the resulting impedance was actually reduced, according to equation 3.

$$Z = \sqrt{R^2 + X_C^2} \quad (3)$$

where X_C is the capacitive reactance and is defined by:

$$X = \frac{1}{2\pi fC} \quad (4)$$

where f is the frequency of the applied waveform. Dependent on the magnitude of the capacitive and resistive changes, the overall impedance decreased dramatically.

This finding of Tsui *et al.*, although it does not demonstrate increased impedance on intraneural needle tip placement, is interesting, because it shows that the complex system time constant changes on close approach to neural tissue when using externally applied electrical fields, an observation I have also made.[5] Also, individual time constants, equation 1, may be derived from the observed charging/decay voltage curve through additional mathematical methods (logarithmic peeling), and the time constants contributed by the nerve, the insulated needle, or the remaining tissue electrical path determined separately.[6]

Philip C. Cory, M.D., St. James Healthcare, Butte, Montana. pcory@littleappletech.com

References

1. 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
2. Cooper MS, Miller JP, Fraser SE: Electrophoretic repatterning of charged cytoplasmic molecules within tissues coupled by gap junctions by externally applied electric fields. Dev Biol 1989; 132:179–88
3. Cory PC: inventor; Nervonix, Inc., assignee: Non-Invasive, Peripheral Nerve Mapping Device and Method of Use. U.S. patent 5 560 372. October 1, 1996
4. Prokhorov E, Llamas F, Morales-Sánchez E, González-Hernández J, Prokhorov A: *In vivo* impedance measurements on nerves and surrounding skeletal muscles in rats and human body. Med Biol Eng Comput 2002; 40:323–6
5. Cory PC: inventor; Nervonix, Inc., assignee: Nerve Stimulator and Method. U.S. patent 7 212 865. May 1, 2007
6. Rall W: Membrane potential transients and membrane time constant of motoneurons. Exp Neurol 1960; 2:503–32

(Accepted for publication January 15, 2009.)

Anesthesiology 2009; 110:1194–5

In Reply:—We are very pleased that our report has stimulated the important comments made by Dr. Cory. We would like to take this opportunity to address the correspondent's concerns and to clarify the simplified electrical circuit depicted in the original manuscript.[1]

Using a clinically relevant low frequency (2 Hz) stimulation, we had hoped to detect any possible warning signs of intraneural needle placement by understanding how to interpret the displayed impedance from one of the common commercial stimulators. We were most encouraged to note the distinct impedance change displayed on the stimulator upon the needle entering the intraneural compartment. The specific concern expressed in the above letter relates to the proposed inaccuracy in the interpretation of the displayed impedance. From observations based on human data, Dr. Cory posits that the maximum voltage may not have been reached within such short pulse duration (0.1 ms).

First of all, it is important to clarify that the simplified circuit of the original manuscript represents only the resistive portions of the circuit. Strictly speaking, an accurately depicted circuit would be much more complex and include the capacitance and inductance of the many tissue types (fig. 1). However, we believed such complex electrical circuitry may have distracted readers from the primary goal of the research. Despite this, there was no intention on our part to undermine the research methodology. Specifically, the effect of capacitance in the porcine model on the dynamic time-dependent component of impedance is negligible when compared with that in humans. This is based on the observed rapid rise in the voltage–time curve, which has a maximum voltage plateau phase near 0.1 ms in a porcine model (fig. 2).[2] Therefore, the displayed impedance from the stimulator is less affected by an increase in pulse duration and is a reasonable approximation. This is in contrast with our unpublished human volunteer data (fig. 3). In humans, the voltage–time response curve takes longer to reach the maximum voltage plateau phase (2–2.5 ms). Therefore, the displayed impedance will change substantially, along with the prolonged pulse duration for extended periods. This is why we clearly pointed out the limitations of our investigation in the manuscript as *"we anticipate that there may be substantial interspecies differences in EI... alternatively a percentage change in EI from the extraneural compartment in humans indicative of intraneural placement would be of high clinical value."* This may rectify the confusion to which Dr. Cory refers, as he may have missed or was unaware of such interspecies differences.

We thank the correspondent for his helpful comments, and we are grateful for the opportunity to clarify our results. We must also emphasize that it was never our intention to relate the absolute mechanism of the complex circuit. Instead, our intent was to examine the

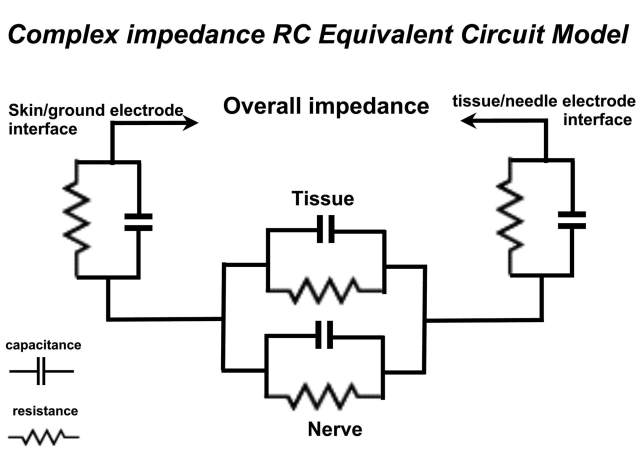

Fig. 1. Schematic complex impedance resistance–capacitance equivalent circuit model.

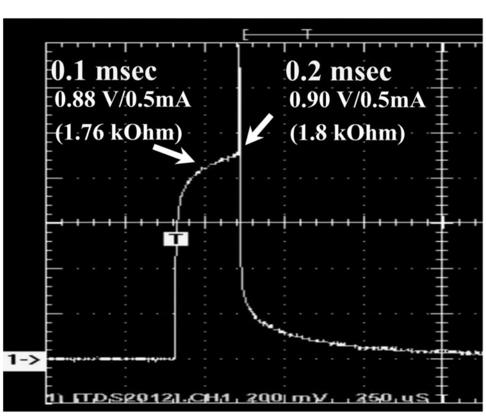

Fig. 2. Voltage–time curve in a porcine model. Example of the voltage response after applying 0.5 mA with a 0.2 ms pulse width *via* an 18-gauge insulated needle placed extraneurally. Adapted from Tsui *et al.*,[2] with permission from Elsevier.

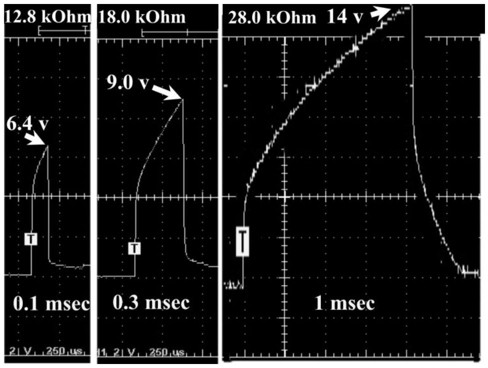

Fig. 3. Voltage–time curve in a human subject. Example of the voltage response after applying 0.5 mA with a 0.1, 0.3, and 1 ms pulse width, respectively, *via* a 24-gauge insulated needle placed extraneurally.

practical interpretation of impedance changes in a commercially available nerve stimulator in a pilot study carried out in a porcine model. The true value of this study lies in the detection of impedance changes that signify intraneural needle placement. Depending on the species, the noted change in impedance may be an increase or a decrease, and it may even be transient in nature. As it is said in a famous Chinese proverb attributed to Deng Xiaoping for his pragmatic policies, *"It doesn't matter if a cat is black or white; as long as it can catch mice, it's a good cat."*

Ban C. H. Tsui, M.D., M.S.C., F.R.C.P.(C.),* Derek Dillane, M.B., B.Ch. *University of Alberta Hospital, Edmonton, Alberta, Canada. btsui@ualberta.ca

References

1. 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
2. Tsui BC, Wagner A, Finucane B: Electrophysiologic effect of injectates on peripheral nerve stimulation. Reg Anesth Pain Med 2004; 29:189–93

(Accepted for publication January 15, 2009.)

Anesthesiology 2009; 110:1195

Nitrous Oxide: A Global Toxicological Effect to Consider

To the Editor:—The recent review article by Sanders *et al.*[1] was informative and comprehensive, with the exception of one important toxicological detail. Nitrous oxide is known to have a significant global climatologic impact as a naturally occurring greenhouse gas. After carbon dioxide and methane, nitrous oxide is the third most climatologically significant greenhouse gas. Greenhouse gases act like a warming blanket in the troposphere and prevent radiative cooling. Nitrous oxide is a particularly potent greenhouse gas with 300 times the global warming potential of carbon dioxide over 100 yr, according to the Intergovernmental Panel on Climate Change.[2] It seems prudent to include the climatologic effects of nitrous oxide as a biologic effect of the gas.

The climatologic effect and global warming potential of all halogenated anesthetic agents was addressed in a 1989 article, in the journal *Nature*, by Brown and colleagues. They concluded that the relatively short atmospheric lifetime of these agents reduces their ozone-depleting impact and global warming potential significantly, relative to other chlorofluorocarbons.[3] Desflurane has a global warming potential 1,341 times more potent than that of carbon dioxide when considered over a 100-yr period.[4] Langbein *et al.* reported that the atmospheric effects of all the halogenated anesthetics combined produce a relative contribution to global warming of .03%.[5] Nitrous oxide, in contrast, has a long atmospheric lifetime of approximately 120 yr.* The vast majority of atmospheric nitrous oxide from human activity is released from combustion and agricultural soils, particularly after the use of nitrogenous fertilizers. Although anesthetic nitrous oxide is believed to constitute a proportionally small amount of all atmospheric nitrous oxide by volume, the exact relative global warming contribution from all medical and dental anesthetic use remains to be studied.

* www.epa.gov/nitrousoxide/scientific.html. Accessed December 2, 2008.

Carbon dioxide regulation has begun, and nitrous oxide emissions are targeted by the 1997 Kyoto Protocol. Nitrous oxide is likely to be further regulated after adoption of the next climate change treaty at the 2009 United Nations Climate Change Conference in Copenhagen, Denmark. Nitrous oxide's potency as a greenhouse gas and the potential for regulation under international climate change accords argue for inclusion in any review of the biologic effects of this gas. Climate change is an important global-scale biologic crisis. International dialogue and reporting are essential to find solutions to this issue.

Nathaniel W. Parker, M.D.,† Elizabeth C. Behringer, M.D. †Cedars-Sinai Medical Center, Los Angeles, California. nathaniel.parker@cshs.org

References

1. Sanders RD, Weimann J, Maze M: Biologic effects of nitrous oxide: A mechanistic and toxicologic review. ANESTHESIOLOGY 2008; 109:707–22
2. Intergovernmental Panel on Climate Change: Climate Change 2001: The Scientific Basis; Cambridge University Press; Cambridge, United Kingdom, p 388
3. Brown AC, Canosa-Mas CE, Parr AD, Pierce JM, Wayne RP: Tropospheric lifetimes of halogenated anaesthetics. Nature 1989; 341:635–7
4. Oyaro N, Sellevåg SR, Nielsen CJ: Atmospheric chemistry of hydrofluoroethers: Reaction of a series of hydrofluoroethers with OH radicals and Cl atoms, atmospheric lifetimes, and global warming potentials. J Phys Chem A 2005; 109:337–46
5. Langbein T, Sonntag H, Trapp D, Hoffmann A, Malms W, Röth EP, Mörs V, Zellner R: Volatile anaesthetics and the atmosphere: Atmospheric lifetimes and atmospheric effects of halothane, enflurane, isoflurane, desflurane and sevoflurane. Br J Anaesth 1999; 82:66–73

(Accepted for publication January 15, 2009.)