Main title: Skin physiological effects of 448 kHz Capacitive Resistive Monopolar Radiofrequency in healthy adults: A randomised crossover study and comparison with Pulsed Shortwave Therapy.

Running title: Physiological effects of radiofrequency treatment.

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ABSTRACT

Background and Purpose: Radiofrequency (RF)-based electrophysical agents (EPAs) are used in therapy practice over several decades, the most common being continuous/pulsed shortwave therapies (CSWT/PSWT) operating at a frequency of 27.12 MHz. There is insufficient evidence to support radiofrequency-based EPAs operating below the shortwave frequency band. This laboratory-based study aimed to investigate the skin physiological effects of 448 kHz capacitive resistive monopolar radiofrequency (CRMRF) and compare them to that of PSWT.

Methods: In a randomised crossover study, seventeen healthy volunteers received four treatment conditions – High, Low and Placebo dose conditions receiving 15-minute CRMRF treatment and a Control condition receiving no intervention. Fifteen participants also attended a fifth session receiving High dose PSWT for comparison. Treatment was applied to the right lower medial thigh. The untreated left leg served as a control. Pre, post and 20-minute follow-up measurements of skin temperature (SKT), skin blood flow (SBF) and nerve conduction velocity (NCV) were obtained using Biopac MP150 physiological measurement system. Core temperature, blood pressure (BP) and pulse rate (PR) were concurrently monitored. Group data were compared using either two-way repeated measures ANOVA or Friedman's ANOVA.

Results: Significant increase and sustenance of SKT with both high and low dose CRMRF was demonstrated over the other groups ($p<0.001$). PSWT increased SKT significantly ($p<0.001$), but failed to sustain it over the follow-up. However, among the five conditions only high dose CRMRF significantly increased and sustained SBF ($p<0.001$). Overall, the CRMRF physiological responses were significantly more pronounced than that of PSWT. No significant changes in NCV, core temperature, BP or PR were noted for any condition. No significant changes were observed in the control limb.

Conclusions: Physiological changes associated with CRMRF were more pronounced when compared to PSWT, placebo or control. Any potential stronger therapeutic benefits of CRMRF need to be confirmed by comparative clinical studies.

KEY WORDS

Electrophysical agents; Physiological effects; Radiofrequency; Skin blood flow; Skin temperature.

INTRODUCTION

Since the early decades of last century, physical therapists world over have used electrophysical agents (EPA) that employ radiofrequency (RF) electromagnetic fields (EMFs) to treat a variety of clinical conditions (Krusen, 1938; Taylor, 1936). Conventionally, the benefits of radiofrequency-based EPAs have been attributed to their ability to influence physiological processes via thermal or non-thermal mechanisms, thereby influencing pain and inflammation and promoting tissue healing (M. Al-Mandeel, M. & Watson, 2008; Foster, 2000). While the radiofrequency spectrum *per se* is broad, in physical therapies the RF frequency ranges used are largely limited to 30 kHz–30 MHz (Kitchen & Partridge, 1992; B. Kumaran & Watson, 2015a; Binoy Kumaran & Watson, 2016; Low & Reed, 1990).

At relatively high doses, the effects of radiofrequency are predominantly thermal (M. M. Al-Mandeel & Watson, 2010; Bricknell & Watson, 1995; Draper, Knight, Fujiwara, & Castel, 1999; Valtonen, Lilius, & Svinhufvud, 1973). The conversion of radiofrequency energy into heat energy in tissues and the ensuing thermophysiological responses can lead to various physiological changes leading to therapeutic benefits. A modest rise in temperature (mild hyperthermia) is sufficient to accelerate and/or increase cellular metabolic activity, and heat-induced vasodilatation can enhance local blood circulation in the tissues (Adair & Black, 2003; Challis, 2005; Jauchem, 2008; Silverman & Pendleton, 1968). Heat can also reduce muscle tone and improve tissue extensibility depending on the level of temperature rise attained in the tissues (Draper, Castro, Feland, Schulthies, & Eggett, 2004; Petrofsky, Laymon, & Lee, 2013; Robertson, Ward, & Jung, 2005). Unlike thermal effects, the non-thermal effects of radiofrequency are believed to occur predominantly at the cellular level (Cleary, 1997; Foster, 2000; Swicord, Balzano, & Sheppard, 2010) although the underpinning mechanism of tissue interaction is less clearly understood. This has led to a rather controversial discourse in contemporary literature.

In current practice the main radiofrequency-based EPA used is shortwave therapy (SWT) that operates at a frequency of 27.12 MHz, and is limited largely to pulsed SWT (PSWT) as a

delivery mode (Kitchen & Partridge, 1992; Shah & Farrow, 2012). Pulsed and continuous (CSWT) shortwaves are also the most widely researched radiofrequency-based EPAs. Nonetheless, EPAs operating at significantly lower RF frequency ranges (<1 MHz) have also been reported in clinical practice, despite their insufficient evidence (B. Kumaran & Watson, 2015a; Binoy Kumaran & Watson, 2016). An example for such EPAs currently used in therapy practice is Capacitive Resistive Monopolar Radiofrequency (CRMRF) that operates at 448 kHz. In this study, the authors aimed to investigate the skin physiological effects of continuous-mode CRMRF therapy in asymptomatic adults and to compare them with those obtained from PSWT.

MATERIALS AND METHODS

Apparatus

CRMRF device: The CRMRF energy at 448 kHz was delivered using 'Indiba Activ 902' (Indiba S. A., Barcelona). This therapeutic device was factory calibrated and pretested for accuracy of output. The peak power of the device was 200 W (450 VA (Volt-Ampere)). It delivers continuous-wave radiofrequency energy in two modes: Capacitive (CAP) and Resistive (RES), using metallic electrodes via a coupling medium. The device is CE marked and fully certified for therapeutic use. The authors did not develop or form part of the team that developed the equipment, and will not profit from sale and use of the equipment.

PSWT device: PSWT was delivered using 'Bosch Ultramed' (Robert Bosch GmbH, Germany) that operates at 27.12 MHz. The pulse duration (PD) was fixed at 400 µs, repeating at (pulse repetition rate; PRR) 15–200 Hz. The peak power (PP) can be varied from 100 to 1000 Watts (W). The desired mean power (MP) can be obtained by manipulating these pulse parameters. The device was calibrated prior to the study. The device is CE marked and fully certified for therapeutic use. The authors did not develop or form part of the team that developed the equipment, and will not profit from sale and use of the equipment.

Data acquisition system: Biopac MP150 (Biopac Systems, CA) physiological measurement system was used to record skin temperature (SKT), skin blood flow (SBF) and nerve conduction velocity (NCV). The cited accuracy of the system was ±0.003% of full scale range. SKT was recorded using SKT100C amplifier module and TSD202A thermistor transducer (response time 0.6 seconds). SBF was recorded using PPG100C

photoplethysmogram (PPG) amplifier module and TSD200 PPG transducer. Nerve conduction velocity was measured using STM100C stimulator and EMG100C electromyography (EMG) amplifier modules.

Other devices: Blood pressure (BP) and pulse rate (PR) were monitored using a digital BP monitor (Omron M2, Omron Healthcare Europe B.V., Netherlands) and core temperature was measured using an infra-red (IR) tympanic thermometer (Braun ThermoScan IRT 4520, Braun GmbH, Germany). A body composition monitor (Omron BF508, Omron Healthcare Europe B.V., Netherlands) was used to obtain the anthropometric data. Room temperature and humidity were monitored using an electronic thermohygrometer (RS 212-124, RS Components Pte Ltd., Singapore).

Sample and groups

Seventeen asymptomatic (self-reported) adults with normal skin thermal perception and no contra-indications to radiofrequency-based therapy were randomly recruited via emails from the 27,000 members of the University of Hertfordshire. They attended four sessions each in a crossover design representing four experimental conditions – CRMRF high (thermal), CRMRF low (sub/minimally thermal) and CRMRF placebo dose conditions, and a control condition with no intervention (Figure 1). The order of attendance was randomised by concealment using a computer generated randomisation chart (IBM SPSS Statistics, Version 20), and blinded from the participants. Fifteen participants attended a fifth session representing 'PSWT high dose' condition. Attendance to PSWT group was neither randomised nor blinded. The study was approved by the Health and Human Sciences Ethics Committee with Delegated Authority (HHSECDA) of the University of Hertfordshire (Protocol number: cHSK/PG/UH/00143). All participants signed an informed consent prior to the study.

Insert Figure 1 here

Experimental procedure

The participants were asked to avoid food, beverages and strenuous exercises before the start of sessions to minimise physiological variation. A minimum gap of 48 hours was allowed between sessions, and similar times (±1 hour) of the day were chosen. Positioned in supine, skin over the medial aspect of both thighs was prepared and marked to deliver treatment and

obtain measurements. For all participants the right leg was chosen for treatment, while the untreated left leg served as control.

The Biopac system probes were attached to the marked areas on both legs (Figure 2). All measurements were performed pre-treatment, immediately post treatment and 20-minutes post treatment for all conditions. After ensuring proper baselining of the data streams, SKT and SBF were recorded for 10 minutes pre-treatment and continuously at post treatment till the 20-minute follow-up. NCV was recorded for 30 seconds at each assessment prior to the other measurements. Core temperature, BP and PR were concurrently monitored. The probes and connecting leads on the treated leg were removed prior to radiofrequency application and reattached post treatment to avoid potential signal interference, probe damage and tissue irritation. Reliability of probe placements was established by extensive pilot work. Sampling rate for Biopac was chosen as 200 per second based on pilot data.

Insert Figure 2 here

Treatment delivery

The CRMRF treatment was delivered for 15 minutes (5 minutes CAP followed by 10 minutes RES) using 20 ml coupling medium for each mode. The return plate electrode was smeared with 20 ml coupling medium and positioned under the calf muscle belly. The dosage was adjusted based on participant feedback. For CRMRF high, the intensity was gradually increased till the participants reported moderate yet comfortable heating, which was then maintained throughout the session. For CRMRF low, the intensity was maintained at a sub/minimally-thermal level throughout. For CRMRF placebo, the device output was turned off (within the first minute) after the participants reported thermal onset. For the control condition the participants rested on the treatment plinth for 15 minutes. The nearest available PSWT dose to the mean CRMRF high dose (42.37 W) used in this study was 47 W (PD–400 µs, PRR–200 Hz, PP–600 W). Hence, 47 W was delivered for 15 minutes to all 15 participants who attended PSWT group, using a drum (monode) applicator placed 1.5 cm from the skin.

Data analysis

All data were analysed using IBM SPSS Statistics ((Version 20) IBM Corporation, USA). Two separate data analyses, with three CRMRF and control groups (17 participants) and with

all five groups (15 participants) were undertaken. To ascertain any statistically significant differences between conditions, group data were compared using either two-way (intervention and time) repeated measures analysis of variance (ANOVA) at three time points (baseline, post treatment, 20-minute follow-up) or using Friedman's two-way ANOVA by ranks, depending on the distribution of data (Shapiro-Wilk). Statistical significance was set at $p \leq 0.05$ (0.8 P, 95% CI). A post-hoc analysis was conducted using G*Power (Version 3.1) to determine the power.

RESULTS

All participants completed the treatments and accompanying assessments. Both types of interventions were well tolerated, with no reports of any adverse events. The demographic and mean (SD) anthropometric data are reported in Table 1. Mean (SD) treatment doses, room temperature and humidity are reported in Table 2. To illustrate the levels of dosage variation among participants, the individual data from the three radiofrequency groups are plotted in Figure 3.

Insert Table 1 here

Insert Table 2 here

Insert Figure 3 here

Skin temperature

Figures 4(a–b) shows the mean (SD) SKTs recorded at three time points and the percentage changes of mean.

Insert Figures 4a & 4b here

A 4*3 (intervention, time) repeated measures ANOVA revealed a significant main effect for intervention [F (3, 48) = 29.545, $p<0.001$]; for time (pre, post, follow-up) [F (2, 32) = 8.458, $p=0.001$]; and a significant interaction between intervention and time [F (2.997, 47.952) = 62.261, $p<0.001$]. Therefore, SKT varied significantly depending on the treatment dose and time point. Groups were not significantly different at baseline. Comparable results were obtained ($p<0.001$) in the five-group analysis. However, the baseline SKT in PSWT group was significantly lower than the rest [F (4, 56) = 10.341, $p<0.001$].

In CRMRF high group there was significant rise in SKT at post treatment [F (1, 16) = 129.695, $p<0.001$, $r=0.943$] and significant retention at follow-up [F (1, 16) = 96.567, $p<0.001$, $r=0.926$]. Similar significant responses, although less strong were noted at post treatment [F (1, 16) = 5.404, $p=0.034$, $r=0.502$] and at follow-up [F (1, 16) = 5.901, $p=0.027$, $r=0.519$] in CRMRF low group. No meaningful changes were noted in the temperature recordings of either placebo or control groups. In PSWT high group significant rise in SKT was noted from baseline to post treatment [F (1, 14) = 146.312, $p<0.001$, $r=0.955$], with no significant retention at follow-up. Key results of pairwise comparisons are reported in Table 3.

Insert Table 3 here

Skin blood flow results

Figures 5(a–b) shows the mean (SD) SBFs recorded at three time points and the percentage changes of mean.

Insert Figures 5a & 5b here

SBF data was analysed using Friedman's two-way ANOVA by ranks. In the four-group analysis, significant main effect for the interventions was found at the post treatment stage [χ^2 (3) = 27.494, $p<0.001$] and the follow-up [χ^2 (3) = 31.047, $p<0.001$]. Therefore, the applied dose significantly influenced the observed SBF. Groups were not significantly different at baseline. In the five-group analysis, similar results were obtained for both the above comparisons ($p<0.001$). As above, there was no significant difference between groups at baseline.

Within CRMRF high group there was substantial rise in SBF at post treatment (Friedman, $p<0.001$, $r=-0.780$), which was retained at the follow-up (Friedman, $p=0.001$, $r=-0.632$). Significant rise (although less strong) at the post (Friedman, $p=0.006$, $r=-0.529$) and retention at the follow-up (Friedman, $p=0.001$, $r=-0.618$) were also noted in the CRMRF low group. No such meaningful changes were noted in the other three groups. Key results of pairwise comparisons are reported in Table 4.

Insert Table 4 here

Nerve conduction velocity results

Figure 6 shows the mean (SD) NCVs recorded at three time points. There were no statistically significant changes in NCV within or between groups at any time point for either the four-group or the five-group analyses (repeated measures ANOVA). The percentage changes of mean are not reported here since there were no meaningful changes.

Insert Figure 6 here

Other results

No physiological parameters from the control leg displayed any changes at any time point. No significant variations were noted in core temperature (tympanic), BP or PR under any test condition at any time point.

Post-hoc analysis revealed that the overall power obtained in both statistical analyses for SKT and SBF were over 80%.

DISCUSSION

Whilst numerous studies have investigated the clinical and other effects of SWT, there is a dearth of evidence to support the use of RF frequencies below shortwaves. Two recent reviews published by the same authors found minimal evidence for radiofrequency-based EPAs below shortwave frequencies (B. Kumaran & Watson, 2015a; Binoy Kumaran & Watson, 2016).

Recently, in a preliminary experimental study we reported the fundamental skin thermal response patterns to incremental doses of 448 kHz CRMRF (B. Kumaran & Watson, 2015b). In the current study more thermophysiological responses to set doses of CRMRF were investigated by employing a randomised controlled design and a comparison was performed with PSWT. Although many similar studies involving shortwaves have been reported over several decades (Abramson et al., 1960; M. Al-Mandeel, M., 2004; M. M. Al-Mandeel & Watson, 2010; Flax, Miller, & Horvath, 1949; Grynbaum, Megibow, & Bierman, 1950; Jan, Yip, & Lin, 1993), to our knowledge this is the first such *in vivo* study employing an RF frequency below the shortwave band.

It is problematic to compare a continuous-mode EPA like CRMRF with a pulsed mode EPA like PSWT because in pulsed mode therapies there is an ‘off cycle’ that enables the body’s circulatory system to dissipate most of the generated heat thus minimising heat accumulation

(M. Al-Mandeel, M. & Watson, 2008). The high PSWT dose (47 W) delivered in this study only produced 'mild' heating at best as reported by the participants. This is consistent with previous PSWT studies (M. M. Al-Mandeel & Watson, 2010; Bricknell & Watson, 1995) although it is interesting to note that those studies had only employed a lower dose. Comparison between CRMRF and PSWT was done on the premise that PSWT is the nearest radiofrequency equivalent to CRMRF in contemporary therapy environment. Clinical use of CSWT, which is the closest to CRMRF in terms of energy delivery, has decreased significantly in the western world over recent decades (Kitchen & Partridge, 1992; Shah & Farrow, 2012).

Temperature and blood flow changes secondary to radiofrequency exposure are largely thermophysiological responses. While the literature suggests that a small rise in tissue temperature of about 1 ^{o}C will help to relieve mild inflammation, many of the clinical benefits of heating such as reduction in pain and inflammation or increasing tissue extensibility occur when temperatures are raised by 2–4 ^{o}C (Lehmann & DeLateur, 1990; Prentice & Draper, 2011). Unlike for temperature rise, there are no recommendations in the literature about what level of rise in blood flow will produce clinical benefits. The substantial gains in SKT and SBF obtained from CRMRF high group would make it potentially suitable for treating chronic pain and inflammation and conditions causing poor tissue extensibility. However, it will be unsuitable for acute conditions since it is widely accepted that high (thermal) dose applications of radiofrequency-based treatments are not advisable for acute conditions (M. Al-Mandeel, M. & Watson, 2008).

The results also showed that a mild increase in SKT of around 1 ^{o}C had no significant/sustained impact on the corresponding SBF. The CRMRF low dose raised the SKT marginally, but not SBF when compared to placebo or control groups. Similar effects were also noted in the PSWT group, where a marginal increase in SKT was obtained with no significant impact on SBF. Hence, the CRMRF low and PSWT high applications are potentially suitable for use in acute conditions. While the modest response in SKT obtained from the PSWT group and/or the lack of sustenance over the follow-up are consistent with several past studies (M. M. Al-Mandeel & Watson, 2010; Bricknell & Watson, 1995; Morrissey, 1966; Valtonen et al., 1973), SBF results are contrary to some others that proposed a significant rise in blood flow post PSWT (Erdman, 1960; Silverman & Pendleton, 1968).

In a recent shortwave study, a significant rise in SBF was reported during PSWT treatment (MP of 24 W), but this effect disappeared post treatment (M. M. Al-Mandeel & Watson, 2010). Other shortwave studies that suggested a much higher and/or sustained increase in temperature (Bennett, Hines Jr, & Krusen, 1941; Verrier, Falconer, & Crawford, 1977); blood flow (Abramson, Harris, & Beaconsfield, 1957; Grynbaum et al., 1950); and both temperature and blood flow (Abramson et al., 1960; Flax et al., 1949) were conducted using CSWT. Comparison of the effects of similar doses of PSWT and CSWT on blood flow is also available (Silverman & Pendleton, 1968).

The contrasting differences between the effects of similar average doses of two types of radiofrequency interventions studied here may be due to various factors. Since PSWT is pulsed, the generated heat is driven away by the circulating blood thus limiting the rise of tissue temperature. Also, PSWT devices are known to cause scattering of the radiofrequency waves. Without the need for a special conducting medium, shortwave devices emit stray radiations in the air (M. Al-Mandeel, M. & Watson, 2008; Scott, 2002). Hence, some of the energy will be lost through scattering, making it difficult to concentrate the energy delivery in the area treated (Docker et al., 1994; Martin, McCallum, Strelley, & Heaton, 1991).

Scattering also makes it challenging to estimate the specific absorption rate (SAR) of radiofrequency energy in the recipient for either intervention. It is challenging also to calculate the SAR for the treated area *per se* since the accurate mass of the area exposed to treatment cannot be determined. If it is assumed that there was zero scattering and that whole of the applied energy was absorbed by the target tissues, the mean (SD) whole body SAR can be estimated to be 0.60 (0.09) W/kg for CRMRF high group, 0.27 (0.07) W/kg for CRMRF low group, 0.04 (0.02) W/kg for CRMRF placebo group and 0.67 (0.10) W/kg for PSWT group. However, although the mean estimated SAR was lower in the CRMRF high group compared to the PSWT high group, its actual SAR is likely to have been higher than PSWT owing to lower scattering.

Another factor that would determine the extent of radiofrequency thermophysiological responses is its ability to penetrate the tissues. Besides the intensity and duration of exposure, frequency of the wave is one of the parameters that influence penetration. Radiofrequency energy gets absorbed at various depths in complex patterns (Adair & Black, 2003). The higher retention of heat and the fact that there was no sharp fall in the post-treatment skin temperature strongly suggests higher energy penetration with CRMRF. Experimental and

theoretical work has suggested that at low intensity exposure levels (such as in this study), 'demodulation' of radiofrequency in tissues is only practical at frequencies that are much lower than a few megahertz (e.g. frequencies significantly lower than shortwaves). In other words, the biological systems cannot 'rectify' radiofrequency fields above a few megahertz efficiently enough to affect the endogenous fields and the biological processes (Swicord et al., 2010).

In the PSWT high group, when the participants were asked to rate their perception of heat on a scale of one to four, where one was 'no heat' and four was 'high heat', the majority (11 participants out of 15) rated the effect as 'mild heating' (score 2 on the scale) at best. Four participants reported that there was no perceptible heat. Such a participant feedback is commensurate with the mild to moderate rise in mean post-treatment SKT noted in the PSWT high group. These findings also agree with some of the previous PSWT studies (M. M. Al-Mandeel & Watson, 2010; Bricknell & Watson, 1995), while at the same time it is interesting to note that those studies had only employed a lower MP dose of PSWT.

When comparing the two high dose groups, the participants described a 'uniform and deep feel' of heating for the CRMRF high intervention, while the feeling of heating was reported to be 'mild at best' for the PSWT high intervention as stated above. However, the reported feeling of deep heating should be interpreted with caution because localised thermal perception is based primarily on cutaneous receptors (Guyton & Hall, 2011) and there remains some controversy as to whether thermal perception at depth is thermal perception *per se* or nociception. To date there is insufficient evidence on the existence of subjective perception of temperature from deeper tissues such as muscles (Graven-Nielsen, Arendt-Nielsen, & Mense, 2002). Hence, the participants' reported perception of deep heating may relate to a variation in the rate and distribution of temperature change in the more superficial tissues such as the skin and superficial fascia, where there is a presence of thermoreceptors (B. Kumaran & Watson, 2015b).

Temperature measurements from the deeper tissues were not attempted in this study as the methods involved are invasive and hence beyond the scope of this study. The Biopac MP150 system used in this study is a popular method to obtain real-time physiological data and has been used widely in research (M. Al-Mandeel, M., 2004; Chakraborty & Pal, 2016; Maity, De, Pal, & Dhara, 2016). PPG and surface thermistors are valid and reliable and have been used since decades to measure SBF and SKT (Alian & Shelley, 2014; Burnham, McKinley,

& Vincent, 2006; Kamal, Harness, Irving, & Mearns, 1989; Kelechi, Michel, & Wiseman, 2006).

There is insufficient evidence available in the literature to show the influence of low frequency RF on nerve conduction in humans, apart from a handful of studies done using shortwave that showed mixed results (Abramson et al., 1966; M. Al-Mandeel, M., 2004; Currier & Nelson, 1969). No such data on nerve conduction exists for radiofrequencies below shortwave. The present study failed to obtain any impact on NCV with either CRMRF or PSWT, although it was anticipated that NCV might change in response to changes in tissue temperature (Rutkove, 2001). On the other hand, it is unsurprising that the core (tympanic) temperature did not change for any of the conditions, since a local application of radiofrequency energy is not expected to influence the core temperature (Adair & Black, 2003). Similar responses were also expected for pulse rate and blood pressure, both of which did not change significantly (Abramson et al., 1960; M. M. Al-Mandeel & Watson, 2010).

Unlike many healthy-participant studies that usually involve young and physically fit participants from a narrow age range, this study recruited deliberately from a wide age range (25–66 years; mean (SD) 45.71 (12.70) years). Also, their physical activity levels were considerably varied, making the sample more representative of the general population. The study was carried out at 'thermoneutral' conditions, where the mean (SD) room temperatures varied between 24.30 (0.56)–25.53 (1.11) ^{o}C. Although the above factors made the results more generalizable, extrapolating the findings from an asymptomatic population to a patient population is problematic, owing to their dissimilar physiological mechanisms, comorbidities and the existence of pathology.

In this study the post-treatment measurements could only be started after a delay of three minutes on average due to skin preparation and probe reattachment. Hence, it is possible that the study failed to capture the absolute peak post treatment responses. Likewise, skin responses during the treatment was also not mapped, unlike in some of the previous PSWT studies (M. M. Al-Mandeel & Watson, 2010; Draper et al., 1999). Together, the above factors somewhat limit the findings; however, in the active CRMRF groups there was no sharp decline in responses through the follow-up period. Hence, extrapolating from the current and past (B. Kumaran & Watson, 2015b) results, it is reasonable to predict that the reported effects would have sustained for more than 30 minutes. From the clinical perspective, this knowledge is valuable as it provides a reasonable 'therapy window' to the treating clinician.

Another limitation was that the researcher (BK) who undertook the interventions and measurements was not blinded, making this study only single-blind at best. Future studies should be fully randomised, double-blinded, employ longer follow-ups and minimise the time delay in post treatment measurements. Additionally, to facilitate a full understanding of the physiological responses, measurements should be obtained during the treatment as well.

CONCLUSIONS

The results suggest that a high as well as low dose of CRMRF can significantly enhance and sustain SKT, while only the high dose CRMRF can meaningfully impact on SBF. An equivalent high dose of PSWT increased SKT only marginally when compared to CRMRF and did not sustain it over the follow-up. PSWT failed to impact on SBF, which meant that overall CRMRF induced a significantly more pronounced physiological response out of the two types of radiofrequency-based treatments. The NCV, BP and PR were not influenced by either type of intervention. The untreated contralateral leg failed to show any meaningful physiological response.

The more pronounced physiological effects of CRMRF in healthy participants compared to PSWT may be indicative of its potentially stronger clinical benefits; however, caution should be exercised in extrapolating these findings to patient populations who could respond differently to the same intervention. Further studies that address the limitations of this study, that explore additional physiological responses and clinical studies that involve patient groups are therefore necessary.

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AUTHOR CONTRIBUTIONS

The study was carried out in the Physiotherapy Research Laboratory of the University of Hertfordshire. The first author (BK) is responsible for the acquisition and analysis of data, and writing up this manuscript. The second author (TW) is responsible for the critical revision of this manuscript and the conception and overall supervision of this research project. Both authors are responsible for the design of the study. Both authors have approved the final version of this manuscript and agree to be accountable for all aspects of the work, its accuracy and integrity. The authors also confirm that all persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

DECLARATION OF INTEREST

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Table 1: Demographic and mean (SD) anthropometric data from the 17 participants who received localised 448 kHz Capacitive Resistive Monopolar Radiofrequency (CRMRF) treatment.

Sample	Demographic data			Mean (SD) anthropometric data				
	Mean (SD) age (years)	Gender: Males	Gender: Females	Height (m)	Weight (kg)	Body fat (%)	Visceral fat	BMI
17	45.71 (12.70)	7	10	1.70 (0.08)	71.48 (10.02)	30.32 (7.61)	7.24 (2.54)	24.68 (2.71)

SD – standard deviation; kg – kilogram; m – metre; BMI – body mass index.

Table 2: Mean (SD) treatment doses received by the participants in the five experimental groups, and mean (SD) room temperature and humidity during the experimental sessions.

	CRMRF High	CRMRF Low	CRMRF Placebo	Control	PSWT High
RF dosage in Watts (W)	42.37 (4.64)	18.77 (3.82)	2.79 (1.23)	0	47
Room temperature (ºC)	25.12 (1.14)	25.53 (1.11)	25.35 (1.06)	25.18 (1.04)	24.30 (0.56)
Humidity (%)	41.21 (6.38)	41.06 (7.40)	39.68 (6.24)	41.79 (6.50)	32.70 (4.37)

CRMRF – Capacitive Resistive Monopolar Radiofrequency; PSWT – Pulsed Shortwave Therapy; RF – radiofrequency.

Table 3: Key results from the planned comparisons (contrasts) on the skin temperature responses across five experimental groups.

Comparisons involving PSWT high group are based on 15 participants, and all others based on 17 participants. Statistical significance was set at $p \leq 0.05$ (two-way repeated measures ANOVA).

Comparison		F-ratio	Significance value (*p*)	Effect size (*r*)	Power (P)
CRMRF high vs.	CRMRF low	9.270	0.008	0.606	0.881
	CRMRF placebo	83.807	< 0.001	0.916	1.000
	Control	31.979	< 0.001	0.816	0.991
	PSWT high	61.449	< 0.001	0.902	0.994
CRMRF low vs.	CRMRF placebo	27.270	< 0.001	0.794	0.987
	Control	11.255	0.004	0.643	0.917
	PSWT high	29.583	< 0.001	0.824	0.982
PSWT high vs.	CRMRF placebo	0.019	0.892 (NS)	0.037	
	Control	12.611	0.003	0.688	0.918

CRMRF – Capacitive Resistive Monopolar Radiofrequency; PSWT – Pulsed Shortwave Therapy; NS – non-significant.

Table 4: Key results from the planned comparisons (contrasts) on the skin blood flow responses across five experimental groups.

Comparisons involving PSWT high group are based on 15 participants, and all others based on 17 participants. Data were not significantly different at the baseline. Statistical significance was set at $p \leq 0.05$ (Friedman's two-way ANOVA).

Comparison		Test statistic	Adjusted significance value (*p*)	Effect size (*r*)	Power (P)	Test statistic	Adjusted significance value (*p*)	Effect size (*r*)	Power (P)
		At post treatment				At follow-up			
CRMRF high vs.	CRMRF low	1.412	0.009	0.546	0.920	1.324	0.017	0.513	0.888
	CRMRF placebo	2.235	< 0.001	0.866	1.000	2.294	< 0.001	0.889	1.000
	Control	1.647	0.001	0.638	0.972	1.912	< 0.001	0.740	0.993
	PSWT high	3.267	< 0.001	1.033	1.000	3.000	< 0.001	0.949	1.000
CRMRF low vs.	CRMRF placebo	0.824	0.377 (NS)	0.319		0.971	0.170 (NS)	0.376	
	Control	0.235	1.000 (NS)	0.091		0.588	1.000 (NS)	0.228	
	PSWT high	1.667	0.039	0.527	0.866	1.333	0.209 (NS)	0.422	
PSWT high vs.	CRMRF placebo	0.867	1.000 (NS)	0.274		0.467	1.000 (NS)	0.148	
	Control	1.533	0.079 (NS)	0.485		0.867	1.000 (NS)	0.274	

CRMRF – Capacitive Resistive Monopolar Radiofrequency; PSWT – Pulsed Shortwave Therapy; NS – non-significant.

Figure 1: Schematic representation of the five study conditions (groups). Groups 1–4 were represented by all 17 participants, with each participant assigned a random order of attendance. Group 5 was represented by 15 participants only, at non-random and was always the last (fifth) session.

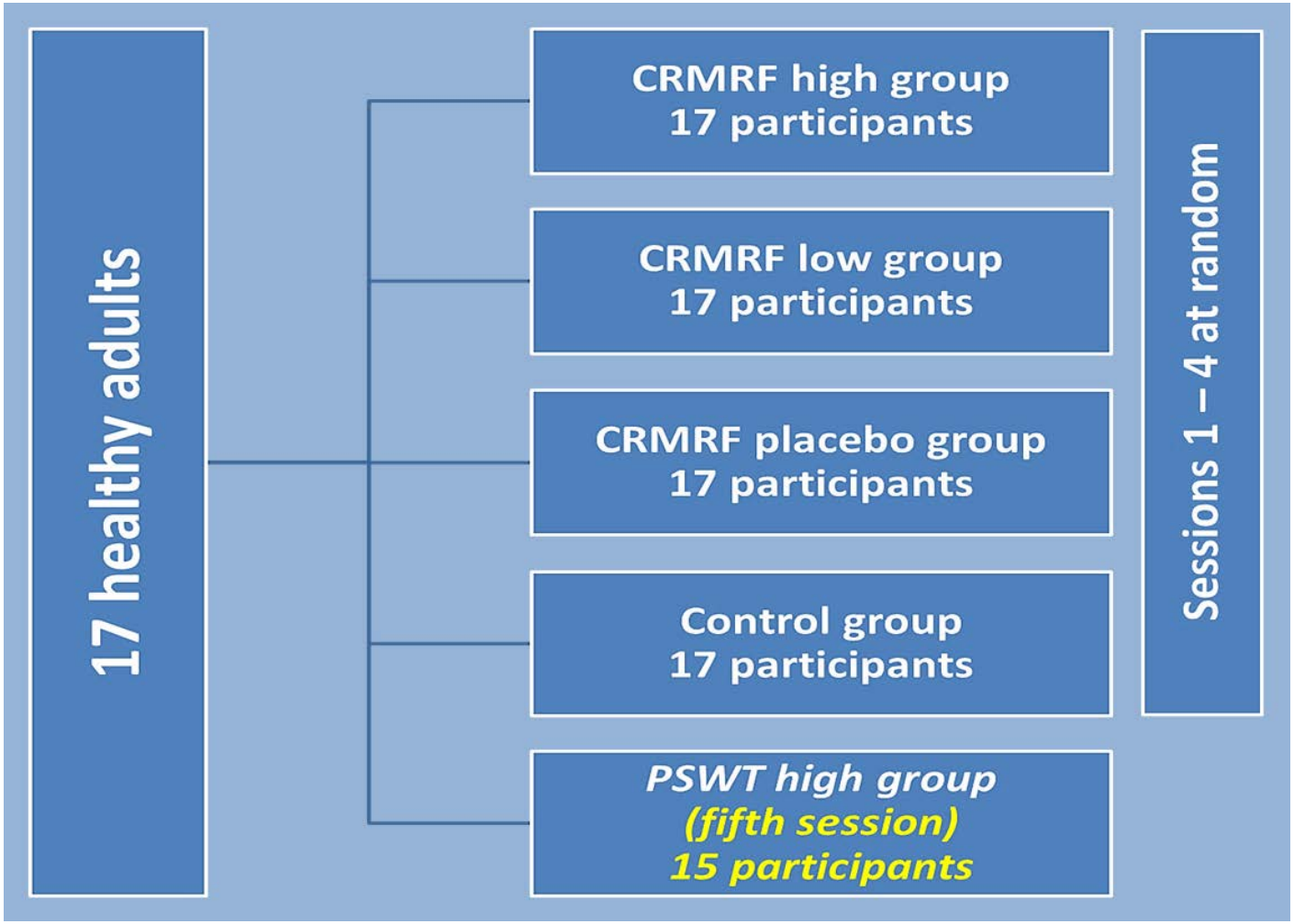

Figure 2: Images showing the Biopac electrode placement and sample data streams for the skin temperature (SKT), photoplethysmography (PPG) and nerve conduction velocity (NCV) modules.

The data streams shown are from participant number 10, after receiving the 'CRMRF high' intervention.

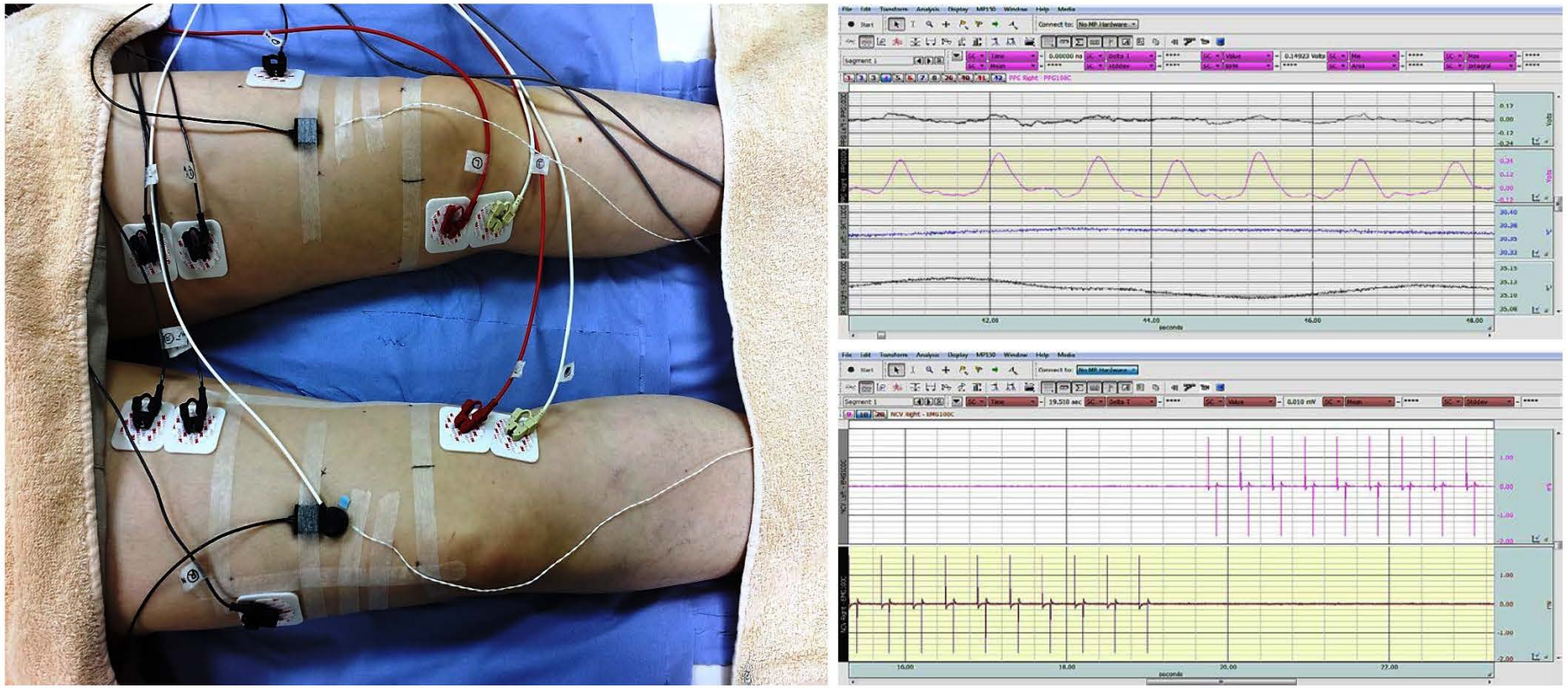

Figure 3: Data from CRMRF high, CRMRF low and PSWT high groups, showing the individual treatment doses delivered.

Participants 9 & 10 did not attend the PSWT session.

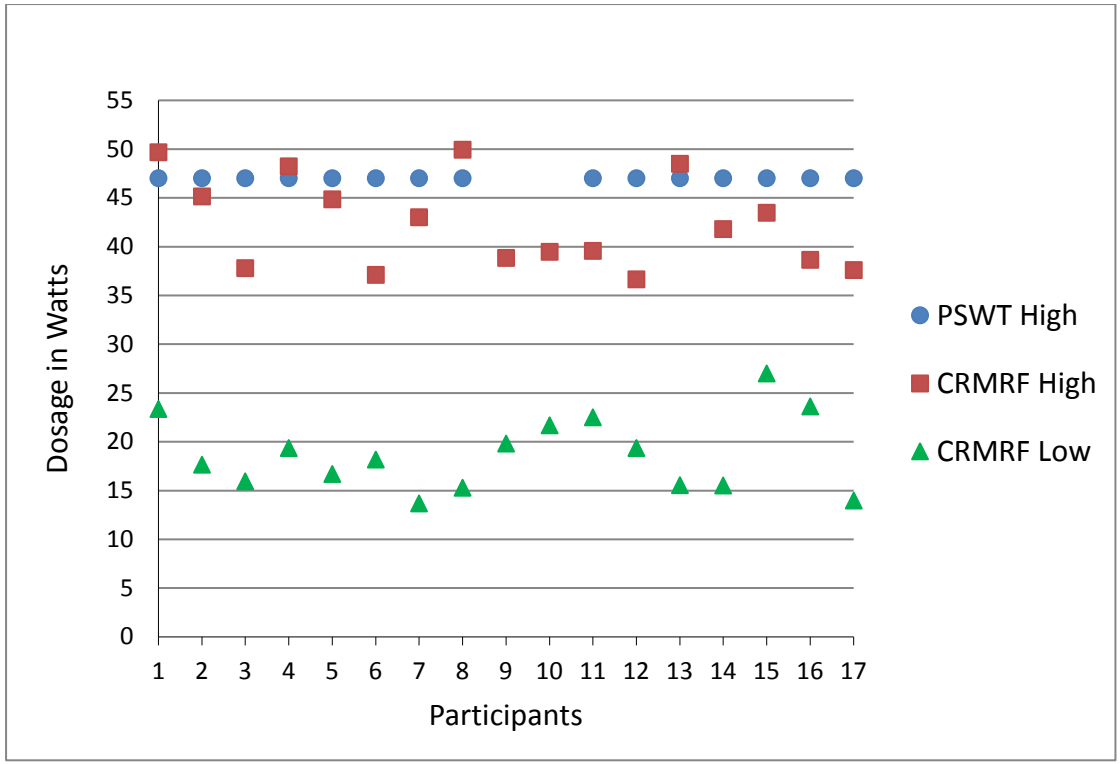

Figure 4a: The mean (SD) skin temperature responses showing the baseline, post treatment and 20-minute follow-up data from all five groups.

The PSWT high group results are based on 15 participants, while the other four groups' results are based on 17 participants. Statistically significant differences (at $p \leq 0.05$) when compared to the baseline are indicated by asterisks (*) above the error bars (two-way repeated measures ANOVA).

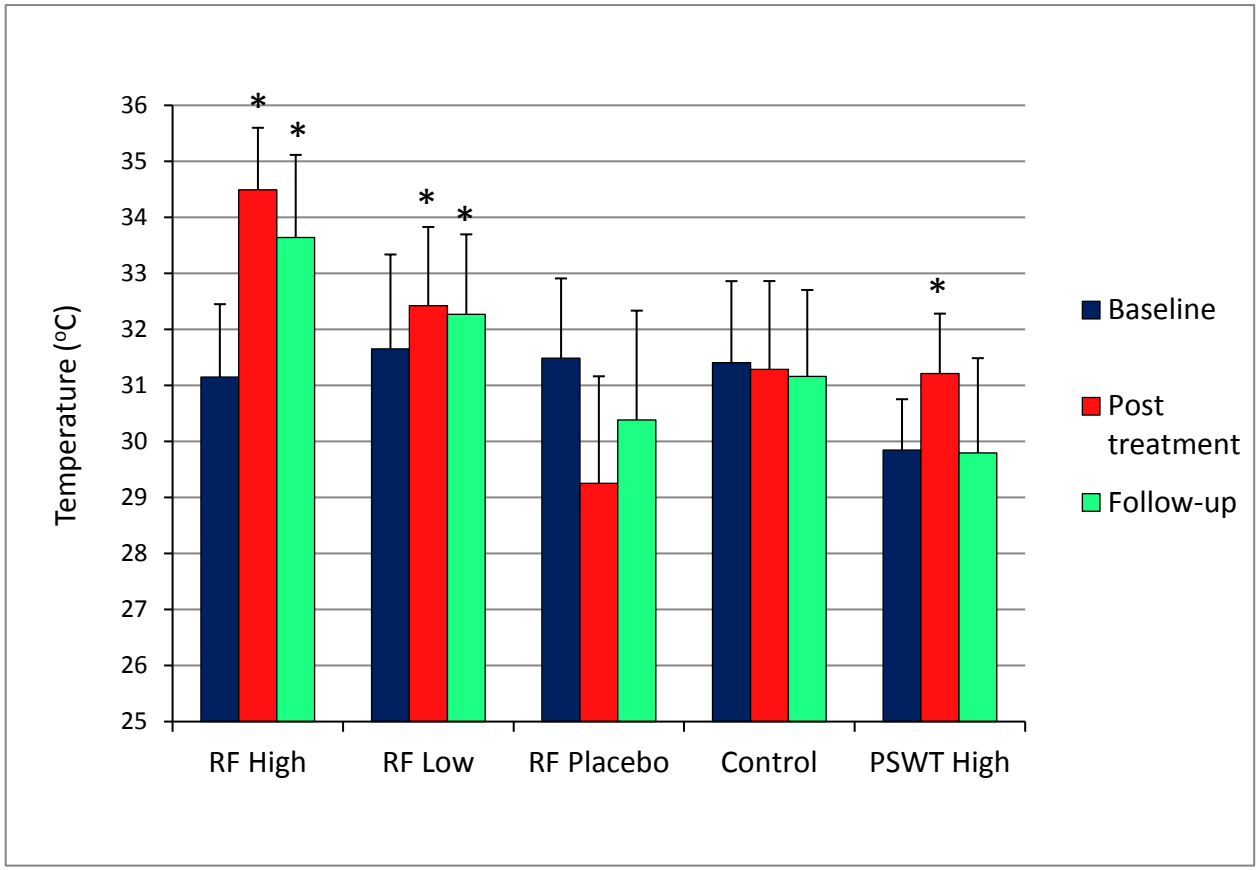

Figure 4b: Percentage change of the mean skin temperature from baseline to post treatment and from baseline to the 20-minute follow-up for all five groups.

The PSWT high group results are based on 15 participants, while the other four groups' results are based on 17 participants. Statistically significant differences (at $p \leq 0.05$) when the groups were compared pairwise are given in Table 3 (two-way repeated measures ANOVA).

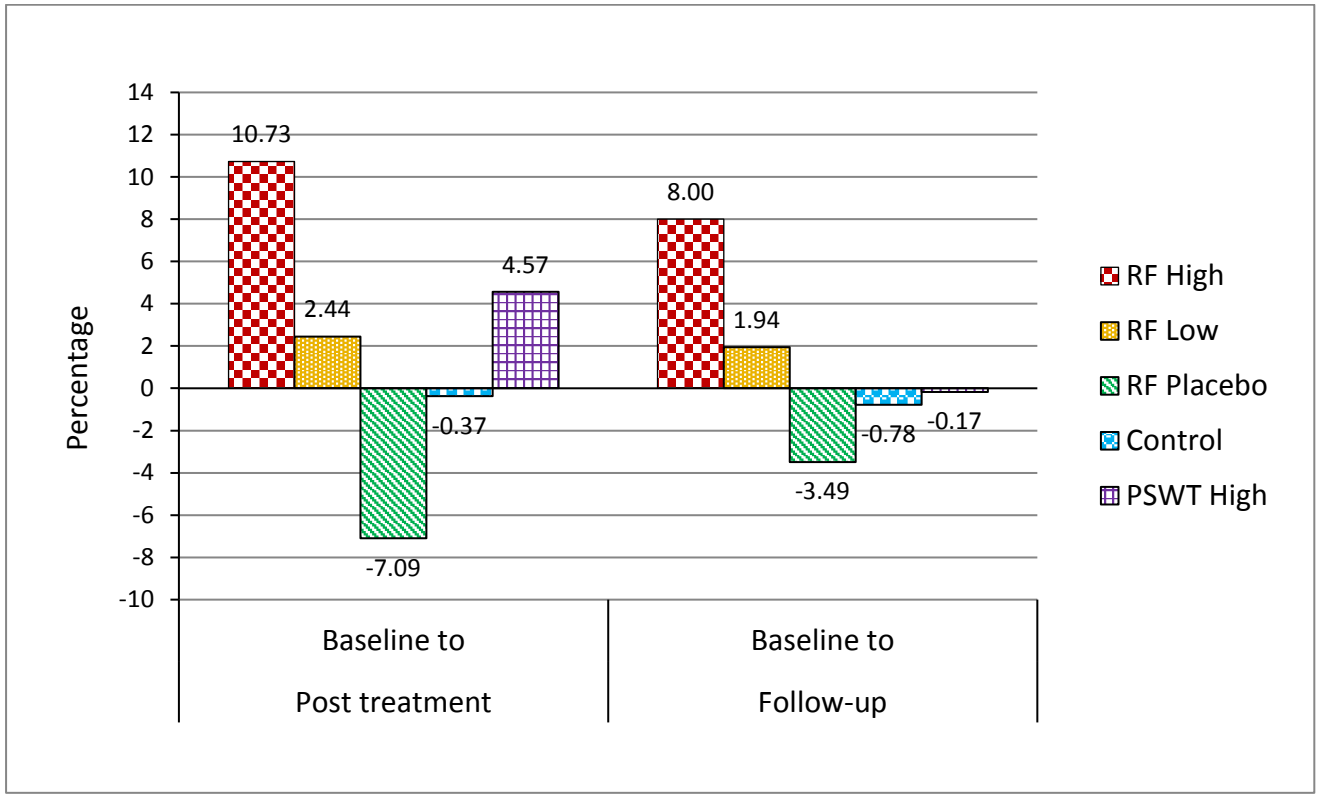

Figure 5a: The mean (SD) skin blood flow responses showing the baseline, post treatment and 20-minute follow-up data from all five groups.

The PSWT high group results are based on 15 participants, while the other four groups' results are based on 17 participants. Statistically significant differences (at $p \leq 0.05$) when compared to the baseline are indicated by asterisks (*) above the error bars (Friedman's two-way ANOVA).

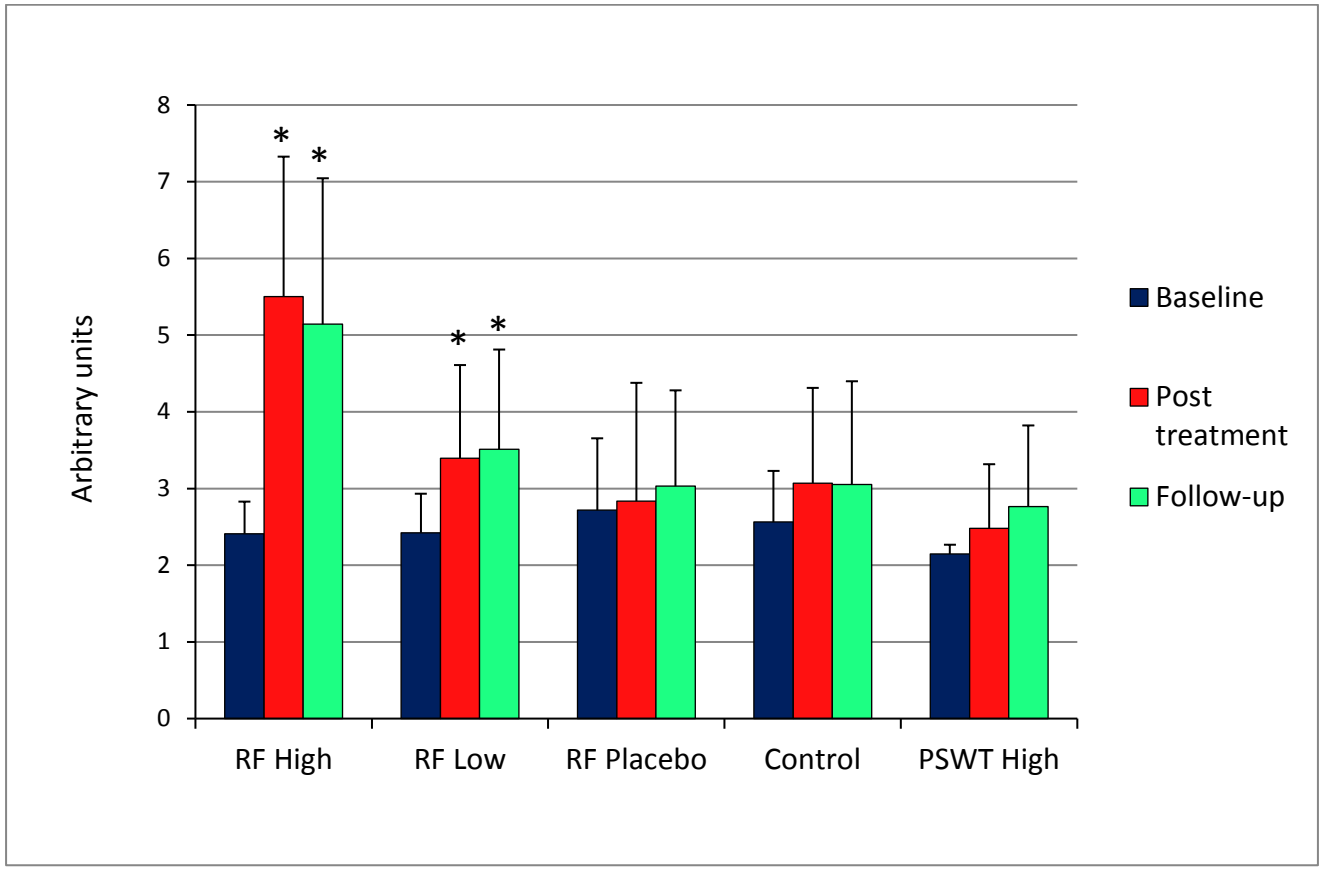

Figure 5b: Percentage change of the mean skin blood flow from baseline to post treatment and from baseline to the 20-minute follow-up for all five groups.

The PSWT high group results are based on 15 participants, while the other four groups' results are based on 17 participants. Statistically significant differences (at $p \leq 0.05$) when the groups were compared pairwise are given in Table 4 (Friedman's two-way ANOVA).

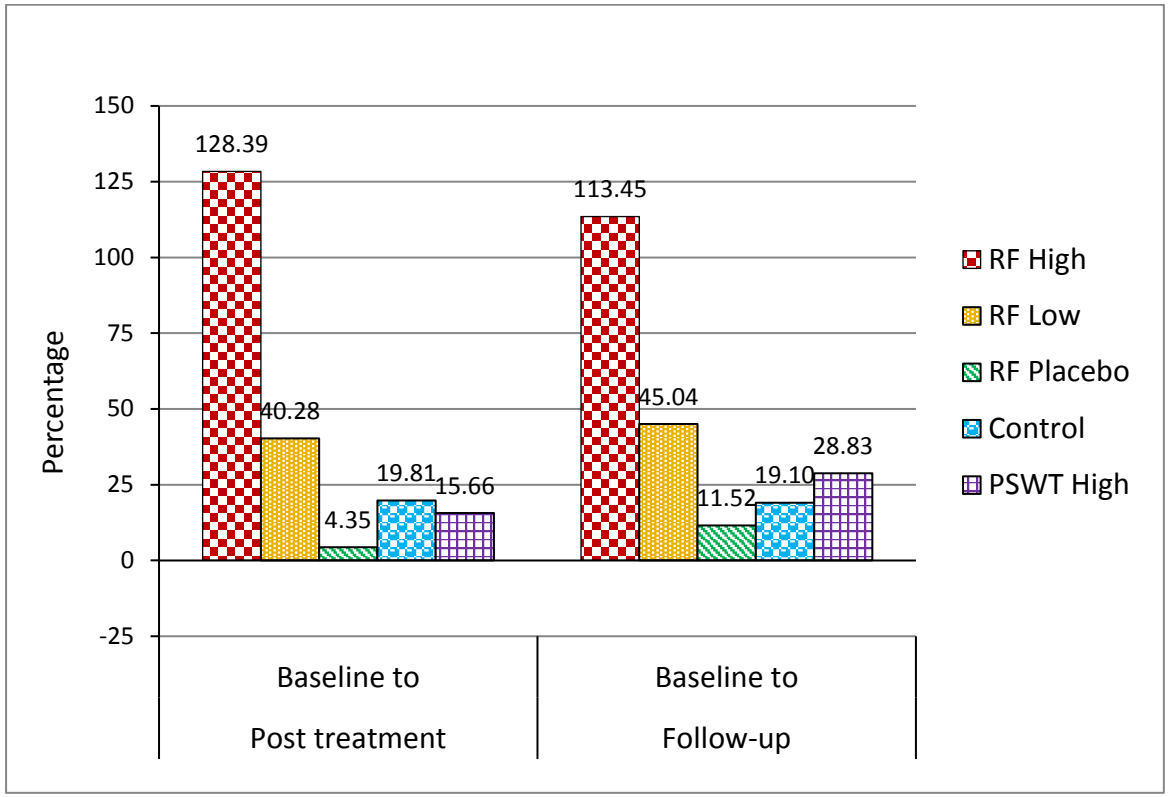

Figure 6: The mean (±SD) nerve conduction velocity responses showing the baseline, post treatment and 20-minute follow-up data from all five groups.

The PSWT high group results are based on 15 participants, while the other four groups' results are based on 17 participants. No statistically significant differences (at $p \leq 0.05$) were obtained within or between any of the groups (two-way repeated measures ANOVA).