Peripheral Nerve Stimulation in Regional Anesthesia

Stephen M. Klein, MD, M. Steve Melton, MD,* Warren M. Grill, PhD,† and Karen C. Nielsen, MD**

Abstract: Peripheral nerve stimulation has a long history in regional anesthesia. Despite the advent of ultrasound-guided peripheral nerve blockade, nerve stimulation remains a popular technique used alone or, now, in combination with ultrasound-guided techniques. In light of this evolving utility of nerve stimulation, this is an appropriate time to review the basic concepts and knowledge base of this historically important tool. Electrical nerve stimulation facilitates nerve localization, using threshold current as a surrogate for needle-to-nerve distance. Preferential activation of motor nerves is possible because motor nerve fibers are more readily activated with a shorter duration of current compared with sensory nerves. The association between current and needle-to-nerve distance predicts that less current is needed to evoke a motor response as the needle moves closer to the nerve. Thus, an elicited motor response at or below 0.5 mA is considered a common end point for successful neural blockade. However, current magnitude is neither 100% sensitive nor specific. Independent of technical ability, both the biological environment and the equipment used impact the current-distance relationship. Thus, successful electrical nerve stimulation is dependent on an anesthesiologist with a solid foundation in anatomy and a thorough understanding of electrophysiology.

(*Reg Anesth Pain Med* 2012;37: 383–392)

Electrical nerve stimulation is used extensively to facilitate and enhance peripheral nerve block performance. Studies using nerve stimulator–based techniques report a high degree of efficacy and reproducibility, making it one of the most prevalent regional anesthesia techniques.[1–3] By providing an objective estimate of needle-to-nerve distance, nerve stimulation enables practitioners to deposit local anesthetic with a high degree of precision. The technique capitalizes on physiology that allows electrical current passing from the needle tip to depolarize a mixed nerve without causing a painful sensory response. As the needle is guided closer to the nerve, less current is required to elicit a motor response of equal magnitude. This relationship serves to approximate needle-to-nerve distance. Whereas nerve stimulation is straightforward in concept and widely applied, the fundamental principles surrounding this technique are more complex. A host of confounding physical and electrical interactions influences nerve stimulation.

When introduced into clinical practice, nerve stimulation was quickly adopted to replace paresthesia techniques because of numerous benefits including (1) the ability to perform regional anesthesia with visual feedback rather than verbal feedback from the patient; (2) improved patient comfort, because a paresthesia technique can be painful or unpleasant compared with nerve stimulation; and (3) a perceived improvement in accuracy.[4–6] This transition in clinical practice preceded a great deal of the literature that describes the principles of electrical nerve localization. Today, a similar, more rapid evolution in technology and practice is occurring between nerve stimulation and ultrasound-guided regional anesthesia. However, despite the popularity of ultrasound-guided peripheral nerve blocks, nerve stimulation remains a common technique used alone or in combination with ultrasound guidance. The developing utility of combining these 2 techniques signals an opportunity to review the history and present the status of nerve stimulation. This review gives an account of events that led to the development and implementation of peripheral nerve stimulation and summarizes the fundamental principles of nerve stimulation as well as the neurostimulation literature that applies to regional anesthesia, including the controversies therein.

METHODS

To conduct the literature search for this review, we used the PubMed database queried before December 2010. Because words such as *nerve* and *stimulation* produce vast lists of references, we used single terms of interest limited to the title field as keywords to achieve search results containing fewer than 400 articles per search, which was deemed manageable for selective individual title, abstract, and/or article review for relevance. Successful terms using this strategy included *nerve stimulator* (327 results) and *nerve localization* (25 results). Unsuccessful terms limited to the title field were adjusted and combined using the "AND" function. One successful combination was *stimulation* (title) AND *block* (title) (352 results). Lastly, we used the "AND" function to search a combination of terms open to all fields. These terms included *stimulation* AND *block* AND *nerve stimulator* (299 results). In addition, we reviewed reference lists from the PubMed articles and found additional articles of interest that were not captured in our original search. Such articles of interest provided additional information about historical milestones and physiologic concepts included in this review. Lastly, we included relevant references that were familiar to us but were not otherwise captured. An English language restriction was applied to all searches. Commentaries, letters to the editor, reviews, and non–peer-reviewed articles were excluded.

HISTORY

The first concept of nerve conduction can be traced back to 260 BC and the hollow nerve doctrine, which described the nerve as a cavity through which messages travel.[7] Over time, tremendous philosophical speculation was devoted to the mechanism responsible for the transmission of messages through the nerve. In the 18th century, when electricity was accepted as a biological property, electricity became the most tangible means to explain neuromuscular conduction. In 1791, Galvani[8] published his theory of "animal electricity," which contended that muscle contraction resulted from latent electricity within the

From the Departments of *Anesthesiology and †Biomedical Engineering, Duke University Medical Center, Durham, NC.
Accepted for publication March 20, 2012.
Address correspondence to: M. Steve Melton, MD, Department of Anesthesiology, Box 3094, Duke University Medical Center, Durham, NC 27710 (e-mail: steve.melton@duke.edu).
The authors declare no conflict of interest.
Departmental financial support was received for this study.

ISSN: 1098-7339
DOI: 10.1097/AAP.0b013e3182576647

nerve. In 1850, however, Helmholtz demonstrated the temporal nature of nerve conduction, distinguishing it from electric current.[9] This was the beginning of our present notion of nerve function, paving the way for the elucidation of peripheral nerve stimulation physiology.[10]

In 1912, von Perthes[11] was the first to describe the use of nerve stimulation. Likely because of the complexity of the equipment at the time, this "impractical" technique was not adopted. In 1955, more than 40 years later, Pearson[12] published a modern description of a neurostimulator-guided peripheral nerve block, and in 1962, Greenblatt and Denson[13] described a system similar to the system used today. They constructed a small portable transistor-based device similar in design and appearance to modern nerve stimulators. This device delivered a square-wave impulse of 0.1 millisecond in duration at 1-Hz frequency, with an adjustable output of 0.3 to 30 V. The block technique described used a needle, insulated with plastic paint except at the tip, as a stimulation probe. Local anesthetic was injected when an appropriate motor response was achieved with 2- to 5-V stimulation amplitude. Using this technique, 87 blocks were performed, including sciatic, femoral, axillary, obturator, median, radial, ulnar, intercostal, and paravertebral approaches. Furthermore, this study[13] evaluated the relationship between voltage and needle-to-nerve distance and selective nerve localization during sciatic nerve blockade. In 1969, Magora et al[14] demonstrated that 0.5 mA is the minimal current needed to elicit a motor response that subsequently corresponded to a successful block.

The commercially available Block-Aid Monitor (Burroughs Wellcome and Co, Tuckahoe, New York) was originally used to assess neuromuscular blockade. In 1969, Koons[15] and Wright[16] proposed modifying this instrument for use as a stimulator-locator for peripheral nerve blocks (Fig. 1). Wright[16] effectively used this modification in 123 blocks, including paravertebral, supraclavicular, axillary, sciatic, and femoral nerve blocks. In 1972, Chapman[17] reported on 68 peripheral nerve blocks that were placed, using the modified Block-Aid Monitor; 60 of these were successful. Chapman[17] reported 100% success with what he described as "easy blocks," which included median, radial, ulnar, and tibial nerve blocks. "Difficult blocks," such as brachial plexus, femoral, and sciatic nerve blocks, were reportedly "less successful."

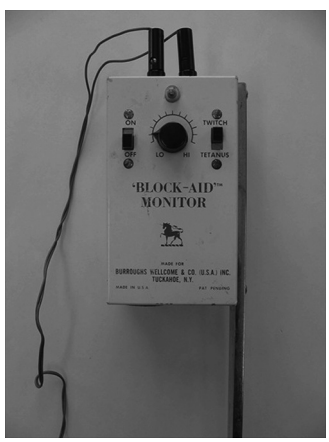


FIGURE 1. The Block-Aid Monitor (Burroughs Wellcome and Co), one of the earlier stimulators used for peripheral nerve blocks. This device was modified from its original purpose, which was to assess neuromuscular blockade. (Image courtesy of the Wood Library–Museum of Anesthesiology.)

In 1973, Montgomery et al[4] described a nerve stimulation technique using standard unsheathed needles, commonly used for paresthesia-guided techniques, and a readily available battery-powered transistor-based peripheral nerve stimulator. Although the success rate was not reported, this technique was described as safe and successful over an 18-month period and involved approximately 1000 peripheral nerve blocks, including interscalene, supraclavicular, infraclavicular, axillary, sciatic, popliteal, femoral, obturator, median, ulnar, and radial nerve blocks. In a separate study, this group reported a 95% success rate in more than 200 cases of electrical stimulation-guided infraclavicular blocks.[5] The reasons for failure included inexperience, a change in needle position after successful nerve localization before injection of local anesthetic, and technical difficulties such as inadequate battery power or bad wiring of the stimulator.[5]

These early reports[4–6] facilitated the gradual transition from mechanical paresthesia to electrical stimulation for nerve localization. Stated benefits of electrical stimulation included perceived improvement in accuracy and visual feedback instead of relying on verbal input from the patient. Despite near universal adoption, conclusive evidence for the efficacy and outcome benefits of electrical stimulation compared with mechanical paresthesia has not yet been presented.[18] Today, a similar but more rapid transition is occurring between nerve stimulation and ultrasound-assisted regional anesthesia.

ELECTROPHYSIOLOGY

To safely and effectively use electrical stimulation to guide peripheral nerve blockade, the anesthesiologist must have a solid foundation in anatomy and a thorough understanding of electrophysiology. Here, we review the relevant principles of electrophysiology.

Current Intensity

Current intensity, a measure of stimulus strength, is the flow of electrical charge used to depolarize the nerve and subsequently produce a motor response, or "twitch." Commercially available nerve stimulators typically allow the anesthesiologist to adjust the current, frequency, and, sometimes, the pulse duration. However, current is the only parameter that is routinely adjusted. For this reason, modern devices are classified as "constant-current" stimulators. The delivered current is described by Ohm law:

$$V = I \times R \text{ or } I = V/R$$

where V is voltage; I, current; R, resistance.

Resistance (R) is primarily independent of the stimulator and is largely a function of tissue impedance encountered by the needle. Therefore, according to Ohm law, nerve stimulators maintain a constant current by raising or lowering the voltage (V) in response to changes in resistance.[19–24] The ability to overcome resistance depends on the voltage source (the battery) and the intrinsic circuitry of the device. For example, in circumstances of high total resistance due to a poor connection of the return electrode, some models will deliver unusually high voltages (70 V) to overcome the load.[20] In other instances, when the resistance is elevated because of a disconnection or battery failure, the current cannot be delivered. Modern devices use a flashing light and/or a change in sound to signal this problem.

Nerve fiber activation occurs when a delivered charge to a nerve results in a change in transmembrane voltage (the difference between the intracellular and extracellular voltage) that exceeds the threshold to generate an action potential. To deliver this charge, a nerve stimulator typically provides a periodic,

pulsed, square-wave current of short duration (0.1 millisecond) to rapidly depolarize the nerve fiber in an effort to overcome accommodation and trigger an action potential. Accommodation is the physiologic process by which a neuron resists a change in its transmembrane potential with prolonged subthreshold stimulation or slowly rising current.[25]

Despite contemporary designs and modern circuitry, nerve stimulators vary in clinical performance.[20,21,23] Barthram[21] demonstrated current output inaccuracies over varying resistance loads among different nerve stimulators used for peripheral nerve blockade. Only 3 of 6 nerve stimulators delivered a target current of 0.3 to 3.0 mA with ±20% accuracy. In a larger study, Hadzic et al[20] found deficient current delivery in 15 commonly used devices. Although these stimulators accurately delivered a 1.0-mA current through a typical 1- or 2-kΩ load resistance, the median error increased significantly for delivery of a 0.1-mA current, with the maximum voltage output ranging from 7.4 to 336 V.

The consistency of nerve stimulators to deliver a square-wave has also been tested.[20,21,23] Jochum et al[23] evaluated the waveforms of 13 nerve stimulators at current intensities 0.1 to 5.0 mA over a constant 1-kΩ resistance. Only 5 of the 13 stimulators demonstrated an ideal rectangular waveform rise and fall time (≤0.003 millisecond) at each current intensity. Hadzic et al[20] demonstrated that resistance loads beyond 1 kΩ were associated with increased waveform distortion. Based on these findings, ensuring a quality connection to the return electrode should improve the ability of the stimulator to deliver a square-wave current[22] by decreasing the impedance load. The variability of device designs has not been correlated with clinical outcome.

Stimulus Strength-Duration Relationship

The total charge (Q) delivered to a nerve is a product of current intensity (I) and pulse duration (t): $Q = I \times t$. The stimulus strength-duration curve illustrates this relationship (Fig. 2). Rheobase and chronaxie are 2 parameters of the stimulus strength-duration relationship. Rheobase is the minimum current needed to depolarize the nerve when using an infinitely long pulse duration.[26] In other words, a current below the rheobase will not generate a motor response. Chronaxie is the minimum pulse duration needed to depolarize the nerve at a current intensity equal to twice the rheobase.[26] Because nerves have the same rheobase, chronaxie values provide an indicator of the relative excitability of a nerve.[27,28] Lower chronaxie values correspond to increased excitability and the ability to elicit a motor response at lower pulse durations.

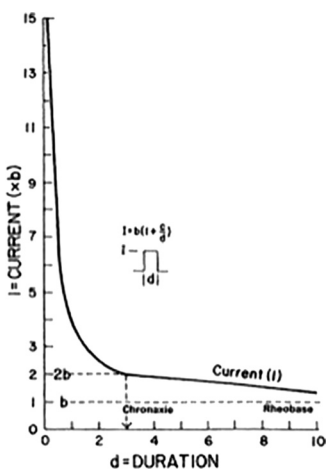


FIGURE 2. Strength-duration curve. The strength-duration curve for current (*I*) versus stimulus duration (pulse width) (*d*) of a classic nerve fiber stimulated with a square-wave current. Rheobase (*b*) is the lowest stimulus amplitude needed for activation when using a very long pulse width. Chronaxie (*c*) is the threshold pulse width needed to depolarize the nerve when the current amplitude is equal to twice the rheobase (2*b*) and permits choice of the optimum stimulus pulse duration, depending on the type of nerve fiber.[26] (Adapted from Geddes and Roeder[28] [permission obtained].)

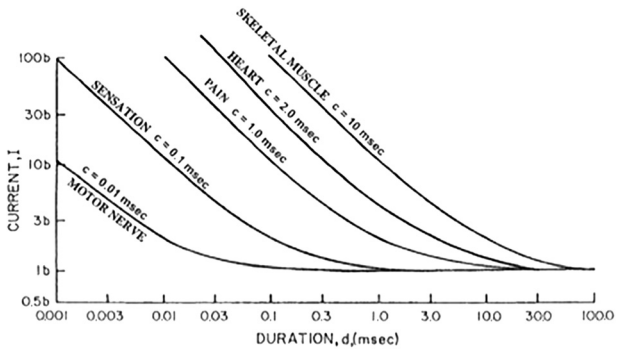


FIGURE 3. Strength-duration curves for tissues with different chronaxies (*c*). (Reproduced from Geddes and Roeder[28] [permission obtained].)

Chronaxie values are influenced by differences in the properties of nerve fibers, such as axon diameter, myelination, and distance between nodes of Ranvier.[28,29] The use of electrical stimulation to guide peripheral nerve blockade exploits these differences, achieving preferential activation of motor nerve fibers. Large A-alpha motor nerve fibers are more readily activated with a shorter pulse duration (≤0.1 millisecond) compared with smaller A-delta and C sensory fibers, which are more readily activated with longer pulse durations (≥0.3 millisecond) (Fig. 3).[27,28,30,31] Therefore, at low current intensities, nerve stimulators can depolarize a mixed nerve and elicit a motor response without causing a painful sensory response.

Although the stimulus strength-duration relationship has been well validated in both physiological and clinical experiments, the effect of pulse duration on pain during block placement is less clear. Studies have demonstrated that discomfort is directly related to contraction force rather than stimulus duration.[32–34] However, longer pulse durations elicited more discomfort contractions at lower currents compared with shorter pulse durations; but when the current was adjusted to maintain uniform intensity of motor response, no significant differences in discomfort were observed among the pulse durations studied. Therefore, these studies concluded that, within the current range used in regional anesthesia, pain is directly related to the total energy delivered.

Frequency

Frequency is the number of repeating events per unit of time. In terms of nerve stimulation, frequency is the number of current pulses (repeated event) delivered from the nerve stimulator in 1 second (unit of time). Frequency is a rate-limiting factor of needle advancement because it correlates with the rate of motor feedback. Nerve stimulator frequency is typically set at 1 or 2 Hz, meaning that a current pulse is delivered in a repeating cycle once or twice per second, respectively. At 1 Hz, the needle must be advanced slowly (in millimeters per second) to allow time for the delivered pulse to elicit a motor response. Many practitioners find this pace too slow. In contrast, at 2 Hz, the needle can be advanced at twice the speed. However, it is possible

to advance the needle at a rate that is faster than pulse delivery. In this case, the needle may pass the appropriate position and fail to elicit a motor response. A 3-Hz stimulus provides faster feedback, but the rapid muscle contractions that result may be unpleasant to the patient. Thus, higher frequencies can be delivered, but these rates do not allow sufficient time for muscle relaxation and are thus uncomfortable.

In their effort to find a method that would more easily target nerves, Urmey and Grossi[35] described a novel 3-Hz stimulation technique called *sequential electrical nerve stimuli*. This technique uses a square-wave current nerve stimulator programmed to deliver a repeating series of alternating sequential pulses of 0.1, 0.3, and 1.0 millisecond at 3 Hz. At a given current, longer pulse duration is associated with increased charge. Therefore, as predicted by the current-distance relationship, a motor response is elicited at a greater distance from the nerve. Conversely, shorter pulse duration is associated with decreased delivered charge and thus requires close needle-to-nerve proximity to elicit a motor response. Using this device, a single motor response per second indicates that the 1.0-millisecond pulse is stimulating the nerve. This provides early feedback at distances farther from the nerve, increasing the range of nerve stimulation. However, 3 motor responses per second indicates that all pulses, including the traditional 0.1-millisecond pulse, are stimulating the nerve, at which point a motor response at a current of 0.5 mA or less is targeted for local anesthetic injection.

Polarity

Electrical polarity is the directional flow of electrons (current) from a negative pole (negative electrode) to a positive pole (positive electrode). In terms of electrical nerve stimulation, the needle and the return electrode, which is attached to the skin, are the electrodes. The orientation of these electrodes, negative and positive, affects the current necessary to elicit a motor response. During electrical nerve stimulation, the needle is oriented as the negative electrode, and the return electrode as the positive electrode. This is referred to as *cathodal* stimulation. Current flowing from the needle electrode (cathode) leads to extracellular voltage distribution, nerve depolarization, and generation of an action potential. Alternatively, if the polarity is reversed, and the needle is oriented as the positive electrode, current flowing into the needle (anode) leads to extracellular voltage distribution and nerve hyperpolarization.[36] In this case, depolarization and initiation of an action potential may occur at a site distant from the hyperpolarized region, termed the *virtual cathode*.[36,37] However, this may occur at the site of hyperpolarization when the anodal stimulus ceases, and the transmembrane potential exceeds the resting value. This is described as anodal break excitation[36,37] and has been observed both experimentally[38] and clinically[39–41] in regional anesthesia because needles as anodes require 2 to 4 times greater current to achieve a motor response compared with properly oriented needles as cathodes.

Traditional teaching emphasized placing the return electrode near the insertion site, but not on the target limb. This was thought to optimize the electrical circuit and direct current flow away from the block site. This practice, however, has not been validated in the anesthesia literature.[32] In fact, return electrode location is not critical, and it can be placed anywhere on the skin. This can be attributed to the fact that the return electrode is relatively distant from the current, and the impedance of the skin is quantitatively great at the voltage and current magnitudes used clinically. Mathematically, the return electrode is assumed to be an infinite distance away from the needle, and hence, its location does not influence depolarization.

Current Density

Current density describes the distribution of current flow in terms of current per cross-sectional area. Loss of motor response upon local anesthetic injection during peripheral nerve blockade is an excellent example of the principle of current density. According to an earlier study, the loss of a motor response after the initial injection of local anesthetic (0.5–1.5 mL), also known as the Raj test, was attributed to the physical displacement of the nerve from the needle.[6] Failure to lose the motor response was indicative of incorrect needle placement. The Raj test was based on the premise that when the needle-to-nerve distance increases, the current threshold increases, and more current is needed to elicit the response. More recent investigations have shown, however, that loss of response is actually due to decreased current density surrounding the needle, caused by the spread of local anesthetic.[42,43] This occurs almost instantaneously and results from a change in the distribution of extracellular voltage around the needle tip. Solutions that conduct electricity, such as local anesthetics or saline, increase the conductive area at the tip of the needle.[43] A greater conductive area leads to decreased current density, and hence, a greater threshold current is needed to evoke an action potential at the same distance. Interestingly, injection of a less conductive solution, such as dextrose 5% in water (D5W), reduces the conductive area at the tip of the needle and increases current density, which results in a similar, or decreased, threshold current than before the injection.[43]

Using finite element analysis, an engineering tool that uses computerized mathematical models to understand complex systems, Ercole demonstrated that a volume of conducting solution (equivalent to saline or local anesthetics) that fills an area measuring 1.5 mm in radius reduces the voltage by 31%.[42] The same volume of a less conductive injectate, such as dextrose solution, increases the voltage by approximately 15%. In practice, clinicians have capitalized on this property when placing continuous stimulating catheters. To facilitate insertion, D5W is injected through the needle to dilate the space while preserving the ability to stimulate.[44] However, an unintended result of this phenomenon occurs after numerous needle passes. In these situations, it is possible to create edema or introduce blood, which act as conductive solutions, increasing the conductive area, decreasing the current density, and increasing the stimulation threshold.

CLINICAL CONCEPTS

Needle-to-Nerve Distance

The success of nerve stimulator–assisted regional anesthesia relies on the reproducible observation that, as the needle moves closer to the nerve, less current is needed to evoke a motor response. This is described by the current-distance relationship, $I_{th}(r) = I_o + kr^2$, where r is the needle-to-nerve distance; I_o, an offset; and k, the current-distance constant. Thus, the threshold current increases as the square of the distance between the needle and the nerve (Fig. 4). When a motor response can be elicited by using less than a minimum current, the needle is sufficiently close to the nerve to predictably block the selected target with injection of local anesthetic.

The ideal minimum current for an insulated needle has been extensively studied.[6,13,14] According to these early investigations, an elevated current, that is, 3 mA, may be required to produce a motor response when the needle tip is only 1 cm from the nerve, but a current of less than 0.5 mA can elicit a motor response when the needle tip is within 5 mm of the nerve. Based

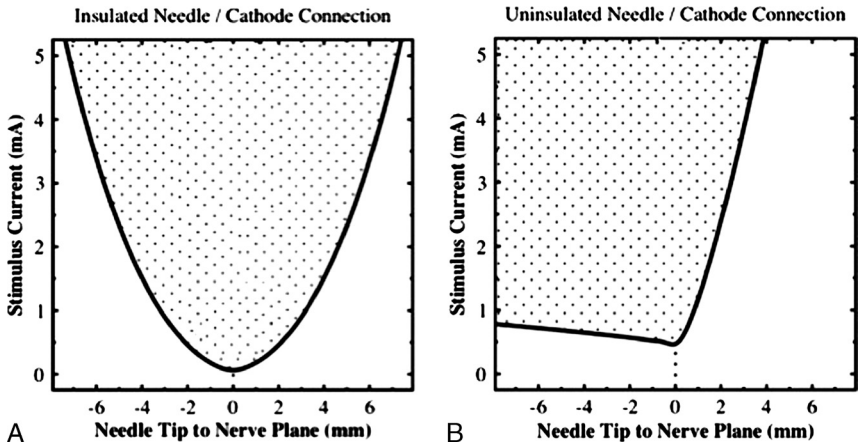


FIGURE 4. Current-distance relationship. The current-distance relationship for (A) insulated and (B) uninsulated needles attached to the cathode of a current stimulator. The shaded areas define current-distance pairs that result in a propagated response along the nerve fiber. (Adapted from Johnson et al[38] [permission obtained].)

on the successful application of these findings in clinical practice, therefore, a motor response at or below 0.5 mA is considered a common end point for predicting successful neural blockade upon local anesthetic injection.[6] More recently, Sung[45] confirmed this relationship using a rabbit model and a micromanipulator to precisely measure needle-to-nerve distance. When a target nerve was stimulated at less than 0.5 mA using pulse durations of 0.1 and 0.250 milliseconds, the center of the block needle bevel was within 5 mm of the nerve.

Despite the clinically reproducible success and common adoption of stimulating currents 0.5 mA or less, controversy persists regarding the ideal current end point, that is, whether minimum current thresholds can be a reliable predictor of needle-to-nerve distance and intraneural needle placement and the effect of disease states on a targeted end point. Inconsistent current end point has prompted some practitioners to warn that ultralow currents (<0.4 mA) may be associated with intraneural needle placement.[46–49] Urmey and Stanton[50] brought this to the forefront when they conducted an evaluation of needle position for interscalene brachial plexus block. They demonstrated that only 30% of patients exhibited a motor response to electrical stimulation (up to 1.0 mA) despite having a paresthesia indicative of sensory nerve contact. Choyce et al[51] performed a study involving 53 axillary blocks. They demonstrated that, upon elicitation of a paresthesia, 77% of subjects produced a motor response at 0.5 mA or less, and 23% produced a motor response at greater than 0.5 mA.[51]

Perlas et al[52] used ultrasound to investigate the reliability of paresthesia and electrical nerve stimulation as an indicator of needle-to-nerve proximity during axillary blocks. They reported a paresthesia in 38% of subjects and a motor response at 0.5 mA or less in 74%, with ultrasound confirmation of needle-to-nerve contact. Using ultrasound in a similar fashion, Al-Nasser et al[53] evaluated motor response during musculocutaneous nerve block and reported disappearance of motor response at current levels of 0.6 mA or greater in 12 of 47 subjects and at 0.3 to 0.5 mA in 20 of 47 subjects and a continued motor response despite a current of 0.3 mA or less in 15 of 47 subjects. In an ultrasound-guided study of electrical stimulation with Tuohy needles for interscalene block and subsequent nonstimulating catheter placement, Fredrickson[54] observed a 57% false-negative rate with an absent motor response at 0.8 mA despite close needle-to-nerve proximity. These studies suggest that, under some conditions, a needle can be in close or direct nerve contact, adequate for a peripheral nerve block but not enough to elicit an appropriate motor response.

In addition, multiple studies have demonstrated intraneural needle position with a motor response at an appropriate current intensity (0.2–0.5 mA) or with lack of a motor response at an elevated current intensity (≥1.5 mA). These scenarios are particularly worrisome because current magnitude is not an indicator of a potentially dangerous needle position. Robards et al[55] demonstrated this in subjects undergoing popliteal fossa sciatic nerve block. Using both nerve stimulator assistance and ultrasound, the end point for needle placement was either an elicited motor response at 0.2 to 0.5 mA or visualized intraneural placement, whichever came first. In 83.3% of subjects, a motor response could be obtained only when the needle entered the intraneural space (subepineurium). In 16.7%, a motor response could not be obtained at a stimulating current of 1.5 mA, despite needle entry into the intraneural space. All evoked motor responses at 0.2 to 0.4 mA were associated with intraneural placement. Sala-Blanch et al[56] demonstrated that 66% of subjects met ultrasound criteria for intraneural injection after nerve stimulator–guided popliteal nerve blocks, with a motor response at less than 0.5 mA. Tsai et al[47] performed sciatic nerve blocks in a pig model and demonstrated that a motor response at less than 0.2 mA was associated with intraneural needle tip location, but that currents as high as 1.7 mA failed to elicit a motor response despite intraneural needle tip location. Using histological techniques, Voelckel et al[57] demonstrated subneural, perineural, and intraneural signs of inflammation in a pig model after sciatic nerve blocks were performed with a motor response at less than 0.2 mA. No signs of inflammation were observed when the target motor response was 0.3 to 0.5 mA. In 55 human subjects, Bigeleisen et al[48] performed ultrasound-guided supraclavicular nerve blocks with purposeful intraneural needle tip placement. They demonstrated that a stimulation current of 0.2 mA or less was associated with intraneural needle location and that a traditional electrostimulation target of 0.2 to 0.5 mA did not exclude intraneural location.

The literature is deficient in describing motor response quality associated with current end point for injection. For example, numerous studies describe "a muscle response below 0.5 mA," but rarely is the magnitude of that response quantified using a dynamometer or similar technology. Motor response quality or strength is a multifactorial event influenced by the muscle and the number of nerve fibers recruited. Although this

parameter could be important in determining current end point, few nerve stimulation studies report this measurement.

In an effort to develop more reliable methods to detect needle placement, several investigators[24,58,59] have examined the disparities among different types of tissue.[21,24,52,53,58,59] Tsui et al[58] investigated the role of electrical impedance as an objective measure of intraneural placement. Using a sciatic nerve model in pigs, this investigation demonstrated that intraneural needle placement, based on direct ultrasound visualization, was associated with increased impedance. These results suggest that, in addition to pain on injection and absolute minimal stimulating current, real-time monitoring of impedance may also be an additional parameter for detecting intraneural needle placement.

Clinical Implications

Although clinically useful and usually predictable, the association between current magnitude and motor response as an indicator of needle-to-nerve distance is neither 100% sensitive nor specific. Furthermore, the relationship between needle and nerve is impacted by a complex biological environment.[60] Experimental conditions in an isolated nerve fiber, a common nerve model, are quite different from clinical conditions. In vitro models assume a source current delivered in a homogeneous medium, spreading uniformly in all directions without barriers such as tissue planes. However, in vivo, the conductivities of skin, nerves, muscles, adipose tissue, and fascia are all different.[61] Boundaries between tissue layers also modify the surrounding electric field.[38,60] Furthermore, current follows the path of least resistance; thus, fluids and blood alter current flow, and needles cannot deliver current uniformly.[62] Finally, the effect of current distribution on stimulation is dependent on the nerve type and condition.[60] Although electrical nerve stimulation is a beneficial aid for peripheral nerve blockade, its limitations, as discussed, must be recognized.

In summary,

- according to the current-distance relationship, the depolarization threshold current is proportional to the distance between the needle and the nerve; the relationship is predictable and obeys a square law;
- low-current nerve stimulation (0.1–0.4 mA) is predictive of a close (1–2 mm) needle-to-nerve distance but, in some anatomic locations and situations, may signal intraneural placement;
- using a low stimulating current to predict intraneural placement is unreliable;
- motor response after intraneural placement is most likely to occur at a lower current but can occur at currents 0.5 mA or greater;
- the absence of a motor response does not preclude intraneural needle placement; and
- needle trauma can create edema or introduce blood, both of which act as conductive solutions, increasing the conductive area, decreasing the current density, and increasing the stimulation threshold.

NEEDLE DESIGN

Needles vary in design characteristics that affect current delivery and nerve stimulation.[63] Such characteristics include length, diameter, lumen size, bevel tip, and degree of insulation. Previous investigations reported in the engineering literature have demonstrated that distributions of current density on electrode surfaces, patterns of current flow in the tissue, and thresholds for neural stimulation are strongly influenced by the size and shape of electrodes.[64–66] For example, although needle surface area is assumed to be perfectly smooth, it is not. Rough areas can increase the geometric surface area, which results in substantial changes in the distribution of current density across the needle surface. Similarly, current is preferentially transferred from needle tips and edges, making the points and sharp bevels the sites of highest current density. Cantrell et al[62] analyzed the effect of needle geometry using finite element analysis. This study determined that, with an insulated Tuohy tip design, maximum current density occurred along the proximal edge of the orifice rather than the tip. Indeed, current density along the proximal edge of the orifice was 1.9 times greater than the current density on the side edges of the orifice and 3.5 times greater than the current density on the distal edge of the orifice. Because of these properties, the needle had asymmetric current flow and was prone to producing different results, depending on its rotation around the axis of the shaft and its relationship to the nerve.

Uninsulated Needles

Initially, needles used in regional anesthesia were also used in spinal anesthetics and phlebotomy. These needles are uninsulated, and current flows along the shaft as well as from the tip (Fig. 5).[38,67,68] Although current density is greatest at the tip, stimulation can occur along the entire length of the needle.[63] Typically, then, the starting current is increased to overcome the diminished current density due to the larger conductive area. Clinically, when target structures are shallow, that is, axillary brachial plexus blocks and most of the needle lies outside the tissue, the small amount of needle below the surface behaves as a single point source similar to an insulated needle. For deeper blocks, however, the needle behaves as a longitudinal series of point sources, creating a linear electrode. This makes it possible to stimulate a nerve with the proximal shaft when the distal tip is far from the target, potentially resulting in incorrect placement of local anesthetic. Despite this drawback, knowledgeable practitioners can achieve a high degree of success with uninsulated needles.[4]

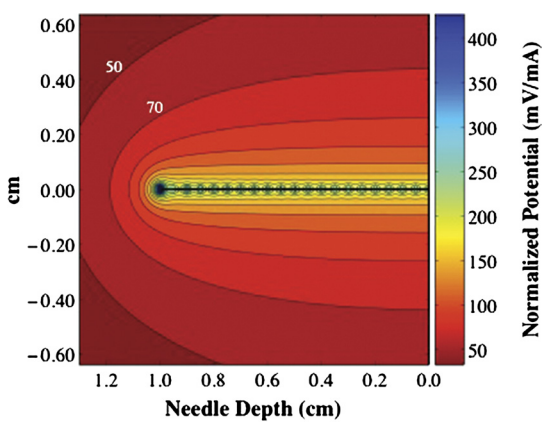


FIGURE 5. Uninsulated needle. Two-dimensional map of the normalized potentials (mV/mA) around an uninsulated needle inserted perpendicular to the skin to a depth of 1 cm. The outer 2 contour lines are labeled, and all lines are equally spaced by 20 mV/mA. The needle location is approximated by a series of current points separated by a distance equal to the radius of the needle (0.05 cm). At this depth, approximately 15% of the total delivered current is concentrated at the tip of the needle. The rest of the current is delivered along the needle shaft. (Adapted from Johnson et al[38] [permission obtained].)

Insulated Needles

The introduction of an insulated needle in clinical practice is attributed to Pearson[12] in 1955, but widespread availability did not occur until insulated needles were commercially manufactured in the 1970s and 1980s. This coincided with a decrease in paresthesia techniques in favor of nerve stimulation. Today, insulated needles are available in different sizes and with numerous options, although most share some common features. They have an integrated wire and attached tubing for injection and are typically insulated along the entire shaft, except for a varying degree and pattern of exposed metal at the tip. Thus, these needles behave as a point source electrode, reducing the ability to stimulate at any point other than close to the injection point at the tip (Fig. 6). Conceptually, this produces a more precise needle, generating stimulation at a point closest to the nerve and reducing activation in areas distant from the tip, that is, the shaft.

NERVE

The influence of nerve composition on electrical nerve stimulation in regional anesthesia has not been well investigated. Because peripheral nerves are heterogeneous structures that carry motor and sensory elements, with neural and nonneural components, fiber composition at 1 anatomic location may be significantly different at another anatomic location. Interestingly, only a small portion of nerve is composed of motor elements. For example, in the rat, the sciatic nerve at the midthigh contains approximately 27,000 axons, but only 6% are myelinated motor axons. Of the remaining axons, 23% are myelinated, 48% are unmyelinated sensory axons, and 23% are unmyelinated sympathetic axons.[69] When examined microscopically, both the upper and lower extremities demonstrate, moving proximal to distal, an increasing ratio of both stromal and connective tissue compared with neural tissue.[70,71] This heterogeneity could influence the ability to stimulate nerves.

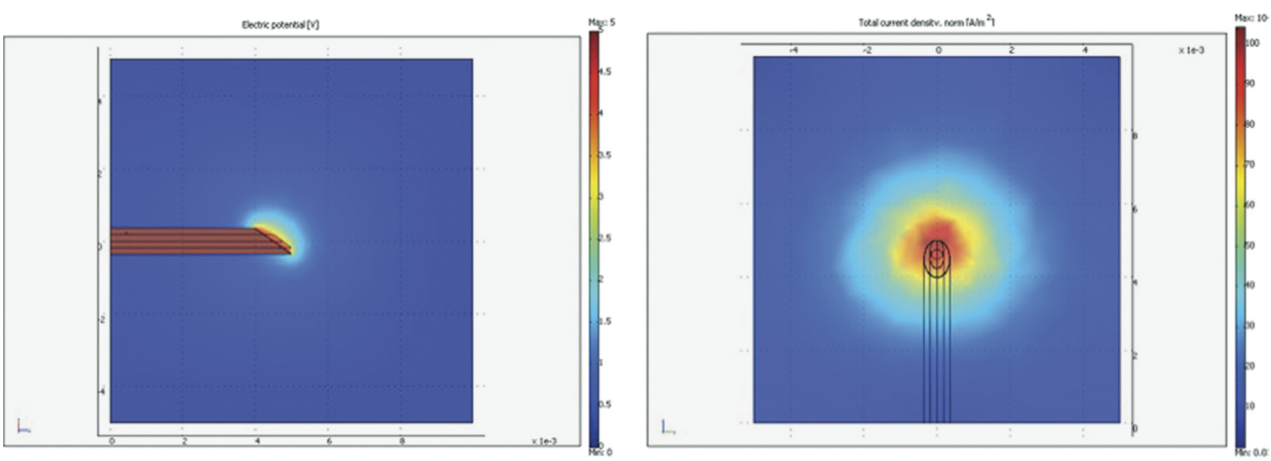
Pathologic processes may significantly alter the ability to elicit a motor response, increasing current threshold or decreasing the magnitude and quality of the motor response. Disease states such as diabetes, Charcot-Marie-Tooth, amyloid polyneuropathy, autoimmune neuropathy, and chemotherapy can influence axonal function and electrical stimulation properties. For example, diabetic neuropathy is associated with decreased conduction velocities due to axonal loss, segmental demyelination, and a host of vascular and membrane changes.[72] Both experimentally[46] and clinically,[73] the presence of diabetic neuropathy has been shown to impair the ability to elicit a muscle contraction. This has resulted in the lack of predictability and inability to detect intraneural needle placement at conventional and elevated (2.4 mA) current levels.[74] There is a paucity of studies in the anesthesia literature that have investigated nerve stimulation in the context of healthy and pathologic nerves.

LITERATURE BASE

The physiology and engineering literature base has been the primary source for the information in this review and can be considered high quality because the research reported therein is extensive and has established the fundamental principles of electrophysiology. Further research, therefore, is very unlikely to change our understanding.[75] The anesthesia literature, however, includes only a small subset of studies in regional anesthesia that have explored the clinical application of these principles during electrical nerve stimulation–guided peripheral nerve blockade. These studies involving a small number of subjects are often observational in design and, in some cases, are based only on expert opinion. This literature base, then, is considered moderate to low quality, suggesting that further research is likely to have an important impact on our understanding and/or clinical practice.[75]

FUTURE DIRECTIONS

Peripheral nerve stimulation has an established, validated role in regional anesthesia and therefore will continue to be used in the future, both alone and in combination with ultrasound. The use of ultrasound guidance for peripheral nerve blockade is supported by strong evidence, and the transition to this advancing technology is happening rapidly. Studies have demonstrated that ultrasound guidance improves outcomes with and without the use of peripheral nerve stimulation.[76–82] Although current end point is a relatively successful surrogate for needle-to-nerve distance, ultrasound guidance provides direct, real-time visualization of needle-to-nerve proximity, surrounding anatomical structures, and local anesthetic spread. However, each technique has limitations.[83,84] By recognizing these limitations, regional anesthesia practitioners can maximize the benefits of each technique,



A B

FIGURE 6. Insulated needle. Three-dimensional representation of the distribution of electrical voltages generated around an insulated needle with a 30-degree bevel and calculated using finite element modeling. Panel A shows the potentials in the x-z plane, and panel B shows the potentials in the y-x plane. The images demonstrate current delivery concentrated at the needle tip without any current delivered along the needle shaft.

whether used alone or in combination. In circumstances such as obesity, deeper blocks, or trauma, ultrasound imaging may be limited, and nerve stimulation can serve as a primary and/or confirmatory end point.[83] In addition, ultrasound guidance is not immune to limitations of stimulation-based techniques, including intraneural and intravascular injection.[85,86] As a result of the dramatic shift toward direct ultrasound visualization, the focus and quantity of research devoted to nerve stimulation will likely diminish. However, numerous undeveloped and/or controversial issues remain and would benefit from further study. These include enhanced reliability in detecting intraneural needle placement and a better understanding of clinical conditions and nerve states that affect the relationship between current, needle-to-nerve distance, and evoked motor response.

CONCLUSIONS

Electrical nerve stimulation is a common technique for nerve localization and has a long history of clinical efficacy and safety. Modification and commercial production of nerve stimulators as well as early reports of success led to a rapid transition from mechanical stimulation, or the "paresthesia technique," to electrical nerve stimulation. Benefits included a perceived improvement in accuracy and visual feedback from the elicited motor response. The successful application of this technique is dependent on a solid foundation in basic anatomy and a thorough understanding of the principles of electrophysiology. Using threshold current as a surrogate for needle-to-nerve distance, practitioners have been able to deposit local anesthetic with a high degree of precision. Nevertheless, the technique is neither 100% sensitive nor specific, because of the complexities of the biologic environment. As a result, important issues, such as the reliability of electrical nerve stimulation as an indicator of intraneural location, have yet to be resolved. With the rapid evolution of technology, however, ultrasound-guided peripheral nerve blockade now provides direct visualization of needle-to-nerve distance, challenging the utility of nerve stimulation.[78,87] Despite this, peripheral nerve stimulation remains a popular and useful method for nerve localization for peripheral nerve blockade, either used alone or in combination with ultrasound guidance.

REFERENCES

1. Franco CD, Vieira ZE. 1,001 Subclavian perivascular brachial plexus blocks: success with a nerve stimulator. *Reg Anesth Pain Med*. 2000;25:41–46.
2. Singelyn FJ, Gouverneur JM, Gribomont BF. Popliteal sciatic nerve block aided by a nerve stimulator: a reliable technique for foot and ankle surgery. *Reg Anesth*. 1991;16:278–281.
3. Silverstein WB, Saiyed MU, Brown AR. Interscalene block with a nerve stimulator: a deltoid motor response is a satisfactory endpoint for successful block. *Reg Anesth Pain Med*. 2000;25:356–359.
4. Montgomery SJ, Raj PP, Nettles D, Jenkins MT. The use of the nerve stimulator with standard unsheathed needles in nerve blockade. *Anesth Analg*. 1973;52:827–831.
5. Raj PP, Montgomery SJ, Nettles D, Jenkins MT. Infraclavicular brachial plexus block—a new approach. *Anesth Analg*. 1973;52:897–904.
6. Raj PP, Rosenblatt R, Montgomery SJ. Use of the nerve stimulator for peripheral blocks. *Reg Anaesth*. 1980;5:7.
7. Clarke E. The doctrine of the hollow nerve in the seventeenth and eighteenth centuries. In: Stevenson L, Multhauf R, eds. *Medicine, Science, Culture*. Baltimore, MD: Johns Hopkins Press; 1968:123–141.
8. Galvani L. De viribus electricitatis in motu musculari commentarius. *Bon Sci Art Inst Acad Comm*. 1791;7:363–418.
9. Clarke E. *Nerve Function Nineteenth-Century Origins of Neuroscientific Concepts*. Los Angeles, CA: University of California Press; 1987.
10. Pither C, Raj PP, Ford DJ. The use of peripheral nerve stimulators for regional anesthesia: a review of experimental characteristics, technique, and clinical applications. *Reg Anaesth*. 1985;10:10.
11. von Perthes G. Uker leitungsanasthesie unter zuhilfenahme elektrischer reizung. *Med Wschr*. 1912;47:2545–2548.
12. Pearson RB. Nerve block in rehabilitation: a technic of needle localization. *Arch Phys Med Rehabil*. 1955;36:631–633.
13. Greenblatt GM, Denson JS. Needle nerve stimulator-locator: nerve blocks with a new instrument for locating nerves. *Anesth Analg*. 1962;41:599–602.
14. Magora F, Rozin R, Ben-Menachem Y, Magora A. Obturator nerve block: an evaluation of technique. *Br J Anaesth*. 1969;41:695–698.
15. Koons RA. The use of the Block-Aid Monitor and plastic intravenous cannulas for nerve blocks. *Anesthesiol*. 1969;31:290–291.
16. Wright BD. A new use for the Block-Aid Monitor. *Anesthesiol*. 1969;30:236–237.
17. Chapman GM. Regional nerve block with the aid of a nerve stimulator. *Anaesth*. 1972;27:185–193.
18. Liguori GA, Zayas VM, YaDeau JT, et al. Nerve localization techniques for interscalene brachial plexus blockade: a prospective, randomized comparison of mechanical paresthesia versus electrical stimulation. *Anesth Analg*. 2006;103:761–767.
19. Hua P, Woo EJ, Webster JG, Tompkins WJ. Finite element modeling of electrode-skin contact impedance in electrical impedance tomography. *IEEE Trans Biomed Eng*. 1993;40:335–343.
20. Hadzic A, Vloka J, Hadzic N, et al. Nerve stimulators used for peripheral nerve blocks vary in their electrical characteristics. *Anesthesiol*. 2003;98:969–974.
21. Barthram CN. Nerve stimulators for nerve location—are they all the same? A study of stimulator performance. *Anaesth*. 1997;52:761–764.
22. Fuhrer MJ, Yegge B. Effects of skin impedance changes accompanying functional electrical stimulation of the peroneal nerve. *Arch Phys Med Rehabil*. 1972;53:276–281.
23. Jochum D, Iohom G, Diarra DP, et al. An objective assessment of nerve stimulators used for peripheral nerve blockade. *Anaesth*. 2006;61:557–564.
24. Sauter AR, Dodgson MS, Kalvoy H, et al. Current threshold for nerve stimulation depends on electrical impedance of the tissue: a study of ultrasound-guided electrical nerve stimulation of the median nerve. *Anesth Analg*. 2009;108:1338–1343.
25. Wessale JL, Geddes LA, Ayers GM, Foster KS. Comparison of rectangular and exponential current pulses for evoking sensation. *Ann Biomed Eng*. 1992;20:237–244.
26. Holsheimer J, Dijkstra EA, Demeulemeester H, Nuttin B. Chronaxie calculated from current-duration and voltage-duration data. *J Neurosci Methods*. 2000;97:45–50.
27. Geddes LA. Accuracy limitations of chronaxie values. *IEEE Trans Biomed Eng*. 2004;51:176–181.
28. Geddes LA, Roeder RA. *Handbook of Electrical Hazards and Accidents*. Tucson, AZ: Lawyers & Judges Pub Co; 2006.
29. Rattay F. Ways to approximate current-distance relations for electrically stimulated fibers. *J Theor Biol*. 1987;125:339–349.
30. Ranck JB Jr. Which elements are excited in electrical stimulation of mammalian central nervous system: a review. *Brain Res*. 1975;98:417–440.
31. Geddes LA. Chronaxie. *Austral Phys Eng Sci Med Biol*. 1999;22:13–17.
32. Hadzic A, Vloka JD, Claudio RE, et al. Electrical nerve localization: effects of cutaneous electrode placement and duration of the stimulus on motor response. *Anesthesiol*. 2004;100:1526–1530.

33. Koscielniak-Nielsen ZJ, Rassmussen H, Jepsen K. Effect of impulse duration on patients' perception of electrical stimulation and block effectiveness during axillary block in unsedated ambulatory patients. *Reg Anesth Pain Med*. 2001;26:428–433.
34. Stone BA. Transcutaneous stimulation of the saphenous nerve to locate injection site. *Reg Anesth Pain Med*. 2003;28:153–154.
35. Urmey WF, Grossi P. Use of sequential electrical nerve stimuli (SENS) for location of the sciatic nerve and lumbar plexus. *Reg Anesth Pain Med*. 2006;31:463–469.
36. Wikswo JP Jr, Lin SF, Abbas RA. Virtual electrodes in cardiac tissue: a common mechanism for anodal and cathodal stimulation. *Biophys J*. 1995;69:2195–2210.
37. Hodgkin AL, Huxley AF. A quantitative description of membrane current and its application to conduction and excitation in nerve. *J Physiol*. 1952;117:500–544.
38. Johnson CR, Barr RC, Klein SM. A computer model of electrical stimulation of peripheral nerves in regional anesthesia. *Anesthesiology*. 2007;106:323–330.
39. Berger JJ, Gravenstein JS, Munson ES. Electrode polarity and peripheral nerve stimulation. *Anesthesiol*. 1982;56:402–404.
40. Tulchinsky A, Weller RS, Rosenblum M, Gross JB. Nerve stimulator polarity and brachial plexus block. *Anesth Analg*. 1993;77:100–103.
41. Rosenberg H, Greenhow DE. Peripheral nerve stimulator performance: the influence of output polarity and electrode placement. *Can Anaesth Soc J*. 1978;25:424–426.
42. Ercole A. The effect of injectate conductivity on the electric field with the nerve stimulator needle: a computer simulation. *Anesth Analg*. 2008;107:1427–1432.
43. Tsui BC, Wagner A, Finucane B. Electrophysiologic effect of injectates on peripheral nerve stimulation. *Reg Anesth Pain Med*. 2004;29:189–193.
44. Tsui BC, Sze CK. An in vitro comparison of the electrical conducting properties of multiport versus single-port epidural catheters for the epidural stimulation test. *Anesth Analg*. 2005;101:1528–1530.
45. Sung DH. Locating the target nerve and injectate spread in rabbit sciatic nerve block. *Reg Anesth Pain Med*. 2004;29:194–200.
46. Rigaud M, Filip P, Lirk P, et al. Guidance of block needle insertion by electrical nerve stimulation: a pilot study of the resulting distribution of injected solution in dogs. *Anesthesiol*. 2008;109:473–478.
47. Tsai TP, Vuckovic I, Dilberovic F, et al. Intensity of the stimulating current may not be a reliable indicator of intraneural needle placement. *Reg Anesth Pain Med*. 2008;33:207–210.
48. Bigeleisen PE, Moayeri N, Groen GJ. Extraneural versus intraneural stimulation thresholds during ultrasound-guided supraclavicular block. *Anesthesiol*. 2009;110:1235–1243.
49. Dufour E, Cymerman A, Nourry G, et al. An ultrasonographic assessment of nerve stimulation–guided median nerve block at the elbow: a local anesthetic spread, nerve size, and clinical efficacy study. *Anesth Analg*. 2010;111:561–567.
50. Urmey WF, Stanton J. Inability to consistently elicit a motor response following sensory paresthesia during interscalene block administration. *Anesthesiol*. 2002;96:552–554.
51. Choyce A, Chan VW, Middleton WJ, et al. What is the relationship between paresthesia and nerve stimulation for axillary brachial plexus block? *Reg Anesth Pain Med*. 2001;26:100–104.
52. Perlas A, Niazi A, McCartney C, et al. The sensitivity of motor response to nerve stimulation and paresthesia for nerve localization as evaluated by ultrasound. *Reg Anesth Pain Med*. 2006;31:445–450.
53. Al-Nasser B, Hubert C, Negre M. Role of local anesthetic spread pattern and electrical stimulation in ultrasound-guided musculocutaneous nerve block. *J Clin Anesth*. 2010;22:334–339.
54. Fredrickson MJ. The sensitivity of motor response to needle nerve stimulation during ultrasound guided interscalene catheter placement. *Reg Anesth Pain Med*. 2008;33:291–296.
55. Robards C, Hadzic A, Somasundaram L, et al. Intraneural injection with low-current stimulation during popliteal sciatic nerve block. *Anesth Analg*. 2009;109:673–677.
56. Sala-Blanch X, Lopez AM, Carazo J, et al. Intraneural injection during nerve stimulator–guided sciatic nerve block at the popliteal fossa. *Br J Anaesth*. 2009;102:855–861.
57. Voelckel WG, Klima G, Krismer AC, et al. Signs of inflammation after sciatic nerve block in pigs. *Anesth Analg*. 2005;101:1844–1846.
58. 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. *Anesthesiol*. 2008;109:479–483.
59. Kalvoy H, Frich L, Grimnes S, et al. Impedance-based tissue discrimination for needle guidance. *Physiol Meas*. 2009;30:129–140.
60. Grill JWM. Modeling the effects of electric fields on nerve fibers: influence of tissue electrical properties. *IEEE Trans Biomed Eng*. 1999;46:918–928.
61. Geddes LA, Baker LE. The specific resistance of biological material—a compendium of data for the biomedical engineer and physiologist. *Med Biol Eng*. 1967;5:271–293.
62. Cantrell MB, Grill WM, Klein SM. Computer-based finite element modeling of insulated Tuohy needles used in regional anesthesia. *Anesth*. 2009;110:1229–1234.
63. Ford DJ, Pither C, Raj PP. Comparison of insulated and uninsulated needles for locating peripheral nerves with a peripheral nerve stimulator. *Anesth Analg*. 1984;63:925–928.
64. Butson CR, McIntyre CC. Role of electrode design on the volume of tissue activated during deep brain stimulation. *J Neural Eng*. 2006;3:1–8.
65. Gimsa U, Schreiber U, Habel B, et al. Matching geometry and stimulation parameters of electrodes for deep brain stimulation experiments—numerical considerations. *J Neurosci Methods*. 2006;150:212–227.
66. Wei XF, Grill WM. Current density distributions, field distributions and impedance analysis of segmented deep brain stimulation electrodes. *J Neural Eng*. 2005;2:139–147.
67. Bashein G, Haschke RH, Ready LB. Electrical nerve location: numerical and electrophoretic comparison of insulated vs uninsulated needles. *Anesth Analg*. 1984;63:919–924.
68. Jones RP, Jonge MD, Smith BE. Voltage fields surrounding needles used in regional anaesthesia. *Br J Anaesth*. 1992;68:515–518.
69. Schmalbruch H. Fiber composition of the rat sciatic nerve. *Anat Rec*. 1986;215:71–81.
70. Moayeri N, Bigeleisen PE, Groen GJ. Quantitative architecture of the brachial plexus and surrounding compartments, and their possible significance for plexus blocks. *Anesthesiol*. 2008;108:299–304.
71. Moayeri N, Groen GJ. Differences in quantitative architecture of sciatic nerve may explain differences in potential vulnerability to nerve injury, onset time, and minimum effective anesthetic volume. *Anesthesiol*. 2009;111:1128–1134.
72. Sharma AK, Thomas PK. Peripheral nerve structure and function in experimental diabetes. *J Neurol Sci*. 1974;23:1–15.
73. Sites BD, Gallagher J, Sparks M. Ultrasound-guided popliteal block demonstrates an atypical motor response to nerve stimulation in 2 patients with diabetes mellitus. *Reg Anesth Pain Med*. 2003;28:479–482.
74. Szerb J, Persaud D. Long current impulses may be required for nerve stimulation in patients with ischemic pain. *Can J Anaesth*. 2005;52:963–966.

75. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ (Clin Res Ed)*. 2008;336:924–926.

76. Neal JM, Wedel DJ. Ultrasound guidance and peripheral nerve injury: is our vision as sharp as we think it is? *Reg Anesth Pain Med*. 2010;35:335–337.

77. Liu SS, Zayas VM, Gordon MA, et al. A prospective, randomized, controlled trial comparing ultrasound versus nerve stimulator guidance for interscalene block for ambulatory shoulder surgery for postoperative neurological symptoms. *Anesth Analg*. 2009;109:265–271.

78. 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;34:251–255.

79. Abrahams MS, Aziz MF, Fu RF, Horn JL. Ultrasound guidance compared with electrical neurostimulation for peripheral nerve block: a systematic review and meta-analysis of randomized controlled trials. *Br J Anaesth*. 2009;102:408–417.

80. Liu SS, John RS. Modeling cost of ultrasound versus nerve stimulator guidance for nerve blocks with sensitivity analysis. *Reg Anesth Pain Med*. 2010;35:57–63.

81. Chan VW, Perlas A, McCartney CJ, et al. Ultrasound guidance improves success rate of axillary brachial plexus block. *Can J Anaesth*. 2007;54:176–182.

82. Beach ML, Sites BD, Gallagher JD. Use of a nerve stimulator does not improve the efficacy of ultrasound-guided supraclavicular nerve blocks. *J Clin Anesth*. 2006;18:580–584.

83. Saranteas T, Karakitsos D, Alevizou A, et al. Limitations and technical considerations of ultrasound-guided peripheral nerve blocks: edema and subcutaneous air. *Reg Anesth Pain Med*. 2008;33:353–356.

84. van Geffen GJ, McCartney CJ, Gielen M, Chan VW. Ultrasound as the only nerve localization technique for peripheral nerve block. *J Clin Anesth*. 2007;19:381–385.

85. Russon K, Blanco R. Accidental intraneural injection into the musculocutaneous nerve visualized with ultrasound. *Anesth Analg*. 2007;105:1504–1505, table of contents.

86. Martinez Navas A, dela Tabla González RO. Ultrasound-guided technique allowed early detection of intravascular injection during an infraclavicular brachial plexus block. *Acta Anaesthesiol Scand*. 2009;53:968–970.

87. Sandhu NS, Sidhu DS, Capan LM. The cost comparison of infraclavicular brachial plexus block by nerve stimulator and ultrasound guidance. *Anesth Analg*. 2004;98:267–268.