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Transcutaneous Oxygen Tension ($tcPO_2$) as a Primary Endpoint to Assess the Efficacy of an Optically Active Vasoactive Garment

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Author Contributions

Drs. Gordon and Coyle collaborated equally in the execution of the study. While both authors were involved in data collection, Dr. Coyle was primarily involved in the data analyses. Both authors contributed to the preparation of the manuscript.

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EFFICACY OF TCPO2 TO ASSESS VASOACTIVE GARMENT

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ABSTRACT

BACKGROUND: Near to far infrared light has been shown to be beneficial to health and cytoprotective. Transcutaneous oxygen tension ($tcPO_2$) is a valid, reliable surrogate for perfusion. In this study, an optically active (OA) garment was evaluated using $tcPO_2$ as a primary endpoint. The OA condition absorbs and reflects IR light back to the skin, which results in skin and tissue vasodilation. RESULTS: Fifty-one subjects enrolled in the study. OA showed an over all treatment effect compared to baseline (BL) (OA, 81.5±14.5 mmHg; BL, 76.6±14.4 mmHg; p. = 0.004). Mean $tcPO_2$ values for the OA were also statistically greater than BL at all time points (10-min (OA, 80.3 mmHg; BL 76.1; p. = 0.012), 30-min (OA, 80.7 mmHg; BL, 75.9 mmHg; p. = 0.003) & 90-min (OA, 83.8; BL 78.6; p. = 0.002). In all cases, the observed mean increases in $tcPO_2$ represented a seven percent (7%) increase in tissue oxygenation in the OA condition when compared to BL. CONCLUSIONS: This optically, vasoactive garment demonstrates that IR light influences cutaneous capillaries and underlying tissue. This vasoactive garment has tremendous potential in athletic performance in the area of thermoregulation, substrate delivery and lactate removal.

INTRODUCTION

All objects with a temperature above absolute zero (-273^{o}C) radiate energy across the electromagnetic spectrum. For example, humans radiate electromagnetic waves as a function of metabolism. It has been shown that certain wavelengths within the electromagnetic spectrum have therapeutic effects (i.e., phototherapy). Photobiomodulation has been demonstrated in near to far infrared (lamda = 670-1000 nm) and has been efficacious in wound healing, growth hormone release, reduced rates of apoptosis, pain reduction, and cytoprotection after myocardial infarcts (7, 11, 15, 23, 27, 30-32) .

The novel optically active garment evaluated in this study (Celliant®, Hologenix, LLC, Santa Monica, CA, USA) is a patented process for adding micron sized optically active quartz, silicon oxide and titanium oxide particles to polymer fibers. The resulting optically active yarns have unique effects on the electromagnetic energy environment of the skin in the visible and near infrared portion of the spectrum leading to increased blood flow and oxygen levels in the tissue and have been described elsewhere (31).

Assessment of oxygenation is useful for determining the health of human tissues. Oxygen delivery is assessed by arterial blood gas evaluation to determine the partial pressure of oxygen in the arteries (P_aO_2). Whereas determination of P_aO_2 involves periodic arterial punctures and subsequent laboratory analysis, transcutaneous oxygen tension ($tcPO_2$) measurements are a non-invasive means of assessing perfusion and under conditions of high skin blood flow approaches P_aO_2 (e.g., 100 mmHg).

Transcutaneous oxygen tension is an endpoint that is widely reported in the literature under a myriad of topics given its close ties to cardiorespiratory function and tissue health (18, 20, 21, 25). The validity of $tcPO_2$ has been well established in the literature under multiple clinical conditions in both animal and human models (19, 22, 25, 29). Although there is a relative dearth of reports on the reliability of $tcPO_2$, Yahav and associates, deemed $tcPO_2$ highly reliable under varying conditions of hypoxia in both children and young adults (29). Heidrich and Lammersen reported that $tcPO_2$ was reliable in distinguishing between healthy normal subjects and diseased individuals (9).

This study was a single blind, within subjects trial, where subjects served as their own control (13, 14). The objective of this efficacy study was to test the hypothesis that a novel, optically active (OA) garment made with an optically active yarn would result in statistically greater mean $tcPO_2$ over a 90-min period when compared to a baseline (BL) period of the same duration. The primary endpoint in this study was transcutaneous partial pressure of oxygen ($tcPO_2$), measured in units of mmHg. Based on the aforementioned, this endpoint is a well-accepted clinical measure for tissue perfusion and oxygenation with well-established norms for reliability intra-subject variability (6, 26).

MATERIALS AND METHODS

Subjects

Fifty-one (51) healthy men and women enrolled in the study (37 men; age 33.4 yrs (SD 9.3) and 14 women; age 37.2 yrs (SD 7.7). Subjects known to be active smokers (8, 16) or engaged in recreational drug use for the six months prior to the start of the study were excluded. Patients were postprandial two (2) hours and refrained from alcohol ingestion (1) within forty-eight (48) hours and caffeine ingestion (24) within four (4) hours prior to testing.

Methods

Skin Preparation. Preparation of the subject was standardized to the following: the hair was shaved from the bicep of dominant arm; the dermis was then abraded with a fine abrasive material; the stratum corneum was then removed by the use of light weight adhesive tape; and finally, the probe site was wiped with an alcohol preparation swab.

Measurement of transcutaneous oxygen ($tcPO_2$). Subjects were seated in a comfortable chair. Room temperature was maintained at a constant temperature over the duration of the study. BL measurements (BL) of $tcPO_2$ were recorded for ninety (90) minutes at the bicep. During this time, the subject wore a standard shirt. After the BL period, subjects donned a OA shirt (Hologenix, LLC, Santa Monica, CA, USA), which has been described elsewhere (31), and subsequent measurements of $tcPO_2$ were recorded at the bicep for ninety (90) minutes. Transcutaneous partial pressure of oxygen ($tcPO_2$) data points were taken at t=10-min, 30-min and 90-min during BL and with OA. All measurements of transcutaneous oxygen tension were recorded using a PeriFlux System 5000 (Perimed, Inc., Kings Park, NY, USA) and modified Clarke Electrodes (Radiometer America, Inc., Ohio, USA). Data were sampled using Perisoft Version 2.10 (Perimed America, Inc., North Royalton, Ohio, USA).

All subjects received the same treatment in the same order: BL followed by OA. Transcutaneous oxygen tension ($tcPO_2$) does not vary significantly over time, therefore, establishing a BL prior to measuring a treatment effect was warranted and, further, the authors felt that the imposed order effect had minimal, if any, influence on the outcome of the study.

STATISTICAL ANALYSES

Continuous variables are summarized with standard descriptive statistics including means, standard deviations (SD) and 95% confidence intervals (95% CI). Inferential analyses were conducted using two-way repeated measures analyses of variance (ANOVA). All data were analyzed using SPSS (12). Alpha was set at 0.05 ($\alpha = 0.05$), *a. priori*, to determine statistical significance. This represents a reasonable and realistic value for research in the medical and biological sciences (4, 5) and suggests that the likelihood is decent that a treatment effect will be detected, assuming a modest effect size (3).

Multiple analyses were executed to evaluate the data. At the highest level, to evaluate whether or not the primary efficacy variable was sensitive enough to detect a difference between the BL and the OA condition, a one-way ANOVA was employed to test the means. The OA treatment was statistically greater than the BL after ninety (90-min) (OA = 81.5 mmHg (SD 14.5), 95% CI [79.1, 83.7]; BL = 76.6 mmHg (SD 14.1), 95% CI [74.3, 78.9], $F(1, 294) = 8.602$, p. = 0.004. This represented a mean percent change from BL of seven percent (7%).

Figure 1 demonstrates the mean treatment difference between OA and BL, as defined by the primary efficacy variable, $tcPO_2$, over the ninety (90) minute measurement period.

FIGURE 1 HERE

A two-way repeated measures ANOVA was employed to evaluate the influence of treatment at the different time points. The interaction between treatments (BL & OA) and time was not significant (($F(1, 45) = 0.012$, p. = 0.914). However, there was a significant within subject contrast for Time ($F(1, 45) = 7.423$), p. = 0.009). Pairwise comparisons were conducted using paired sample *t*-tests to evaluate the differences between the means to identify statistical differences between specific time points. To insulate against multiplicity, and therefore committing a type I error, alpha was adjusted down for the number of comparisons (i.e., 3) (2, 10). Thus, to achieve statistical significance, alpha ($\alpha = 0.05/3$) was set at 0.017. At all time points, the OA condition was statistically greater than the BL as assessed by two-tailed, paired *t*-tests and corresponded to a mean change from the BL condition of seven percent (7%). See Table 1 for a summary of these data.

TABLE 1 HERE

Graphically these data are represented by figure 2.

FIGURE 2 HERE

To be certain that mean $tcPO_2$ did not significantly increase over time during the BL, as well as to show that the BL did not influence the OA condition (i.e., cross over effect), a two-tailed paired *t*-test was executed in the BL condition between t=10-min (76.2 mmHg (SD 14.2)) and t=90-min (77.8 mmHg (SD 14.1), $t(49) = -1.18$, p. = 0.242. This comparison was not statistically significant.

A boxplot of the treatment means (Figure 3) is helpful to identify skewed data. The median is the line in the middle of the box; the upper edge of the box is the 75th percentile and the lower edge is the 25th percentile. The ends of the vertical bars or "whiskers" indicate the minimum and maximum data values. A datum outside the whiskers is an outlier, in this case there were none (17). This graphic suggests that these data show good symmetry and are not skewed.

FIGURE 3 HERE

DISCUSSION

Adequate blood supply is necessary for many physiologic processes. However, there are few valid, reproducible, non-invasive methods with which to assess it. One such measure is transcutaneous partial pressure of oxygen ($tcPO_2$). This measurement is a non-invasive method of measuring oxygen tension at the skin surface; represents the amount of oxygen diffusing outward across the skin (28); and can be used as a surrogate for arterial perfusion.

In this study a shirt made with optically active yarn, known to cause capillary vasodilation secondary to the reabsorption of IR light (31), was evaluated using $tcPO_2$ as a primary endpoint to assess efficacy compared to a baseline period of ninety (90) minutes. It has been suggested that nitric oxide, a potent vasodilator within the endothelium, may be a key molecule in the mechanism of action (15, 32).

It is conceivable that a garment such as this may have a significant influence on the body's ability to thermoregulate. It is well known that cutaneous blood flow is approximately

250 $ml \cdot min^{-1}$ in a thermoneutral environment, however, this value may change depending on individual subcutaneous fat stores. During strenuous exercise, a significant portion of cardiac output is diverted to the skin in order to shed heat from the core. It is plausible to assume that if one were wearing a garment made with the optically active yarn evaluated in this study the observed increase in $tcPO_2$ and, therefore skin perfusion, would likely result in greater heat loss across the skin.

Further investigation into the mechanism of action, as well as to evaluate the extent to which heat loss during warm environments and or exercise is warranted. One such study might be to evaluate core and skin temperature while subjects sit in an environmental chamber at different temperatures. This new and exciting textile and its ability to vasodilate capillaries in the skin and underlying tissue, has many applications in athletic performance, ranging from thermoregulation, to the evaluation of increased delivery of substrate to exercising skeletal muscle, to the potential for the reduction of fatigue and faster recovery via increased lactate clearance post exercise.

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DISCLOSURES

This study was funded by a grant from Hologenix, LLC. Dr. Coyle serves as Chief Science Officer for Hologenix.

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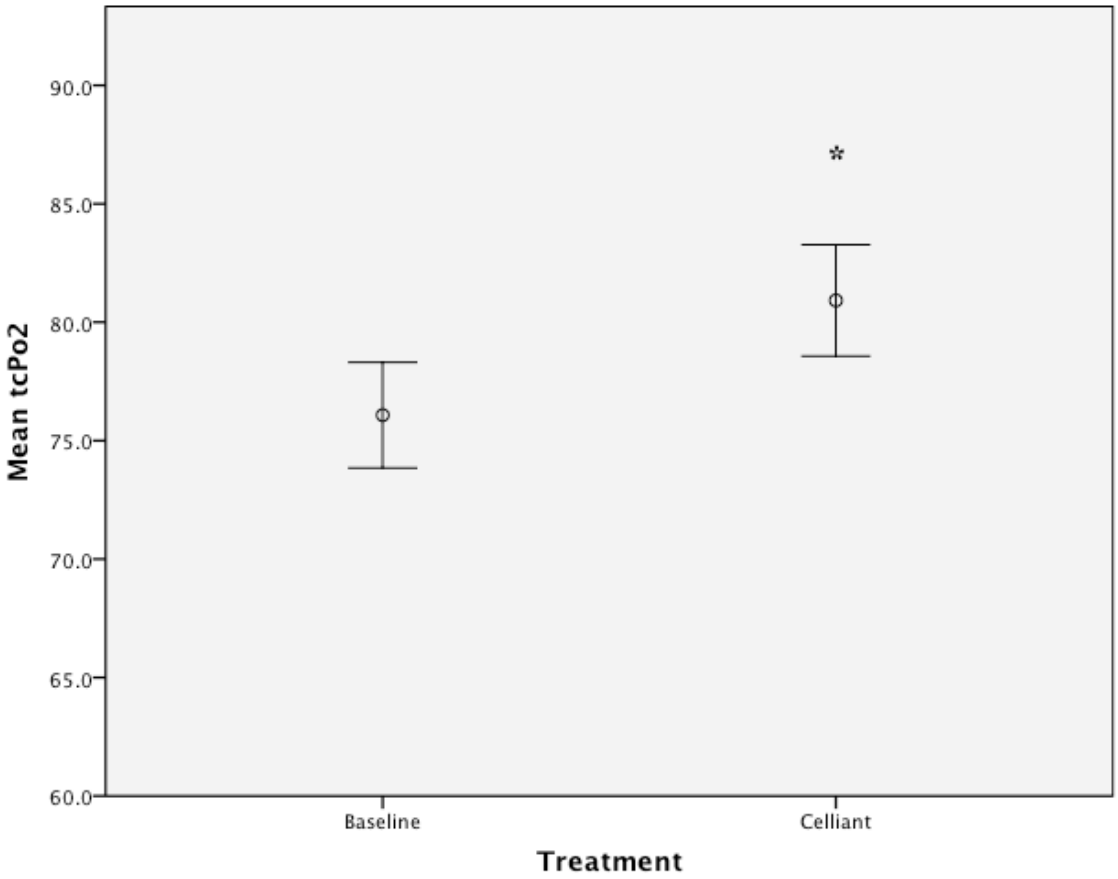
Figure 1. Difference in Treatments as Measured by tcPO2



Error Bars: 95% CI

* p. = 0.004

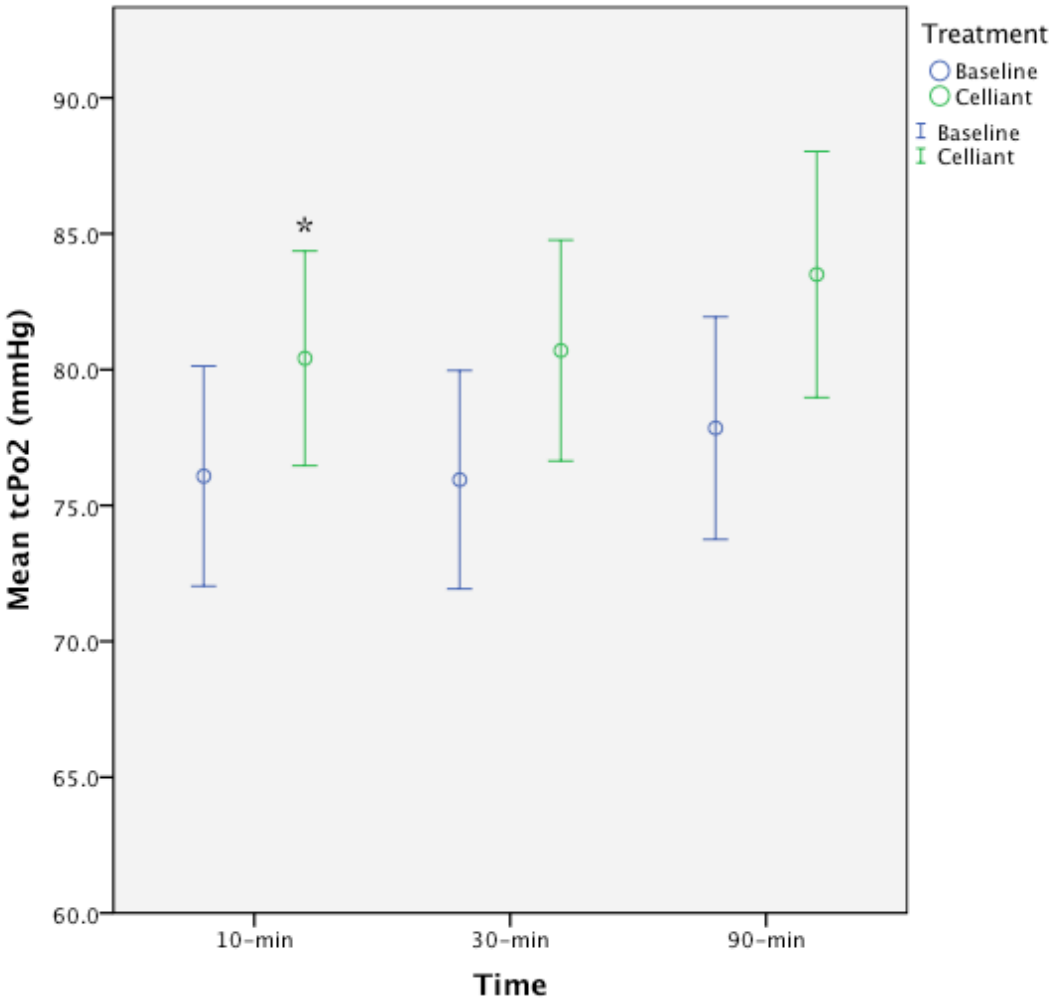
¶Optically Active = Celliant

Table 1. Summary of Two-tailed Paired *t*-tests vs. Time

Time	Mean CL tcPO2 mmHg	Mean BL tcPO2 mmHg	*t* statistic	d.f.	P-value
10-min	80.3	76.1	-2.60	50	0.012*
30-min	80.7	75.9	-3.14	50	0.003*
90-min	83.8	78.6	-3.22	46	0.002*

*OA condition statistically greater than BL.

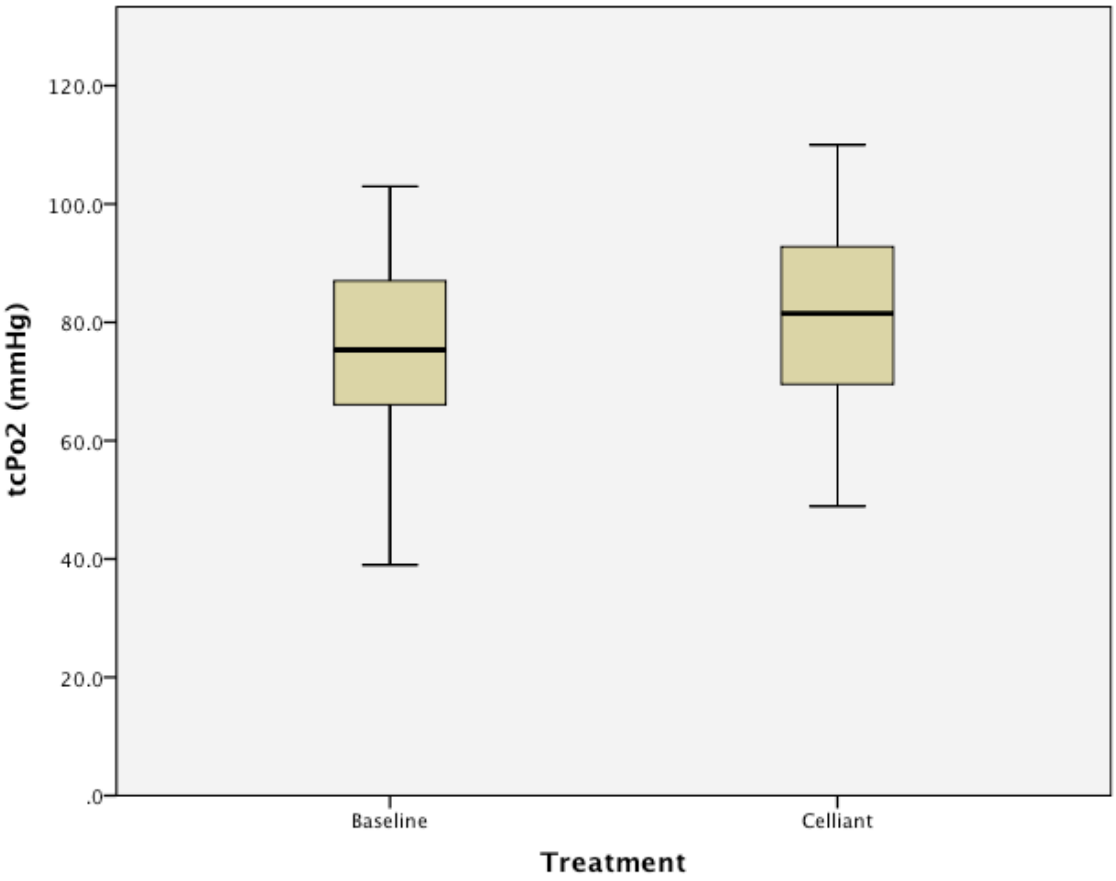
Figure 2. Mean tcPO2 by Condition Over Time



* At all time points, Celliant was statistically greater than Baseline. See Table 1 for p values.

Optically Active condition = Celliant

Figure 3. Distribution of tcPO2 values Between Baseline & Celliant



¶Optically Active = Celliant