
# Transcutaneous Partial Pressure of Oxygen (tcPO2) as a Primary Endpoint to Assess the Efficacy of Celliant® as a Vasoactive Material

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## INTRODUCTION

Celliant® technology is a patented process for adding micron sized optically active quartz, silicon oxide and titanium oxide particles to polymer fibers. The resulting Celliant® 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.

This report is a summary of data collected under the auspices of Ian Gordon, M.D., Ph.D., Associate Clinical Professor of Surgery at the University of California- Irvine Medical School. Fifty-one (51) healthy men and women were enrolled in the study. This study was a within subjects trial, which is noted for its ability to control for individual differences among subjects. Since each subject is assessed under each level of the independent variable or condition, the subjects serve as their own control, with the result that one of the largest sources of between treatment differences, inter-subject variation, is controlled (Keppel, 1991; Lindquist, 1953).

In the medical sciences, statistical significance levels are stated, *a. priori*, to know whether or not the treatment was efficacious relative to the control or baseline. A stringent statistical significance level (alpha = 0.05) is typically chosen so that if the study were to be reproduced, one would get the exact same results 95 times out of 100. Therefore, a p-value of *less* than 0.05 is perfunctory to meet this requirement. This represents a reasonable and realistic value for research in the medical and biological sciences (Cohen, 1965, 1977) and suggests that the likelihood is decent that a treatment effect will be detected, assuming a modest effect size (Chase & Tucker, 1976).

## OBJECTIVES

The objective of this pilot study was to test the null hypothesis that a novel, optically active garment made with Celliant® (CL) material would not influence mean $tcPO_2$ over a 90-min period differently than when compared to a baseline (BL) period of the same duration (90-min).

## PRIMARY ENDPOINT

The primary endpoint in this study was transcutaneous partial pressure of oxygen (tcPO2), measured in units of mmHg, which was used to assess treatment efficacy. This endpoint has been

used in numerous clinical trials and is a well-accepted clinical measure for tissue perfusion and oxygenation (Burgess, Matsen, Wyss, & Simmons, 1982; Dooley, Schirmer, Slade, & Folden, 1996; Franzeck, Talke, Bernstein, Golbranson, & Fronek, 1982; Hanna et al., 1997; Jaszczak, 1988; Le Devehat & Khodabandehlou, 1990; Le Devehat, Khodabandehlou, & Vimeux, 2001; Matsen, Bach, Wyss, & Simmons, 1980; Matsen et al., 1980; Matsi, Manninen, Suhonen, Pirinen, & Soimakallio, 1993; Shoemaker & Vidyasagar, 1981; White et al., 1982) with well established norms for intra-subject variability (Coleman, Dowd, & Bentley, 1986; Wagener & Hendricker, 1987)

## MATERIALS AND METHODS

### Subjects

Fifty-one (51) heathy 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 (Fewings, Rand, Scroop, & Whelan, 1966; Mayhan & Patel, 1997) 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 (Altura & Altura, 1982; Fewings, Hanna, Walsh, & Whelan, 1966) within forty-eight (48) hours and caffeine ingestion (Umemura et al., 2006) 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. Baseline 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 baseline period, subjects donned a Celliant® shirt 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 CL. 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: Baseline (BL) followed by Celliant® (CL). Transcutaneous oxygen tension ($tcPO_2$) does not vary significantly over time, therefore, establishing a baseline prior to measuring a treatment effect was warranted.

**STATISTICAL ANALYSES**

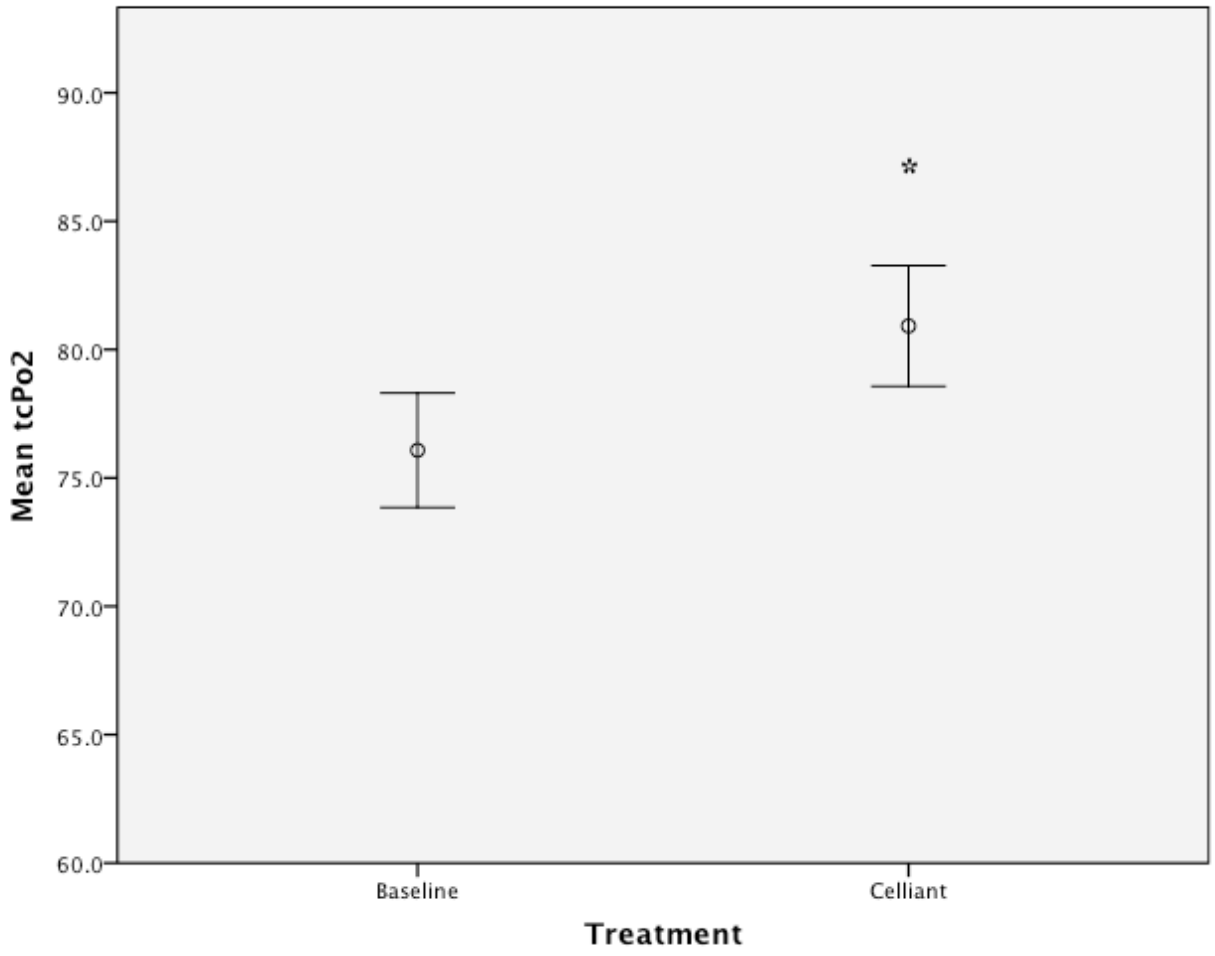
Continuous variables are summarized with standard descriptive statistics including means, standard deviations (SD) and 95% confidence intervals (95% CI). Inferential analyses were conducted using two-way repeated measures analyses of variance (ANOVA). All data were analyzed using SPSS (IBM, 2011). Statistical significance for this study was set at alpha = 0.05. Thus, a p-value < 0.05 was necessary to be considered statistically significant.

An analysis of the entire data set identified four (4) missing data points (three (3) data points from the Celliant® condition and one (1) data point from the Baseline condition). This resulted in a data set equal to 98.7% of the total expected data.

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 Baseline and the Celliant® conditions, a one-way ANOVA was employed to test the means. The Celliant® treatment was statistically greater than the Baseline after ninety (90-min) (CL = 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 Baseline of seven percent (7%).

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

**Figure 1. Difference in Treatments as Measured by tcPO2**




A two-way Repeated Measures ANOVA was employed to evaluate the influence of treatment at the different time points. The interaction between Condition (BL & CL) 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 dependent sample *t*-tests to evaluate the differences between the means to identify statistical differences between specific time points. At all time points, the Celliant® condition was statistically greater than the Baseline as assessed by two-tailed, paired *t*-tests and corresponded to

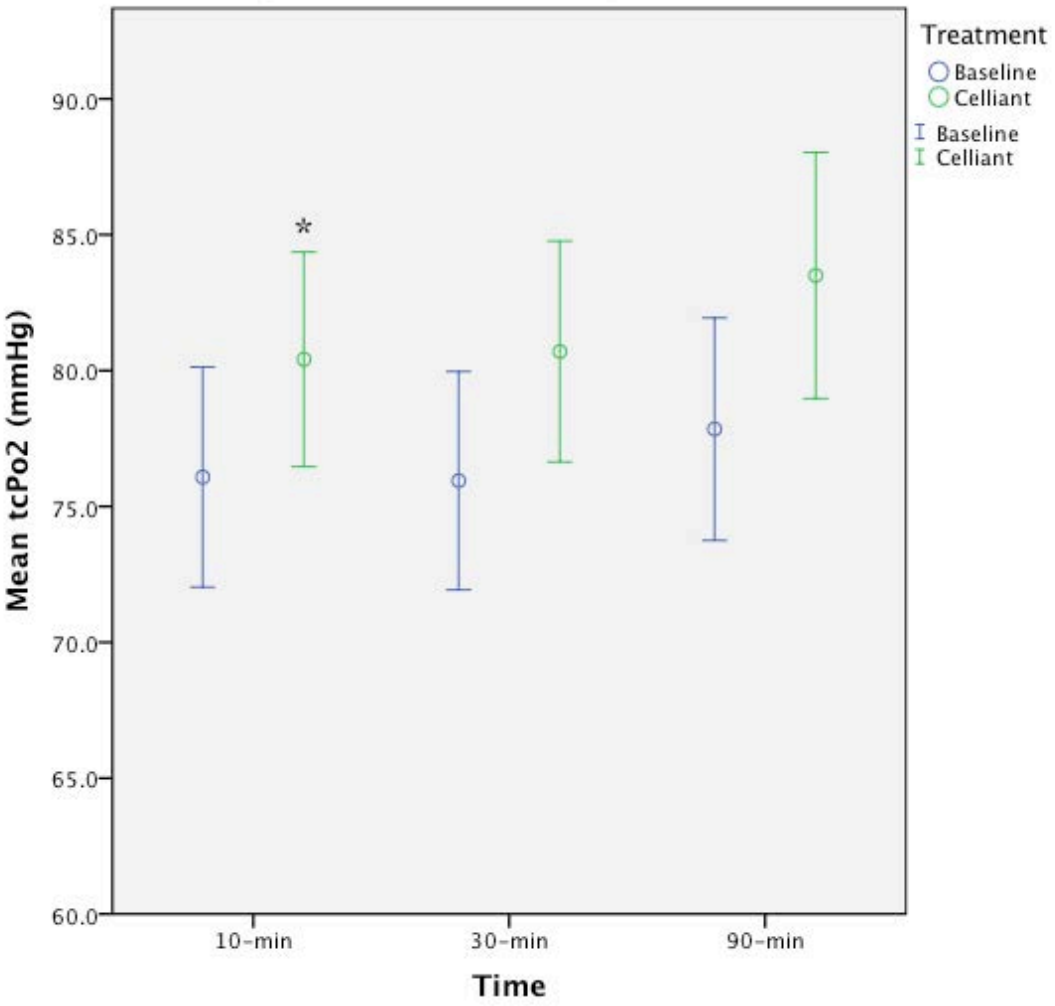
a mean change from the Baseline condition of seven percent (7%). See Table 1 for a summary of these data.

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 |

To be certain that mean $tcPO_2$ did not significantly increase over time during the Baseline, as well as to show that the Baseline did not influence the Celliant® condition, a two-tailed paired *t*-test was executed in the Baseline 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. Figure 2 shows the difference in treatment means graphically.

**Figure 2. Mean tcPO2 by Condition Over Time**

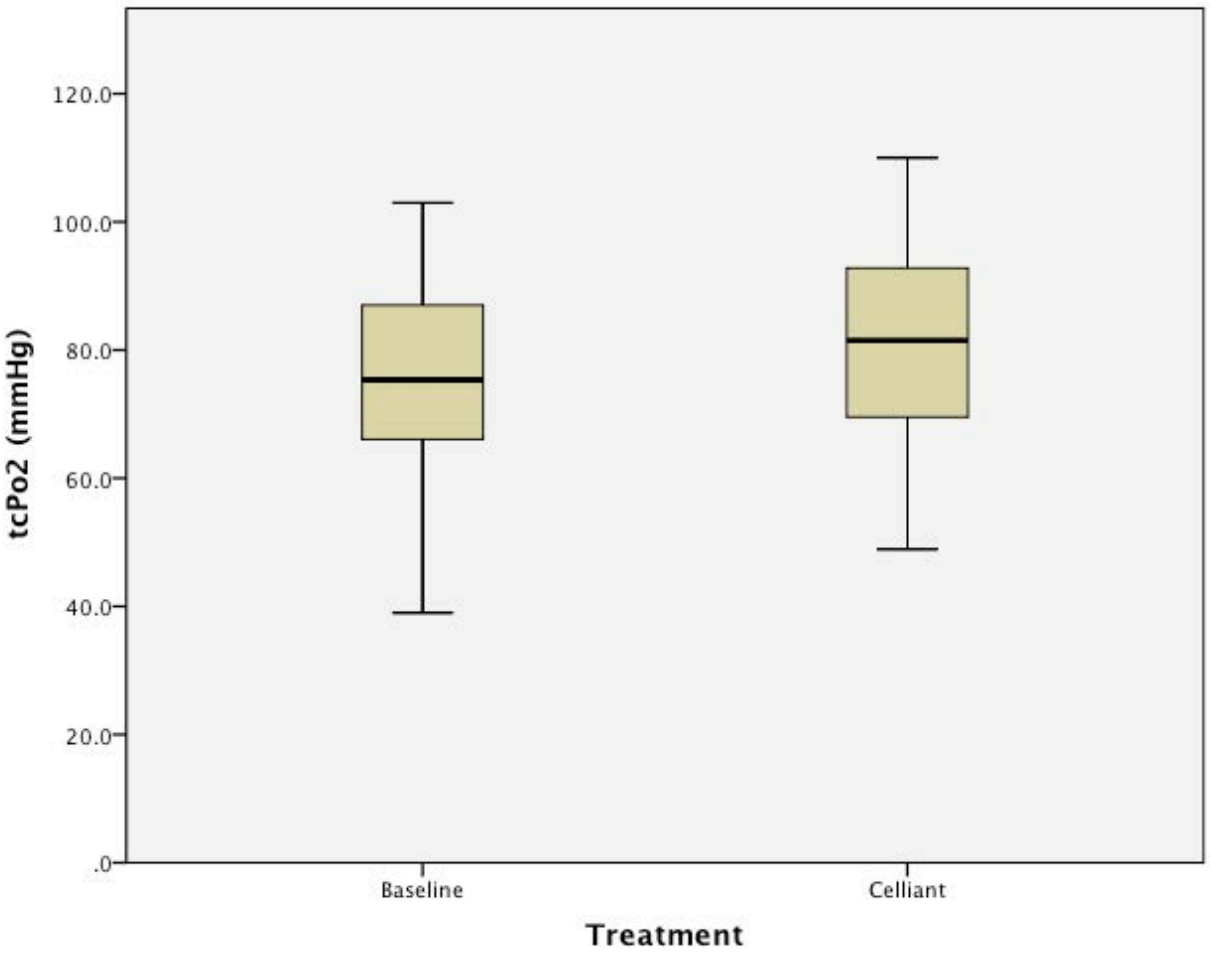



Error Bars: 95% CI

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

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 75$^{th}$ percentile and the lower edge is the 25$^{th}$ 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 (McGill, Tukey, & Larsen, 1978). This graphic suggests that these data show good symmetry and are not skewed.

**Figure 3. Distribution of tcPO2 values Between Baseline & Celliant**



**SUMMARY**

Fifty-one subjects underwent separate ninety (90) minute testing periods where transcutaneous partial pressure of oxygen ($tcPO_2$), a well-accepted clinical measurement for tissue perfusion and oxygenation, was used as the primary endpoint. First, a Baseline was established. Then, a shirt made with Celliant® material was worn during a subsequent session. All measurements were taken at the bicep.

**Transcutaneous oxygen tension proved to be a sensitive measure of efficacy, which resulted in the rejection of the null hypothesis. Thus, mean $tcPO_2$ values for the Celliant® garment were statistically greater than the Baseline at all time points (t= 10-min, 30-min & 90-min), as well as showed an over all treatment effect when mean $tcPO_2$ values were condensed across time. In all cases, the observed mean increases in $tcPO_2$ represented a seven percent (7%) increase in tissue oxygenation in the Celliant® condition when compared to Baseline.**

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