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Acute Effects of Ultrasonic Shears and Monopolar Electrosurgery on Sciatic Nerve Electrophysiology

Chaoyang Chen[1], John M. Cavanaugh[1], Srinivasu Kallakuri[1], Katsumasa Tanimoto[2], Duan Broughton[3], Jeffrey W. Clymer[3*], Tamara V. Widenhouse[3] and Joseph F. Amaral[3]

[1]Spine Research Laboratory, Bioengineering Center, Wayne State University, Detroit, MI, USA.
[2]Department of Orthopaedic Surgery, Sapporo Medical University, Sapporo, Japan.
[3]Ethicon, Inc., Cincinnati, OH, USA.

Authors' contributions

This work was carried out in collaboration between all authors. Authors CC, JMC and DB were responsible for the study protocol. Authors CC, SK and KT designed and performed the experiments. Authors CC and JWC performed the statistical analysis and wrote the draft manuscript. Authors JMC, TVW and JFA contributed to the interpretation of the results. All authors provided critical evaluation of the manuscript and approve of its contents.

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Original Research Article

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ABSTRACT

Background: When using energized surgical devices in the vicinity of nerves, care must be taken to reduce the risk of thermal or electrical injury. For example, during thyroidectomy, it is critical to avoid damage to the recurrent laryngeal nerve while dissecting and coagulating nearby tissue.
Methods: We compared use of Harmonic ACE+ and Focus ultrasonic shears and monopolar electrosurgery to scissors as a control applied to make incisions in muscle 2 mm from the sciatic nerve in rats. Via electrophysiological monitoring, the compound action potential and conduction velocity were determined over a three hour post-application period. Neuromuscular response was observed by von Frey hair stimulation. Leukocyte infiltration was measured via H&E staining, and impaired axonal transport via β-APP immunohistology.
Results: None of the energized devices had a significantly different compound action potential

**Corresponding author: E-mail: jclymer@its.jnj.com;*

than scissors, although electrosurgery exhibited prolonged depolarization and repolarization times. Electrosurgery had significantly slower conduction velocity and increased von Frey stimulation force compared to scissors, whereas both ultrasonic devices were not different from the control. No difference was observed between devices for leukocyte infiltration, but electrosurgery had significantly greater β-APP levels than scissors, while again ultrasonic devices were not different.
Conclusion: Electrosurgery caused significantly more neurophysiological damage than scissors. In contrast, the ultrasonic shears were not statistically different than scissors in terms of nerve injury. Harmonic ACE+ and Focus can be used to cut and coagulate tissue near nerves with a low risk of electrophysiological injury.

Keywords: Ultrasonic; harmonic; electrophysiology; surgery; nerve injury; focus; ACE+.

ABBREVIATIONS

β-APP : Beta amyloid precursor protein
CAP : Compound action potential
CV : Conduction velocity
H&E : Hematoxylin & eosin
HPF : High power field
MES : Monopolar electrosurgery

1. BACKGROUND

When operating in the vicinity of nerves using energized surgical devices, care must be taken to avoid injury both from heat transfer and the passage of electrical current. Such procedures as hysterectomy, prostatectomy, and head and neck surgery all entail an increased risk of nerve injury if energy is used indiscriminately. For example, during thyroid surgery, meticulous dissection and hemostasis is needed when using energized surgical devices to dissect close to the ligament that attaches the thyroid gland to the cricoid cartilage and tracheal rings in order to reduce the risk of injury to the recurrent laryngeal nerve.

Monopolar electrosurgery (MES), via the passage of electrical current and heat, has been shown to produce significant nerve cell injury [1]. In contrast, devices powered by ultrasonic energy pass no electrical current [2]. Harmonic® devices (Ethicon Endo-Surgery, Inc., Cincinnati OH) cut and coagulate tissue by means of the frictional energy of mechanical motion at ultrasonic speeds (55 kHz). This mechanism, when used in Harmonic Blades, has been shown to produce less electrophysiological nerve damage than MES when used at a distance of 1-4 mm from the rat sciatic nerve, and, in fact, is similar in effect to dissection with cold scalpel [3,4]

This study was undertaken to determine whether ultrasonic shears, like blades, are also less likely to produce nerve injury than electrosurgery. Two versions of Harmonic shears, ACE+ and Focus, were compared to conventional monopolar surgery and cold steel scissors for their acute effects on nerve electrophysiology via conduction velocity studies and histological assessment. Harmonic ACE+ shears are designed for laparoscopic applications in soft tissue incisions when bleeding control and low thermal injury are desired. Harmonic Focus shears are used in open procedures for fine dissection and sealing of blood vessels and lymphatics. Both shear devices, like the Harmonic Blade, use a strictly mechanical mechanism of action, and thus cannot injure nerve via the passage of electrical current, as can an MES device.

2. METHODOLOGY

All surgical procedures were performed after approval by the Institutional Animal Care and Use Committee of Wayne State University.

The devices tested were HARMONIC ACE®+ Shears with Adaptive Tissue Technology (Ethicon Endo-Surgery, Inc., Cincinnati, OH), HARMONIC FOCUS® Long Curved Shears (Ethicon Endo-Surgery), Electrosurgical Pencil (ConMed, Utica, NY), and sharp-tipped steel surgical scissors. ACE+ and Focus were used at Power Level 5. The Electrosurgical (MES) device was used at 30 W in coagulation mode, which provides similar cutting and coagulation speed and functionality as do ACE+ and Focus at Power Level 5. [3]

Sciatic nerves from 32 male Sprague-Dawley rats were tested, eight per treatment leg. Rats were anesthetized via intraperitoneal injection of ketamine (60-80 mg/kg) and xylazine (8-13 mg/kg). Depth of anesthesia was continuously monitored via paw pinch. A tracheotomy was performed with intubation of a PE240 tracheal tube. The animal was ventilated with room air at a tidal volume of 2.5 ml and a rate of 90-100 respiratory cycles per minute. Pancuronium bromide was administered intravenously (2.5 mg/kg) to paralyze the skeletal muscles and further muscle paralysis was maintained using 1.5 mg/kg pancuronium bromide. Following muscle paralysis, the depth of anesthesia was monitored based on heart rate.

2.1 Surgical Procedures

Laminectomy: A midline dorsal longitudinal incision was made over the lumbar spine. The paraspinal muscles were retracted and the L2 to L5 spinous processes were removed. An L2-L5 laminectomy was then performed to expose the spinal canal. The dura mater was cut to expose the nerve roots for electrophysiological neural activity recordings. Exposed left L5 dorsal spinal nerve roots were kept intact with their connection to the spinal cord. The nerve roots were kept in mineral oil heated to 37 C.

Sciatic nerve exposure: A dorsal lateral skin incision between the lateral aspect of knee joint and greater trochanter of femur bone was made to expose muscles and fascia. Scissors were used to separate vastus lateralis cranially and rectus femoris muscles caudally to expose the sciatic nerve (Fig. 1). A stimulating electrode was placed at the distal end of the sciatic nerve, and a recording electrode was placed under the L5 dorsal root.

Fig. 1. Wound location in the muscle associated with the sciatic nerve

Device applications: Scissors were used to create a hole in the caudofemoralis muscle 2 mm away from the sciatic nerve. Using the hole, the devices were used to create a 10 mm long cut. ACE+ and Focus were applied twice for each cut of 5 mm. Focus was operated with the active blade up with upward tension on the muscle. For both Harmonic devices, the incision created was 10 mm long by 2 mm wide by 5 mm deep. MES was used to create a 10 mm incision with a depth of 5 mm. Scissors were used to create a 5 mm incision twice (Fig. 2).

2.2 Neurophysiological Recordings

Baseline neural discharges and evoked compound action potentials (CAP) were recorded prior to using each device. To activate myelinated axons, a 3 V followed by a 5 V electrical stimulus with a duration of 300 μs and a frequency of 1 Hz was applied to the sciatic nerve. Neural activity was amplified with an AC preamplifier (x1000) and recorded on an FM tape recorder, while being simultaneously monitored on an audio speaker [3]. Data were digitized prior to analysis. Hind paw probing was performed at each timepoint using calibrated pressure aesthesiometer nylon filaments [3]. Minimal force required to evoke sensory receptor response was determined and defined as the threshold force. Neurophysiological readings were taken prior to incisions (baseline) and at 2, 10, 30, 60, 120, and 360 minutes after the incisions.

2.3 Data Analysis

The conduction velocity (CV) was calculated by dividing the distance between the stimulating and recording electrodes by the latency between the onset of the stimulus pulse and the onset of the CAP. The area under the CAP curve (AUC) was calculated by integrating the area under the rectified CAP obtained from the recording electrodes. The depolarization time was estimated as the time from initial increase in the CAP curve to the peak (timepoints i to ii in Fig. 3). During depolarization, the voltage-gated sodium channels are activated. The repolarization time was estimated as the time from the peak in the CAP curve to the beginning of the hyperpolarization, or “overshoot,” period (timepoints ii to iii in Fig. 3). During repolarization, the voltage-gated potassium channels are activated.

2.4 Histology

After completion of the 3-hour neurophysiology recordings, the sciatic nerve was harvested and fixed in 4% paraformaldehyde and processed for paraffin infiltration and sectioning (7-10 μm).

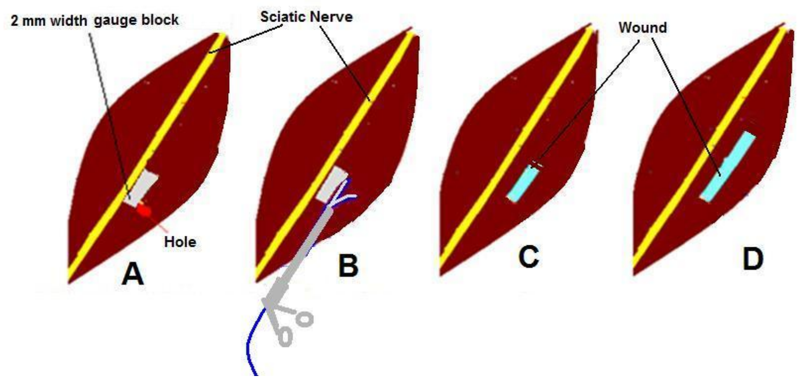

Fig. 2. Use of Harmonic ACE+ with two 5 mm cuts adjacent to the sciatic nerve

A. The distance between the nerve and cutting device was measured using a gauge block that was removed just before the actual cutting. The red dot was the location where a hole was made with a depth of 5 mm. After placing the 2 mm width gauge block next to the nerve, sharp surgical scissors was used to punch a 5 mm deep hole in the muscle. B. ACE+ was used to clamp a 5 mm length of muscle and the jaw was closed. The ACE+ was activated and upward force was applied to cut the muscle. C. Procedures A and B produced a 5 x 5 x 2 mm^3 wound. D. Procedures A and B were repeated to produce a 10 x 5 x 2 mm^3 wound.

Sections were stained with hematoxylin and eosin (H&E), and analyzed for the presence of white blood cells as an indicator of acute inflammatory changes. Sections were analyzed by β-amyloid precursor protein (β-APP) immunostaining [3] to assess axonal injury. For each staining technique digital images taken at 400x magnification, defined as a high power field (HPF), were analyzed to determine morphological changes. Scores were assigned by the investigator blinded to the treatment device.

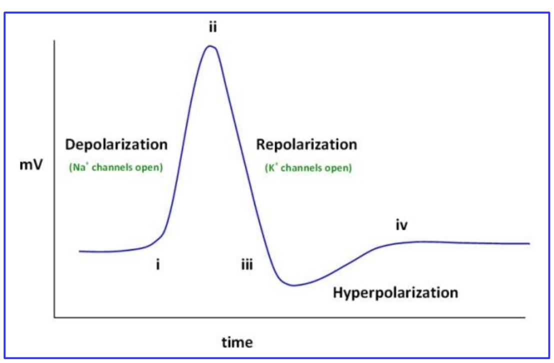

Fig. 3. Schematic of the compound action potential showing the depolarization time (timepoints i to ii) and repolarization time (timepoints ii to iii)

2.5 Statistical Analysis

A time-weighted average was calculated for each response over the 3-hr observation period. These time-weighted averages were then compared via ANOVA for the four treatments. Dunnett simultaneous tests were also performed between Scissors, as a control, and each of the energized devices. The Dunnett tests used a family-wise value of alpha of 0.05.

3. RESULTS

Results for the time-weighted averages of all responses are given in Table 1. The difference in compound action potential was not significant, although MES had the highest value and the greatest variability among treatments. Because of the variability, a post-hoc calculation indicated that study only had an 80% (1-β) power to detect a difference in the compound action potential of more than 1447 mV·ms. There was a significant difference in conduction velocity between treatments, with MES significantly slower than Scissors, whereas there was no difference between Scissors and either ACE+ or Focus. For both depolarization and repolarizations times, there was a significant difference between devices. MES had significantly longer times than Scissors, and again there was no difference in times between Scissors and the ultrasonic devices. The repolarization times at each experimental timepoint for all devices are shown in Fig. 4. For the von Frey hair stimulation force, there was a significant difference between devices but no energized device was individually different from Scissors. There were no significant differences observed between devices for H&E granulocyte incidence. For β-APP, there was a significant difference between devices (Figs. 5,6,7). MES had significantly higher infiltration of β-APP than Scissors, whereas there was no difference between Scissors and the ultrasonic devices.

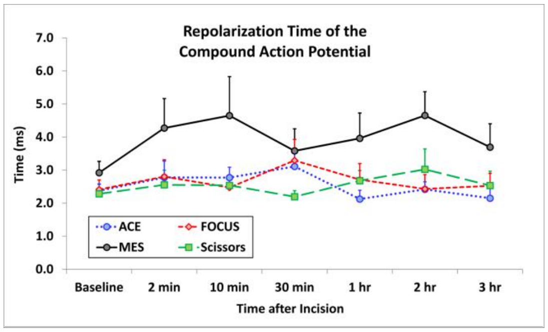

Fig. 4. Repolarization times of the compound action potential for the 3 hr period post-surgery with each of the devices

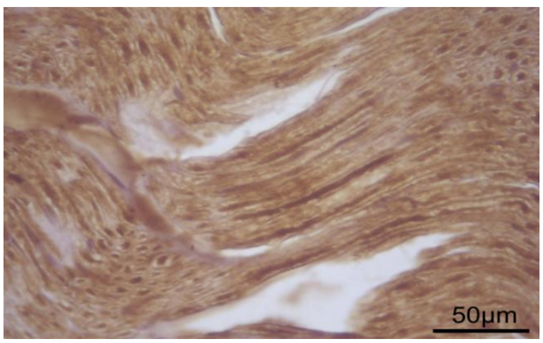

Fig. 5. A sciatic nerve section from exposure to scissors showing β-APP stained axons

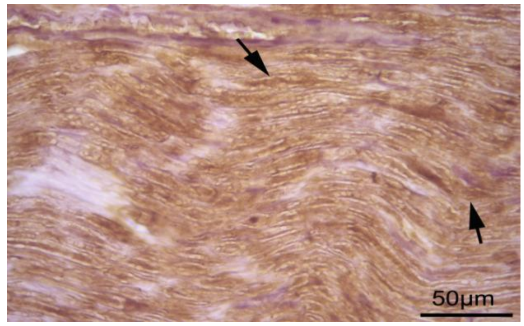

Fig. 6. A sciatic nerve section from exposure to MES showing IAT in the form of swellings (arrowheads)

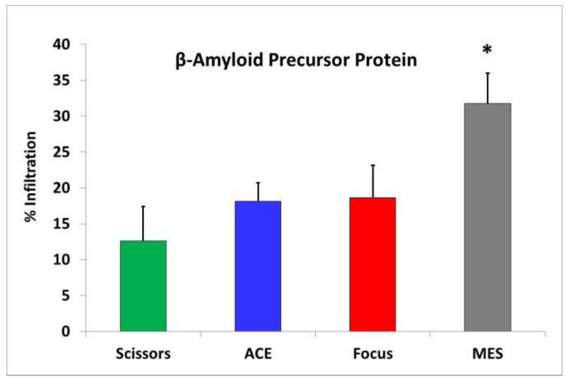

Fig. 7. Infiltration of β-amyloid precursor protein after application of the devices. Error bars represent two standard errors of the mean. MES was significantly greater than scissors (p<0.001)

Table 1. Summary of results (Mean ± Standard Deviation). The p-values in the scissors column are for ANOVA across all four devices. The p-values in the other three columns are for comparisons via the Dunnett Simultaneous Test between Scissors as a control and the device of that particular column

Measure	Scissors	MES	ACE+	Focus
Compound action potential (mV·ms)	1621±647	2457±2107	1519±362	1803±701
p-value	0.118	0.124	0.990	0.948
Conduction velocity (mm/ms)	61.8±1.7	58.5±3.5	62.3±2.1	60.3±1.5
p-value	**<0.001**	**<0.001**	0.867	0.212
Depolarization time (μs)	229.5±25.3	283.1±83.7	211.6±20.9	248.1±37.6
p-value	**0.001**	**0.008**	0.607	0.579
Repolarization time (μs)	2687±1017	4150±2021	2435±882	2650±1653
p-value	**0.005**	**0.017**	0.929	1.000
Von Frey Hair Stim force (g)	20.2±9.9	28.5±8.2	17.0±1.8	19.1±4.7
p-value	**0.017**	0.070	0.698	0.982
H&E (% incidence)	16.3±8.8	14.0±6.7	13.2±10.0	8.6±6.4
p-value	0.268	0.898	0.766	0.150
β-APP (% incidence)	12.6±5.9	31.8±6.0	18.1±4.0	18.6±6.7
p-value	**<0.001**	**<0.001**	0.156	0.121

4. DISCUSSION

With any surgical procedure that is performed near a nerve, there is always a risk of unintended injury to the nerve and loss of electrophysiological function. For example, in thyroidectomy, injury to the recurrent laryngeal nerve is of paramount concern to the surgeon. Harmonic Focus has a long history of use in thyroidectomy, and a recent network meta-analysis [5] shows that ultrasonic devices provide significantly faster operative time, less intraoperative and postoperative blood loss, and shorter hospital stay with no detriment to safety outcomes, such as recurrent laryngeal nerve paresis or hypocalcemia, compared to conventional surgery. Likewise, Harmonic ACE+ is useful in laparoscopic applications, where dissection efficiency and meticulous hemostasis is of paramount importance. [6] This preclinical study shows how ultrasonic devices can improve operative efficiency without increasing the risk of nerve injury as has been observed in clinical studies.

Previous studies have shown that ultrasonic energy when used in the form of a blade produces less inflammation, [7], provides faster healing, [8], and induces lower levels of gene and protein biomarkers of injury and inflammation [9] than conventional monopolar electrosurgery. In electrophysiological studies, where electrosurgery produces substantial nerve trauma as evidenced by reduced compound action potential and slower conduction velocity, the Harmonic Blade is essentially similar in these measures to sham surgery, both acutely [3] and subacutely. [4] The current study is the first in which we have directly compared the shears form of ultrasonic devices instead of the blade to monopolar electrosurgery. In general, the same advantages with regard to reduced risk of nerve trauma carry over from blades to shears.

We have demonstrated here that use of monopolar electrosurgery within 2 mm of a nerve causes loss of nerve function and axonal injury, whereas ultrasonic shears cause no more damage than cold steel scissors. After use of MES, alterations in the compound action potential were clear; both the depolarization and repolarization times increased and the conduction velocity slowed down. In contrast, both ACE+ and Focus showed no difference from use of scissors in any of these parameters.

Depolarization occurs at the beginning of the action potential when voltage-gated Na^+ channels open, allowing sodium influx into the axon, causing the membrane voltage to become less negative. Damage to the Na^+ channels would decrease influx and prolong depolarization time, as observed for MES where the depolarization time was 23% longer than for scissors, along with a decreased peak amplitude of the CAP.

Repolarization occurs after the Na^+ channels close and voltage-gated K^+ channels open, allowing potassium outflow and causing the membrane voltage to decrease. Damage to either the Na^+ or K^+ channels would prolong the repolarization time. [10] The repolarization time for MES was 150% longer than that for scissors, implying substantial alteration to the ion channels and ion flow. Neither ACE+ nor Focus had significantly different depolarization or repolarization times than scissors. Prolonged hyperpolarization was also observed for some of the MES samples, which can indicate malfunction of the Na^+/ K^+-ATPase pumps that restore the membrane voltage to its resting level.

The longer polarization times for MES resulted in a greater area under the curve for the compound action potential, but not significantly different from the value for scissors. This lack of significance is likely due to the much greater variability in CAP observed for MES. Most of the tracings showed extended polarization times, but a few showed virtually no response to the stimulating voltage, leading to a high standard deviation for the CAP AUC of MES. The CAP's of ACE+ and Focus were more consistent, as were those for cold scissors.

The conduction velocity for MES was slowed by 5% relative to scissors. Besides injury to the nerve itself, damage to the myelin sheath can also result in decreased velocity of propagation of the action potential. The alterations in the electrophysiological parameters were manifested in the functional response of the muscle to von Frey hair stimulation. The MES treatment required 40% greater stimulating force than scissors, while again the ultrasonic devices were not different than scissors.

Although no statistical difference was seen between treatments in inflammatory markers via H&E for this acute study, there was a significant difference for β-APP infiltration. Accumulation of β-APP indicates impaired axoplasmic transport from damage to the neurofilaments in the axon. Axons with impaired transport are less likely to be recruited to be part of the compound action potential due to conduction block, leading to increased polarization times. The level of β-APP was 150% higher after MES incisions than after application of scissors. No difference was seen between β-APP levels in scissors and either ACE+ or Focus.

Limitations of the study include the small sample size and short duration. For both AUC and H&E, no significant differences were observed between devices. Because of the high standard deviations for these two measures, a substantially larger sample size would have been necessary to detect a difference, and the effect size was small enough to make the measurement of little clinical relevance. The study's duration only lasted for 3 hours, so no conclusions can be drawn about long-term effects. However in a study involving blade devices, the differences between devices at 3 hours were also observed after a 7-day subacute study [4].

This study was carried out with the currently-marketed version of ACE+, but used the previous version of Focus. The new, recently-developed, Focus+ has a smaller end effector, lower thermal spread, and faster transection time, yet produces vessel seals that are just as strong and durable [11]. As does ACE+, Focus+ incorporates Adaptive Tissue Technology, [6,12,13] which permits more intelligent control of energy delivery to produce optimal seal strength with minimal thermal damage. Preliminary testing with the new version of Focus+ indicates that the same benefits as shown above for cutting and coagulating in the vicinity of nerves are achieved.

5. CONCLUSIONS

This study shows that ultrasonic shears provide the same benefits in operating near nerves as has been shown previously for ultrasonic blades. While MES causes lengthening of the polarization times, slows conduction velocity, and impairs axoplasmic transport, the ultrasonic shears are no different in any of these parameters than scissors. These results are consistent with earlier observations that the cause of nerve injury from MES is primarily from the passage of electrical current rather than from heat, as at the power level at which MES was used, the tissue temperatures generated were not substantially different than those generated by the ultrasonic devices. [3] Based on these results and similar findings in the literature, [14] MES should not be used within 2 mm of a nerve. Ultrasonic devices, such as Harmonic ACE+ and Focus, showed no more detrimental effect than scissors when used at a distance of 2 mm. Of course, surgeons must always use appropriate caution whenever using any energized device in the vicinity of nerves.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

DISCLAIMER

This manuscript was presented in the conference "84th Annual Meeting of the American Thyroid Association" available link is"
http://www.thyroid.org/wp-content/uploads/2014_84th_annualmeeting/ATA_2014_Full_Meeting_Program.pdf"
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COMPETING INTERESTS

Authors DB, JWC, TVW and JFA are employees of Ethicon Inc., manufacturer of the Harmonic ACE+ and Harmonic Focus. This study was supported with funding from Ethicon Inc.

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