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Electrical Impedance to Distinguish Intraneural from Extraneural Needle Placement in Porcine Nerves during Direct Exposure and Ultrasound Guidance

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Background: **Intraneural injection during peripheral nerve blockade can cause neurologic injury. Current approaches to prevent or detect intraneural injection lack reliability and consistency, or only signal intraneural injection upon the event. A change in electrical impedance (EI) could be indicative of intraneural needle placement before injection.**

Methods: **After animal care committee approval, eight pigs were anesthetized and kept spontaneously breathing. In four pigs (part 1), the sciatic nerves were exposed bilaterally for direct needle placement; in a further four pigs (part 2), the tissue was kept intact for ultrasound-guided needle placement. An insulated needle (Sprotte 24 gauge; Pajunk GmbH Medizintechnologie, Geisingen, Germany), attached to a nerve stimulator displaying EI (Braun Stimuplex HNS 12; B. Braun Medical, Bethlehem, PA), was placed extraneurally and then advanced to puncture the nerve sheath. Five punctures within approximately a 1-cm length of each nerve were performed. For each Part, overall EI at each compartment and EI after individual punctures were compared using a general linear model, with *post hoc* analysis using the Duncan multiple range test.**

Results: **The EI was lower extraneurally compared with intraneurally during open dissection (12.1 ± 1.8 *vs.* 23.2 ± 4.4 kΩ; $P < 0.0001$; n = 8) and when using ultrasound guidance (10.8 ± 2.9 *vs.* 18.2 ± 6.1 kΩ; $P < 0.0001$; n = 7 nerves were visualized adequately). The EI difference was maintained despite performing five sequential punctures.**

Conclusions: **With further study, EI could prove to be a quantifiable warning signal to alert clinicians to intraneural needle placement, preventing local anesthetic injection and subsequent nerve injury.**

OPTIMAL performance of peripheral nerve block techniques requires precise placement of needles and catheters immediately adjacent to but not within peripheral nerves. Intraneural injection during peripheral nerve blocks can be a cause of significant neurologic injury.[1–3] From animal studies, the nerve injury seems to be associated with a high injection pressure in the intrafascicular (subperineural) space, particularly with the introduction into this space of highly concentrated local anesthetic solutions.[2–6] Regardless of intraneural location or injection pressure, Borgeat's[7] reiteration in a recent editorial is apt: "the basic rule [that remains is] not to inject local anesthetics into the nerve."

Current approaches to prevent intraneural injection of local anesthetic occur during nerve localization and include patient reports of paresthesias, adherence to current threshold criteria (>0.4 mA) when using a nerve stimulation technique, and visualizing the needle tip in the near vicinity of the nerve using ultrasound. Injection into the intraneural compartment is sometimes but not always heralded by pain on injection and, potentially, by ultrasound visualization of local anesthetic within the nerve.[8–11] Subjective reports of paresthesia and the use of nerve stimulation parameters can at times be inconsistent and unreliable.[10,12–15] A minimal stimulating current that is normally considered indicative of a close needle-to-nerve proximity (0.43 mA) has been shown during ultrasound imaging to be associated with intraneural needle placement.[11] Consistent visualization of the needle tip is a prerequisite of ultrasound-guided regional anesthesia, but rather than preventing intraneural puncture, its use may lead to inadvertent intraneural injection if this principle is abandoned.[16] In addition, the potential for ultrasound visualization of local anesthetic injection into the intraneural compartment has the overriding limitation that, with current technology, intraneural injection has to occur to enable diagnosis. Because even small-volume injections of local anesthetic may cause damage (especially within areas devoid of substantial protective stroma such as nerve roots),[10] the search for a warning sign before such injection is crucial.

The use of electrical impedance (EI) to detect intraneural needle puncture in animals or humans has not been reported. Through a small conductive surface of an insulated needle tip, EI is highly sensitive to tissue composition and has been shown to vary greatly between structures with varying water content; *e.g.*, the impedance of white and gray matter is considerably higher as compared with cerebrospinal fluid.[17] This reliance on structural characteristic differences, contributing to conductivity patterns, has helped various investigators use high-frequency (KHz) stimulation to map various brain structures,[18,19] including tumors (high fluid content)[17] and to detect penetration of the spinal cord from the subarachnoid space.[20] The disparity between extraneural and intraneural impedance during low-frequency (1- to 2-Hz) stimulation at the needle tip, on the basis of differences in the physical composition of the tissue components, has not been explored to any extent in peripheral nerves. Nevertheless, a readily detectable

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variation in EI can be expected to exist between intraneural and extraneural tissues. EI could provide a quantifiable warning signal to alert clinicians to intraneural needle placement. The major advantage of this technique is that intraneural needle placement could be identified before injection, thus avoiding potential chemical and mechanical injury from injection.

Our hypothesis was that there is a detectable and significant difference in EI as measured at the needle tip between the extraneural and intraneural compartments. We studied EI during sciatic nerve punctures in an animal model, with the needle advanced both during direct vision and during ultrasound guidance, to confirm that such an EI difference does exist and is measurable. The dissected model was a necessary control because the use of ultrasound, being an indirect visualization aid, warranted the establishment of the premise during direct vision. Because nerves can potentially be punctured on multiple occasions, either in a single-block procedure or during the performance of rescue blocks, our secondary goal was to demonstrate that the EI values would remain stable after multiple nerve punctures.

Materials and Methods

After institutional animal care committee (Edmonton, Alberta, Canada) approval, a two-part study using direct (*i.e.*, dissection) and indirect visualization (*i.e.*, ultrasound) was conducted using a total of eight Duroc pigs (30–35 kg). The pigs were anesthetized with intravenous ketamine (5 mg/kg), maintained with isoflurane, and kept spontaneously breathing. Neuromuscular blocking drugs were not used during either study.

Part 1: Punctures during Direct Nerve Exposure

The sciatic nerves were exposed bilaterally (n = 8) in the subgluteal region. The nerves were then kept intact and moist with normal saline. An insulated needle (Sprotte 24 gauge; Pajunk GmbH Medizintechnologie, Geisingen, Germany) was attached to a nerve stimulator (set at 1 Hz, 0.1 ms, 0.5 mA) that measures and continually displays EI (Stimuplex HNS 12; B. Braun Medical, Bethlehem, PA). During direct vision, the needle was first placed immediately outside, and in contact with, the nerve (extraneural compartment). An independent observer recorded the EI and the motor response characteristics. The needle was then advanced by the investigator until the noninsulated portion of the needle tip was seen to enter the nerve (intraneural compartment), at which time the EI was again recorded. The investigator performing the nerve punctures was blinded to both the extraneural and intraneural EI measurements. Five punctures within a 1-cm length of each nerve were performed.

Part 2: Ultrasound-guided Nerve Punctures

The same needle type, nerve stimulator (set at 1 Hz, 0.5 mA), and approximate location of the sciatic nerve were used for part 2. The needle was advanced to a point in the interstitial (extraneural) tissue near the sciatic nerve during real-time ultrasound imaging (M-Turbo with HFL 38x 13-6 MHz linear array probe; SonoSite Inc., Bothell, WA) using in-plane needle alignment to a probe positioned to capture the longitudinal axis of the nerve. An independent observer recorded the EI and the motor response characteristics, although no further assessment of nerve stimulation parameters was undertaken. Ultrasonography was used to place the needle approximately 1–2 mm from the nerve, defining the initial extraneural location, and the first EI measurement was taken. The intraneural EI was recorded after the needle was directed to puncture the nerve during ultrasound guidance, and the extraneural EI was again recorded when the needle was subsequently advanced further to transect the nerve. Five punctures within a 1-cm length of each nerve were performed.

Statistical Analysis

For part 1 and part 2, the overall mean and SD of EI at each compartment were calculated. Impedance between intraneural and extraneural needle placement was compared using a general linear model (PROC GLM in SAS for Windows version 8.2; Cary, NC), in which impedance was the sole dependent variable, and individual nerve identity, location of needle tip (intraneural *vs.* extraneural), and sequential puncture number at each site were the independent variables. The sequential puncture number was a repeated-measures factor. No interaction terms were used. Separate models were constructed for the exposed nerve and ultrasound-guided experiments. *Post hoc* analysis using the Duncan multiple range test was performed to determine whether EI was significantly different between intraneural and extraneural needle placement (for the individual nerves and in all nerves in combination) but that it did not differ between the five sequential punctures in each nerve.

Results

Part 1: Punctures during Direct Nerve Exposure

All punctures were completed in a technically satisfactory manner; 40 punctures in eight nerves were completed and used for analysis. A hoof twitch motor response was observed for all cases. The experimental extraneural impedance was 12.1 ± 1.8 kΩ for all 40 punctures, which was significantly ($P < 0.0001$) lower than the EI of 23.2 ± 4.4 kΩ in the intraneural compartment. The general linear model F value was 43.38 with 79 *df* ($P < 0.0001$). The Duncan multiple range test showed that EI was significantly different between intra-

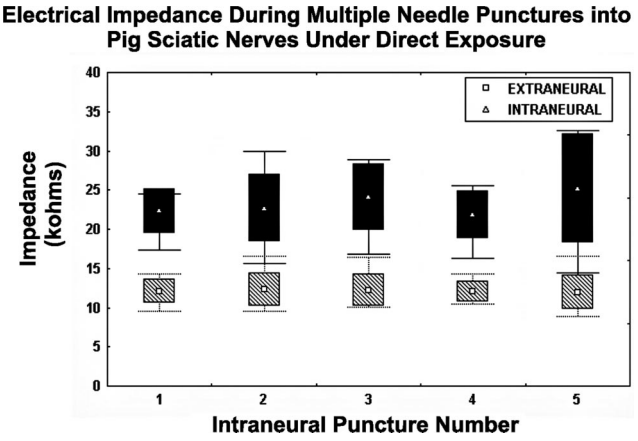

Fig. 1. Electrical impedance values at the extraneural and intraneural compartments during each puncture (n = 40) in the exposed nerves (part 1). The *filled rectangles* represent the SD, and the *whiskers* represent the minimum and maximum values for each electrical impedance measurement.

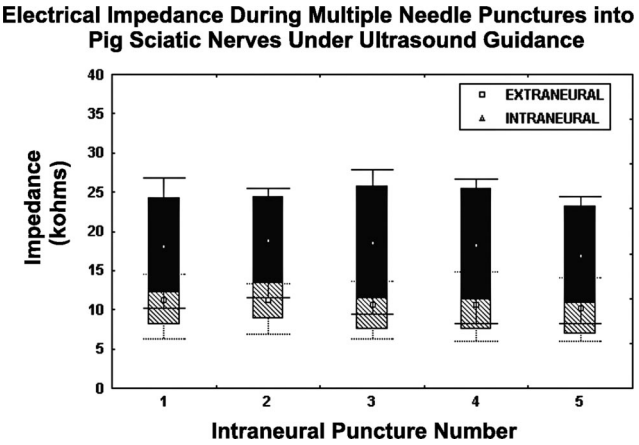

Fig. 3. Electrical impedance values at the extraneural and intraneural compartments during each ultrasound-guided nerve puncture (n = 35) (part 2). The *filled rectangles* represent the SD, and the *whiskers* represent the minimum and maximum values for each electrical impedance measurement.

neural and extraneural needle placement (for the individual nerves and in all nerves in combination) but that it did not differ between the five sequential punctures in each nerve (fig. 1). The EI returned to baseline (12.3 ± 2.3 kΩ) when the needle was withdrawn to the extraneural compartment (not shown in the figure).

Part 2: Ultrasound-guided Nerve Punctures

One nerve was not adequately visualized, leaving seven nerves with 35 punctures available for analysis. The difference in mean EI values between compartments for all 35 punctures (10.8 ± 2.9 kΩ extraneurally *vs.* 18.2 ± 6.13 kΩ intraneurally) was statistically significant ($P < 0.0001$). After the needle transected the nerve and reached the opposing extraneural tissue (fig. 2), the EI approached the baseline extraneural value (10.9 ± 3.2 kΩ). A hoof twitch motor response was observed for all cases. Interestingly, the process of transection often displayed a visibly distinct distension in the epineurium on the opposite side from the puncture. The model F value was 35.75 with 69 *df* ($P < 0.0001$). Similar to part 1, the Duncan multiple range test showed that the impedance was significantly different between intraneural and extraneural needle placement but that it did not differ between the five sequential punctures in each nerve (fig. 3).

Discussion

This study confirmed our hypothesis that there is a detectable difference in EI measured between the extraneural and intraneural compartments in porcine sciatic nerves. In fact, the EI difference between compartments in this model seems to be more than 50%. Furthermore, this EI difference is maintained upon multiple nerve punctures.

The variation in the EI of tissues throughout the body is dependent on their nonhomogeneity, primarily due to the variation in water and lipid content. The peripheral nerve is a complex structure consisting of fascicles (each a bundle of nerve fibers surrounded by a perineurium) that are held together by the epineurium, an enveloping external connective tissue sheath. The various fibrous tissues within the intraneural compartment contain much greater amounts of nonconducting lipids (*e.g.*, myelin sheaths) and lower water content (5–20% by weight) than do muscle (73–78% water by weight) and the surrounding interstitial fluid.[21] Therefore, the change in EI that occurs on entering a nerve from the

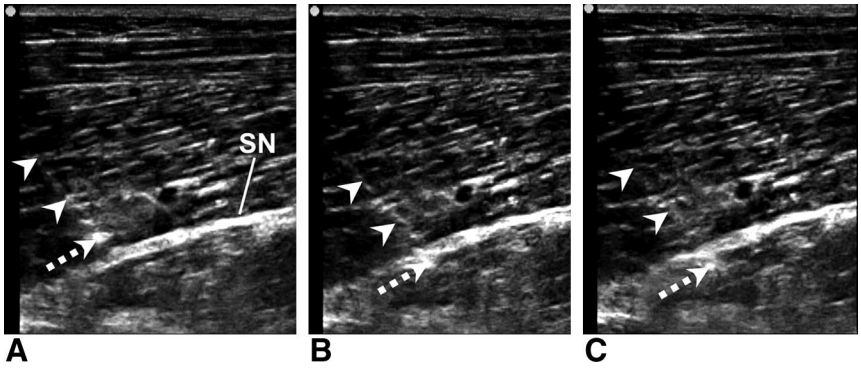

Fig. 2. Ultrasound images illustrating the in-plane needle positioning (*arrowheads*) to place the needle tip (*dashed arrows*) (*A*) first in the extraneural compartment and then (*B*) into the intraneural space of the longitudinally viewed sciatic nerve (SN) before transecting the nerve (*C*) to enter the opposing extraneural compartment. Immediately before the transection, the needle tip was often seen to distend the opposing epineurium (*B*).

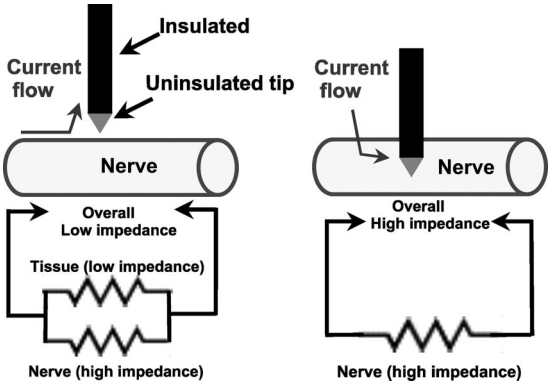

Fig. 4. Schematics of electrical impedance in the extraneural and intraneural compartments. *Upper left and right*: needle placements. *Lower left and right*: simplified equivalent circuit diagrams. The extraneural tissue, with low electrical impedance, provides a path through which most of the stimulating current will conduct. As the needle tip punctures the nerve, the low-resistance path is no longer available and a substantial increase in the electrical impedance of the circuit occurs.

surrounding tissue should be readily detectable. Indeed, in our experiments, the observer found that the EI increased abruptly, without any increments, upon entrance into the intraneural compartment.

Sources of EI during peripheral nerve stimulation are found in the grounding electrode, the stimulating needle, the connecting wire, and the biologic tissue that completes the electrical circuit. Because the EI is a combination of these influences, we must question why it increases so dramatically after entering the nerve.[18] In general, it is expected that impedance increases with length in a uniform electric current path, and this certainly occurs if the path is in a length of resistance wire or any other uniform linear conductor.[22] In biologic tissue, however, the dominant portion of the impedance is that which occurs close to the actual electrodes (a "volume-conductor" effect). Only in this area is the density of current high.[22] Beyond this zone, current flow spreads out across a large cross-sectional area, current density decreases dramatically, and the surrounding tissue in all three dimensions effectively displays very low impedance. Varying the spacing distance between the electrodes introduces little or no extra impedance into the system. The key determining factor for total EI in the entire circuit is the high current density at the needle tip.[22] Therefore, when the needle comes in close proximity to the nerve (or touches the nerve but remains extraneural), the EI of the circuit remains low (fig. 4). This is because the tissue, with low EI, provides a path through which most of the stimulating current will conduct. As the noninsulated needle tip punctures and becomes embedded in the nerve, the low-impedance path is no longer available and a substantial increase in the EI of the circuit occurs.

Nerve stimulators are designed to deliver precisely calibrated electrical signals *via* insulated needles during peripheral nerve blockade. Modern nerve stimulators produce a constant current (I) regardless of variations in resistance (R). For direct currents, the electrical resistance may be either measured or calculated when the voltage is known (V = IR). Recently available nerve stimulators display calculated EI for pulsatile stimulation (as per the User Manual for the Stimuplex HNS 12, B. Braun Medical). That is, the information is accessible in commercially available nerve stimulators, but the question remains as to how it should be interpreted. This study provides preliminary data to support the use of EI measurement during the performance of peripheral nerve blocks to help warn of intraneural needle placement.

There are limitations to this study. An obvious limitation of part 1 relates to the fact that the nerve was directly exposed and thus this model may not accurately reflect what happens clinically. The extent of intraneural placement can be determined accurately with direct visual observation; however, the dissection required to expose the nerve may have caused distortion in the data. Air has a high EI value, and therefore, the EI measurements may have been altered by the presence of air near the needle tip. Saline was used in this experiment to moisten the surface of the nerve in an attempt to minimize interference from conductance changes, although air may still have influenced the results due to the thin layer of the air–saline interface. On the other hand, the saline itself may have also introduced other possible artifacts, including a reduction of the impedance within the extraneural compartment, thus artificially leading to a greater change in EI between this and the intraneural compartment. Another variable that may have influenced (increased) the measured extraneural EI was the removal of surrounding extraneural tissue (*e.g.*, muscles) superficial to the exposed nerve, which normally would impart a significant conductive area. These confounding elements were the justification for part 2 of this study, the objective of which was to address these issues by leaving the tissue intact with no disruption.

During ultrasound guidance, the overall mean extraneural EI value seemed to be lower than that measured during open dissection. We speculate that the higher extraneural EI in the exposed system may relate to the presence of air or to the reduction in conductive extraneural tissue matter. Even though the difference between intraneural and extraneural EI values reached high statistical significance in both the open system with dissection and the closed system during ultrasound guidance using this small sample size, it is noteworthy that the EI variance was noticeably larger in the closed system. This may imply that it may be more difficult to make a general recommendation for detecting whether the needle is placed intraneurally *versus* extraneurally simply based on an absolute EI value. In these circumstances, a relative (*i.e.*, percentage) change of EI upon entrance into the intraneural compartment may be more

appropriate. Obviously, further study is needed to confirm this speculation.

During the part 2 experimentation of this study, it was critical to have the ability to observe the entire process of needle penetration to determine the needle tip location at all times (fig. 2). Unfortunately, we had difficulty clearly visualizing one of the eight sciatic nerves. We decided to exclude this nerve from the experimental procedure because the extent of needle penetration could not be ascertained with any certainty. This finding, in fact, closely resembles the clinical scenario, because ultrasound may not always accurately delineate nerve structures and, more importantly, enable consistent observation of needle advancement.

Another limitation regarding the specificity of this new method for detecting intraneural needle placement may be the similarity of EI changes found in other nonhydrated structures, such as tendons. This could be considered a negative aspect of the use of EI in some circumstances and is an area in which further study is warranted. Nevertheless, our group advocates for the use of combined nerve-stimulation and ultrasound-guided nerve localization, because nerve stimulation may aid to distinguish between nerves and tendons by their different physiologic responses to electricity.

Although the premise of our study was to assess a novel approach for avoiding injection of local anesthetic into the nerve at any intraneural location, it may be of future interest to perform tissue staining and/or pathology to examine whether EI can differentiate between extrafascicular (beyond the epineurium) and intrafascicular (beyond the perineurium) compartments within the nerve. This could be of particular value because ultrasound imaging currently does not allow this differentiation.[7] Unfortunately, correlating specific intraneural needle tip locations, *via* injection of a marker solution, with individual EI values would have been impractical in this study because of the secondary objective of determining whether EI measurement could be beneficial after multiple punctures in close proximity within each nerve. Furthermore, the injection itself may confound the results, because even very-small-volume injections (1–3 ml) have been shown to expand nerves,[10,11] and a set volume of solution that may lead to nerve damage *via* mechanical means is not known at this time.[7] Finally, the solution itself may vary the EI values, depending on its intrinsic conductive properties.[23]

Obviously, we anticipate that there may be substantial interspecies differences in EI. Although the absolute EI values may vary between species, further study is important to establish whether the changes in EI between the extraneural and intraneural compartments in humans are of a magnitude similar to those of the porcine model. Establishing an absolute EI value, or alternatively a percentage change in EI from the extraneural compartment, in humans indicative of intraneural placement would be of high clinical value.

In conclusion, EI was significantly different upon penetration of porcine sciatic nerves during open exposure and during ultrasound guidance. Despite the fact that only eight pigs were used during these experiments, the results obtained are highly significant, and therefore, the additional value of further study in animal nerves is questionable. Further studies are planned to investigate the feasibility of EI changes in humans.

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References

1. Fremling MA, Mackinnon SE: Injection injury to the median nerve. Ann Plast Surg 1996; 37:561–7
2. Gentili F, Hudson AR, Hunter D, Kline DG: Nerve injection injury with local anesthetic agents: A light and electron microscopic, fluorescent microscopic, and horseradish peroxidase study. Neurosurgery 1980; 6:263–72
3. Selander D, Sjostrand J: Longitudinal spread of intraneurally injected local anesthetics: An experimental study of the initial neural distribution following intraneural injections. Acta Anaesthesiol Scand 1978; 22:622–34
4. 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
5. 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
6. Mackinnon SE, Hudson AR, Llamas F, Dellon AL, Kline DG, Hunter DA: Peripheral nerve injury by chymopapain injection. J Neurosurg 1984; 61:1–8
7. Borgeat A: Regional anesthesia, intraneural injection, and nerve injury: Beyond the epineurium. ANESTHESIOLOGY 2006; 105:647–8
8. Al-Nasser B: Intraneural injection of local anesthetics during ultrasound-guided peripheral nerve block may lead to nerve injury. ANESTHESIOLOGY 2007; 106:1245–6
9. Baciarello M, Casati A, Fanelli G: Ultrasound-guided intraneural injections and neurologic injury. ANESTHESIOLOGY 2007; 106:1244–5
10. 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
11. 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
12. 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
13. Hadzic A, Vloka J, Hadzic N, Thys DM, Santos AC: Nerve stimulators used for peripheral nerve blocks vary in their electrical characteristics. ANESTHESIOLOGY 2003; 98:969–74
14. Perlas A, Niazi A, McCartney C, Chan V, Xu D, Abbas S: The sensitivity of motor response to nerve stimulation and paresthesia for nerve localization as evaluated by ultrasound. Reg Anesth Pain Med 2006; 31:445–50
15. Urmey WF, Stanton J: Inability to consistently elicit a motor response following sensory paresthesia during interscalene block administration. ANESTHESIOLOGY 2002; 96:552–4
16. 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
17. Organ L, Tasker RR, Moody NF: Brain tumor localization using an electrical impedance technique. J Neurosurg 1968; 28:35–44
18. Nicholson PW: Specific impedance of cerebral white matter. Exp Neurol 1965; 13:386–401
19. Robinson BW: Localization of intracerebral electrodes. Exp Neurol 1962; 6:201–23
20. 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. J Neurosurg 1969; 30:87–92
21. Pethig R: Electrical properties of biological tissue, Modern Bioelectricity. Edited by Marino A. New York, Marcel Dekker, 1988, pp 125–80
22. Suckling EE: Bioelectricity. New York, McGraw-Hill, 1961, pp 1–27
23. Tsui BC, Wagner A, Finucane B: Electrophysiologic effect of injectates on peripheral nerve stimulation. Reg Anesth Pain Med 2004; 29:189–93