The biophysical effects of ultrasound on median nerve distal latencies

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Abstract:

Purpose: Previous studies have documented the lack of ultrasound's non-thermal effects on nerve conduction using frequencies of 1 MHz and 870 kHz. The analyses and conclusions were reached, despite only one study incorporating pulsed ultrasound. The purpose of this study was to determine the biophysical effects of continuous wave (CW) and pulsed wave (PW) ultrasound on median nerve motor and sensory latencies using common frequencies of 1.0 and 3.0 MHz.

Subjects: Fifteen healthy subjects (8 males, 7 females, age = 23.5 + 4.44 yrs, height = 171.2 + 10.7 cm, weight = 67.5 + 7.9 kg) without a history of neurological or musculoskeletal injury to their non-dominant arm volunteered for testing. Methods and materials: Subjects were exposed in counterbalanced order to five ultrasound treatment conditions: (1) 1 MHz, 1.0 W/cm², 8 min., (2) 1 MHz, 1.0 W/cm², 50% PW, 8 min., (3) 3.0 MHz, 1.0 W/cm², CW, 8 min., (4) 3.0 MHz, 1.0 W/cm², 50% PW, 8 min., (5) placebo, 0.0 W/cm², 8 min. Dependent measures for motor and sensory latencies, and subcutaneous temperatures were taken pretreatment, at 2, 4 and 6 minutes during treatment, and immediately post-treatment. Separate two within repeated measures ANO VA were used for each dependent measure.

Results: Analysis revealed significant interactions for motor latencies [F (16,224) = 52.77, p < .001] , sensory latencies [F (16,224) = 41.10, p < .001J, and subcutaneous temperatures [F (16,224) = 52.77, p < .001] . Tukey's HSD post hoc analyses confirmed that nerve latencies responded similarly to subcutaneous temperature changes during and after ultrasound treatment.

Conclusions: Alterations in nerve latencies from ultrasound on healthy nerves appeared to be related to temperature changes induced by ultrasound's thermal effects, and not by non-thermal or mechanical effects.

Article:

INTRODUCTION

Therapeutic ultrasound is commonly prescribed and administered by physical therapists and athletic trainers for a variety of musculoskeletal conditions. Clinicians have traditionally used ultrasound to elevate tissue temperature and reduce pain with generators set at a frequency of l.0 megahertz (MHz). The introduction of 3.0 MHz ultrasound allows for faster heating with greater soundwave absorption in superficial tissues (34). Both frequencies produce biophysical effects in tissues, characterized by thermal or non- thermal (mechanical) mechanisms which are

administered clinically through either continuous or pulsed duty cycles (32, 34). Among the various physiological responses noted (15, 27, 18, 23, 32, 36), the thermal effect of raising tissue temperature has demonstrated faster nerve conduction (9, 10, 24, 27-30). In theory, the therapeutic benefit from this physiological response suggests the pain threshold within the area treated can be elevated through an analgesic effect.

The biophysical effects of continuous ultrasound on sensory or motor nerve conduction have been documented using the more commonly prescribed frequency of l.0 MHz (8-10, 24, 33). Additional studies on nerve conduction velocity (NCV) have been performed with an ultrasound frequency of 870 kHz (19, 27-30, 40). The earlier studies provided conflicting reports of both increased and decreased ulnar motor NCV following various continuous ultrasound intensities (19, 33, 40). Review of their methodology suggests the inconsistent findings are possibly attributed to the large areas sonated. Studies examining the effects of continuous l.0 MHz ultrasound on distal sensory latencies noted an inverse relationship between increases in tissue temperature and latency decreases of the superficial radial nerve (9, 10, 24). Halle et al. (24), while comparing ultrasound to infrared radiation on sensory latencies further noted the findings were similar between modalities, concluding the non-thermal effects from ultrasound were not a factor in nerve rate changes.

Of the reported studies on the effect of ultrasound on nerve conduction, only Kramer (27) included the use of pulsed ultrasound at 870 kHz to assess potential non-thermal effects. He noted significant increases in both ulnar NCV and subcutaneous tissue temperatures with continuous ultrasound and infrared radiation, attributing these responses to the thermal effects of the respective modalities. Whereas the effects of pulsed and placebo ultrasound both produced decreased NCV and subcutaneous tissue temperatures, to which he attributed these findings to the cooling effect of the ultrasonic transmission gel.

The effects of continuous 870 kHz ultrasound at various clinical intensities on subcutaneous tissue temperature and ulnar NCV have been studied separately for motor (28) and sensory (29) nerve fibers. Kramer (30) later used the same ultrasound parameters, comparing the treatment effects simultaneously on both ulnar motor and sensory NCV. In these studies he observed that intensities above 0.5 W/cm2 produced significant increases in NCV, but subcutaneous temperatures only increased significantly at intensities greater than 1.0 W/cm2. His observation was that it took an intensity of 1.5 W/cm2 to overcome the cooling effect on the tissue brought about by the transmission gel. He further noted that increased velocities were attributed to the heating effect of ultrasound on subcutaneous tissue and selectively on nerve tissue, accounting for the faster nerve conduction at 1.0 W/cm2, despite no significant changes in temperature at that intensity.

There is little doubt that nerve latencies should decrease as a result of elevating subcutaneous tissue temperature with heating modalities. However, there is insufficient evidence at this point to conclude that ultrasound's non-thermal effects will not effect nerve conduction. Authors have proposed that non-thermal ultrasound increases cellular membrane permeability and sodium ion transfer (17, 18, 32, 34) and that increases in sodium ion conductance in healthy peripheral nerve increases the rate of depolarization (5). Yet we have failed to demonstrate the extent of this relationship through laboratory or clinical research.

The lack of consistent findings in the literature on changes in nerve conduction across various ultrasound parameters, coupled with a poor understanding as to the significance of this physiological response, warrants further investigation. Additionally no documented studies have examined the effects of continuous or pulsed ultrasound at 3.0 MHz frequency on nerve conduction. Therefore, the purpose of this study was to compare the effects of l.0 MHz versus 3.0 MHz continuous and pulsed ultrasound on distal motor and sensory latencies of the median nerve and to determine whether ultrasound's non-thermal mechanisms would alone increase nerve conduction. We hypothesized that the non-thermal effects of pulsed ultrasound at l.0 and 3.0 MHz would decrease median nerve distal latencies.

METHODOLOGY

Subjects

The effects of therapeutic ultrasound on distal median motor and sensory nerve latencies, and subcutaneous temperatures in the distal non-dominant forearm and wrist were analyzed on 15 healthy volunteers (Table l). Inclusion criteria for this study were male or female, with an age range between 18 and 45 years. Subjects had no known medical history of central or peripheral neurological injury or disease, and had not sustained a musculoskeletal injury to their non-dominant upper extremity within 6 months prior to data collection. All subjects read and signed an informed consent form approved by a university Human Investigations Committee.

Table 1. – *Descriptive statistics on 15 subjects (8 males and 7 females)*

Characteristic	Mean	SD	Range
Age (years)	23.47	4.44	19-34
Height (cm)	171.19	10.74	147.32-185.42
Weight (kg)	67.54	7.90	56.80-82.50
Body fat (%)	15.64	7.56	4.8-29.10

Instrumentation

Nerve conduction latencies were recorded from a Cadwell Sierra LT, 2 Channel Electromyograph (EMG) machine (Cadwell Laboratories, Inc., 1021 Kellgg St., Kennewick, WA 99336). Instrumentation settings were selected according to the manufacturer and standard electroneuromyographic protocol for normal nerve (22, 25, 26, 35, 39). The low and high frequency amplifier settings were 32 hertz (Hz) and 2 KHz respectively, with a sensitivity of 20 microvolts per division and a sweep speed velocity of 2 milliseconds (msec) per division. The constant current stimulator was set with a rectangular pulse stimulus of 0.l msec, delivered at a frequency of 1 pulse per second, at supramaximal intensity. All recordings were obtained through extracellular techniques with the use of a disc ground electrode, surface disc electrodes for motor latencies and wire ring electrodes for sensory latencies. Electrodes were new and examined prior to initial testing for evidence of loose or frayed wires. They were then subjected to serial testing on a median nerve for reliable latency, amplitude and duration measures. Electrodes which failed this criteria were omitted from the study. The dependent variables recorded with the Cadwell Sierra LT were distal median nerve motor and sensory latencies measured in msec.

Ultrasound treatments were performed with an Omnisound 3000 (PTI, Topeka, KS 66619). The Omnisound 3000 provides a dual frequency capability of l.0 MHz ± 10% or 3.0 MHz ± 10%. A 2.0 cm² transducer head was used containing a lead ziconate titanate crystal. The effective radiating area of the soundhead was l.5 cm² with a beam nonuniformity ratio of 3:l for l.0 MHz and 4:l for 3.0 MHz. The same transmission gel was used for all nerve conduction testing and ultrasound treat ments (Aquasonic 100, Parker LaboratorIes, 307 Washington St., Orange, NJ 07050).

Subcutaneous temperatures were recorded with either a 5 cm 23-gauge, or 4 cm 26 gauge thermistor microprobe (Physitemp MT-23/5, Physitemp Instruments, Clifton, NJ). The thermistor was connected to a monitor (BAT-10, Physitemp Instruments, Clifton, NJ) which provided a digital temperature reading in degrees Celsius (°C). The indwelling thermistor was gas sterilized prior to insertiOn in each subject. According to the manufacturer, the accuracy for temperature readings was within 0.1°C for the indwelling thermistor, and monitor. All instruments were calibrated and assessed for reliability prior to data collection.

Procedure

Subjects reported to the McCue Center Sports Medicine Clinic at the University of Virginia for testing. They were instructed to rest comfortably in the area of examination 30 minutes prior to testing in order to allow for acclimatization with room temperature (35). Each subject was exposed to 5 ultrasound treatment conditions (Table 2). Subject treatment order was counterbalanced to reduce potential carry-over effects from previous treatments. Distal motor and sensory latencies, and subcutaneous temperature measurements were recorded serially for pre and post treatment conditions and on 2 minute intervals during each treatment for all subjects. The same clinician performed all nerve conduction testing, and was blinded from the ultrasound parameters to reduce potential bias when measuring nerve latencies.

Subject's non-dominant forearm, wrist and hand were exposed and anatomical landmarks for

Table 2. – *Five ultrasound treatment conditions*

	Frequency	Intensity	Duty cycle	Duration
Treatment 1	1 MHz	1.0 W/cm^2	continuous	8 minutes
Treatment 2	1 MHz	1.0 W/cm^2	50% pulsed	8 minutes
Treatment 3	3 MHz	1.0 W/cm^2	continuous	8 minutes
Treatment 4	3 MHz	1.0 W/cm^2	50% pulsed	8 minutes
Treatment 5	Sham	0.0 W/cm^2		8 minutes

nerve latency measurements and ultrasound treatments identified and marked with indelible ink. The EMG ground and recording electrodes were then positioned for testing, utilizing standardized procedures (22, 25, 26, 35, 39). With electrodes secured in place, the thermistor for recording subcutaneous temperatures was inserted into the mid-portion of the treatment area, medially to the palmaris longus tendon, so the temperature sensitive tip lay in the subcutaneous tissue above and medially to the course of the median nerve. The area of insertion was initially cleansed with isopropyl alcohol swabs. Once the thermistor was in place and secured with gauze and tape, the subject was allowed to rest 2 minutes before temperatures were recorded at 1 minute intervals. Subcutaneous temperature was considered stabilized after two successive recordings were within l.0°C of one another. A physician was present to insert the thermistor and

monitor each subject's condition throughout the testing procedure. The thermistor remained in place throughout the testing period.

Subsequent to subcutaneous temperature stabilization, temperatures were recorded, followed immediately by simultaneous motor and sensory latency measurements. The stimulating electrode was positioned over the median nerve between the palmaris longus and flexor carpi radialis tendons with the cathode of the stimulator positioned 10 cm proximal to the active recording electrode over the abductor pollicis muscle belly. The location of the stimulating electrode was the same for both motor and sensory latencies. Unlike the standard distance of 8 cm, the additional 2 cm allowed for an adequate area to administer the ultrasound treatments.

Ultrasound treatments were applied over the course of the median nerve beginning 2 cm distal to the stimulating electrode. The treatment area was 6 cm in length by 4 cm in width to insure the size of area treated did not exceed three times the soundhead's ERA. The area was marked with indelible ink to provide a point of reference for the examiner, and to also prevent transmission gel from touching the recording or stimulating electrodes. The conventional stroking technique was used with the soundhead moving at approximately 2 cm/sec, with each stroke overlapping the previous stroke by approximately 50%. The soundhead was lifted from the arm for less than 2 seconds at 2, 4, and 6 minutes during treatment to allow for nerve latencies to be recorded. Subcutaneous temperatures were also recorded during the same time intervals. A plastic syringe was used to measure 3 cubic centimeters (cc) of transmission gel for each treatment. Both the ultrasound transmission gel and soundhead were at room temperature prior to treatment.

Immediately following termination of an ultrasound treatment, gel was wiped from the treated area. Post-treatment subcutaneous temperatures were recorded, followed immediately by motor and sensory nerve latency measurements. The stimulus intensity for measuring nerve latencies remained constant to the pre-treatment intensity established separately for each condition. The remaining treatments were carried out using the same process, with an approximate 30 minute break between treatments to allow for subcutaneous temperature to return within + 01.°C of the original pre-treatment baseline temperature.

Statistical analysis

Separate two within (ultrasound treatments x time) repeated measures analysis of variance (RM-ANOVA) were analyzed for median nerve distal motor and sensory latencies respectfully. Post hoc analysis on significant interactions were assessed with a Tukey H.S.D. analysis. An alpha level of .05 was used for all tests. It was decided a priori not to adjust the alpha level with a Bonferroni's correction in order to maximize the results despite potentially creating a Type I error.

Intraclass correlation coefficients (ICC) (2,l) (13, 18) and standard error of measurement (SEM) data on instruments for measuring motor and sensory nerve latencies, and subcutaneous temperatures were collected and analyzed on the first five subjects to determine intra-tester reliability prior to testing (Table 3).

RESULTS

Room temperature throughout the three week testing period fluctuated from 25.3° to 29.0°C with a mean of 26.7°C (SD + l.013).

Table 3. – *Intraclass correlation coefficients (ICC) (2,1) and standard error of measurement (SEM) values for intra-tester reliability on instruments prior to subject testing for measuring distal motor and sensory latencies, and subcutaneous temperatures*

Measure	ICC	SEM
Distal motor latencies	.98	.03
Distal sensory latencies	.98	.03
Subcutaneous temperatures	.98	.07

SEM units are milliseeonds for distal lateneies and degrees Celsius for temperatures.

Distal motor latencies

Median nerve distal motor latency (DML) means and standard deviations for the 5 levels of ultrasound treatment conditions across the 5 levels of time during each condition are presented in Table 4. Latency fluctuations are illustrated in Figure 1.

The two within RM-ANOVA on DMLs revealed significant main effects for ultrasound treatment conditions ($F(4,56) = 11.26, p < .0001$], and for the time increments during each treatment [$F(4,56) = 13.97, p < .0001$]. The analysis also revealed a significant interaction between the ultrasound treatment conditions and time increments during treatment [$F(16,224) = 52.77, p < .0001$]. The magnitude of the interaction is appreciated by analyzing the effect size of a partial eta², which revealed that 79% of the total variance was accounted for between these factors.

Tukey's post hoc analysis revealed significant pre to post-treatment DML changes for all treatment conditions. There were no significant differences between pre-treatment latencies. With exception to treatments 2 and 4, all post-treatment latencies were significantly different from each other. The thermal ultrasound conditions produced significantly shorter latencies for treatments 1 and 3 at the post-treatment recording. Treatment 3 also produced significantly shorter latency changes from its pre-treatment measures at 4 and 6 minutes. The three non-thermal ultrasound conditions produces significantly longer latencies at 4 and 6 minutes and again at the post-treatment recordings. The non- thermal conditions were not significantly different from one another until the post-treatment recording, at which time treatment 5 was significantly prolonged from treatments 2 and 4.

Distal sensory latencies

Median nerve distal sensory latency (DSL) means and standard deviations for the 5 levels of

Table 4. – *Distal motor latency means (msec.) and (standard deviations) for each ultrasound treatment condition at the five levels of time*

	Pre Mean (SD)	2 Min. Mean (SD)	4 Min. Mean (SD)	6 Min. Mean (SD)	Post (8 Min.) Mean (SD)
Treatment 1	3.961	4.003	3.962	3.937	3.912[b,d]
	(.234)	(.237)	(.230)	(.227)	(.222)
Treatment 2	3.963	3.993	4.015[a]	4.030[a]	4.047[a]
	(.281)	(.277)	(.274)	(.266)	(.276)
Treatment 3	3.918	3.889[c]	3.843[c]	3.813[c]	3.783[b,c,d]
	(.204)	(.210)	(.203)	(.206)	(.208)
Treatment 4	3.935	3.991	4.011[a]	4.017[a]	4.033[a]
	(.207)	(.205)	(.203)	(.211)	(.207)
Treatment 5	3.933	3.977	4.046[a]	4.083[a]	4.112[a,b]
	(.233)	(.221)	(.222)	(.221)	(.223)

[a] $p < .05$ (treatments 2, 4 and 5 were significantly different from pre measures at 4 and 6 minutes, and post treatment)
[b] $p < .05$ (except treatments 2 and 4, all post treatment latencies were significantly different from one another)
[c] $p < .05$ (significant differences between treatment 1 and 3 at all recording times except pre)
[d] $p < .05$ (treatment 3 was significantly different from its pre treatment measures at all recording times)

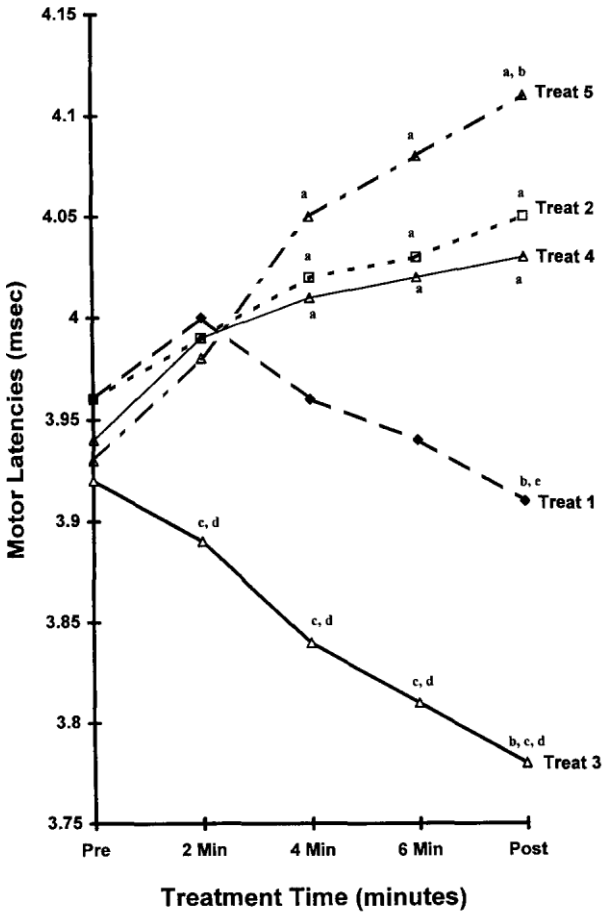

Fig. 1. – Median nerve distal motor latency means for ultrasound treatment conditions by time interaction.

[a] $p < .05$ (treatments 2, 4 and 5 were significantly different from pre measures at 4 and 6 minutes, and post treatment)

[b] $p < .05$ (except treatments 2 and 4, all post treatment latencies were significantly different from one another)

[c] $p < .05$ (significant differences between treatment 1 and 3 at all recording times except pre)

[d] $p < .05$ (treatment 3 was significantly different from its pre treatment measures at all recording times)

[e] $p < .05$ (treatment 1 was significantly different from pre treatment measures at post treatment)

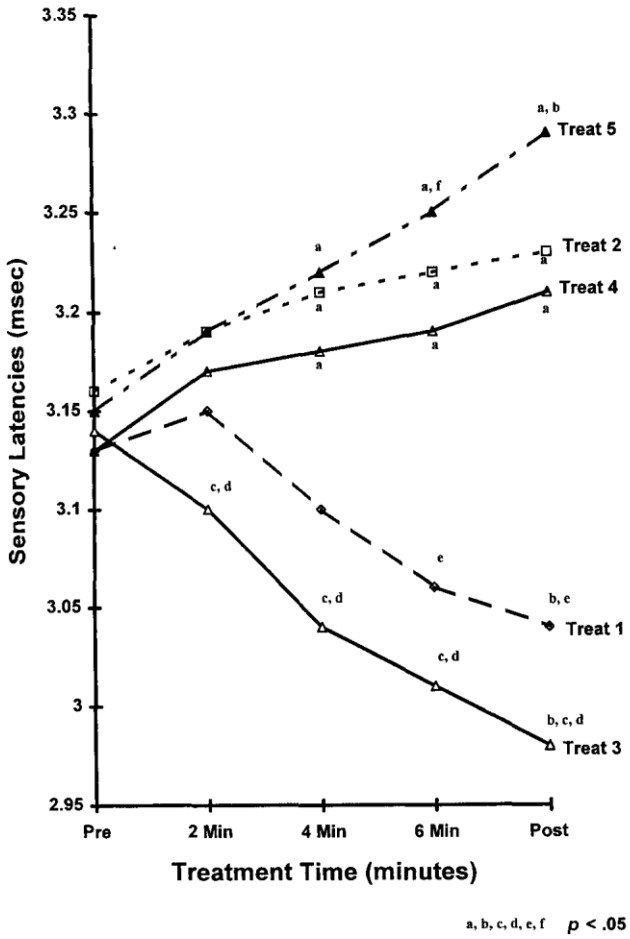

Fig. 2. – Median nerve sensory latency means for ultrasound conditions by time interaction.

[a] $p < .05$ (treatments 2, 4 and 5 were significantly different from pre measures at 4 and 6 minutes, and post treatment)

[b] $p < .05$ (except treatments 2 and 4, all post treatment latencies were significantly different from one another)

[c] $p < .05$ (significant differences between treatment 1 and 3 at all recording times except pre)

[d] $p < .05$ (treatment 3 was significantly different from its pre treatment measures at all recording times)

[e] $p < .05$ (treatment 1 was significantly different from pre treatment measures at 6 minutes and post treatment)

[f] $p < .05$ (treatment 5 was significantly different from treatment 4 at 6 minutes)

ultrasound treatment conditions across the 5 levels of time are presented in Table 5. Differences in latency means are illustrated in Figure 2.

The two within RM-ANOVA on DSLs revealed a significant main effect for ultrasound treatment conditions [F (4,56) = 12,31, p < .0001], but not for the time increments during each treatment [F (4,56) = 2.34, p > .066]. The analysis did reveal a significant interaction between

ultrasound conditions and time increments during treatment [F (16,224) = 41.10, p < .0001]. The interaction effect size produced a partial eta² of .741.

Tukey's post hoc analysis revealed significant pre to post-treatment DSL changes similar to the

Table 5. – *Distal sensory latency means (msec.) and (standard deviation) for each ultrasound treatment condition at the five levels of time*

	Pre Mean (SD)	2 Min. Mean (SD)	4 Min. Mean (SD)	6 Min. Mean (SD)	Post (8 Min.) Mean (SD)
Treatment 1	3.129	3.151	3.101	3.059[e]	3.041[b,e]
	(.192)	(.203)	(.187)	(.188)	(.190)
Treatment 2	3.163	3.193	3.209[a]	3.219[a]	3.233[a]
	(.147)	(.134)	(.126)	(.114)	(.138)
Treatment 3	3.139	3.097[c,d]	3.044[c,d]	3.006[c,d]	2.984[b,c,d]
	(.138)	(.143)	(.142)	(.126)	(.126)
Treatment 4	3.132	3.167	3.185[a]	3.190[a]	3.201[a]
	(.180)	(.185)	(.173)	(.177)	(.181)
Treatment 5	3.147	3.185	3.221[a]	3.248[a,f]	3.291[a,b]
	(.178)	(.171)	(.170)	(.161)	(.166)

[a] $p < .05$ (treatments 2, 4 and 5 were significantly different from pre measures at 4 and 6 minutes, and post treatment)
[b] $p < .05$ (except treatments 2 and 4, all post treatment latencies were significantly different from one another)
[c] $p < .05$ (significant differences between treatment 1 and 3 at all recording times except pre)
[d] $p < .05$ (treatment 3 was significantly different from its pre treatment measures at all recording times)
[e] $p < .05$ (treatment 1 was significantly different from pre treatment measures at 6 minutes and post treatment)
[f] $p < .05$ (treatment 5 was significantly different from treatment 4 at 6 minutes)

DMLs in that significant delays were noted with treatments 2, 4 and 5 and shorter latencies with treatments 1 and 3. Again there were no significant differences between pre-treatment measures. Treatments 2, 3 and 4 produced significant changes across recording times similar to the DMLs. In slight contrast with motor latency findings, treatment 1 produced significantly shorter latencies from pre-treatment measures at 6 minutes and posttreatment. Treatment 5 was also significantly prolonged from treatment 4 at the 6 minute recording period.

Subcutaneous temperature

Subcutaneous temperature means and standard deviations are presented in Table 6.

Relationships of distal latencies and subcutaneous temperatures

Relevant combinations of the dependent measures were extracted from a correlation matrix and presented in Table 7. The analysis revealed significant relationships between each of the dependent measures but varied in terms of which ultrasound treatment was administered. Meaningfulness of significant correlations are best put in perspective by assessing the explained variance shared by the combinations of dependent variables. Coefficients of determination (r^2) (Table 7) were calculated to analyze the explained variance between latencies and subcutaneous temperatures. In looking at the highest correlation coefficient between distal motor and sensory latencies, treatment 3 produced an r2 = .47, or 47% of the total variance accounted for between these variables.

DISCUSSION

The primary purpose of this study was to ascertain the thermal and non-thermal effects of therapeutic ultrasound on healthy nerve latencies using the more common frequencies of l.0 and 3.0 MHz. Our findings were consistent with previous studies in which ultrasound's thermal effects were considered responsible for significant decreases in distal nerve latencies (9, 10, 24). Despite not measuring the differences between motor and sensory latencies across factors for practical reasons, their relationship was addressed and found to be significant, consistent with findings reported by Kramer (30).

Table 6. – *Subcutaneous temperature means (degrees Celsius) and (standard deviation) for each ultrasound treatment condition at the five levels of time*

	Pre Mean (SD)	2 Min. Mean (SD)	4 Min. Mean (SD)	6 Min. Mean (SD)	Post (8 Min.) Mean (SD)
Treatment 1	32.033	31.607	31.947	32.267	32.493
	(.708)	(.633)	(.703)	(.911)	(.948)
Treatment 2	32.053	31.413	31.133	30.947	30.887
	(.674)	(.549)	(.590)	(.639)	(.650)
Treatment 3	32.027	32.440	32.893	33.293	33.893
	(.708)	(.705)	(.695)	(.771)	(.701)
Treatment 4	32.047	31.560	31.247	31.127	31.033
	(.691)	(.580)	(.630)	(.590)	(.603)
Treatment 5	32.020	31.407	30.900	30.520	30.267
	(.719)	(.672)	(.674)	(.648)	(.713)

Table 7. – *Pearson product correlation coefficients for relationships of distal motor (DML) and sensory latencies (DSL), and subcutaneous temperature (Temp) across the five ultrasound treatment conditions*

	Treat 1	Treat 2	Treat 3	Treat 4	Treat 5
DML:DSL	.5824	.5264	.6873	.5298	.5656
	(.339)	(.277)	(.472)	(.281)	(.320)
	$p = .023$	$p = .044$	$p = .005$	$p = .042$	$p = .028$
DML:Temp	– .4964	– .5311	– .5799	– .5072	– .5898
	(.246)	(.282)	(.336)	(.257)	(.348)
	$p = .060$	$p = 0.42$	$p = .023$	$p = .054$	$p = .021$
DSL:Temp	– .5615	– .6203	– .6991	– .5391	– .6683
	(.315)	(.385)	(.489)	(.291)	(.447)
	$p = .029$	$p = .014$	$p = .004$	$p = .038$	$p = .006$

Coefficients of determination (r^2) are included below each correlation coefficient.

Ultrasound's thermal effects on nerve latencies

Our findings expectantly revealed that continuous 1.0 and 3.0 MHz ultrasound resulted in significantly decreased median nerve DMLs and DSLs. This is consistent with previous studies which measured superficial radial DSLs following treatment with continuous l.0 Mhz ultrasound (9, 10, 24). In slight contrast to these studies we found significant DSL decreases with continuous l.0 MHz at the 6 minute recording period and again at posttreatment. This frequency also produced a significant decrease with median nerve DMLs, but not until the post-treatment

recording. These findings would suggest that length of treatment is important if nerve rate changes are considered when utilizing continuous l.0 MHz ultrasound. Currier et al. (9) and Currier and Kramer (10) reported significant sensory latency changes after 5 minutes of continuous ultrasound at l.0 MHz. However, they used a higher intensity at l.5 W/Cm², and sonated the area of the distal superficial radial nerve, which provides less soft tissue between the roundhead and distal radius. One or both of these factors could explain why they found significant differences in a shorter duration than ours.

Of notable interest were the significant decreases observed in motor and sensory latencies utilizing continuous 3.0 MHz ultrasound. Unlike the casual latency changes with l.0 MHz, continuous 3.0 MHz produced significant decreases from pretreatment measures at all recording times. Post hoc analysis further revealed significant differences between continuous 1.0 and 3.0 MHz ultrasound for both motor and sensory latencies at all recording times except for pretreatment. The faster rate of tissue heating with continuous 3.0 MHz could easily account for the differences noted between the two frequencies across the recording periods (16).

Relationships of thermal effects between dependent measures

The findings of our study produced new information regarding the thermal effects of continuous 3.0 MHz ultrasound on nerve latency changes. Studies reporting the effects of elevation in subcutaneous temperatures with faster nerve latency changes have been documented (l, 2, 4, 6, 7, 9-11, 14, 20, 21, 24, 27-30, 33). However, only a few of the reported studies used continuous ultrasound as a means to investigate nerve latency changes resulting from the modality, correlating those findings with subcutaneous temperatures (9, 10, 24, 27-30, 33). These studies all reported a linear relationship between increasing temperatures and speed of the evoked response.

The purpose of our study was never to question ultrasound's thermal effects on the relationship of subcutaneous temperature with nerve latency changes. Therefore we did not feel it was necessary to include another heating modality to confirm what has been well documented (9, 24, 27). These studies demonstrated that continuous ultrasound and infrared radiation produced significant increases in subcutaneous temperatures and faster evoked responses, with neither modality significantly different from the other in their results.

Ultrasound's non-thermal effects

The non-thermal effects of ultrasound on nerve conduction have been addressed in the literature (9, 24, 27). However, only one study directly investigated these effects through the use of pulsed 870 kHz ultrasound (27). The purpose of our study in addressing the non-thermal effects of ultrasound on median nerve DMLs and DSLs was to not only look at the more common frequencies of 1.0 and 3.0 MHz, but to also maximize the treatment dosage without creating a thermal effect. Our treatment dosage was derived from previous studies by Kramer (27-30), and from pilot testing. We speculated that if a non-thermal response in nerve latencies was to be achieved, our ultrasound parameters should have been sufficient.

Ultrasound's non-thermal effects on nerve latencies

The non-thermal effects produced by pulsed l.0 and 3.0 MHz ultrasound on median nerve DMLs and DSLs did not support our hypothesis. In fact, increased latencies were noted with the respective treatments. Our findings demonstrated that significant increases in DMLs and DSLs were also noted with sham ultrasound. Further analysis revealed the pulsed and sham ultrasound treatments were not significantly different from each other until the post-treatment recording period. The exception was pulsed 3.0 MHz ultrasound on DSLs, which became significantly different from the sham treatment at the 6 minute time period. Also of note was that both pulsed ultrasound treatments responded similarly on DMLs and DSLs, and that they were never significantly different from each other.

The reality of these findings were not surprising, and perhaps as previously reported, resulted from the cooling effect produced by the ultrasound transmission gel (27-30). However, it has created a slight dilemma as to why the latencies did not decrease, or at least stay the same. Our study was performed in vivo on normal healthy tissue, recording dependent measures related to nerve latencies and not directly on microscopic cellular changes. The results of our findings with regard to nerve latencies from pulsed ultrasound are perhaps more related to the anatomical and physiological aspects of healthy peripheral nerves in general, and the median nerve specifically, and not necessarily due to a lack of non-thermal effects.

Relationships of non-thermal effects between dependent measures

We believe our findings on ultrasound's non- thermal effects on nerve latencies provided conclusive evidence to suggest these effects do not influence healthy nerve function. Our findings support previous studies reporting on the lack of ultrasound's mechanical effects on nerve conduction (9, 24, 27).

The relationships of subcutaneous temperatures with nerve latencies, although significant were again not found to be strong. This further suggests that tissue exposure to ultrasound energy produces enough variability within the relationship between subcutaneous temperature and nerve latencies that caution must prevail when interpreting the results. Certainly a topically applied thermal application provides more uniform distribution of energy as it dissipates along a temperature gradient through tissue.

Summary of thermal & non-thermal effects

We hoped our study would produce nerve latency changes in the absence of a thermal effect with pulsed l.0 and 3.0 MHz ultrasound. Despite our study not providing evidence to support changes in peripheral nerve function induced from pulsed ultrasound does not preclude the presence of non-thermal effects within the tissues. It simply implies that in healthy peripheral nerves, in the absence of soft tissue trauma, and for the dependent measures we analyzed, no significant findings were produced.

A criticism of our findings would suggest that we should have waited longer between treatments to permit tissue homeostasis and avoid carry-over effects. Kramer (28-30) chose to wait 48 hours between treatments to avoid contaminating results. Our decision to use baseline subcutaneous temperatures as a reference for measuring subsequent temperatures to within 0.1 degree Celsius before initiating the next treatment proved to be valid and more efficient than having subjects return at a later time.

Post hoc analysis on nerve latencies revealed pre-treatment data recordings for each of the dependent measures were not significantly different from each other. This would suggest tissue cellular membrane stability and electrolyte homeostasis had occurred before the next treatment was initiated. This was a logical assumption, and inferred without directly investigating respective cellular physiology.

Clinical implications

Continuous ultrasound treatments produced expected thermal effects with increased subcutaneous temperatures and decreased DMLs and DSLs. Of these treatments, clinicians should be aware of potential problems associated with each. The 3.0 MHz treatment produced immediate and significant temperature and latency changes. In our study this presented no problems for the subjects tested. However, we only used an intensity of l.0 W/cm². Using higher intensities would not only generate more heat within the tissue, but also potentially cause discomfort to the patient.

Continuous 1.0 MHz ultrasound is also used by clinicians for its thermal effects on deeper structures. However, since not all facilities have a 3.0 MHz ultrasound unit, it is not uncommon for clinicians to use 1.0 MHz over joints such as the wrist. Of notable interest with continuous 1.0 MHz was the time factor necessary to elevate subcutaneous temperature and decrease motor and sensory latencies. The results of our study would suggest that at least 6 minutes of treatment time would be necessary to promote a thermal effect, and that 8 minutes would be more beneficial. Draper et al. (16) also advocated using an 8 minute treatment time to be more effective when using continuous 1.0 MHz ultrasound to elevate tissue temperature, as opposed to the traditional 5 minutes.

Future research

A positive aspect of our findings is that practical issues might be investigated. First, what effects would pulsed ultrasound have on nerve conduction in traumatized tissue? We can now assume, with a certain degree of confidence, that pulsed ultrasound has no effect on nerve conduction in healthy tissue. A study could be designed similar to ours; except without the thermal treatments, in which a controlled delayed onset muscle soreness group could be added to the study. Could peripheral nerves within inflamed tissue be more sensitive to pulsed ultrasound?

A second important issue would address the question of what relevance changes in nerve conduction have when treated with ultrasound. Studies could address issues related to pain modulation through differentiating nerve fiber recruitment, or by measuring plasma beta-endorphin levels. Significant findings in one of these studies would provide clinicians and researchers with important information to address the potential role of nerve function with ultrasound.

Laboratory studies could also be designed on animal specimens using in vivo and in vitro approaches to not only again look at the issue of pulsed ultrasound on nerve function, but to hopefully address the issues related to cellular function. The effectiveness of in vitro research, and its contribution to further understanding cellular physiology has more recently been documented on the effects of pulsed ultrasound on the nucleus of human fibroblasts (12), and with continuous ultrasound on collagen synthesis and fibroblast proliferation (37). Therefore, to actually measure ion diffusion rates across peripheral nerve tissue cell membranes with ultrasound intervention should be feasible and of interest.

CONCLUSION

Our findings further support previous studies which have reported that alterations in nerve conduction are related to temperature changes induced by ultrasound's thermal effects, and not by non-thermal or mechanical effects (9, 10, 24, 27). Unlike these studies, we included analysis on both commonly used frequencies of l.0 and 3.0 MHz, comparing continuous and pulsed duty cycles at 50% to a sham treatment. Despite the sensitivity of the instruments utilized for both treatment and data collections, no significant evidence was found to support the hypothesis of ultrasound's non- thermal effects changing median nerve motor or sensory latencies. The lack of evidence in this study to support our hypothesis does not mean the mechanical effects are not present within the tissue. It merely infers that in healthy human tissue in vivo, no significant differences were found to suggest a non-thermal effect on nerve latencies.

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