 53: 1098-102.

59. Claudio R, Hadzic A, Shih H, Vloka JD, Castro J, Koscielniak-Nielsen Z, Thys DM, Santos AC. Injection pressures by anesthesiologists during simulated peripheral nerve block. Reg Anesth Pain Med 2004; 29: 201-5.

60. Gadsden JC, Choi JJ, Lin E, Robinson A. Opening injection pressure consistently detects needle–nerve contact during ultrasound-guided interscalene brachial plexus block. Anesthesiology 2014; 120: 1246-53.

61. Marhofer P, Harrop-Griffiths W, Kettner SC, Kirchmair L. Fifteen years of ultrasound guidance in regional anaesthesia: Part 1. Br J Anaesth 2010; 104: 538-46.

62. French JLH, Raine-Fenning NJ, Hardman JG, Bedforth NM. Pitfalls of ultrasound guided vascular access: The use of three/four-dimensional ultrasound. Anaesthesia 2008; 63: 806-13.

63. Feinglass NG, Clendenen SR, Torp KD, Wang RD, Castello R, Greengrass RA. Real-time three-dimensional ultrasound for continuous popliteal blockade: A case report and image description. Anesth Analg 2007; 105: 272-74.

64. Foxall GL, Hardman JG, Bedforth NM. Three-dimensional, multiplanar, ultrasound-guided, radial nerve block. Reg Anesth Pain Med 2007; 32: 516-21.

65. Clendenen SR, Riutort K, Ladlie BL, Robards C, Franco CD, Greengrass RA. Real-time three-dimensional ultrasound-assisted axillary plexus block defines soft tissue planes. Anesth Analg 2009; 108: 1347-50.

66. Choquet O, Capdevila X. Three-dimensional high-resolution ultrasound-guided nerve blocks: A new panoramic vision of local anesthetic spread and perineural catheter tip location. Anesth Analg 2013; 116: 1176-81.

67. Tang R, Sawka A, Vaghadia H, Umbarje K. Sonixgps™ needle tracking system for out-of-plane brachial plexus block in human cadavers. Acta Anaesthesiol Scand 2013; 57: 398-99.

68. Tighe PJ, Badiyan SJ, Luria I, Boezaart AP, Parekattil S. Robot-assisted regional anesthesia: A simulated demonstration. Anesth Analg 2010; 111: 813-16.

69. Morse J, Terrasini N, Wehbe M, Philippona C, Zaouter C, Cyr S, Hemmerling TM. Comparison of success rates, learning curves, and inter-subject performance variability of robot-assisted and manual ultrasound-guided nerve block needle guidance in simulation. Br J Anaesth 2014; 112: 1092-7.

70. Sites BD, Spence BC, Gallagher JD, Wiley CW, Bertrand ML, Blike GT. Characterizing novice behavior associated with learning ultrasound-guided peripheral regional anesthesia. Reg Anesth Pain Med 2007; 32: 107-15.

71. Ting CK, Tsou MY, Chen PT, Chang KY, Mandell MS, Chan KH, Chang Y. A new technique to assist epidural needle placement: Fiberoptic-guided insertion using two wavelengths. Anesthesiology 2010; 112: 1128-35.

72. Doornbos RMP, Lang R, Aalders MC, Cross FW, Sterenborg HJCM. The determination of in vivo human tissue optical properties and absolute chromophore concentrations using spatially resolved steady-state diffuse reflectance spectroscopy. Phys Med Biol 1999; 44: 967.

73. Desjardins AE, Hendriks BHW, van der Voort M, Nachabé R, Bierhoff W, Braun G, Babic D, Rathmell JP, Holmin S, Söderman M, Holmström B. Epidural needle with embedded optical fibers for spectroscopic differentiation of tissue: Ex vivo feasibility study. Biomed Opt Express 2011; 2: 1452-61.

74. Colak SB, Van Der Mark MB, Hooft GWt, Hoogenraad JH, Van Der Linden ES, Kuijpers FA. Clinical optical tomography and nir spectroscopy for breast cancer detection. IEEE J Sel Top Quantum Electron 1999; 5: 1143-58.

75. Bigio IJ, Mourant JR. Ultraviolet and visible spectroscopies for tissue diagnostics: Fluorescence spectroscopy and elastic-scattering spectroscopy. Phys Med Biol 1997; 42: 803.

76. Sharma V, Kashyap D, Mathker A, Narvenkar S, Bensalah K, Kabbani W, Tuncel A, Cadeddu JA, Liu H. Optical reflectance spectroscopy for detection of human prostate cancer. Conf Proc IEEE Eng Med Biol Soc 2009; 2009: 118-21.

77. Utzinger U, Brewer M, Silva E, Gershenson D, Blast RC, Jr., Follen M, Richards-Kortum R. Reflectance spectroscopy for in vivo characterization of ovarian tissue. Lasers Surg Med 2001; 28: 56-66.

78. Giller CA, Liu H, German DC, Kashyap D, Dewey RB. A stereotactic near-infrared probe for localization during functional neurosurgical procedures: Further experience. J Neurosurg 2009; 110: 263-73.

79. Liese GJ, Pong W, Brandt DE. Fiber-optic stylet for needle tip localization. Appl Opt 1985; 24: 3125-26.

80. Balthasar A, Desjardins AE, van der Voort M, Lucassen GW, Roggeveen S, Wang K, Bierhoff W, Kessels AGH, Sommer M, van Kleef M. Optical detection of vascular penetration during nerve blocks: An in vivo human study. Reg Anesth Pain Med 2012; 37: 3-7.

81. Balthasar A, Desjardins AE, van der Voort M, Lucassen GW, Roggeveen S, Wang K, Bierhoff W, Kessels AG, van Kleef M, Sommer M. Optical detection of peripheral nerves: An in vivo human study. Reg Anesth Pain Med 2012; 37: 277-82.

82. Brynolf M, Sommer M, Desjardins AE, van der Voort M, Roggeveen S, Bierhoff W, Hendriks BH, Rathmell JP, Kessels AG, Soderman M, Holmstrom B. Optical detection of the brachial plexus for peripheral nerve blocks: An in vivo swine study. Reg Anesth Pain Med 2011; 36: 350-7.

83. Grimnes S, Martinsen ØG. Bioimpedance. Wiley encyclopedia of biomedical engineering. John Wiley & Sons, Inc., 2006.

84. Dean DA, Ramanathan T, Machado D, Sundararajan R. Electrical impedance spectroscopy study of biological tissues. J Electrostat 2008; 66: 165-77.

85. Miklavčič D, Pavšelj N, Hart FX. Electric properties of tissues. Wiley encyclopedia of biomedical engineering. John Wiley & Sons, Inc., 2006.

86. Gitter AH, Fromm M, Schulzke J-D. Impedance analysis for the determination of epithelial and subepithelial resistance in intestinal tissues. J Biochem Biophys Methods 1998; 37: 35-46.

87. Schwan HP. Linear and nonlinear electrode polarization and biological materials. Ann Biomed Eng 1992; 20: 269-88.

88. Bayford RH. Bioimpedance tomography (electrical impedance tomography). Annu Rev Biomed Eng 2006; 8: 63-91.

89. Riu PJ. Preface. Ann N Y Acad Sci 1999; 873: xi-xi.

90. Brown BH. Electrical impedance tomography (eit): A review. J Med Eng Technol 2003; 27: 97-108.

91. Holder DS. Electrical impedance tomography of brain function. Automation Congress, 2008 WAC 2008 World 2008: 1-6.

92. Zou Y, Guo Z. A review of electrical impedance techniques for breast cancer detection. Med Eng Phys 2003; 25: 79-90.

93. Hope T, Iles S. Technology review: The use of electrical impedance scanning in the detection of breast cancer. Breast Cancer Res 2003; 6: 1-6.

94. Stojadinovic A, Nissan A, Gallimidi Z, Lenington S, Logan W, Zuley M, Yeshaya A, Shimonov M, Melloul M, Fields S, Allweis T, Ginor R, Gur D, Shriver CD. Electrical impedance scanning for the early detection of breast cancer in young women: Preliminary results of a multicenter prospective clinical trial. J Clin Oncol 2005; 23: 2703-15.

95. Kun S, Ristic B, Peura RA, Dunn RM. Algorithm for tissue ischemia estimation based on electrical impedance spectroscopy. IEEE Trans Biomed Eng 2003; 50: 1352-9.

96. Baxter AJ, Mangnall YF, Loj EH, Brown B, Barber DC, Johnson AG, Read NW. Evaluation of applied potential tomography as a new non-invasive gastric secretion test. Gut 1988; 29: 1730-35.

97. Mangnall YF, Baxter AJ, Avill R, Bird NC, Brown BH, Barber DC, Seagar AD, Johnson AG, Read NW. Applied potential tomography: A new non-invasive technique for assessing gastric function. Clin Phys Physiol Meas 1987; 8 Suppl A: 119-29.

98. Avill R, Mangnall YF, Bird NC, Brown BH, Barber DC, Seagar AD, Johnson AG, Read NW. Applied potential tomography. A new noninvasive technique for measuring gastric emptying. Gastroenterology 1987; 92: 1019-26.

99. Soulsby CT, Khela M, Yazaki E, Evans DF, Hennessy E, Powell-Tuck J. Measurements of gastric emptying during continuous nasogastric infusion of liquid feed: Electric impedance tomography versus gamma scintigraphy. Clin Nutr 2006; 25: 671-80.

100. Lukaski HC. Requirements for clinical use of bioelectrical impedance analysis (bia). Ann N Y Acad Sci 1999; 873: 72-6.

101. Hoffer EC, Meador CK, Simpson DC. A relationship between whole body impedance and total body water volume*. Ann N Y Acad Sci 1970; 170: 452-61.

102. Dua R, Beetner DG, Stoecker WV, Wunsch DC, 2nd. Detection of basal cell carcinoma using electrical impedance and neural networks. IEEE Trans Biomed Eng 2004; 51: 66-71.

103. Emtestam L, Nicander I, Stenstrom M, Ollmar S. Electrical impedance of nodular basal cell carcinoma: A pilot study. Dermatology 1998; 197: 313-6.

104. Aberg P, Nicander I, Hansson J, Geladi P, Holmgren U, Ollmar S. Skin cancer identification using multifrequency electrical impedance--a potential screening tool. IEEE Trans Biomed Eng 2004; 51: 2097-102.

105. Aberg P, Geladi P, Nicander I, Hansson J, Holmgren U, Ollmar S. Non-invasive and microinvasive electrical impedance spectra of skin cancer - a comparison between two techniques. Skin Res Technol 2005; 11: 281-6.

106. Aberg P, Nicancer I, Ollmar S. Minimally invasive electrical impedance spectroscopy of skin exemplified by skin cancer assessments. Conf Proc IEEE Eng Med Biol Soc 2003; 4: 3211-14.

107. Beetner DG, Kapoor S, Manjunath S, Zhou X, Stoecker WV. Differentiation among basal cell carcinoma, benign lesions, and normal skin using electric impedance. IEEE Trans Biomed Eng 2003; 50: 1020-5.

108. Nyren M, Kuzmina N, Emtestam L. Electrical impedance as a potential tool to distinguish between allergic and irritant contact dermatitis. J Am Acad Dermatol 2003; 48: 394-400.

109. Nicander I, Ollmar S, Rozell BL, Emtestam L. Allergic contact reactions in the skin assessed by electrical impedance – a pilot study. Skin Res Technol 1997; 3: 121-25.

110. Lindholm-Sethson B, Han S, Ollmar S, Nicander I, Jonsson G, Lithner F, Bertheim U, Geladi P. Multivariate analysis of skin impedance data in long-term type 1 diabetic patients. Chemometr Intell Lab Syst 1998; 44: 381-94.

111. Nicander I, Åberg P, Ollmar S. The use of different concentrations of betaine as a reducing irritation agent in soaps monitored visually and non-invasively. Skin Res Technol 2003; 9: 43-49.

112. Nicander I, Rantanen I, Rozell BL, Söderling E, Ollmar S. The ability of betaine to reduce the irritating effects of detergents assessed visually, histologically and by bioengineering methods. Skin Res Technol 2003; 9: 50-58.

113. Blichmann CW, Serup J. Assessment of skin moisture. Measurement of electrical conductance, capacitance and transepidermal water loss. Acta Derm Venereol 1988; 68: 284-90.

114. Van De Water JM, Miller TW, Vogel RL, Mount BE, Dalton ML. Impedance cardiography: The next vital sign technology? Chest 2003; 123: 2028-33.

115. Fellahi JL, Caille V, Charron C, Deschamps-Berger PH, Vieillard-Baron A. Noninvasive assessment of cardiac index in healthy volunteers: A comparison between thoracic impedance cardiography and doppler echocardiography. Anesth Analg 2009; 108: 1553-9.

116. Gildenberg PL, Zanes C, Flitter M, Lin PM, Lautsch EV, Truex RC. Impedance measuring device for detection of penetration of the spinal cord in anterior percutaneous cervical cordotomy. Technical note. J Neurosurg 1969; 30: 87-92.

117. Kalvøy H, Frich L, Grimnes S, Martinsen ØG, Hol PK, Stubhaug A. Impedance-based tissue discrimination for needle guidance. Physiol Meas 2009; 30: 129.

118. Broggi G, Franzini A. Value of serial stereotactic biopsies and impedance monitoring in the treatment of deep brain tumours. J Neurol Neurosurg Psychiatry 1981; 44: 397-401.

119. Broggi G, Franzini A, Peluchetti D, Servello D. Treatment of deep brain abscesses by stereotactic implantation of an intracavitary device for evacuation and local application of antibiotics. Acta neurochir 1985; 76: 94-98.

120. Kimura S, Morimoto T, Uyama T, Monden Y, Kinouchi Y, Iritani T. Application of electrical impedance analysis for diagnosis of a pulmonary mass. Chest 1994; 105: 1679-82.

121. Lee BR, Roberts WW, Smith DG, Ko HW, Epstein JI, Lecksell K, Partin AW. Bioimpedance: Novel use of a minimally invasive technique for cancer localization in the intact prostate. Prostate 1999; 39: 213-8.

122. Halter RJ, Schned AR, Heaney JA, Hartov A. Passive bioelectrical properties for assessing high- and low-grade prostate adenocarcinoma. Prostate 2011; 71: 1759-67.

123. Hernandez DJ, Sinkov VA, Roberts WW, Allaf ME, Patriciu A, Jarrett TW, Kavoussi LR, Stoianovici D. Measurement of bio-impedance with a smart needle to confirm percutaneous kidney access. J Urol 2001; 166: 1520-3.

124. Tsui BC, Pillay JJ, Chu KT, Dillane D. Electrical impedance to distinguish intraneural from extraneural needle placement in porcine nerves during direct exposure and ultrasound guidance. Anesthesiology 2008; 109: 479-83.

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