

# Monochromatic Infrared Irradiation (890 nm): Effect of a Multisource Array upon Conduction in the Human Median Nerve

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## ABSTRACT

**Objective:** Antidromic conduction studies in the human median nerve were used to assess the neurophysiological effects of irradiation of the skin overlying the nerve using a novel treatment unit comprising a multisource monochromatic infrared diode array (Equilight, Denver, CO). **Materials and Methods:** Healthy human volunteers ( $n = 40$ ) were recruited and randomly allocated to one of four groups: control, placebo, or one of two treatment groups (1.7 and 4.0 J/cm<sup>2</sup>). After baseline recordings of negative peak latency (NPL) were completed on the nondominant arm, subjects were treated according to group allocation. Recordings were subsequently repeated at 5-min intervals over a 45-min period. **Results:** Analysis of negative peak latency difference scores (ANOVA) demonstrated significant differences in NPL between groups and over time ( $p < 0.05$ ). While in the control and placebo groups NPL values remained relatively stable, in the two treatment groups such values decreased marginally, with the greatest effects observed in the 4.0 J/cm<sup>2</sup> group (e.g., at 5 min, differences in NPL [mean  $\pm$  SEM]: control group,  $0.02 \pm 0.03$  msec; treatment group 2, 4 J/cm<sup>2</sup>,  $-0.07 \pm 0.03$  msec). Similar significant differences were observed in skin temperature; correlation analysis indicated a weak (but expected) positive linear relationship between skin temperature and nerve conduction velocity ( $r = 0.125$ ). **Conclusion:** These results suggest that irradiation at the parameters and under the conditions used here produce a direct neurophysiological effect. The magnitude of such effects are in keeping with previous findings using single source arrays at higher radiant exposures or thermal effects of the treatment unit.

## INTRODUCTION

SO-CALLED LASER THERAPY, the use of low-intensity lasers and superluminous diodes as a therapeutic modality at radiant exposures typically under 30 J/cm<sup>2</sup>, has been investigated and clinically applied for nearly 30 years. Over this period, technological advances have led to the replacement of gaseous He-Ne systems with smaller, more portable laser-diode-based devices as the mainstay of treatment; additionally, multisource treatment arrays based upon clusters of diodes, which allow treatment of larger tissue areas, have become increasingly popular with clinical practitioners.<sup>1</sup> While this therapy has been promoted (and researched) as an effective treatment option for various pathologies such as delayed wound healing and pain,<sup>1–3</sup> controversy and skepticism has surrounded its use, particularly for the relief of pain.<sup>4,5</sup> Such controversy is based in part upon

the lack of an obvious mechanism for the putative treatment effects associated with laser therapy;<sup>4,6</sup> as a result, a significant proportion of the studies completed to date within this field have aimed to establish definitively the basic physiological and biological processes that may underlie any claimed clinical benefits of laser therapy.

In assessing putative mechanisms of action, a number of studies have assessed the effects of irradiation upon various neurophysiological functions.<sup>6–15</sup> Findings from such studies in animals include reports of laser-generated or delayed action potentials *in vitro*,<sup>7</sup> and laser-mediated increases in conduction latencies in the isolated frog sciatic nerve (820 nm; 2.38–3.57 J).<sup>8</sup> In humans, most work to date has concentrated on assessment of the effects of laser upon peripheral nerve conduction, with variable effects reported.<sup>9–14</sup> While one of the earliest reports in this area noted an apparent increase in nerve conduction latency

in the superficial radial nerve,<sup>9</sup> other studies in the same nerve have produced variable findings using He-Ne<sup>10</sup> or infrared diode irradiation.<sup>11</sup> Perhaps most interestingly, Kramer and Sandrin<sup>12</sup> compared He-Ne (632.8 nm, 10 mW), GaAlAs (780 nm, 12 mW) and placebo laser irradiation (using white light) and found no significant effects upon sensory latencies in the superficial radial nerve.

Studies at this center have similarly yielded variable results.<sup>13,14</sup> Infrared laser irradiation (830 nm; continuous wave [CW]; 9.6 J/cm<sup>2</sup>) was found to produce a significant increase of approximately 0.4 msec in median nerve negative peak latency (NPL).<sup>14</sup> In contrast, no significant results were found using pulsed irradiation (73 Hz versus 5 kHz; 820 nm; 1.5 J/cm<sup>2</sup>).<sup>13</sup> Interestingly, when the relevance of radiant exposures (830 nm; CW; 1.5–12 J/cm<sup>2</sup>) upon conduction velocity in the human median nerve was investigated, a significant increase in negative peak latency was reported (magnitude of change = ~0.2 msec), but only for the lowest radiant exposure (i.e., 1.5 J/cm<sup>2</sup>); such effects were coupled with a decrease in recorded skin temperature.<sup>15</sup> Finally, laser-mediated *decreases* in motor and sensory distal latencies after laser irradiation have also been demonstrated, using higher levels of radiant exposure (magnitude of change = ~0.18 msec); GaAlAs; 830 nm; 40 mW; CW; 1.2 J/point).<sup>16</sup>

While such investigations have been based upon the use of single source lasers or superluminescent diodes, no study has yet attempted to quantify the putative effects of multisource treatment arrays. Thus, despite their increasing popularity over the last 10 years,<sup>3,5</sup> the precise effects of this type of device remain unknown. Therefore, the aim of this current study was to examine the effects of a multisource array upon median nerve conduction in humans, as this is a well-established and characterized model of nerve conduction. For this study, a novel flexible treatment device was used to optimize application of radiation to the skin overlying the nerve in the forearm.

## MATERIALS AND METHODS

### Preliminaries

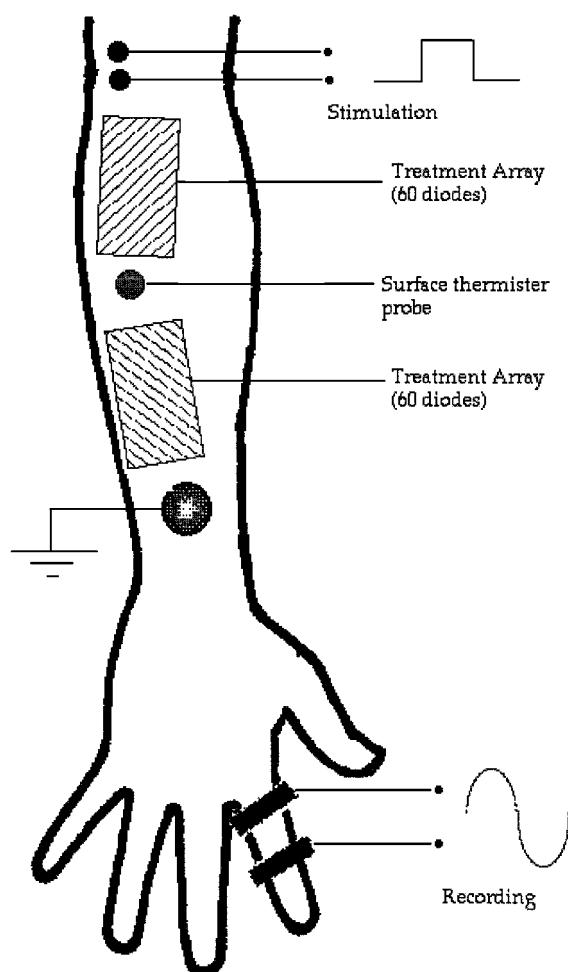
Following approval by the University of Ulster's Research Ethics Committee, healthy human volunteers ( $n = 40$ ; male and female; 20–40 years old) were recruited and screened for history or current signs/symptoms of neuromuscular disorders or peripheral neuropathy. The experimental procedure was explained to subjects, who were then asked to sign a simple consent form and randomly assigned to one of four experimental groups under single-blinded conditions. Subjects were randomly allocated to groups and remained supine for the duration of the experiment. The volar surface of the right forearm and hand was prepared using alcohol, and the stimulation and recording sites, at the elbow and second digit, respectively, were cleaned with a colloidal abrasive (Omniprep [Weaver, Aurora, CO]) to improve electrical conductance.

### Recording procedures

A bipolar muscle stimulator was used to identify the median nerve at the elbow for the purposes of antidromic stimulation; a monopolar muscle stimulator was further used to map the

course of the nerve along the forearm to the palmar surface of the hand to facilitate the accurate positioning of the treatment arrays (Fig. 1). A bar stimulating electrode was attached at the elbow, and two digital ring recording electrodes to the second digit, with the active electrode on the proximal phalanx and the reference electrode 3 cm distally on the middle phalanx. An earth electrode was also attached approximately 2 cm above the wrist, and all electrodes connected to a Mystro<sup>+</sup> electrophysiological stimulation and recording system (Medelec Ltd., Surrey, U.K.). The nerve was stimulated supramaximally (at 20%) using 100- $\mu$ sec pulses, delivered at a frequency of 1 Hz; averaged responses to a train of 16 pulses were recorded and stored digitally for subsequent analysis. Recordings were taken at 2-min intervals until three consecutive readings showed constant negative peak latencies (less than 0.01 msec). Once stabilized in this way, action potentials were recorded at 5-min intervals for the remainder of the experimental period (i.e., 45 min).

Ambient and skin temperature were recorded concomitantly throughout the procedure at 1-min intervals. For this, one ambient probe and one skin thermistor (model EU-U-V3-2; Grant Instruments Ltd., Cambridge, U.K.) were used, with the latter attached to the skin overlying the mid-point between the elbow and the wrist. All were connected to a Squirrel data logger



**FIG. 1.** Experimental procedure, showing electrical stimulation, electrode placement, and area of irradiation.

(Squirrel meter, 1200 series; Grant Instruments Ltd.) interfaced with a microcomputer; both thermistors were sensitive to temperature changes of  $\pm 0.05^\circ\text{C}$ .

### Irradiation parameters

A multisource monochromatic treatment unit (Equilight, Denver, CO) was used to irradiate the skin overlying the course of the nerve, after baseline recording of NPL was complete. This device produced infrared radiation (890 nm; pulsed at 270 Hz; average irradiance set at  $0.42\text{ mW/cm}^2$ ) via two multisource arrays, each containing 60 diodes (irradiation area:  $22.5\text{ cm}^2$  per array); the unit was applied to deliver radiant exposures of  $1.7\text{ J/cm}^2$  (treatment group 1) or  $4.0\text{ J/cm}^2$  (treatment group 2) dependent upon group allocation.

For the placebo condition, the procedure was repeated as for the  $4\text{ J/cm}^2$  group (treatment group 2) without activating the unit, thus allowing no active radiation to be delivered. Furthermore, the device was hidden from the subjects' view in all groups, in order to maintain blinding conditions.

### Analysis

NPL, that is, the time (msec) from onset (stimulus artefact) to the maximum negative deflection of the recorded action potential, or negative peak latency, was measured by an independent investigator. To allow for variation between subjects' baseline values, NPL difference scores were calculated for each subject by subtracting initial NPL values (time = 0 min) from subsequent measurements. Ambient and skin temperature readings were treated similarly. All such results were analyzed using repeated measures analysis of variance (ANOVA) and appropriate *post hoc* Fisher tests to determine whether any differences between conditions were statistically significant. The signifi-

cance level was set at  $p < 0.05$  for all tests. All statistical analyses were completed using the Statview statistical analysis package (Abacus Concepts Inc., Berkeley, CA).

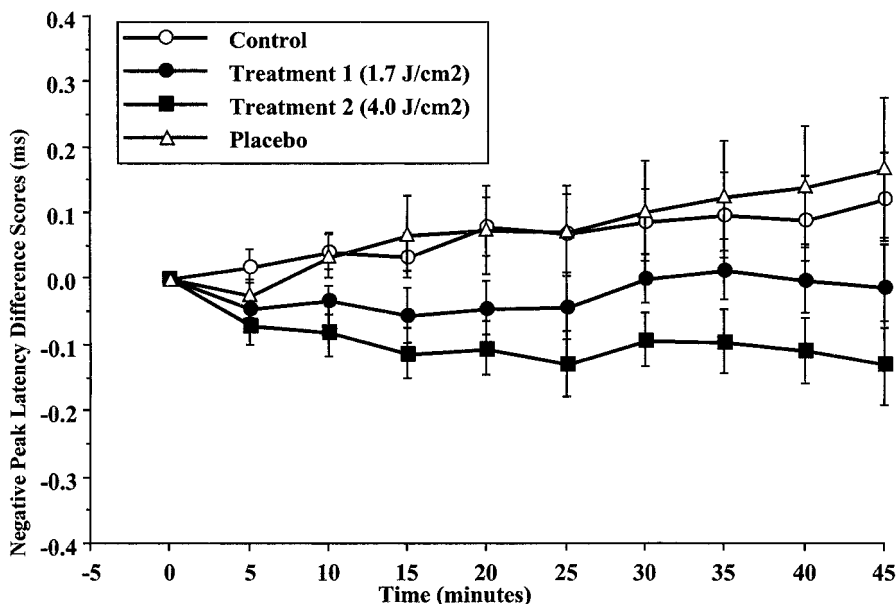
### Ambient temperature

Shift in ambient temperature of more than  $\pm 0.5^\circ\text{C}$  in any one experiment was used as the basis for exclusion of relevant data for that subject. This did not occur for any of the subjects. Beyond this, analysis of collected ambient temperature data indicated no significant differences between groups.

## RESULTS

Figure 2 shows NPL differences (msec; means  $\pm$  SEM) plotted against time in minutes for control, placebo, and both treatment groups. Although values in the control and placebo groups increased slightly over the 45 min of the experiment, NPLs in the two treatment groups *decreased* over the same period. Statistical analysis (ANOVA) of these data indicated significant differences among groups ( $p = 0.0281$ ), over time ( $p = 0.012$ ), and an interactive effect ( $p = 0.0066$ ). *Post hoc* Fisher tests further showed significant differences between control and treatment 2, treatment 1, and placebo, as well as treatment 2 and placebo groups at the 5-min interval. At 10-, 15-, 20-, and 45-min points, significant differences were found between treatment group 2 (i.e.,  $4\text{ J/cm}^2$ ) versus control and placebo groups.

Concomitant skin temperature recordings for all four groups are summarized in Figure 3, which shows temperature differences ( $^\circ\text{C}$ ; means  $\pm$  SEM) plotted against time in minutes. At baseline (i.e., 0 min), the mean skin temperature value for all groups was  $31.42 \pm 0.18^\circ\text{C}$  (mean  $\pm$  SEM), and at the 45-min



**FIG. 2.** Negative peak latency difference scores (NPLDs; msec) against time in minutes (points represent means  $\pm$  SEM;  $n = 10$  for all groups).

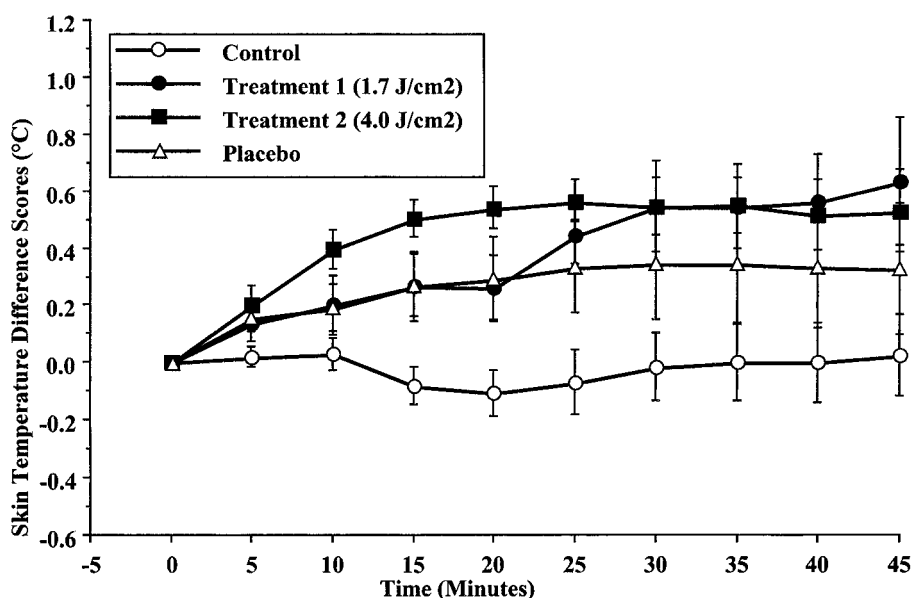


FIG. 3. Skin temperature difference scores ( $^{\circ}\text{C}$ ) against time in minutes (points represent means  $\pm$  SEM;  $n = 10$  for all groups).

time point the mean value was  $31.8 \pm 0.2^{\circ}\text{C}$  (mean  $\pm$  SEM). Results for the control group remained relatively stable over the experiment period; in contrast, skin temperature for both treatment groups and the placebo group increased. Statistical analysis confirmed that there were significant differences in skin temperature among groups ( $p = 0.007$ ), over time ( $p = 0.0001$ ), and an interactive effect between the time points and experimental groups ( $p = 0.0289$ ). *Post hoc* Fisher tests further showed significant differences between control and both treatment groups at the 10- and 30-min points. At 15, 20, and 25 min, *post hoc* Fisher tests showed significant differences among control and the other three experimental groups.

In summary, while there were some differences seen between groups, the most consistent findings indicated that the  $4.0 \text{ J/cm}^2$  treatment group demonstrated significant (and the greatest) decreases in negative peak latency values, coupled with increases in skin temperature values.

## DISCUSSION

Despite nearly 30 years of research and clinical application, there is still considerable debate regarding the efficacy of laser therapy, in part due to the lack of an obvious mechanism of action underlying the claimed effects of such devices.<sup>5</sup> In the laboratory, previous studies have demonstrated variable effects of irradiation upon nerve conduction, based exclusively upon single source devices;<sup>8,9,13,14</sup> the effects of irradiation using multi-source arrays have not previously been investigated. Previous research at this center has examined the effects of irradiation of the current multisource array ( $0.18$ ,  $0.54$ , and  $1.45 \text{ J/cm}^2$ ; GaAlAs,  $890 \text{ nm}$ ) upon wound healing in murine skin; that study concluded that irradiation at these parameters did not affect the rate of wound healing ( $0.18$  and  $0.54 \text{ J/cm}^2$ ) but rather seemed to produce an inhibitory effect ( $1.45 \text{ J/cm}^2$ ).<sup>17</sup> There-

fore, the aim of the current study was to examine the neurophysiological effects of such multisource monochromatic infrared irradiation upon conduction in the human median nerve; previous investigations in this nerve have demonstrated direct neurophysiological effects of laser irradiation.<sup>8,13-16</sup>

Analysis of negative peak latencies in the current study indicate that monochromatic infrared irradiation of the volar forearm overlying the nerve can significantly alter nerve conduction. In the present study, irradiation at the parameters indicated resulted in a decrease in latency, and thus an increase in conduction velocity. Further analysis showed that the effects of irradiation were relatively long lasting: decreases in NPL lasted for the duration of the experimental period (up to 45 min).

The finding of concomitant increases in skin temperature may provide an explanation for the observed findings, as it has been well recognized that a variation in tissue temperature will cause a corresponding alteration in nerve conduction velocities.<sup>18-20</sup> This is interesting as the irradiation parameters ( $1.7$  and  $4.0 \text{ J/cm}^2$ ) used in the present study would typically be classified as low intensity and, therefore, essentially athermal. The concomitant increase in skin temperature reported here contrasts with the findings of previous studies. Basford et al.,<sup>16</sup> similarly demonstrated a laser-mediated decrease in motor and sensory latency of the median nerve ( $1.25 \text{ J/point}$ ;  $890 \text{ nm}$ ; CV; infrared), but found no significant alterations in skin temperature. In contrast, Greathouse et al.<sup>11</sup> reported significant reductions in skin temperature following laser irradiation at 20 or 120 sec to five  $1\text{-cm}^2$  segments along the course of the superficial radial nerve. As a result, Greathouse and colleagues<sup>11</sup> discounted the observed (significant) increases in conduction, positing that unacceptable fluctuations in room temperature had produced the effects upon skin temperature and nerve conduction; this has been subsequently challenged by Baxter et al.<sup>14</sup> Such an explanation is clearly not applicable in the current study, as ambient temperature remained stable, and skin tem-

perature differences did not occur in the control group. It must therefore be assumed that changes in the measured skin temperature were treatment mediated; however, the precise mechanism underlying this effect is unknown. This notwithstanding, a conductive heating effect cannot be discounted as the treatment arrays were found (even at the relatively low settings used here) to produce a mild level of heat. One possible explanation may lie in the high level of total energy delivered over the course of the nerve in the current study; at 164 J for treatment group 2 (i.e., 4 J/cm<sup>2</sup>), this would be over 10-fold greater than levels used in previous experiments (based upon single point sources). Given such high levels of delivered energy, a significant increase in skin temperature might reasonably be expected in the treatment groups, along with a parallel increase in nerve conduction velocity. Correlation analysis between skin temperature difference score values and NPL difference score values did provide evidence for such a relationship ( $r = -0.562$ ); in other words, an increase in skin temperature was accompanied by a decrease in NPL and therefore representative of an increase in median nerve conduction velocity. This observation suggests that the effects observed in the current study may have been based upon a thermal mechanism, rather than the result of a direct photobiological effect. However, this is largely speculative. More detailed investigation is required before this can be definitively demonstrated.

In the final analysis, the present study has demonstrated a significant effect upon nerve conduction *in vivo*. However, analysis of results indicates that infrared irradiation delivered by this device may have produced a thermal rather than the expected photobiological effect. The significance of such an effect in the clinical application of this therapy has yet to be defined and requires further research; in particular, the (marginal) thermal effects reported here may be produced, and possibly more simply and effectively, with other electrophysical agents.

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