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THERMAL BUILD-UP, DECAY AND RETENTION RESPONSES TO LOCAL THERAPEUTIC APPLICATION OF 448 KHZ CAPACITIVE RESISTIVE MONOPOLAR RADIOFREQUENCY: A PROSPECTIVE RANDOMISED CROSSOVER STUDY IN HEALTHY ADULTS.

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INTRODUCTION

Electrophysical agents (EPAs) are used by therapists to treat a wide variety of conditions. Some of these agents can induce hyperthermia in tissues without being invasive or ablative. While some produce superficial heating to the area of the body where the modality is applied (e.g. infrared (IR) therapy), others such as radiofrequency (RF) electromagnetic field-based EPAs are capable of heating the skin as well as deeper structures (such as muscles and joint tissues) [1].

In therapy, heat application is often used as a mode to relieve pain and inflammation and potentially enhance tissue healing. Therapeutically, a rise in tissue temperature by more than 1 ºC will help to relieve mild inflammation and an increase of 2–3 ºC will help to reduce pain and muscle spasm, whereas an increase of 3–4 ºC can produce changes in tissue extensibility [2,3].

Among the EPAs that are used to induce mild hyperthermia, longwave diathermy (which employed RF fields of around 0.5–1 MHz) became obsolete in the 1950s due to practical limitations and the severe disturbances it caused to communication and broadcasting [4]. Shortwave therapy commonly operates at 27.12 MHz, and microwave therapy operates at up to 2.45 GHz

The majority of research on the biological effects of RF is centered on the higher frequency (microwaves), particularly areas such as mobile telephony [5]. However, recent reviews indicated that the RF currently used in therapy-related clinical practice is predominantly within the relatively lower frequency range of 30 kHz–30MHz and largely limited to the shortwave range of 10–30MHz [6-9].

EPAs operating at significantly lower RF ranges (<1 MHz) have also been reported and used to induce mild hyperthermia and other physiological effects [10–13]. An example is capacitive resistive monopolar radiofrequency (CRMRF), which operates at a frequency of 448 kHz. In this study the authors aimed to investigate the skin thermal responses (thermal effects) to the cutaneous application of continuous mode CRMRF therapy in healthy adults.

MATERIALS AND METHODS

Apparatus

The CRMRF energy was delivered using an INDIBA® device (Indiba S. A., Barcelona, Spain). It delivers RF energy in two modes: capacitive (CAP) and resistive (RES).

A hand-held contactless IR skin surface thermometer and an IR tympanic thermometer were used for skin surface and core temperature measurements respectively.

Sample and groups

A randomly selected cohort of 15 asymptomatic adults participated in the study. The study was approved by the Health and Human Sciences Ethics Committee with Delegated Authority (HHSECDA) of the University of Hertfordshire.

Each participant attended two sessions; one each for the CAP and the RES modes thus forming two separate treatment groups. The order of attendance was randomized. There were no control or placebo groups. Based on pilot experiments, a minimum gap of 48 h was allowed between the two sessions so that no residual effects from the first session were present at the time of the second. Similar times of the day (± 1 h) were chosen for either session for each participant.

Experimental procedure

The participants were screened using an eligibility questionnaire. Subsequently, their 'skin thermal sensitivity' was tested using test tubes filled with water at approximately three different temperatures (± 0.5 ºC): 45 ºC (warm), 35 ºC (neutral) and 25 ºC (cold). The participants were required to distinguish between the three temperatures in order to continue with their participation in the study. After, demographic and anthropometric data were collected.

To receive treatment, a square area covering the lower quarter of the anterior aspect of the right thigh was marked with tape (Figure 1). The local skin temperature was recorded from the centre of the marked square area on the treated leg and the corresponding area of the untreated leg (control). The core (tympanic) temperature was also concurrently monitored. The local skin temperature measurements were repeated every 2 min until it stabilised, (baseline skin temperature).

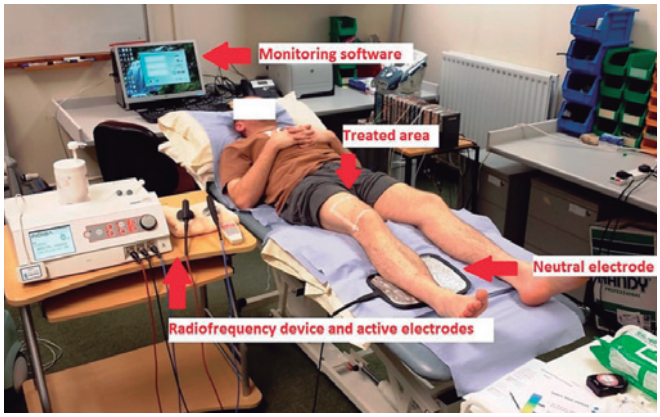

Figure 1. The experimental setting with the 448 kHz capacitive resistive monopolar radiofrequency (CRMRF) device (INDIBA®), electrodes and the computer based monitoring software.

For the experiment, the treatment intensity started at the lowest level permitted by the device and was raised by one level every 30 s. The active electrode produced firm circles on the skin, at a rate of 'one per second' as guided by a metronome. The participants were instructed to report clearly and promptly at three time points: Firstly, when they start to feel heat on the skin (thermal onset), secondly, when they feel moderate yet comfortable heat (definite thermal sensation), and thirdly, when the heat starts to become uncomfortable (onset of thermal discomfort). The treatment was stopped once the 'onset of thermal discomfort' was reached.

After clearing the treated area, the post-treatment (peak) skin temperature was recorded from either leg from the same spot used for the baseline measurement. The core temperature was also recorded at this time. The skin temperature measurements were repeated subsequently every 30 s on the treated leg and every 5 min on the control leg for the next 45 min or until the temperature reached the baseline level.

In addition, a second brief experiment was conducted separately, to map the temperature changes in the active treatment electrodes at various stages of testing in response to set intensities (expressed as percentages) of application of the CRMRF energy. For this purpose three arbitrary intensity levels were chosen, alongside a fourth level which would be the mean peak power reached during each mode of the main experiment.

Data analysis

All data was processed and analysed using Microsoft Office Excel (Version 2010, Microsoft Corporation) and IBM SPSS Statistics (Version 20) for Windows. The group data were compared using a two-way repeated measures analysis of variance (ANOVA) model with a Bonferroni post-hoc comparison for the thermal responses of the CAP and RES modes at three time points (baseline, post-treatment and 45-minute follow-up). The statistical significance was set at $p \leq 0.05$ (0.8 P, 95% CI).

RESULTS

The RF treatment was well tolerated and there were no reports of any adverse events that may be a consequence of the intervention.

The mean (± SD) skin thermal responses as well as individual thermal response patterns obtained from all 15 participants to both CAP and RES modes of CRMRF therapy are plotted in Figures 2. The baseline, post-treatment and 45-min follow-up mean (± SD) skin temperatures obtained for the CAP mode were 30.9 (± 1.1) ºC, 34.3 (± 1.6) ºC and 31.5 (± 1.4) ºC respectively, and for the RES mode were 31.1 (± 1.0) ºC, 35.0 (± 1.2) ºC and 33.2 (± 1.4) ºC respectively.

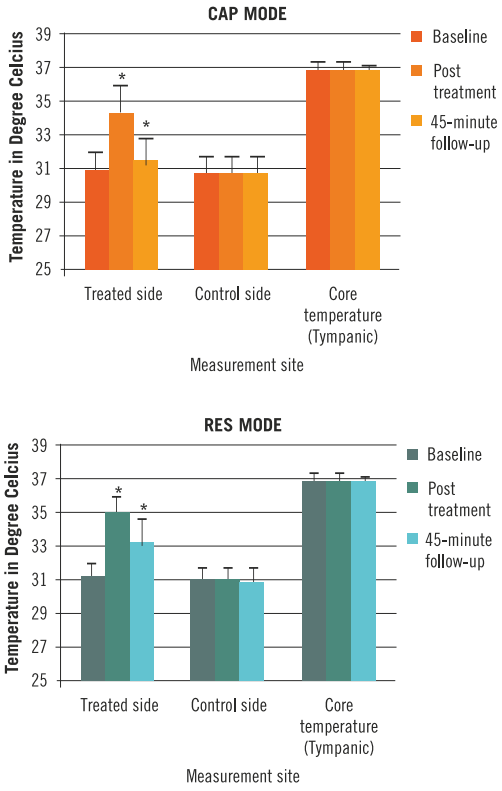

Figure 2. Capacitive (CAP) and resistive (RES) mode mean skin thermal responses to localised 448 kHz capacitive resistive monopolar radiofrequency (CRMRF) treatment. The data shown (baseline, post-treatment and 45-min follow-up) are from 15 participants. *Statistically significant differences when compared to the baseline (at $p<0.05$) (two-way repeated measures ANOVA).

Table 1 shows the mean mean (± SD) time taken, energy delivered and the peak power output to reach each thermal stage.

Overall, there was statistically significant difference between the thermal response patterns produced by the CAP and RES modes ($p=0.001$) although their peak skin temperatures obtained at the end of treatment were not significantly different. From baseline to peak there was 11.1% increase in the mean skin temperature of CAP mode, and 12.7% increase in that of RES mode.

	CAP MODE			RES MODE		
STAGE	**Mean (±SD) time (s)**	**Mean (±SD) energy (J)**	**Mean (±SD) peak power (W)**	**Mean (±SD) time (s)**	**Mean (±SD) energy (J)**	**Mean (±SD) peak power (W)**
Thermal onset	159.1 (55.2)	664.7 (405.2)	6.1 (2.3)	285.5 (109.9)	3417.3 (2299.9)	21.3 (9.6)
Definite thermal	261.5 (56.9)	1635.1 (635.3)	13.2 (3.5)	463.9 (116.2)	8867.6 (4531.4)	42.5 (16.9)
Thermal discomfort	399.7 (70.2)	4764.0 (1467.6)	32.4 (11.8)	656.0 (64.4)	19137.5 (5087)	81.5 (20.1)

Table 1. Mean time, mean energy and mean peak power reached at each of the three thermal stages for 15 participants who received localised 448 kHz capacitive resistive monopolar radiofrequency (CRMRF) treatment.

Both CAP and RES modes also showed a significant retention of the gained temperature at the 45-min follow-up compared to their baseline (CAP: p=0.011; RES: p<0.001). However, the rate of temperature retention at the 45-min follow-up was significantly higher for the RES mode compared to that of the CAP mode (53.6% and 17.5% retention respectively) (p<0.001).

No meaningful change was noted in the thermal response of either the untreated control side or the core (tympanic) temperature at any time point in either group.

DISCUSSION

Radiofrequency waves may interact with the biological tissues through a number of mechanisms. While the theory underpinning the thermal effects of RF interaction is well established, arguably the claims about the 'so called' low level non-thermal (LLNT) effects are somewhat controversial and lack sufficient experimental support [5]. Thermal effects do occur even at very low levels because all interactions between the RF fields and the biological tissues will result in energy transfer to the tissues, ultimately leading to an increase in temperature [14]. For example, cell metabolism can be affected by changes in temperature that are as small as a fraction of a degree [5]. However, many of the physiological benefits of heating occur when temperatures are raised by at least 2 ºC.

The results show significant differences between the patterns of heating produced by the CAP and RES modes of CRMRF therapy. The CAP mode response in relation to the three thermal stages (onset, definite and discomfort) was achieved considerably faster, but the built-up temperature decayed faster and was retained less compared to that of the RES mode. However, the lack of linearity between the intensity settings of the two modes renders any further comparison problematic. Similarly, the peak power achieved at each time point would also have been influenced by the lack of linearity.

The highest temperature recorded for any particular participant was 37.4 ºC for the CAP mode and 37.0 ºC for the RES mode. *Per se*, these values are below or barely at the level of the core temperature. Hence, what is achieved is only 'mild hyperthermia' at best, and solely in relation to the baseline skin temperatures recorded at the treatment site. To be termed hyperthermia, the temperature would have to be raised to supra-physiological levels, that is, to around 40–45 ºC.

More than 60% of the gained heat (Mean (± SD) of 60.3 (± 34.5)%) has been retained in the RES mode at the end of the 45-min follow-up, as against 15% (Mean (± SD) of 15.5 (± 20.1)%) in the CAP mode (Figure 3). The untreated control side and the core temperatures did not change significantly at any point for either condition.

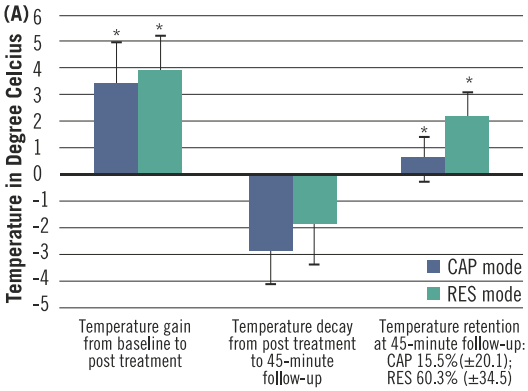

Figure 3. Capacitive (CAP) and resistive (RES) mode mean skin thermal changes after localised 448 kHz capacitive resistive monopolar radiofrequency (CRMRF) treatment (treated side). The data shown (thermal build-up, thermal decay and thermal retention) are the changes in relation to the baseline from 15 participants. *Statistically significant differences when compared to the baseline (at p<0.05) (two-way repeated measures ANOVA).

The faster heating and faster thermal decay associated with the CAP mode CRMRF may be indicative of its relatively superficial nature of penetration.

Similarly, in the RES mode, the higher retention of heat and the fact that there was no sharp fall in the post-treatment skin temperature might suggest an increased penetration of the RF energy. However, it should be noted that the temperature at depth was not measured in this study.

A limitation commonly found in laboratory studies is that the participants may be young and physically fit, limiting the generalisability of the results. In this study, although the participants were physically fit and active; their age range (19–59 years) was purposefully kept wide to improve generalisability. In any case, extrapolation of these results to a patient population is problematic as their physiological responses will be different due to the underlying pathology.

CONCLUSIONS

This study confirms that both the CAP and the RES modes of CRMRF therapy can significantly increase and sustain local skin temperature in healthy adults.

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INDIBA®

CAPACITIVE RESISTIVE MONOPOLAR RADIOFREQUENCY (CR-MRF) THERAPY AT 448 kHz: THE EFFECTS ON DEEP BLOOD FLOW AND ELASTICITY OF TISSUES

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PURPOSE

This study aimed to investigate the changes in blood flow and elasticity in tissues at least at two centimetres depth from the skin in response to cutaneous application of CRMRF (administered using INDIBA® device; Indiba S. A., Barcelona, Spain) in healthy adult volunteers, in order to examine its physiological effects

METHODS

Participants: Seventeen healthy volunteers (10 females, 7 males).

Design: Single-blind randomized crossover study comprising four groups, with all 17 participants attending all four groups in a random order – high, low and placebo dose groups and a control group.

Intervention: The high, low and placebo dose groups received CR-MRF therapy for 15 minutes given to the medial aspect of the lower end of thigh. The control group did not receive any intervention and simply rested for 15 minutes.

Measurements: Baseline and post treatment blood flow velocity, blood volume and tissue elasticity were recorded using Doppler Ultrasound and Ultrasound Elastography (Esaote MyLab70 XVG, Italy). The core temperature, blood pressure and pulse rate were concurrently monitored.

Data analysis: Computational analysis of ultrasound images was performed using MATLAB codes (MathWorks, Massachusetts). Group data were compared using a two-way repeated measures ANOVA model using SPSS Statistics (v20). Statistical significance was set at $p \leq 0.05$ (0.8 P, 95% CI).

RESULTS

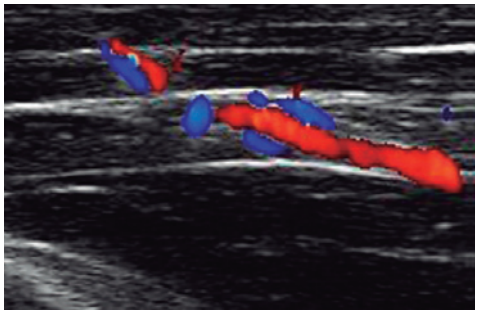
A significant overall difference in both volume (p=0.047, 0.82 P) and intensity (p=0.009, 0.98 P) of blood flow was demonstrated between the four conditions.

No significant differences were noted between the high and low dose groups although the high dose response was greater.

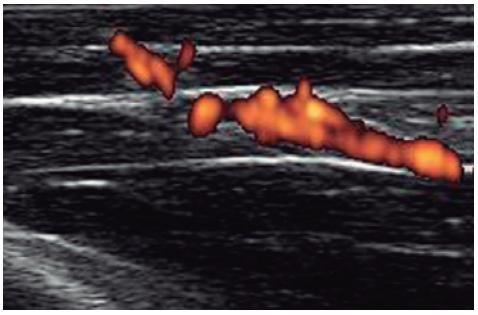
No significant changes were noted in the blood flow velocity, tissue elasticity measurements, blood pressure or pulse rate.

CONCLUSIONS

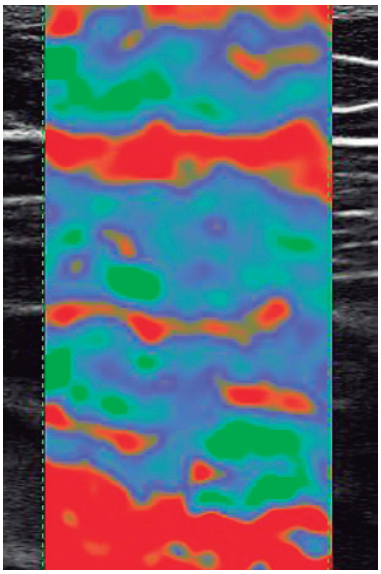
Both the high and low doses of CRMRF at 448 kHz are capable of significantly increasing the volume and intensity of blood flow at depth, but not the velocity of flow or elasticity of tissues.



IColour Doppler image showing blood velocity



Power Doppler image showing blood volume



Elastography image showing information on tissue elasticity

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