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Improving Blood Flow with Holofiber in the Hands and Feet of High-Risk Diabetics

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Improving Blood Flow with Holofiber in the Hands and Feet of High-Risk Diabetics

Objective: To evaluate changes in peripheral blood flow in the hands and feet of persons with diabetes when Holofiber gloves and stockings are worn. We expect that patients that wear the Holofiber garments will have an increase in local tissue perfusion compared to baseline and control garments. The study outcomes are transcutaneous oxygen and laser Doppler flowometry measurements over the course of one hour while the study subjects wear Holofiber garments and placebo garments.

Study Design: This will be a double blind evaluation of changes in peripheral perfusion. Subjects will act as their own controls. We plan to enroll 20 subjects with a history of diabetes and vascular impairment. Subjects will be evaluated for baseline blood flow status. They will then have transcutaneous oxygen (Perimed Inc. North Royalton, Ohio, PF5040 transcutaneous module) and laser Doppler flowometry measurements (PF5010 Laser Doppler Perfusion module) with stockings and gloves made with and without Holofiber. Measurements will be made prior to wearing the garments and continuously over a one hour period. We will analyze data at ten minute intervals. The tester and subject will be blinded to the study garment. Garments will be randomly selected and tested from a computer generated randomization list. We will take measurements of both the hand and foot with study subjects wearing Holofiber versus standard fiber gloves and stockings.

The diagnosis of diabetes mellitus will be based on World Health Organization criteria.⁸ For the purposes of this study, the diagnosis of peripheral vascular disease will be a transcutaneous oxygen measurement > 30mm Hg taken at the transmetatarsal level on the day of enrollment.^{5,9}

Inclusion Criteria:

1. Diagnosis of Diabetes Mellitus by the World Health Organization Criteria
2. Patient 18 -80 years old.

Exclusion Criteria:

1. Patient currently being treated by dialysis, or having serum creatinine greater than or equal to 3.0 mg/dl.
2. Patient known to be an active alcohol or substance abuser for the six months prior to the start of the study.
3. Patient currently receiving systemic corticosteroids in a dose equivalent to greater than or equal to 10 mg of prednisone per day.
4. Patient currently receiving immunosuppressive agents.
5. Patient currently receiving radiation therapy.
6. Patient currently receiving cytotoxic agents.
7. Patient currently receiving antiviral agents.
8. Patient having history of widespread malignant or systemically immunocompromising disease.
9. Patient is a female who is breast feeding, pregnant, or attempting to become pregnant.
10. Patient has other conditions considered by the investigator to be sound reasons for disqualification (e.g., acute illness or exacerbation of chronic illness, lack of motivation, and history of poor compliance).
11. Amputation proximal to Lisfranc's (tarsometatarsal) joint or if amputation/surgical debridement has destroyed the venous plexus of the plantar arch.
12. Acute deep venous thrombosis.
13. Active congestive heart failure.
14. Uncontrolled osteomyelitis.
15. Vascular surgery in the past 4 weeks.
16. Patient has a full thickness skin ulcer.

The dynamic non-invasive vascular assessment will consist of transcutaneous oxygen pressure (TcPO₂) measurement, and laser Doppler flowmetric measurement. We will use the PeriFlux 5000 System. It is a multifunctional system that incorporates four functional units that combine transcutaneous oxygen and laser Doppler function units.

The transcutaneous oxygen electrodes are warmed to 44°C and allowed to equilibrate on the skin for 5 minutes (until stable values are achieved). The resultant values are measured in mmHg.^{5,9} The laser Doppler monitor will be used to continuously measure tissue blood perfusion (PF5010 Laser Doppler Perfusion module). The application is non-invasive. Two stick-on probes similar to standard EKG probes are applied to the skin. In the tissue, the laser light is scattered and Doppler shifted by interaction with the moving blood cells according to the well-known Doppler principle. The sampling depth is on the order of 200-500 micrometers. A fraction of the backscattered light is detected by a remotely positioned photo detector.

We will measure transcutaneous oxygen and laser Doppler flowometry measurements continuously during the one hour evaluation period and record values for 60 seconds at ten minute intervals on the dorsum of the foot and hand. In addition, we will measure a two minute interval at the conclusion of each data collection period to compare the change in blood flow parameters in placebo and Holofiber treatment groups.

Results:

We used a paired t-test to compare transcutaneous oxygen (TCOM) and laser Doppler (LD) values on the hand and foot. Transcutaneous oxygen measures the partial pressure of oxygen at the surface of the skin, and the laser Doppler measures capillary blood flow. As part of the descriptive evaluation of the data we, stratified TCOM and LD into three levels: increase when comparing Holofiber to placebo, no change or a decrease when comparing Holofiber to placebo. If there was less than a 4% change when the placebo vs. Holofiber was used, this was determined to represent “no change”. TCOM's in the hand showed 10 subjects with an increase, 4 unchanged and 6 with a decrease when using Holofiber compared to the placebo garment. TCOM's in the foot again showed 10 subjects with an increase when using Holofiber, 4 were unchanged and 6 were decreased.

There was a statistically significant change in transcutaneous oxygen or the oxygen delivery to the skin in the hand and foot when using the paired t-test to compare data collected at time periods 40 and 50 minutes after initiation of testing. The Laser Doppler

studies did not show a difference in blood flow in placebo versus Holofiber in either the hand or the foot. The significant changes observed are very compelling for this type of product. An 8-12% improvement in skin oxygenation could improve marginal circulation enough to improve wound healing or eliminate ischemic pain of the legs.

All 10 Minute Interval Data (Paired)

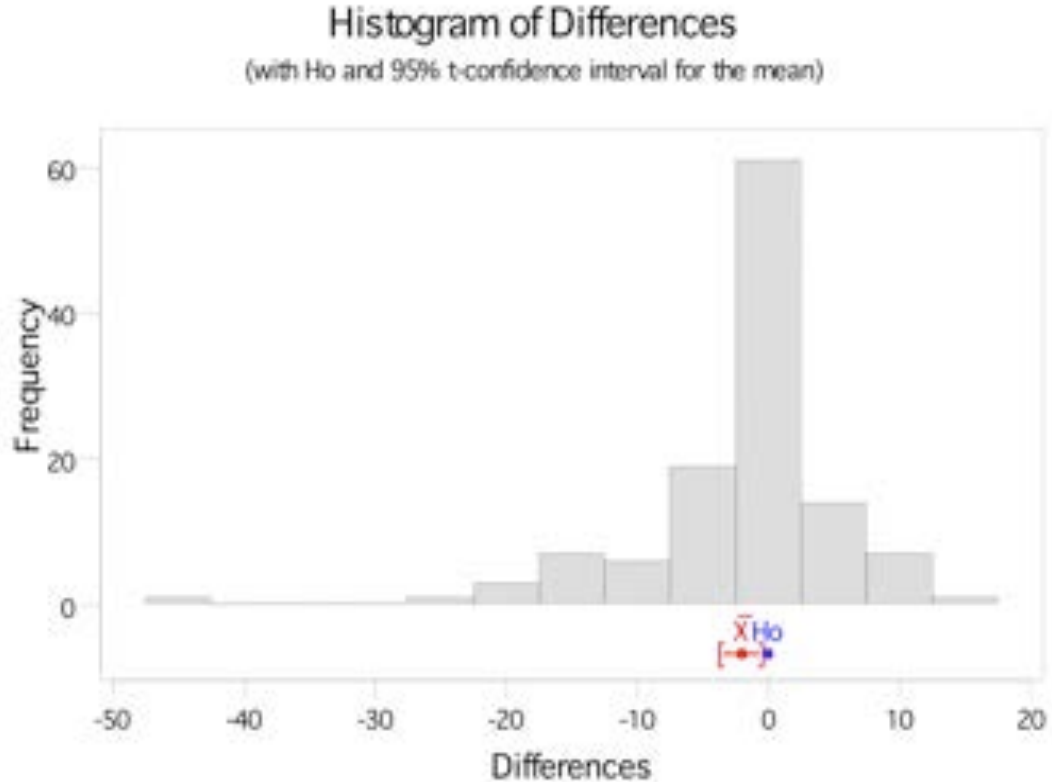
Paired T-Test and CI: TCOM HAND-Placebo, TCOM HAND-Holofiber

Paired T for TCOM HAND-Placebo - TCOM HAND-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|-----|--------|--------|---------|
| TCOM HAND-Pl | 120 | 15.284 | 7.613 | 0.695 |
| TCOM HAND-ho | 120 | 17.323 | 10.505 | 0.959 |
| Difference | 120 | -2.039 | 7.718 | 0.705 |

95% CI for mean difference: (-3.434, -0.644)

T-Test of mean difference = 0 (vs not = 0): T-Value = -2.89 P-Value = 0.005



All 10 Minute Interval Data (Paired)

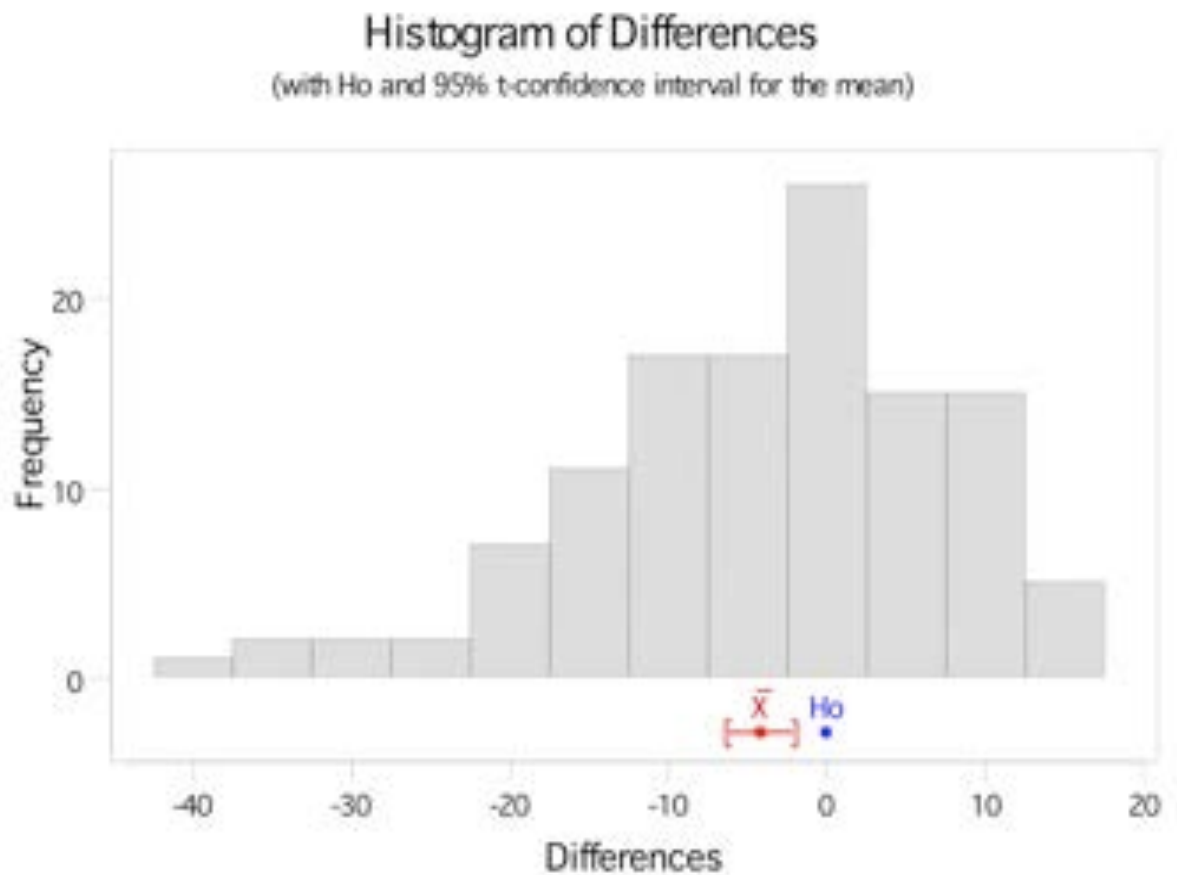
Paired T-Test and CI: TCOM FOOT-Placebo, TCOM FOOT-Holofiber

Paired T for TCOM FOOT-Placebo - TCOM FOOT-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|-----|-------|--------|---------|
| TCOM FOOT-pl | 120 | 52.22 | 20.39 | 1.86 |
| TCOM FOOT-ho | 120 | 56.35 | 20.01 | 1.83 |
| Difference | 120 | -4.13 | 11.25 | 1.03 |

95% CI for mean difference: (-6.16, -2.10)

T-Test of mean difference = 0 (vs not = 0): T-Value = -4.02 P-Value = 0.000



All 10 Minute Interval Data (Paired)

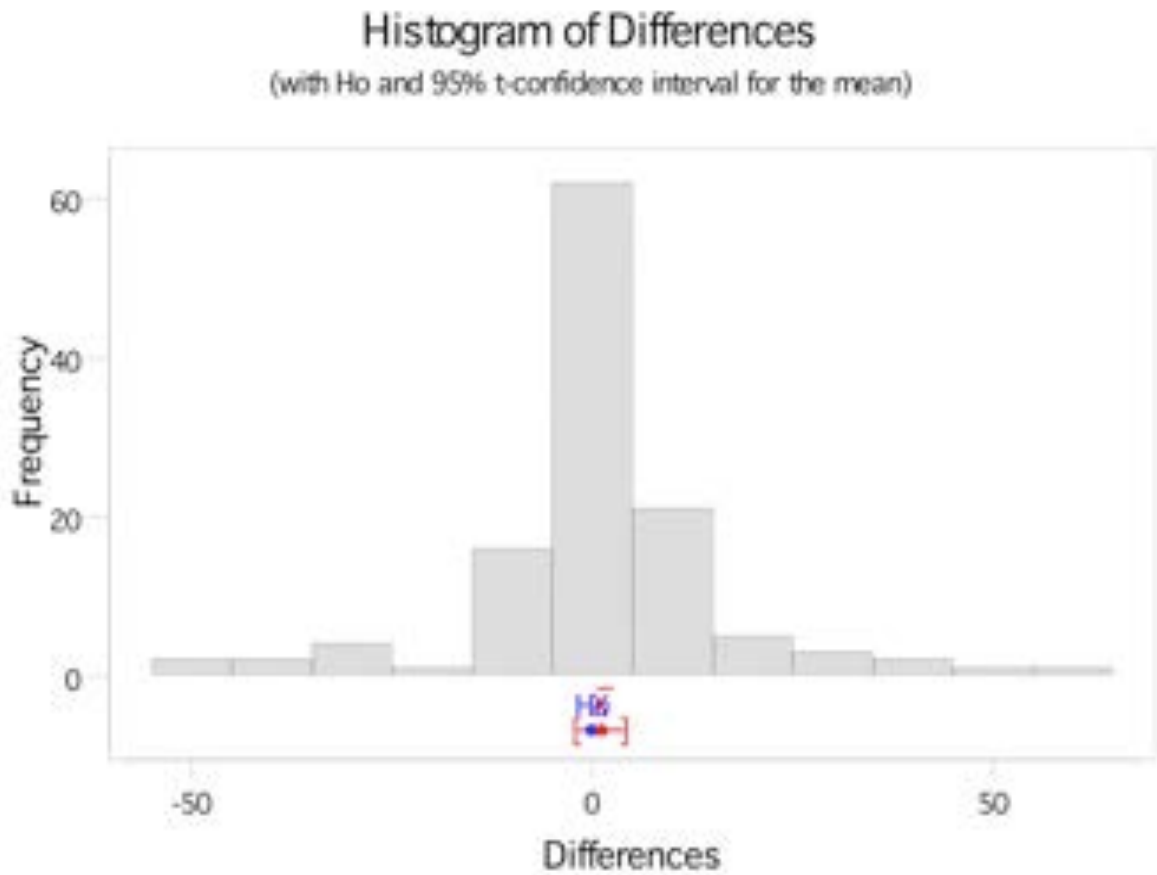
Paired T-Test and CI: LASER HAND-Placebo, LASER HAND-Holofiber

Paired T for LASER HAND-Placebo - LASER HAND-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|-----|-------|--------|---------|
| LASER HAND-p | 120 | 35.00 | 28.84 | 2.63 |
| LASER HAND-h | 120 | 33.91 | 25.62 | 2.34 |
| Difference | 120 | 1.09 | 15.67 | 1.43 |

95% CI for mean difference: (-1.74, 3.92)

T-Test of mean difference = 0 (vs. not = 0): T-Value = 0.76 P-Value = 0.447



All 10 Minute Interval Data (Paired)

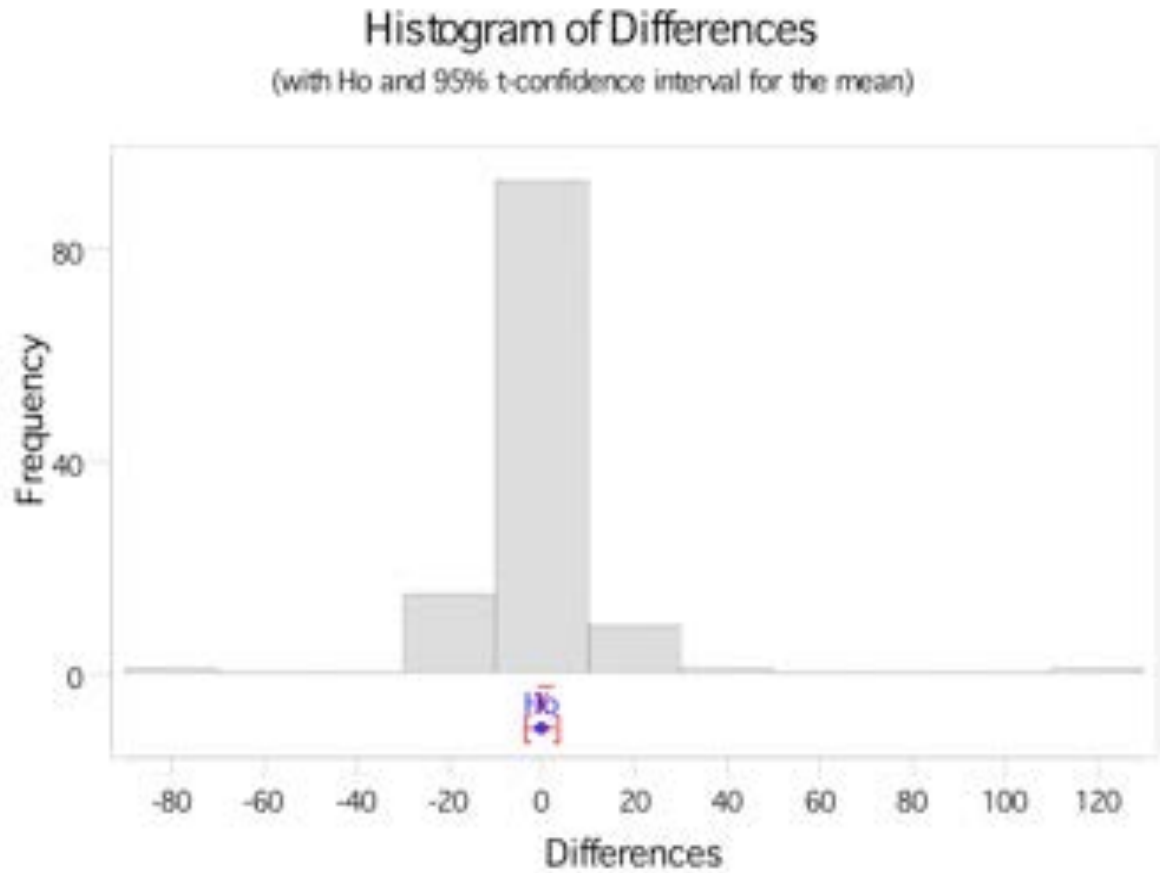
Paired T-Test and CI: LASER FOOT-Placebo, LASER FOOT-Holofiber

Paired T for LASER FOOT-Placebo - LASER FOOT-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|-----|-------|--------|---------|
| LASER FOOT-p | 120 | 49.68 | 21.12 | 1.93 |
| LASER FOOT-h | 120 | 49.64 | 19.55 | 1.78 |
| Difference | 120 | 0.04 | 15.79 | 1.44 |

95% CI for mean difference: (-2.81, 2.90)

T-Test of mean difference = 0 (vs. not = 0): T-Value = 0.03 P-Value = 0.976



Last Three Points of 10 Minute Interval Data (Paired)

Paired T-Test and CI: TCOM HAND-Placebo, TCOM HAND-Holofiber

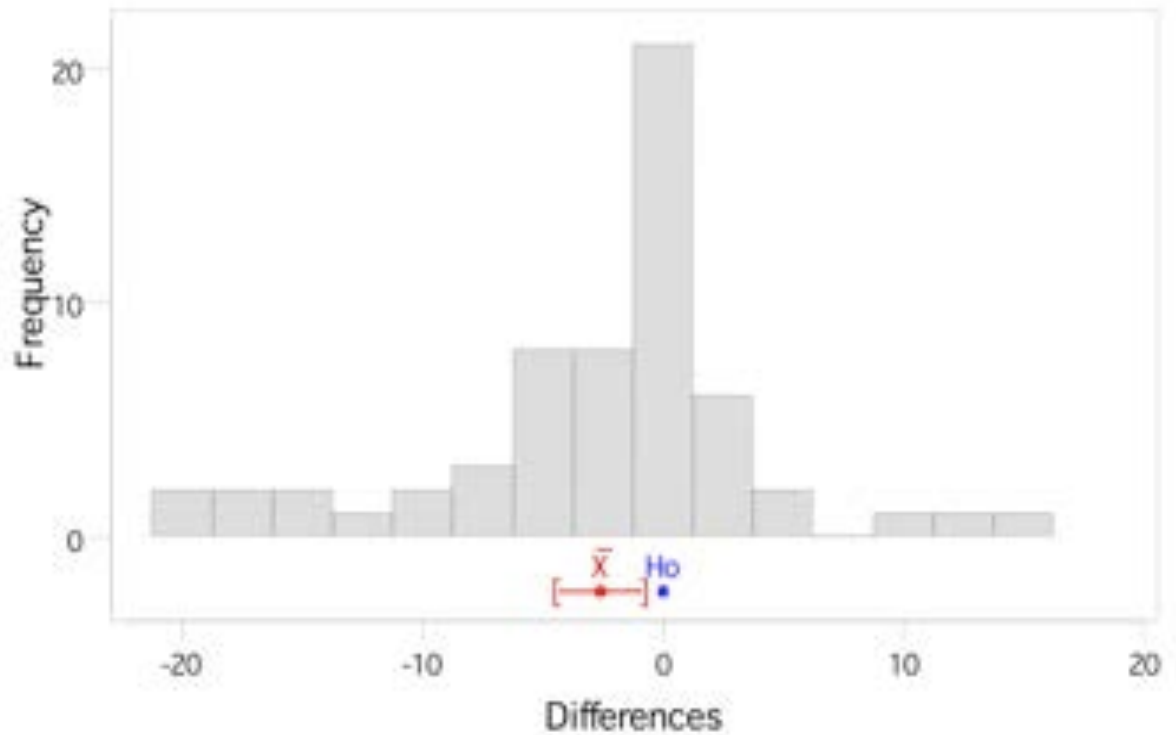
Paired T for TCOM HAND-Placebo - TCOM HAND-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|----|--------|--------|---------|
| TCOM HAND-Pl | 60 | 14.62 | 7.08 | 0.91 |
| TCOM HAND-ho | 60 | 17.19 | 9.75 | 1.26 |
| Difference | 60 | -2.572 | 6.784 | 0.876 |

95% CI for mean difference: (-4.325, -0.819)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -2.94 P-Value = 0.005

Histogram of Differences
(with Ho and 95% t-confidence interval for the mean)



Last Three Points of 10 Minute Interval Data (Paired)

Paired T-Test and CI: TCOM FOOT-Placebo, TCOM FOOT-Holofiber

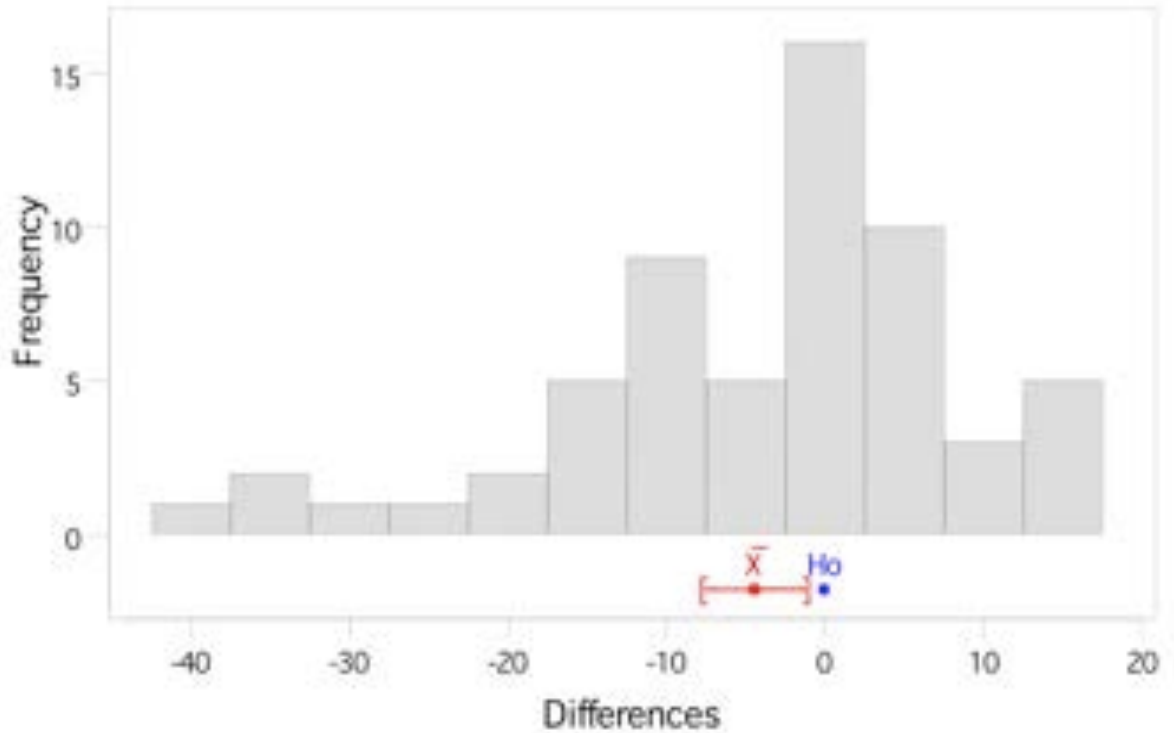
Paired T for TCOM FOOT-Placebo - TCOM FOOT-Holofiber

| | N | Mean | St Dev | St Dev | SE Mean |
|--------------|----|-------|--------|--------|---------|
| TCOM FOOT-pl | 60 | 54.19 | 19.90 | 2.57 | |
| TCOM FOOT-ho | 60 | 58.57 | 21.29 | 2.75 | |
| Difference | 60 | -4.38 | 12.27 | 1.58 | |

95% CI for mean difference: (-7.55, -1.21)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -2.76 P-Value = 0.008

Histogram of Differences
(with H_0 and 95% t-confidence interval for the mean)



Last Three Points of 10 Minute Interval Data (Paired)

Paired T-Test and CI: LASER HAND-Placebo, LASER HAND-Holofiber

Paired T for LASER HAND-Placebo - LASER HAND-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|----|-------|--------|---------|
| LASER HAND-p | 60 | 33.52 | 28.32 | 3.66 |
| LASER HAND-h | 60 | 33.48 | 25.89 | 3.34 |
| Difference | 60 | 0.05 | 15.24 | 1.97 |

95% CI for mean difference: (-3.89, 3.98)

T-Test of mean difference = 0 (vs. not = 0): T-Value = 0.02 P-Value = 0.981

Paired T-Test and CI: LASER FOOT-Placebo, LASER FOOT-Holofiber

Paired T for LASER FOOT-Placebo - LASER FOOT-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|----|-------|--------|---------|
| LASER FOOT-p | 60 | 49.90 | 19.48 | 2.51 |
| LASER FOOT-h | 60 | 51.56 | 21.49 | 2.77 |
| Difference | 60 | -1.65 | 14.80 | 1.91 |

95% CI for mean difference: (-5.48, 2.17)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -0.86 P-Value = 0.391

Last Point of 10 Minute Interval Data (Paired)

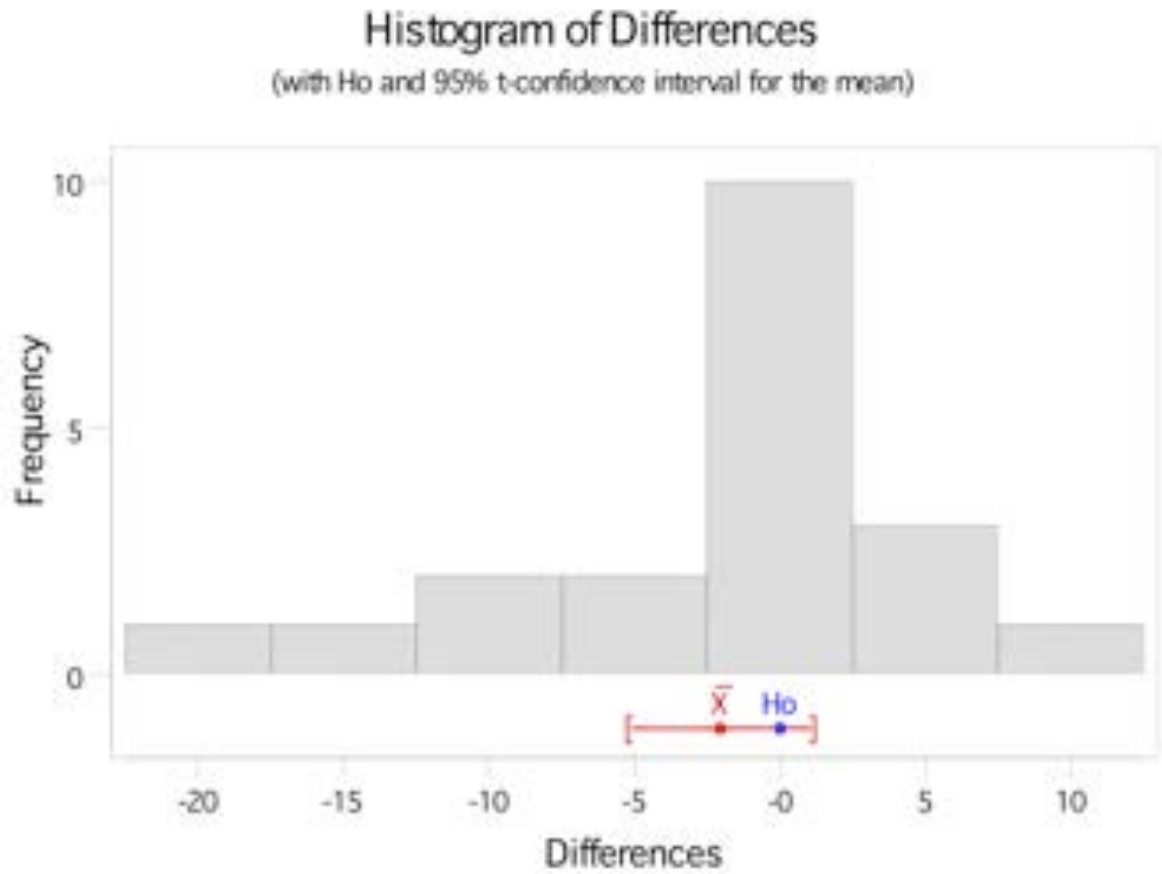
Paired T-Test and CI: TCOM HAND-Placebo, TCOM HAND-Holofiber

Paired T for TCOM HAND-Placebo - TCOM HAND-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|----|-------|--------|---------|
| TCOM HAND-Pl | 20 | 15.15 | 8.08 | 1.81 |
| TCOM HAND-ho | 20 | 17.17 | 10.17 | 2.28 |
| Difference | 20 | -2.02 | 6.60 | 1.48 |

95% CI for mean difference: (-5.11, 1.07)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -1.37 P-Value = 0.187



Last Point of 10 Minute Interval Data (Paired)

Paired T-Test and CI: TCOM FOOT-Placebo, TCOM FOOT-Holofiber

Paired T for TCOM FOOT-Placebo - TCOM FOOT-Holofiber

| | N | Mean | S Dev | SE Mean |
|--------------|----|-------|-------|---------|
| TCOM FOOT-pl | 20 | 55.42 | 20.54 | 4.59 |
| TCOM FOOT-ho | 20 | 59.48 | 21.65 | 4.84 |
| Difference | 20 | -4.05 | 11.61 | 2.60 |

95% CI for mean difference: (-9.49, 1.38)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -1.56 P-Value = 0.135

Paired T-Test and CI: LASER HAND-Placebo, LASER HAND-Holofiber

Paired T for LASER HAND-Placebo - LASER HAND-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|----|-------|--------|---------|
| LASER HAND-p | 20 | 33.87 | 26.02 | 5.82 |
| LASER HAND-h | 20 | 33.69 | 27.39 | 6.13 |
| Difference | 20 | 0.18 | 15.89 | 3.55 |

95% CI for mean difference: (-7.26, 7.62)

T-Test of mean difference = 0 (vs. not = 0): T-Value = 0.05 P-Value = 0.960

Paired T-Test and CI: LASER FOOT-Placebo, LASER FOOT-Holofiber

Paired T for LASER FOOT-Placebo - LASER FOOT-Holofiber

| | N | Mean | St Dev | SE Mean |
|--------------|----|-------|--------|---------|
| LASER FOOT-p | 20 | 52.52 | 22.57 | 5.05 |
| LASER FOOT-h | 20 | 54.97 | 27.41 | 6.13 |
| Difference | 20 | -2.45 | 24.05 | 5.38 |

95% CI for mean difference: (-13.70, 8.80)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -0.46 P-Value = 0.654

1st Half to 2nd Half of Test

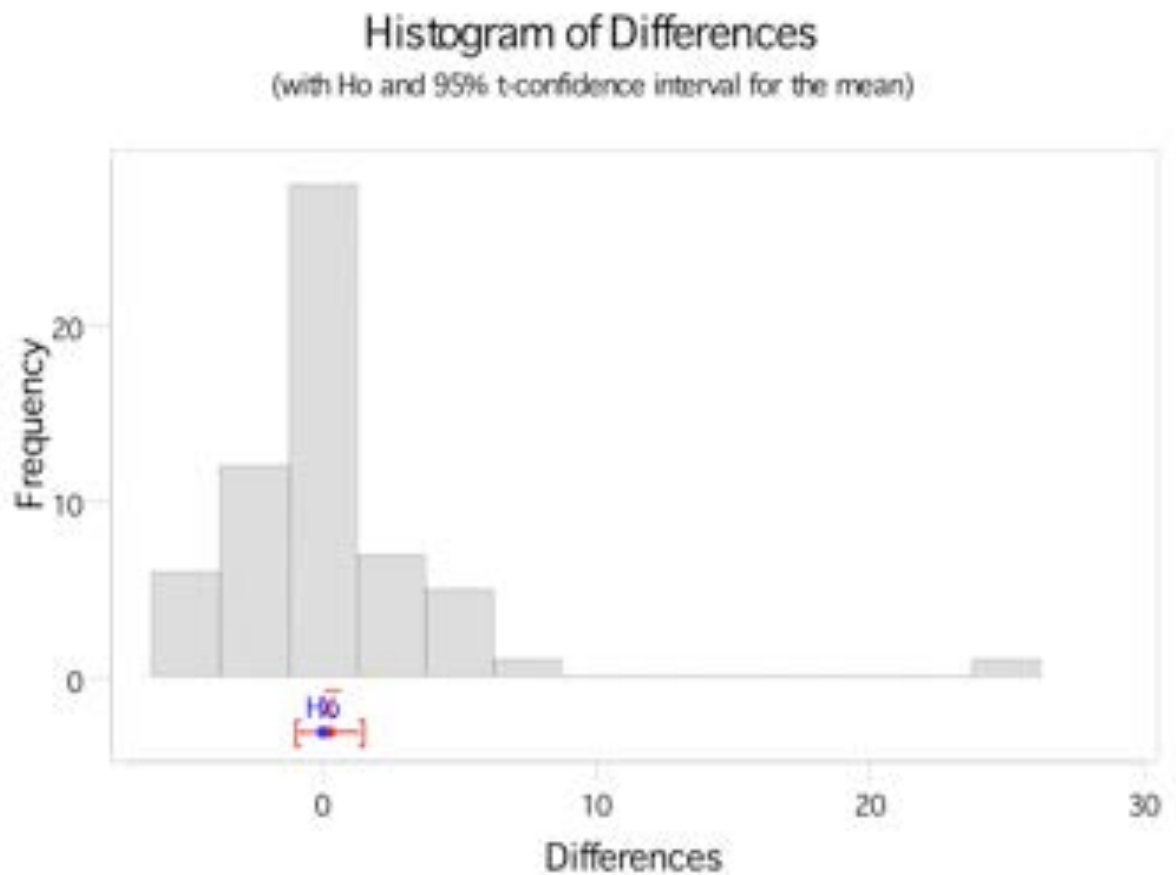
Paired T-Test and CI: 1 Holofiber-TCOM Hand, 2 Holofiber-TCOM Hand

Paired T for 1 Holofiber-TCOM Hand - 2 Holofiber-TCOM Hand

| | N | Mean | St Dev | SE Mean |
|------------------|----|-------|--------|---------|
| 1 Holofiber-TCOM | 60 | 17.45 | 11.29 | 1.46 |
| 2 Holofiber-TCOM | 60 | 17.19 | 9.75 | 1.26 |
| Difference | 60 | 0.256 | 4.321 | 0.558 |

95% CI for mean difference: (-0.860, 1.372)

T-Test of mean difference = 0 (vs. not = 0): T-Value = 0.46 P-Value = 0.648



1st Half to 2nd Half of Test

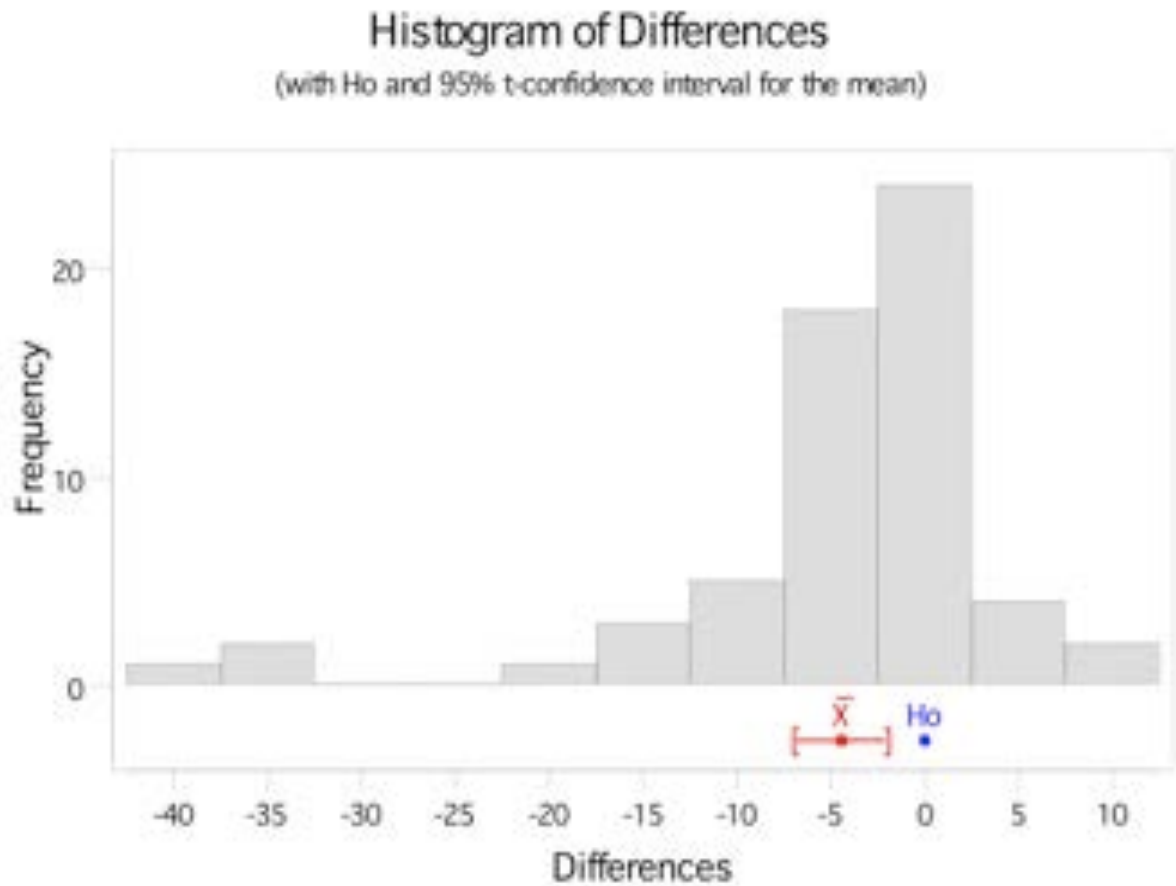
Paired T-Test and CI: 1 Holofiber-TCOM Foot, 2 Holofiber-TCOM Foot

Paired T for 1 Holofiber-TCOM Foot - 2 Holofiber-TCOM Foot

| | N | Mean | St Dev | SE Mean |
|------------------|----|-------|--------|---------|
| 1 Holofiber-TCOM | 60 | 54.14 | 18.55 | 2.39 |
| 2 Holofiber-TCOM | 60 | 58.57 | 21.29 | 2.75 |
| Difference | 60 | -4.43 | 9.14 | 1.18 |

95% CI for mean difference: (-6.79, -2.07)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -3.76 P-Value = 0.000



1st Half to 2nd Half of Test

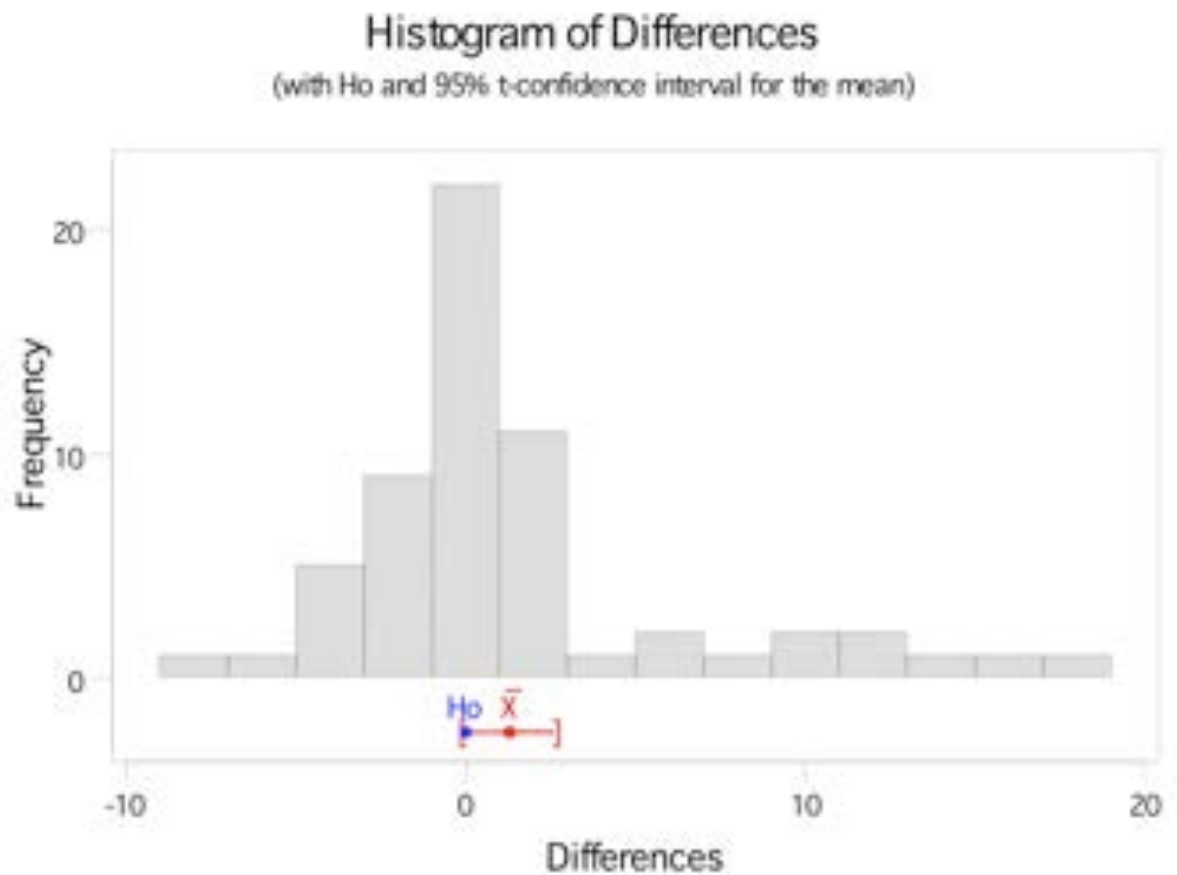
Paired T-Test and CI: 1 Placebo-TCOM Hand, 2 Placebo-TCOM Hand

Paired T for 1 Placebo-TCOM Hand - 2 Placebo-TCOM Hand

| | N | Mean | St Dev | SE Mean |
|---------------|----|-------|--------|---------|
| 1 Placebo -TC | 60 | 15.94 | 8.12 | 1.05 |
| 2 Placebo -TC | 60 | 14.62 | 7.08 | 0.91 |
| Difference | 60 | 1.322 | 5.102 | 0.659 |

95% CI for mean difference: (0.004, 2.640)

T-Test of mean difference = 0 (vs. not = 0): T-Value = 2.01 P-Value = 0.049



1st Half to 2nd Half of Test

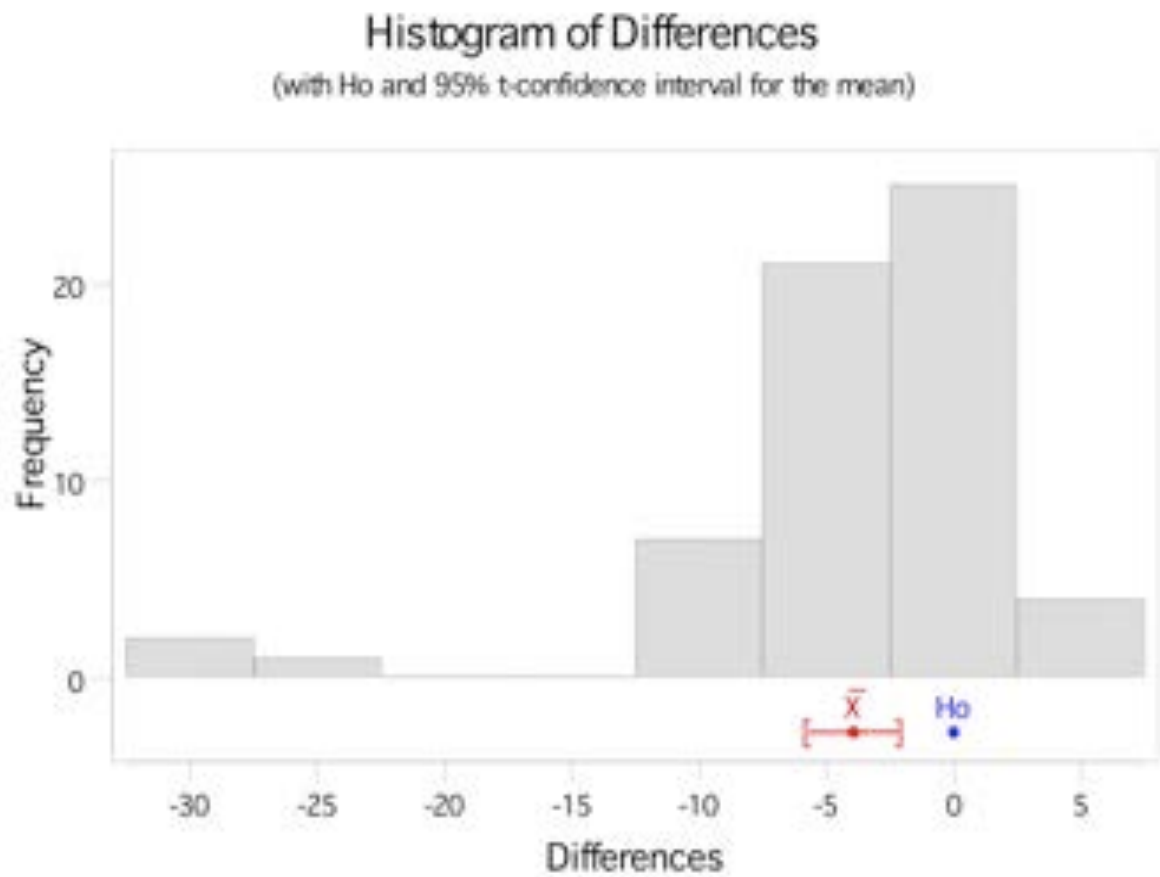
Paired T-Test and CI: 1 Placebo-TCOM Foot, 2 Placebo-TCOM Foot

Paired T for 1 Placebo-TCOM Foot - 2 Placebo-TCOM Foot

| | N | Mean | St Dev | SE Mean |
|--------------|----|--------|--------|---------|
| 1 Placebo-TC | 60 | 50.26 | 20.85 | 2.69 |
| 2 Placebo-TC | 60 | 54.19 | 19.90 | 2.57 |
| Difference | 60 | -3.930 | 6.726 | 0.868 |

95% CI for mean difference: (-5.668, -2.192)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -4.53 P-Value = 0.000



Last Two Points 10 Minute Interval Data (Paired)

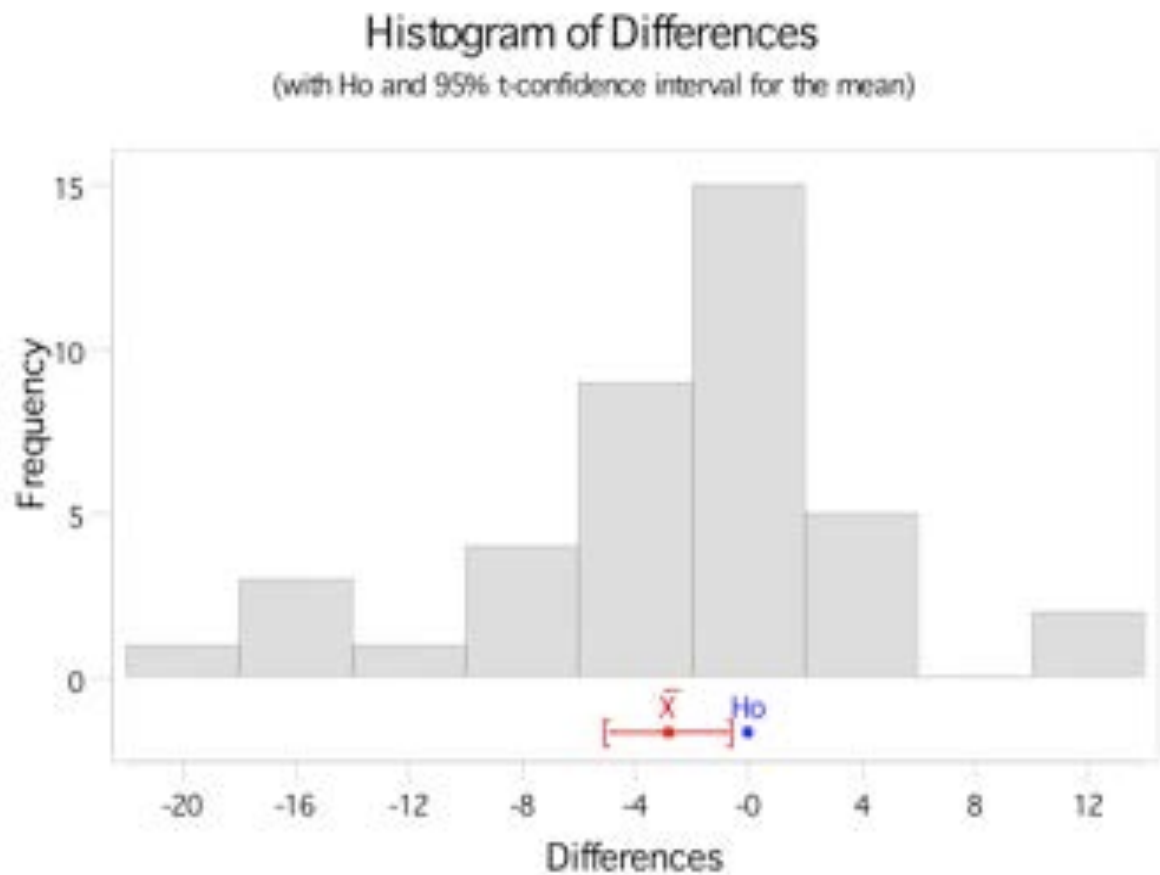
Paired T-Test and CI: Placebo-TCOM Hand, Holofiber-TCOM Hand

Paired T for Placebo-TCOM Hand - Holofiber-TCOM Hand

| | N | Mean | St Dev | SE Mean |
|-------------------|----|-------|--------|---------|
| Placebo-TCOM | 40 | 14.68 | 7.32 | 1.16 |
| Holofiber-TCOM Ha | 40 | 17.49 | 9.91 | 1.57 |
| Difference | 40 | -2.82 | 6.67 | 1.05 |

95% CI for mean difference: (-4.95, -0.68)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -2.67 P-Value = 0.011



Last Two Points 10 Minute Interval Data (Paired)

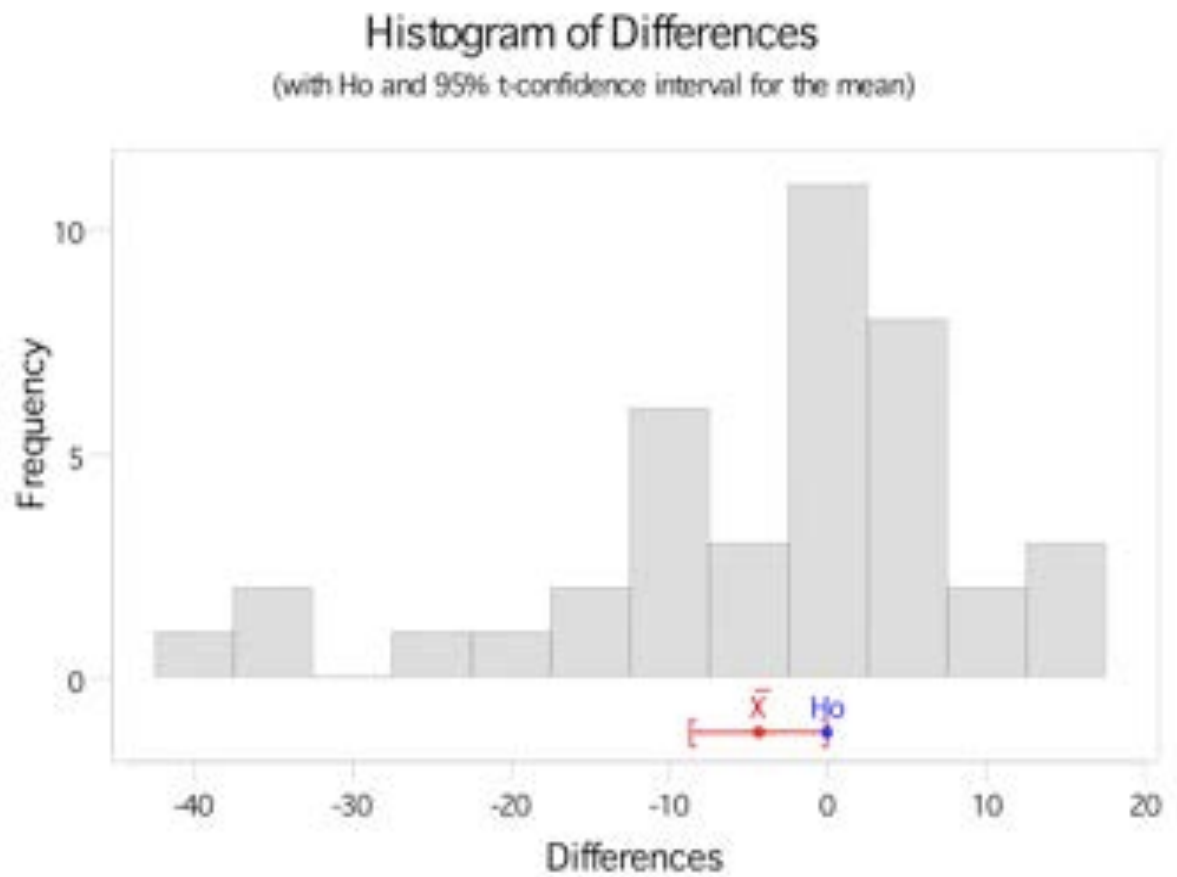
Paired T-Test and CI: Placebo-TCOM Foot, Holofiber-TCOM Foot

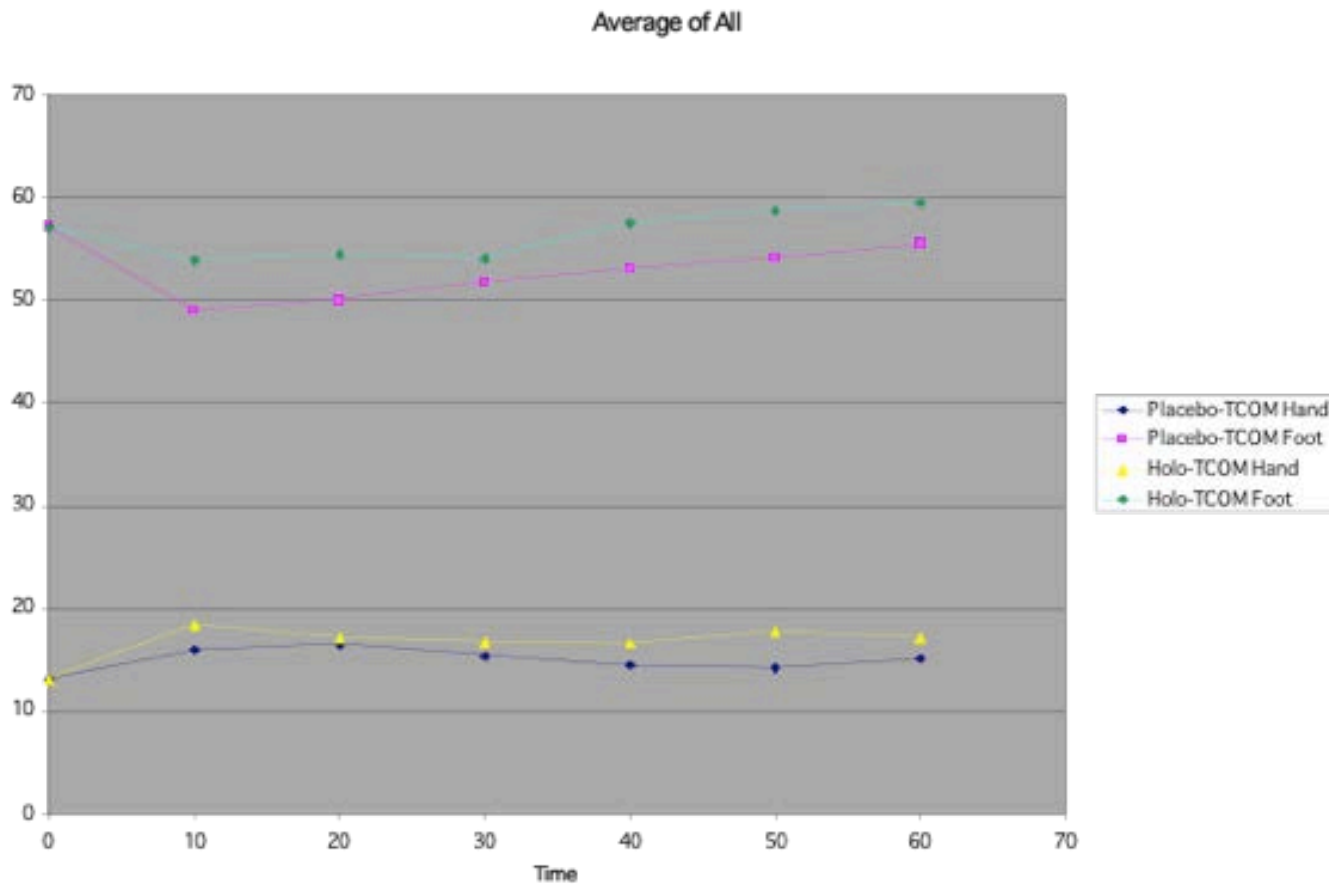
Paired T for Placebo-TCOM Foot - Holofiber-TCOM Foot

| | N | Mean | St Dev | SE Mean |
|----------------|----|-------|--------|---------|
| Placebo-TCOM | 40 | 54.76 | 19.92 | 3.15 |
| Holofiber-TCOM | 40 | 59.10 | 21.02 | 3.32 |
| Difference | 40 | -4.33 | 12.85 | 2.03 |

95% CI for mean difference: (-8.44, -0.22)

T-Test of mean difference = 0 (vs. not = 0): T-Value = -2.13 P-Value = 0.039





Limitations: This preliminary study provides some insight into the potential for Holofiber. This project should be considered as a pilot project to build on. Prior to beginning the project we had little scientific information about the effect that Holofiber might have on perfusion to the extremities. There is obviously a lot that we still do not understand about Holofiber and the best way to optimize its use.

Patient selection: We enrolled diabetic males with an abnormal clinical vascular examination. Our results may have been better if we included patients with more severe vascular impairment. The subjects that may benefit the most may be diabetics with very severe disease, patients with Raynaud's disease, or peripheral arterial occlusive disease.

For instance, in the future we may want to include patients with baseline transcutaneous oxygen values less than 20 or 30 mm Hg.

Duration of the evaluation: The study period for this project was one hour. This may not have been a long enough period to observe the greatest impact of the product. Several of the patients that have voiced strong subjective improvement related their symptoms did not change until they wore the garment for more than an hour.

Wash out period: It is unclear if a “wash out” period was needed for subjects that were treated with the Holofiber and subsequently were treated with the placebo garments. This would suggest that there was a lasting effect of the Holofiber material. The current analysis did not indicate there was a trend to support this theory.

Light Exposure: Since one of the theories regarding the mechanism of action of Holofiber involves infrared light, Holofiber may be more effective when the patient is exposed to natural light during the evaluation period. The current study was conducted in a room without any exposure to natural light.

Recommendations: The pilot data is compelling. I am very optimistic that we could pursue additional funding through the National Institute of Health. Probably the best bet would be to apply for a Technology Transfer Grant or through an award from the Alternative Medicine Institute of the NIH.

Future research should focus on the target markets for this product. In addition, we should identify the mechanism of action of Holofiber, if that is possible. Initially, I would build on the data from the current project and focus on vascular improvement and subjective improvement in persons with diabetes mellitus. My recommendations would be to expand the scope of the pilot study. We should expand the study population and evaluate specific “risk groups” within the diabetic population that would benefit from the product such as dialysis patients. We need to evaluate patients after they wear Holofiber over the course of hours days or weeks. We should measure vascular parameters as well

as subjective improvement in functional status, sleep habits, and perhaps even glucose control. A long term, multi-million dollar project would evaluate if Holofiber helps to prevent lower extremity complications such as ulceration, gangrene, and amputation in high-risk persons with diabetes. This type of outcome would be better than discovering penicillin.

The athletic market probably has the most potential. There are a number of sports activities and levels of competition that we could evaluate. In general, we should focus on measuring improvement in performance in athletes that use Holofiber. I would additionally evaluate subject responses from athletes after using the product, but every shoe company has a celebrity spokesman that loves the product. I know it is a cliché from the 60's, but if we can show that Holofiber helps you run faster and jump higher (like PF Flyers) you will not be able to keep it on the shelf.

Performance outcomes are easy to measure. We can measure changes in speed, jumping, weight lifting, rowing, cycling or a number of other athletic endeavors. The easiest approach would be to conduct a classic randomized clinical trial and evaluate two groups of athletes that use Holofiber or placebo garments. We could evaluate military recruits, high school, college or professional athletes. Another approach would be to use subjects as their own control and measure pre versus post Holofiber athletic performance. We could relatively easily evaluate if exposure to the product in the course of a few hours, improves a specific athletic event like weight lifting or the time to run 2 miles.

Funding for these types of projects will be harder to obtain. The NIH's focus is on disease states. We would also need pilot data that supports the hypothesis of our athletic performance research in order to obtain advanced funding.

Is there any evidence that Holofiber improves sleep patterns? This could be measured from subjective patient feedback using a pre – post evaluation of Holofiber pajamas and sheets. A more expensive approach would be to measure sleep patterns in a sleep lab. The laboratory approach will be more objective and more expensive. Objective data of

enhanced REM sleep and other sleep parameters would attract significant attention to the product.

There are a number of areas and questions that we could pursue.

1. Does Holofiber improve in persons with diabetes?

Does Holofiber improve blood flow in diabetics?

Does Holofiber improve pain-free walking in diabetic with intermittent claudication?

Does Holofiber improve wound healing in venous stasis ulcers, diabetic neuropathic ulcers, and ischemic ulcers?

| Transcutaneous measurement of the foot | | | | | |
|--|---------------------|--------|--------|-------------------|-----------------------|
| id no. | Order of treatment | mean | mean | Percentage change | Change with Holofiber |
| | | values | values | | |
| 121 | placebo - Holofiber | 14.48 | 27.39 | 89.07 | increase |
| 119 | placebo - Holofiber | 78.74 | 70.92 | -9.93 | decrease |
| 118 | placebo - Holofiber | 20.3 | 43.9 | 116.3 | increase |
| 116 | placebo - Holofiber | 82.35 | 92.58 | 12.42 | increase |
| 113 | placebo - Holofiber | 45.76 | 52.44 | 14.61 | increase |
| 112 | placebo - Holofiber | 57.88 | 60.65 | 4.79 | increase |
| 102 | placebo - Holofiber | 54.65 | 50.82 | -7 | decrease |
| 104 | placebo - Holofiber | 65.5 | 57.96 | -11.52 | decrease |
| 105 | placebo - Holofiber | 68.51 | 106.61 | 55.61 | increase |
| 109 | placebo - Holofiber | 91.73 | 85.74 | -6.53 | decrease |
| 106 | placebo - Holofiber | 35.79 | 23.17 | -35.25 | decrease |
| 107 | placebo - Holofiber | 53.42 | 37.5 | 29.8 | increase |
| 108 | placebo - Holofiber | 55.63 | 53.63 | 3.59 | no change |
| 101 | placebo - Holofiber | 54.34 | 55.82 | -2.72 | no change |
| 110 | placebo - Holofiber | 92.91 | 81.88 | 11.86 | increase |
| 111 | placebo - Holofiber | 57.53 | 48 | 16.58 | increase |
| 114 | placebo - Holofiber | 60.69 | 62.37 | -2.77 | no change |
| 115 | placebo - Holofiber | 55.1 | 57.75 | -4.81 | decrease |
| 117 | placebo - Holofiber | 44.28 | 40.93 | 7.56 | increase |
| 120 | placebo - Holofiber | 51.06 | 51.92 | -1.69 | no change |

| Transcutaneous measurement of the hand | | | | | |
|--|---------------------|-------------|-------------|-------------------|-----------------------|
| id no. | Order of treatment | mean values | mean values | Percentage change | Change with Holofiber |
| 121 | placebo - Holofiber | 14.82 | 12.63 | -14.81 | decrease |
| 119 | placebo - Holofiber | 21.19 | 31.45 | 48.4 | increase |
| 118 | placebo - Holofiber | 32.5 | 42.77 | 31.61 | increase |
| 116 | placebo - Holofiber | 5.91 | 5.98 | 1.23 | no change |
| 113 | placebo - Holofiber | 13.63 | 14.35 | 5.34 | decrease |
| 112 | placebo - Holofiber | 14.72 | 15.04 | 2.18 | no change |
| 102 | placebo - Holofiber | 9.51 | 13.33 | 40.22 | increase |
| 104 | placebo - Holofiber | 11.19 | 9.95 | -11.08 | decrease |
| 105 | placebo - Holofiber | 7.28 | 9.31 | 27.91 | increase |
| 109 | placebo - Holofiber | 11.64 | 11.95 | 2.69 | no change |
| 106 | placebo - Holofiber | 5.57 | 7.86 | 41.18 | increase |
| 107 | placebo - Holofiber | 5.64 | 4.36 | 22.69 | increase |
| 108 | placebo - Holofiber | 16.18 | 14.6 | 9.73 | increase |
| 101 | placebo - Holofiber | 19.91 | 14.46 | 27.36 | increase |
| 110 | placebo - Holofiber | 9.56 | 9.64 | -0.89 | no change |
| 111 | placebo - Holofiber | 32.73 | 17.34 | 47.02 | increase |
| 114 | placebo - Holofiber | 22.13 | 28.45 | -28.53 | decrease |
| 115 | placebo - Holofiber | 14.58 | 29.75 | -104.02 | decrease |
| 117 | placebo - Holofiber | 25.59 | 12.93 | 49.47 | increase |
| 120 | placebo - Holofiber | 25.81 | 27.42 | -6.27 | decrease |

| id no. | Order of treatment | Laser doppler of the hand | | | |
|--------|---------------------|---------------------------|-------------|-------------------|-----------------------|
| | | mean values | mean values | percentage change | Change with Holofiber |
| 121 | placebo - Holofiber | 33.81 | 43.19 | 27.74 | increase |
| 119 | placebo - Holofiber | 84.94 | 69.28 | -18.44 | decrease |
| 118 | placebo - Holofiber | 46.02 | 46.49 | 1.03 | no change |
| 116 | placebo - Holofiber | 51.9 | 30.88 | -40.51 | decrease |
| 113 | placebo - Holofiber | 20.18 | 14.83 | -26.5 | decrease |
| 112 | placebo - Holofiber | 26.66 | 29.35 | 10.08 | increase |
| 102 | placebo - Holofiber | 34.82 | 46.63 | 33.93 | increase |
| 104 | placebo - Holofiber | 27.83 | 29.44 | 5.8 | increase |
| 105 | placebo - Holofiber | 18.17 | 13.44 | -26.03 | decrease |
| 109 | placebo - Holofiber | 15.75 | 15.22 | -3.33 | no change |
| 106 | placebo - Holofiber | 6.6 | 5.5 | -16.6 | increase |
| 107 | placebo - Holofiber | 12.64 | 19.07 | -50.93 | decrease |
| 108 | placebo - Holofiber | 12.96 | 18.07 | -39.48 | decrease |
| 101 | placebo - Holofiber | 15.52 | 22.87 | -47.4 | decrease |
| 110 | placebo - Holofiber | 11.47 | 17.05 | -48.7 | decrease |
| 111 | placebo - Holofiber | 24.55 | 22.46 | 8.52 | increase |
| 114 | placebo - Holofiber | 105.44 | 104.88 | 0.53 | no change |
| 115 | placebo - Holofiber | 93.59 | 23.89 | 74.47 | increase |
| 117 | placebo - Holofiber | 62.58 | 75.88 | -21.25 | decrease |
| 120 | placebo - Holofiber | 33.81 | 43.19 | -27.74 | decrease |

| Laser doppler of the foot | | | | | |
|---------------------------|---------------------|-------------|-------------|-------------------|-----------------------|
| Id no. | Order of treatment | mean values | mean values | Percentage change | Change with Holofiber |
| 121 | placebo - Holofiber | 47.9 | 60.84 | 27.01 | increase |
| 119 | placebo - Holofiber | 84.28 | 75.54 | -10.37 | decrease |
| 118 | placebo - Holofiber | 53.29 | 62.79 | 17.84 | increase |
| 116 | placebo - Holofiber | 2.71 | 5.57 | 105.29 | increase |
| 113 | placebo - Holofiber | 63.47 | 64.87 | 2.2 | no change |
| 112 | placebo - Holofiber | 63.47 | 64.87 | 2.2 | no change |
| 102 | placebo - Holofiber | 50.23 | 140.23 | 179.18 | increase |
| 104 | placebo - Holofiber | 65.84 | 63.16 | -4.08 | no change |
| 105 | placebo - Holofiber | 56.78 | 61.78 | 8.79 | increase |
| 109 | placebo - Holofiber | 49.26 | 50.22 | 1.96 | increase |
| 106 | placebo - Holofiber | 61.37 | 57.53 | -6.25 | decrease |
| 107 | Holofiber - placebo | 59.35 | 63.08 | -6.27 | decrease |
| 108 | Holofiber - placebo | 57.21 | 79.87 | -39.61 | decrease |
| 101 | Holofiber - placebo | 49.06 | 45.84 | 6.55 | increase |
| 110 | Holofiber - placebo | 40.44 | 43.57 | -7.73 | decrease |
| 111 | Holofiber - placebo | 31.69 | 32.89 | -3.81 | no change |
| 114 | Holofiber - placebo | 59.05 | 62.31 | -5.52 | decrease |
| 115 | Holofiber - placebo | 58 | 59.67 | -2.87 | no change |
| 117 | Holofiber - placebo | 4.31 | 2.3 | 46.72 | increase |
| 120 | Holofiber - placebo | 46.13 | 52.08 | -12.89 | decrease |

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| Patient ID: 101 | Holofiber - placebo | | | |
|------------------------------|---------------------|------------|-----------|------------|
| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| Mean value (Unit) | 24.52 | 16.82 | 55.6 | 49.82 |
| Standard Deviation (Unit) | 3.57 | 6.9 | 0.48 | 0.29 |
| Standard Error (Unit) | 0.13 | 0.24 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 1228.34 | 842.67 | 2785.16 | 2495.65 |
| 10 MINUTES HOLOFIBER | | | | |
| Mean value (Unit) | 19.89 | 13.29 | 54.6 | 44.08 |
| Standard Deviation (Unit) | 3.24 | 3.48 | 1.36 | 0.34 |
| Standard Error (Unit) | 0.11 | 0.12 | 0.05 | 0.01 |
| Area under curve (Unit*sec.) | 994.9 | 664.9 | 2731.59 | 2205.26 |
| 20M MINUTES HOLOFIBER | | | | |
| Mean value (Unit) | 17.93 | 12.42 | 53.86 | 44.25 |
| Standard Deviation (Unit) | 7.33 | 1.97 | 1.22 | 0.87 |
| Standard Error (Unit) | 0.26 | 0.07 | 0.04 | 0.03 |
| Area under curve (Unit*sec.) | 899.19 | 622.89 | 2701.65 | 2219.58 |
| 30 MINUTES HOLOFIBER | | | | |
| Mean value (Unit) | 16.01 | 13.11 | 55.61 | 48.34 |
| Standard Deviation (Unit) | 3.63 | 3.99 | 1.86 | 0.32 |
| Standard Error (Unit) | 0.13 | 0.14 | 0.07 | 0.01 |
| Area under curve (Unit*sec.) | 794.3 | 650.01 | 2758.62 | 2397.88 |
| 40 MINUTYES HOLOFIBER | | | | |
| Mean value (Unit) | 20.84 | 12.41 | 50.05 | 46.7 |
| Standard Deviation (Unit) | 4.55 | 1.68 | 1.05 | 0.21 |
| Standard Error (Unit) | 0.16 | 0.06 | 0.04 | 0.01 |
| Area under curve (Unit*sec.) | 1032.44 | 615.01 | 2479.3 | 2313.27 |
| 50 MINUTES HOLOFIBER | | | | |
| Mean value (Unit) | 23.19 | 15.32 | 51.7 | 49.39 |
| Standard Deviation (Unit) | 3.51 | 13.77 | 0.98 | 0.5 |
| Standard Error (Unit) | 0.12 | 0.48 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 1157.26 | 764.74 | 2580.38 | 2464.88 |
| 60 MINUTES HOLOFIBER | | | | |
| Mean value (Unit) | 18.76 | 12.15 | 54.42 | 46.87 |
| Standard Deviation (Unit) | 4.06 | 1.84 | 1.52 | 0.48 |
| Standard Error (Unit) | 0.14 | 0.06 | 0.05 | 0.02 |
| Area under curve (Unit*sec.) | 948.83 | 614.15 | 2752.92 | 2371.13 |
| 10 MINUTES PLACEBO | | | | |
| Mean value (Unit) | 17.96 | 16.39 | 48.23 | 48.87 |
| Standard Deviation (Unit) | 6 | 4.72 | 1.01 | 0.43 |
| Standard Error (Unit) | 0.22 | 0.17 | 0.04 | 0.02 |
| Area under curve (Unit*sec.) | 876.49 | 800.13 | 2353.08 | 2384.35 |
| 20 MINUTES PLACEBO | | | | |
| Mean value (Unit) | 16.23 | 14.01 | 50.2 | 43.88 |

| | | | | |
|------------------------------|--------|---------|---------|---------|
| Standard Deviation (Unit) | 2.58 | 1.66 | 1.43 | 0.55 |
| Standard Error (Unit) | 0.09 | 0.06 | 0.05 | 0.02 |
| Area under curve (Unit*sec.) | 821.9 | 709.8 | 2542.56 | 2222.42 |
| 30 MINUTES PLACEBO | | | | |
| Mean value (Unit) | 17.15 | 14.56 | 56.02 | 46.79 |
| Standard Deviation (Unit) | 2.84 | 2.43 | 2.03 | 0.52 |
| Standard Error (Unit) | 0.1 | 0.09 | 0.07 | 0.02 |
| Area under curve (Unit*sec.) | 859.03 | 729.36 | 2805.87 | 2343.65 |
| 40 MINUTES PLACEBO | | | | |
| Mean value (Unit) | 16.14 | 13.25 | 52.87 | 45.3 |
| Standard Deviation (Unit) | 3.11 | 2.62 | 0.59 | 0.69 |
| Standard Error (Unit) | 0.11 | 0.09 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 809.73 | 664.6 | 2651.61 | 2272.11 |
| 50 MINUTES PLACEBO | | | | |
| Mean value (Unit) | 15.44 | 14.36 | 60.51 | 58.32 |
| Standard Deviation (Unit) | 4.63 | 2.19 | 0.95 | 1.29 |
| Standard Error (Unit) | 0.17 | 0.08 | 0.03 | 0.05 |
| Area under curve (Unit*sec.) | 775.33 | 721.12 | 3038.74 | 2928.89 |
| 60 MINUTES PLACEBO | | | | |
| Mean value (Unit) | 16.08 | 22.06 | 55.53 | 48.87 |
| Standard Deviation (Unit) | 7.18 | 15.94 | 1.14 | 2.56 |
| Standard Error (Unit) | 0.26 | 0.57 | 0.04 | 0.09 |
| Area under curve (Unit*sec.) | 803.07 | 1100.69 | 2771.29 | 2439.26 |

| Patient ID: 102 | placebo-Holofiber | | | |
|---------------------------------|-------------------|---------------|--------------|---------------|
| | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| BASELINE | | | | |
| Mean value (Unit) | 8.66 | 45.65 | 55.22 | 40.67 |
| Standard Deviation (Unit) | 2.72 | 4.5 | 0.86 | 0.38 |
| Standard Error (Unit) | 0.1 | 0.16 | 0.03 | 0.01 |
| Area under curve (Unit*sec.) | 438.71 | 2312.2 | 2797.32 | 2059.9 |
| 10 MINUTE PLACEBO | | | | |
| Mean value (Unit) | 10.27 | 40.1 | 5.75 | 37.56 |
| Standard Deviation (Unit) | 3.28 | 6.94 | 0.96 | 0.44 |
| Standard Error (Unit) | 0.08 | 0.17 | 0.02 | 0.01 |
| 20 MINUTE PLACEBO | | | | |
| Mean value (Unit) | 10.15 | 36.71 | 22.45 | 40.96 |
| Standard Deviation (Unit) | 2.82 | 6.14 | 0.62 | 0.26 |
| Standard Error (Unit) | 0.1 | 0.22 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 501.22 | 1813.7 | 1109.29 | 2023.98 |
| 30 MINUTE PLACEBO | | | | |
| Mean value (Unit) | 10.13 | 36.2 | 30.28 | 41.9 |
| Standard Deviation (Unit) | 3.92 | 3.14 | 0.83 | 0.75 |
| Standard Error (Unit) | 0.14 | 0.11 | 0.03 | 0.03 |
| Area under curve (Unit*sec.) | 514.53 | 1837.85 | 1537.66 | 2127.42 |
| 40 MINUTE PLACEBO | | | | |
| Mean value (Unit) | 11.57 | 34.57 | 33.95 | 47.01 |
| Standard Deviation (Unit) | 2.78 | 3.53 | 0.35 | 0.2 |
| Standard Error (Unit) | 0.1 | 0.12 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 593.38 | 1772.94 | 1740.97 | 2410.22 |
| 50 MINUTE PLACEBO | | | | |
| Mean value (Unit) | 9.58 | 35.59 | 52.67 | 47.78 |
| Standard Deviation (Unit) | 1.97 | 3.18 | 0.1 | 0.16 |
| Standard Error (Unit) | 0.07 | 0.11 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 484.85 | 1800.54 | 2664.69 | 2417.03 |
| 60 MINUTE PLACEBO | | | | |
| Mean value (Unit) | 8.99 | 33.82 | 55.02 | 50.6 |
| Standard Deviation (Unit) | 2.11 | 6.96 | 0.4 | 0.45 |
| Standard Error (Unit) | 0.07 | 0.24 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 455.18 | 1712.98 | 2787.02 | 2563.31 |
| 10 MINUTE HOLOFIBER | | | | |
| Mean value (Unit) | 8.93 | 43.3 | 37.54 | 59.37 |
| Standard Deviation (Unit) | 1.85 | 3.14 | 0.27 | 0.3 |
| Standard Error (Unit) | 0.07 | 0.11 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 444.79 | 2155.53 | 1869.08 | 2955.84 |

| | | | | |
|---------------------------------|--------|---------|---------|----------|
| 20 MINUTE HOLOFIBER | | | | |
| Mean value (Unit) | 9.53 | 41.92 | 38.65 | 57.8 |
| Standard Deviation (Unit) | 1.77 | 2.95 | 0.13 | 0.16 |
| Standard Error (Unit) | 0.06 | 0.1 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 477.24 | 2099.87 | 1936.15 | 2895.57 |
| 30 MINUTE HOLOFIBER | | | | |
| Mean value (Unit) | 9.67 | 40.85 | 40.17 | 59.47 |
| Standard Deviation (Unit) | 1.86 | 3.69 | 0.34 | 0.96 |
| Standard Error (Unit) | 0.07 | 0.13 | 0.01 | 0.03 |
| Area under curve (Unit*sec.) | 474.01 | 2003.64 | 1969.91 | 2915.9 |
| 40 MINUTES HOLOFIBER | | | | |
| Mean value (Unit) | 12.06 | 41.65 | 40.43 | 57.87 |
| Standard Deviation (Unit) | 2.54 | 3.65 | 0.28 | 0.64 |
| Standard Error (Unit) | 0.09 | 0.13 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 607.67 | 2099.4 | 2037.75 | 2916.84 |
| 50 MINUTRE HOLOFIBER | | | | |
| Mean value (Unit) | 13.04 | 43.7 | 39.8 | 59.2 |
| Standard Deviation (Unit) | 2.62 | 3.7 | 0.4 | 0.15 |
| Standard Error (Unit) | 0.09 | 0.13 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 637.89 | 2137.86 | 1946.79 | 2895.96 |
| 60 MINUTES HOLOFIBER | | | | |
| Mean value (Unit) | 13.61 | 46.5 | 50.5 | 140.59 |
| Standard Deviation (Unit) | 3.61 | 5.91 | 1.13 | 2.51 |
| Standard Error (Unit) | 0.11 | 0.17 | 0.03 | 0.07 |
| Area under curve (Unit*sec.) | 978.71 | 3343.47 | 3630.78 | 10108.81 |

| Patient ID:104 | placebo - Holofiber | | | |
|------------------------------|------------------------|------------|-----------|------------|
| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| Mean value (Unit) | 9.59 | 27.27 | 58.95 | 74.86 |
| Standard Deviation (Unit) | 4.17 | 5.27 | 0.52 | 0.61 |
| Standard Error (Unit) | 0.15 | 0.19 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 467.46 | 1330.34 | 2876.43 | 3652.55 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 22.31 | 43.44 | 65.31 | 68.88 |
| Standard Deviation (Unit) | 10.72 | 6.89 | 0.5 | 0.16 |
| Standard Error (Unit) | 0.39 | 0.25 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 1057.09 | 2057.66 | 3093.45 | 3262.85 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 19.91 | 26.3 | 63.01 | 64.9 |
| Standard Deviation (Unit) | 11.08 | 7.04 | 0.65 | 0.24 |
| Standard Error (Unit) | 0.28 | 0.18 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 1876.28 | 2478.22 | 5938.24 | 6116.34 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.19 | 28.63 | 67.04 | 65 |
| Standard Deviation (Unit) | 5.24 | 5.72 | 1.51 | 0.98 |
| Standard Error (Unit) | 0.14 | 0.15 | 0.04 | 0.03 |
| Area under curve (Unit*sec.) | 1147.35 | 2489.99 | 5831.53 | 5654.23 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 11.83 | 29.71 | 64.06 | 63.89 |
| Standard Deviation (Unit) | 2.87 | 17.62 | 1.09 | 0.84 |
| Standard Error (Unit) | 0.07 | 0.44 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 1200.52 | 3015.51 | 6502.62 | 6485.27 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 12.13 | 28.64 | 66.07 | 66.32 |
| Standard Deviation (Unit) | 6.49 | 5.6 | 1.09 | 0.86 |
| Standard Error (Unit) | 0.16 | 0.14 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 1231.21 | 2907.27 | 6706.28 | 6731.59 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 11.52 | 27.4 | 63.88 | 63.7 |
| Standard Deviation (Unit) | 3.33 | 4.68 | 0.7 | 1.02 |
| Standard Error (Unit) | 0.12 | 0.17 | 0.02 | 0.04 |
| Area under curve (Unit*sec.) | 563.45 | 1339.87 | 3124.95 | 3116.03 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.06 | 29.95 | 59.11 | 64.74 |
| Standard Deviation (Unit) | 6.26 | 5.17 | 0.51 | 2.42 |
| Standard Error (Unit) | 0.23 | 0.19 | 0.02 | 0.09 |
| Area under curve (Unit*sec.) | 619.53 | 1420.55 | 2803.78 | 3070.87 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.21 | 28.82 | 55.27 | 59.2 |
| Standard Deviation (Unit) | 4.51 | 4.23 | 0.52 | 0.59 |
| Standard Error (Unit) | 0.16 | 0.15 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 661.85 | 1444.08 | 2768.75 | 2965.68 |

| | | | | |
|------------------------------|--------|---------|---------|---------|
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.79 | 26.41 | 55.19 | 61.7 |
| Standard Deviation (Unit) | 9.57 | 6.77 | 1.25 | 0.46 |
| Standard Error (Unit) | 0.33 | 0.24 | 0.04 | 0.02 |
| Area under curve (Unit*sec.) | 699.18 | 1338.76 | 2798.95 | 3129.3 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 9.03 | 33.09 | 63.95 | 68.85 |
| Standard Deviation (Unit) | 2.84 | 8.03 | 0.37 | 0.38 |
| Standard Error (Unit) | 0.1 | 0.28 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 448.06 | 1642.01 | 3172.03 | 3414.72 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 14.5 | 31.61 | 61.32 | 67.89 |
| Standard Deviation (Unit) | 26.64 | 5.31 | 0.79 | 0.52 |
| Standard Error (Unit) | 0.94 | 0.19 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 717.52 | 1563.87 | 3034.01 | 3359.13 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 8.52 | 31.54 | 56.9 | 64.22 |
| Standard Deviation (Unit) | 2.5 | 5.65 | 1.04 | 0.69 |
| Standard Error (Unit) | 0.09 | 0.2 | 0.04 | 0.02 |
| Area under curve (Unit*sec.) | 427.27 | 1581.51 | 2853.88 | 3221.07 |

Patient ID:105

placebo - Holofiber

| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 6.83 | 12.06 | 76.89 | 57.94 |
| Standard Deviation (Unit) | 0.58 | 1.88 | 0.27 | 0.18 |
| Standard Error (Unit) | 0.02 | 0.07 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 349.89 | 617.69 | 3937.57 | 2967.1 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 8.72 | 17.24 | 67.06 | 52.94 |
| Standard Deviation (Unit) | 2.44 | 1.29 | 0.17 | 0.13 |
| Standard Error (Unit) | 0.08 | 0.04 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 447.72 | 884.73 | 3442.6 | 2717.89 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 7.63 | 12.91 | 69.95 | 53.39 |
| Standard Deviation (Unit) | 0.99 | 8.66 | 0.27 | 0.42 |
| Standard Error (Unit) | 0.03 | 0.3 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 386.29 | 654.39 | 3543.14 | 2704.38 |
| Slope (Unit/sec.) | 0.01 | -0.11 | -0.01 | 0 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 7.22 | 9.8 | 74.77 | 62.03 |
| Standard Deviation (Unit) | 0.61 | 1.66 | 0.18 | 0.43 |
| Standard Error (Unit) | 0.02 | 0.06 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 369.02 | 500.96 | 3824.49 | 3172.94 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 7.32 | 9.89 | 72.97 | 60.38 |
| Standard Deviation (Unit) | 0.78 | 1.41 | 0.43 | 0.4 |
| Standard Error (Unit) | 0.03 | 0.05 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 374.1 | 505.5 | 3727.86 | 3084.74 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 7.28 | 11.94 | 68.44 | 57.22 |
| Standard Deviation (Unit) | 0.39 | 1.7 | 0.35 | 0.62 |
| Standard Error (Unit) | 0.01 | 0.06 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 372.44 | 610.92 | 3500.89 | 2926.78 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 7.33 | 12.98 | 68.36 | 57.73 |
| Standard Deviation (Unit) | 0.4 | 1.86 | 0.21 | 0.34 |
| Standard Error (Unit) | 0.01 | 0.07 | 0.01 | 0.01 |
| Maximum value (Unit) | 8.24 | 18.49 | 68.79 | 58.47 |
| Area under curve (Unit*sec.) | 360.89 | 638.56 | 3364.02 | 2840.72 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 8.39 | 12.97 | 67.4 | 64.54 |
| Standard Deviation (Unit) | 0.96 | 1.22 | 0.33 | 0.25 |
| Standard Error (Unit) | 0.03 | 0.04 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 427.72 | 660.83 | 3434.87 | 3289.18 |
| 20 MIN HOLO | | | | |
| Mean value (Unit) | 8.21 | 15.47 | 68.53 | 63.36 |
| Standard Deviation (Unit) | 0.59 | 2.04 | 0.09 | 0.09 |

| | | | | |
|------------------------------|--------|--------|---------|---------|
| Standard Error (Unit) | 0.02 | 0.07 | 0 | 0 |
| Area under curve (Unit*sec.) | 414.41 | 780.64 | 3458.52 | 3197.45 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 8.09 | 13 | 69.57 | 61.65 |
| Standard Deviation (Unit) | 0.86 | 1.28 | 0.09 | 0.24 |
| Standard Error (Unit) | 0.03 | 0.04 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 412.29 | 662.46 | 3545.72 | 3141.67 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 7.94 | 10.71 | 100.73 | 63.74 |
| Standard Deviation (Unit) | 0.53 | 1.04 | 0.11 | 0.29 |
| Standard Error (Unit) | 0.02 | 0.04 | 0 | 0.01 |
| Minimum value (Unit) | 6.68 | 8.36 | 100.53 | 63.05 |
| Area under curve (Unit*sec.) | 406.62 | 548.54 | 5158.38 | 3264.19 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 12.99 | 14.31 | 105.67 | 62.23 |
| Standard Deviation (Unit) | 10.5 | 3.56 | 0.46 | 0.27 |
| Standard Error (Unit) | 0.36 | 0.12 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 667.91 | 735.84 | 5431.38 | 3198.7 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 8.95 | 10.29 | 107.61 | 60.69 |
| Standard Deviation (Unit) | 2.4 | 1.61 | 0.11 | 0.18 |
| Standard Error (Unit) | 0.08 | 0.06 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 456.04 | 524.2 | 5484.28 | 3092.83 |

Patient ID: 106

placebo - Holofiber

| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 4.97 | 12.13 | 44.65 | 55.53 |
| Standard Deviation (Unit) | 2.5 | 7.93 | 0.5 | 0.17 |
| Standard Error (Unit) | 0.09 | 0.28 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 250.45 | 610.53 | 2248 | 2795.7 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 6.72 | 11.8 | 33.25 | 55.67 |
| Standard Deviation (Unit) | 5.08 | 13.08 | 1.14 | 0.46 |
| Standard Error (Unit) | 0.18 | 0.46 | 0.04 | 0.02 |
| Area under curve (Unit*sec.) | 339.01 | 595.11 | 1675.82 | 2806.24 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 6.56 | 18.81 | 33.39 | 56.16 |
| Standard Deviation (Unit) | 3.11 | 17.69 | 0.58 | 0.5 |
| Standard Error (Unit) | 0.11 | 0.62 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 333.41 | 955.97 | 1695.63 | 2851.61 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 6.58 | 15.75 | 31.28 | 55.92 |
| Standard Deviation (Unit) | 2.5 | 17.71 | 0.51 | 0.57 |
| Standard Error (Unit) | 0.09 | 0.62 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 334.68 | 801 | 1590.1 | 2843.11 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 5.61 | 9.79 | 40.6 | 57.55 |
| Standard Deviation (Unit) | 1.19 | 6.29 | 1.02 | 0.32 |
| Standard Error (Unit) | 0.04 | 0.22 | 0.04 | 0.01 |
| Area under curve (Unit*sec.) | 286.31 | 499.27 | 2071.89 | 2936.59 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 5.56 | 11.51 | 37.27 | 60.23 |
| Standard Deviation (Unit) | 2.11 | 3.21 | 0.74 | 0.5 |
| Standard Error (Unit) | 0.07 | 0.11 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 281.46 | 581.88 | 1885.38 | 3047.07 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 5.74 | 11.77 | 35.16 | 61.53 |
| Standard Deviation (Unit) | 2.03 | 12.41 | 0.46 | 0.57 |
| Standard Error (Unit) | 0.07 | 0.41 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 324.7 | 665.94 | 1988.04 | 3478.76 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 6.72 | 16.89 | 22.6 | 59.07 |
| Standard Deviation (Unit) | 2.81 | 11.83 | 0.06 | 0.32 |
| Standard Error (Unit) | 0.1 | 0.41 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 342.8 | 862.07 | 1153.21 | 3014.17 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 8.77 | 16.54 | 24.39 | 60.86 |
| Standard Deviation (Unit) | 2.97 | 7.36 | 0.22 | 0.21 |
| Standard Error (Unit) | 0.1 | 0.26 | 0.01 | 0.01 |
| Minimum value (Unit) | 3.97 | 6.84 | 24.11 | 60.55 |

| | | | | |
|------------------------------|---------|---------|----------|----------|
| Area under curve (Unit*sec.) | 444.86 | 839.7 | 1238.67 | 3090.46 |
| 30 MIN HOLOFIBER | | | | |
| Item | 1 PU #1 | 2 PU #2 | 3 pO2 #3 | 4 pO2 #4 |
| Mean value (Unit) | 3.38 | 12.52 | 23.67 | 60.29 |
| Standard Deviation (Unit) | 1.68 | 5.84 | 0.06 | 0.42 |
| Standard Error (Unit) | 0.06 | 0.21 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 167.23 | 618.67 | 1169.58 | 2979.33 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 5.66 | 20.19 | 24.11 | 61.86 |
| Standard Deviation (Unit) | 5.75 | 11.57 | 0.1 | 0.58 |
| Standard Error (Unit) | 0.2 | 0.41 | 0 | 0.02 |
| Area under curve (Unit*sec.) | 283.09 | 1011.32 | 1209.52 | 3102.92 |
| 50 MIN HOLOFIBER | | | | |
| Item | 1 PU #1 | 2 PU #2 | 3 pO2 #3 | 4 pO2 #4 |
| Mean value (Unit) | 5.75 | 14.06 | 23.58 | 58.75 |
| Standard Deviation (Unit) | 3.19 | 9.45 | 0.19 | 0.43 |
| Standard Error (Unit) | 0.11 | 0.33 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 286.12 | 700.39 | 1174.03 | 2925.03 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 5.89 | 7.45 | 23.33 | 57.99 |
| Standard Deviation (Unit) | 2.92 | 2.55 | 0.15 | 0.13 |
| Standard Error (Unit) | 0.1 | 0.09 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 284.39 | 359.42 | 1125.44 | 2797.23 |

Patient ID:107

Holofiber - placebo

BASELINE

| Item | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 3.52 | 6.05 | 80.02 | 63.82 |
| Standard Deviation (Unit) | 0.37 | 0.32 | 0.35 | 2.4 |
| Standard Error (Unit) | 0.01 | 0.01 | 0.01 | 0.09 |
| Area under curve (Unit*sec.) | 170.78 | 293.47 | 3879.61 | 3094.13 |

10 MIN HOLOFIBER

| | | | | |
|------------------------------|--------|--------|---------|---------|
| Mean value (Unit) | 4.04 | 6.07 | 60.06 | 52.45 |
| Standard Deviation (Unit) | 0.06 | 0.46 | 0.1 | 0.16 |
| Standard Error (Unit) | 0 | 0.02 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 190.98 | 286.62 | 2837.57 | 2477.93 |

20 MIN HOLOFIBER

| | | | | |
|------------------------------|--------|-------|---------|---------|
| Mean value (Unit) | 4.31 | 6.69 | 61.73 | 57.14 |
| Standard Deviation (Unit) | 0.19 | 1.03 | 0.18 | 0.17 |
| Standard Error (Unit) | 0.01 | 0.04 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 216.08 | 335.6 | 3096.23 | 2865.82 |

30 MIN HOLOFIBER

| | | | | |
|------------------------------|--------|--------|--------|---------|
| Mean value (Unit) | 4.51 | 5.9 | 57.26 | 55.5 |
| Standard Deviation (Unit) | 0.15 | 0.8 | 0.1 | 0.22 |
| Standard Error (Unit) | 0.01 | 0.03 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 227.14 | 297.47 | 2886.1 | 2797.45 |

40 MIN HOLOFIBER

| | | | | |
|------------------------------|--------|--------|---------|---------|
| Mean value (Unit) | 4.54 | 5.84 | 58.9 | 55.27 |
| Standard Deviation (Unit) | 0.27 | 1.35 | 0.11 | 0.09 |
| Standard Error (Unit) | 0.01 | 0.05 | 0 | 0 |
| Area under curve (Unit*sec.) | 227.57 | 292.61 | 2950.67 | 2768.95 |

50 MIN HOLOFIBER

| | | | | |
|------------------------------|-------|--------|---------|---------|
| Mean value (Unit) | 4.41 | 4.82 | 56.98 | 54.73 |
| Standard Deviation (Unit) | 0.15 | 0.23 | 0.15 | 0.2 |
| Standard Error (Unit) | 0.01 | 0.01 | 0.01 | 0.01 |
| Minimum value (Unit) | 4.27 | 4.52 | 56.58 | 54.32 |
| Area under curve (Unit*sec.) | 221.8 | 242.44 | 2864.96 | 2752.06 |

60 MIN HOLOFIBER

| | | | | |
|------------------------------|--------|--------|---------|---------|
| Mean value (Unit) | 4.59 | 6.18 | 48.35 | 60.3 |
| Standard Deviation (Unit) | 0.37 | 0.87 | 0.36 | 0.31 |
| Standard Error (Unit) | 0.01 | 0.03 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 228.04 | 306.87 | 2401.39 | 2994.84 |

10 MIN PLACEBO

| | | | | |
|------------------------------|--------|--------|---------|---------|
| Mean value (Unit) | 4.55 | 6.92 | 37.97 | 62.03 |
| Standard Deviation (Unit) | 0.31 | 4.71 | 0.23 | 2.04 |
| Standard Error (Unit) | 0.01 | 0.17 | 0.01 | 0.07 |
| Area under curve (Unit*sec.) | 227.99 | 347.09 | 1904.27 | 3111.28 |

20 MIN PLACEBO

| | | | | |
|-------------------|------|------|-------|-------|
| Mean value (Unit) | 4.53 | 5.56 | 36.89 | 65.09 |
|-------------------|------|------|-------|-------|

| | | | | |
|------------------------------|--------|--------|---------|---------|
| Standard Deviation (Unit) | 0.52 | 0.2 | 0.45 | 1.24 |
| Standard Error (Unit) | 0.02 | 0.01 | 0.02 | 0.04 |
| Area under curve (Unit*sec.) | 226.19 | 277.55 | 1841.35 | 3248.56 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 5.01 | 4.89 | 38.65 | 64.81 |
| Standard Deviation (Unit) | 1.49 | 0.32 | 0.4 | 1.65 |
| Standard Error (Unit) | 0.05 | 0.01 | 0.01 | 0.06 |
| Area under curve (Unit*sec.) | 250.25 | 244.58 | 1931.42 | 3238.84 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 4.54 | 5.83 | 37.83 | 62.23 |
| Standard Deviation (Unit) | 0.5 | 0.93 | 0.04 | 0.36 |
| Standard Error (Unit) | 0.02 | 0.03 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 228.01 | 292.78 | 1899.64 | 3125.22 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 4.57 | 7.16 | 37.71 | 62.6 |
| Standard Deviation (Unit) | 0.32 | 2.74 | 0.07 | 1.08 |
| Standard Error (Unit) | 0.01 | 0.1 | 0 | 0.04 |
| Area under curve (Unit*sec.) | 226.17 | 354.81 | 1868.13 | 3100.91 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 4.51 | 5.44 | 37.1 | 63.37 |
| Standard Deviation (Unit) | 0.34 | 0.28 | 0.15 | 0.77 |
| Standard Error (Unit) | 0.01 | 0.01 | 0.01 | 0.03 |
| Area under curve (Unit*sec.) | 226.15 | 272.75 | 1860.74 | 3178.5 |

Patient ID:108

Holofiber - placebo

| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 10.99 | 12.62 | 64.67 | 65.36 |
| Standard Deviation (Unit) | 1.58 | 8.11 | 0.54 | 0.33 |
| Standard Error (Unit) | 0.06 | 0.28 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 557.28 | 640.06 | 3279.66 | 3315.06 |
| Duration (sec.) | 50.78 | 50.78 | 50.78 | 50.78 |
| 10 min HOLOFIBER | | | | |
| Mean value (Unit) | 19.38 | 14.83 | 51.17 | 51.83 |
| Standard Deviation (Unit) | 2.02 | 6.5 | 0.93 | 1.97 |
| Standard Error (Unit) | 0.07 | 0.23 | 0.03 | 0.07 |
| Area under curve (Unit*sec.) | 976.89 | 747.25 | 2579.49 | 2612.72 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 17.08 | 11.45 | 49.79 | 50.6 |
| Standard Deviation (Unit) | 1.6 | 1.84 | 0.26 | 0.28 |
| Standard Error (Unit) | 0.06 | 0.06 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 860.7 | 577.1 | 2509.51 | 2550.36 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 16.32 | 12.18 | 49.5 | 48.66 |
| Standard Deviation (Unit) | 1.83 | 4.92 | 0.18 | 0.29 |
| Standard Error (Unit) | 0.06 | 0.17 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 829.66 | 618.74 | 2516.66 | 2473.87 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 17.07 | 12.71 | 53.03 | 50.48 |
| Standard Deviation (Unit) | 1.82 | 7.25 | 0.75 | 0.65 |
| Standard Error (Unit) | 0.05 | 0.21 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 1212.43 | 902.93 | 3767.74 | 3586.89 |
| 50 MIN HOLOFIBER 6 | | | | |
| Mean value (Unit) | 16.77 | 19.04 | 52.31 | 51.16 |
| Standard Deviation (Unit) | 2.71 | 10.84 | 0.35 | 0.5 |
| Standard Error (Unit) | 0.09 | 0.38 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 854.54 | 970.53 | 2665.87 | 2607.19 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 15.99 | 12.58 | 55.56 | 57.65 |
| Standard Deviation (Unit) | 1.62 | 1.9 | 0.33 | 0.22 |
| Standard Error (Unit) | 0.06 | 0.07 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 809.26 | 636.3 | 2810.94 | 2916.88 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 12.9 | 14.1 | 52.2 | 164 |
| Standard Deviation (Unit) | 1.9 | 3.18 | 0.28 | 7.88 |
| Standard Error (Unit) | 0.07 | 0.11 | 0.01 | 0.28 |
| Area under curve (Unit*sec.) | 644.7 | 704.93 | 2608.34 | 8197.44 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.6 | 16.22 | 51.1 | 43.19 |
| Standard Deviation (Unit) | 4 | 7.43 | 0.36 | 0.47 |
| Standard Error (Unit) | 0.14 | 0.26 | 0.01 | 0.02 |

| | | | | |
|------------------------------|--------|--------|---------|---------|
| Area under curve (Unit*sec.) | 674.31 | 804.35 | 2534.63 | 2142.27 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.69 | 14.34 | 51.85 | 44.83 |
| Standard Deviation (Unit) | 2.96 | 4.03 | 0.12 | 0.22 |
| Standard Error (Unit) | 0.1 | 0.14 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 684.38 | 716.98 | 2591.1 | 2240.1 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 12.48 | 15.28 | 51.48 | 44.11 |
| Standard Deviation (Unit) | 1.86 | 5.77 | 0.36 | 0.51 |
| Standard Error (Unit) | 0.07 | 0.2 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 622.25 | 761.74 | 2565.95 | 2198.53 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.56 | 16.21 | 52.09 | 41.92 |
| Standard Deviation (Unit) | 3.79 | 5.05 | 0.15 | 0.26 |
| Standard Error (Unit) | 0.13 | 0.18 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 681.12 | 814.34 | 2615.75 | 2105.18 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.9 | 15.36 | 54.05 | 107.15 |
| Standard Deviation (Unit) | 2.87 | 5.2 | 0.23 | 8.2 |
| Standard Error (Unit) | 0.1 | 0.18 | 0.01 | 0.29 |
| Area under curve (Unit*sec.) | 692.65 | 765.29 | 2692.18 | 5337.14 |

| Patient ID:109 | placebo - HoloFiber | | | |
|------------------------------|------------------------|------------|-----------|------------|
| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| Mean value (Unit) | 12.37 | 17.97 | 69.93 | 22.66 |
| Standard Deviation (Unit) | 1.33 | 3.93 | 0.33 | 1.09 |
| Standard Error (Unit) | 0.05 | 0.14 | 0.01 | 0.04 |
| Area under curve (Unit*sec.) | 627.48 | 910.86 | 3546.44 | 1149.41 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 10.94 | 16.36 | 80.45 | 39.43 |
| Standard Deviation (Unit) | 1.31 | 4.65 | 0.42 | 0.43 |
| Standard Error (Unit) | 0.05 | 0.16 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 542.22 | 810.41 | 3985.22 | 1953.28 |
| Slope (Unit/sec.) | 0.02 | 0.01 | -0.01 | 0.02 |
| 20 MIN PLACEBO 3 | | | | |
| Mean value (Unit) | 11.01 | 18.53 | 78.56 | 39.61 |
| Standard Deviation (Unit) | 1.2 | 2.43 | 0.51 | 0.74 |
| Standard Error (Unit) | 0.04 | 0.09 | 0.02 | 0.03 |
| Area under curve (Unit*sec.) | 543.17 | 914.79 | 3877.33 | 1954.83 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 11.41 | 20.12 | 78.08 | 39.34 |
| Standard Deviation (Unit) | 1.05 | 2.77 | 0.56 | 0.67 |
| Standard Error (Unit) | 0.04 | 0.1 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 559.43 | 986.78 | 3829.11 | 1929.46 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 11.25 | 18.91 | 86.07 | 45.31 |
| Standard Deviation (Unit) | 1.01 | 3.88 | 0.46 | 0.39 |
| Standard Error (Unit) | 0.03 | 0.1 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 980.23 | 1648.17 | 7501.65 | 3949.1 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 11.31 | 16.76 | 90.1 | 48.17 |
| Standard Deviation (Unit) | 1.19 | 2.06 | 1.21 | 0.53 |
| Standard Error (Unit) | 0.03 | 0.06 | 0.03 | 0.01 |
| Area under curve (Unit*sec.) | 923.86 | 1369.05 | 7361.88 | 3935.63 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 12.13 | 20.15 | 90.4 | 48.59 |
| Standard Deviation (Unit) | 1.21 | 2.28 | 0.63 | 0.44 |
| Standard Error (Unit) | 0.04 | 0.08 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 613.82 | 1019.33 | 4573.49 | 2458.45 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 11.92 | 14.63 | 80.47 | 40.44 |
| Standard Deviation (Unit) | 1.42 | 1.9 | 2.72 | 1.24 |
| Standard Error (Unit) | 0.05 | 0.07 | 0.1 | 0.04 |
| Area under curve (Unit*sec.) | 599.46 | 735.61 | 4046.39 | 2033.34 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 11.88 | 13.37 | 72.12 | 38.02 |
| Standard Deviation (Unit) | 0.95 | 2.01 | 0.58 | 0.57 |
| Standard Error (Unit) | 0.03 | 0.07 | 0.02 | 0.02 |

| | | | | |
|------------------------------|--------|--------|---------|---------|
| Area under curve (Unit*sec.) | 602.5 | 677.87 | 3657.6 | 1928.26 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 11.77 | 16.7 | 76.19 | 42.17 |
| Standard Deviation (Unit) | 1.27 | 2.06 | 0.99 | 1.12 |
| Standard Error (Unit) | 0.04 | 0.07 | 0.03 | 0.04 |
| Area under curve (Unit*sec.) | 592.39 | 841.03 | 3835.59 | 2122.75 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 12.15 | 11.44 | 83.75 | 47.17 |
| Standard Deviation (Unit) | 1 | 0.92 | 0.68 | 0.64 |
| Standard Error (Unit) | 0.04 | 0.03 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 609.21 | 573.86 | 4200.81 | 2365.71 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 12.43 | 18.18 | 76.08 | 44.63 |
| Standard Deviation (Unit) | 1.38 | 1.67 | 0.36 | 0.25 |
| Standard Error (Unit) | 0.05 | 0.06 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 614.44 | 898.5 | 3759.35 | 2205.23 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 11.87 | 13.32 | 88.75 | 53.17 |
| Standard Deviation (Unit) | 1.91 | 1.82 | 1.58 | 0.67 |
| Standard Error (Unit) | 0.07 | 0.06 | 0.06 | 0.02 |
| Area under curve (Unit*sec.) | 592.94 | 665.79 | 4435.1 | 2657.24 |

| Patient ID:110 | Holofiber - placebo | | | |
|------------------------------|---------------------|------------|-----------|------------|
| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| Mean value (Unit) | 6.29 | 12.12 | 64.93 | 52.82 |
| Standard Deviation (Unit) | 0.57 | 1.56 | 0.77 | 0.24 |
| Standard Error (Unit) | 0.02 | 0.05 | 0.03 | 0.01 |
| Maximum value (Unit) | 7.48 | 15.66 | 66.35 | 53.28 |
| Minimum value (Unit) | 5.13 | 8.06 | 63.78 | 52.55 |
| Area under curve (Unit*sec.) | 321.5 | 619.35 | 3317.14 | 2698.66 |
| Slope (Unit/sec.) | 0 | 0.03 | -0.05 | -0.02 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 8.38 | 14.3 | 90.03 | 43.66 |
| Standard Deviation (Unit) | 0.7 | 2.06 | 0.25 | 0.12 |
| Standard Error (Unit) | 0.02 | 0.07 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 428.97 | 732.38 | 4610.73 | 2235.98 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 8.69 | 14.92 | 100.01 | 43.02 |
| Standard Deviation (Unit) | 0.98 | 2.13 | 0.31 | 0.12 |
| Standard Error (Unit) | 0.03 | 0.07 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 440.17 | 755.67 | 5065.99 | 2178.95 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 9.12 | 15.77 | 84.96 | 41.59 |
| Standard Deviation (Unit) | 0.59 | 2.17 | 0.6 | 0.13 |
| Standard Error (Unit) | 0.02 | 0.08 | 0.02 | 0 |
| Area under curve (Unit*sec.) | 466.04 | 805.7 | 4340.29 | 2124.97 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 9.36 | 15.97 | 89.88 | 40.61 |
| Standard Deviation (Unit) | 0.71 | 2.96 | 0.81 | 0.12 |
| Standard Error (Unit) | 0.02 | 0.1 | 0.03 | 0 |
| Area under curve (Unit*sec.) | 471.94 | 805.31 | 4530.55 | 2047.06 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 9.33 | 15.41 | 89.14 | 40.4 |
| Standard Deviation (Unit) | 0.72 | 2.58 | 0.83 | 0.17 |
| Standard Error (Unit) | 0.02 | 0.09 | 0.03 | 0.01 |
| Area under curve (Unit*sec.) | 475.87 | 786.19 | 4548.24 | 2061.61 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 9.45 | 14.8 | 92.8 | 40.26 |
| Standard Deviation (Unit) | 0.53 | 2.42 | 0.26 | 0.03 |
| Standard Error (Unit) | 0.02 | 0.09 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 455.86 | 713.73 | 4476.48 | 1942.11 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 8.16 | 15.96 | 78.26 | 48.44 |
| Standard Deviation (Unit) | 0.72 | 2.4 | 1.72 | 0.74 |
| Standard Error (Unit) | 0.03 | 0.08 | 0.06 | 0.03 |
| Area under curve (Unit*sec.) | 414.14 | 810.73 | 3974.03 | 2459.69 |
| 20 MIN PLACEBO | | | | |

| | | | | |
|------------------------------|--------|---------|---------|---------|
| Mean value (Unit) | 8.49 | 17.29 | 83.83 | 47.58 |
| Standard Deviation (Unit) | 0.85 | 2.65 | 2.09 | 0.88 |
| Standard Error (Unit) | 0.03 | 0.09 | 0.07 | 0.03 |
| Area under curve (Unit*sec.) | 430.46 | 877.06 | 4251.55 | 2412.81 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 8.56 | 18.64 | 83.54 | 46.22 |
| Standard Deviation (Unit) | 0.97 | 3.92 | 0.28 | 0.14 |
| Standard Error (Unit) | 0.03 | 0.14 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 431.51 | 939.79 | 4211.12 | 2329.88 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 8.96 | 17.94 | 79.84 | 42.63 |
| Standard Deviation (Unit) | 0.95 | 2.99 | 0.65 | 0.28 |
| Standard Error (Unit) | 0.03 | 0.1 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 456.31 | 913.03 | 4064.21 | 2169.69 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 9.16 | 20.65 | 83.29 | 44.54 |
| Standard Deviation (Unit) | 1.04 | 4.5 | 0.5 | 0.08 |
| Standard Error (Unit) | 0.04 | 0.16 | 0.02 | 0 |
| Area under curve (Unit*sec.) | 465.88 | 1050.09 | 4234.54 | 2264.57 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 9.99 | 22.16 | 91.47 | 48.61 |
| Standard Deviation (Unit) | 1.57 | 6.96 | 1.86 | 1.09 |
| Standard Error (Unit) | 0.04 | 0.18 | 0.05 | 0.03 |
| Area under curve (Unit*sec.) | 897.12 | 1989.09 | 8211.3 | 4363.73 |

Patient ID:111

Holofiber - placebo

| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 33.49 | 8.71 | 57.58 | 68.57 |
| Standard Deviation (Unit) | 6.41 | 2.61 | 1.93 | 3.38 |
| Standard Error (Unit) | 0.09 | 0.04 | 0.03 | 0.05 |
| Maximum value (Unit) | 71.81 | 42.51 | 61.22 | 77.76 |
| Minimum value (Unit) | 17.27 | 5.07 | 54.87 | 63.23 |
| Area under curve (Unit*sec.) | 10328.53 | 2684.65 | 17756.92 | 21146.53 |
| Slope (Unit/sec.) | 0.01 | 0.01 | 0.02 | 0.03 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 25.68 | 10.68 | 61.46 | 28.98 |
| Standard Deviation (Unit) | 3.14 | 2.6 | 1.09 | 0.41 |
| Standard Error (Unit) | 0.06 | 0.05 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 4869.38 | 2025.36 | 11652.76 | 5495.14 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 30.11 | 10.61 | 59.18 | 28.57 |
| Standard Deviation (Unit) | 4.43 | 2.14 | 2.06 | 1.44 |
| Standard Error (Unit) | 0.09 | 0.04 | 0.04 | 0.03 |
| Area under curve (Unit*sec.) | 5050.32 | 1780.16 | 9925.2 | 4791.03 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 28.25 | 9.94 | 58.3 | 29.19 |
| Standard Deviation (Unit) | 4.34 | 1.65 | 2.66 | 2.33 |
| Standard Error (Unit) | 0.08 | 0.03 | 0.05 | 0.04 |
| Area under curve (Unit*sec.) | 4738.63 | 1666.57 | 9777.08 | 4895.74 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 26.16 | 11.55 | 61.93 | 33.59 |
| Standard Deviation (Unit) | 2.94 | 2.21 | 2.88 | 2.44 |
| Standard Error (Unit) | 0.06 | 0.04 | 0.06 | 0.05 |
| Area under curve (Unit*sec.) | 4195.76 | 1853.45 | 9934.88 | 5389.17 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 31.71 | 12.47 | 60.23 | 32.63 |
| Standard Deviation (Unit) | 2.81 | 2.27 | 0.92 | 0.75 |
| Standard Error (Unit) | 0.06 | 0.05 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 4855.39 | 1909.35 | 9221.95 | 4997.09 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 32.53 | 12.07 | 57.38 | 31.65 |
| Standard Deviation (Unit) | 3.11 | 2.27 | 0.52 | 0.71 |
| Standard Error (Unit) | 0.07 | 0.05 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 4271.81 | 1585.26 | 7534.79 | 4155.52 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.34 | 22 | 50.03 | 31.34 |
| Standard Deviation (Unit) | 2.72 | 4.44 | 0.91 | 0.78 |

| | | | | |
|---------------------------------|---------|---------|----------|---------|
| Standard Error (Unit) | 0.05 | 0.08 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 2629.01 | 4337.03 | 9861.82 | 6176.8 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 15.35 | 18.41 | 50.46 | 31.39 |
| Standard Deviation (Unit) | 4.78 | 3 | 0.62 | 0.64 |
| Standard Error (Unit) | 0.09 | 0.06 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 2689.27 | 3225.25 | 8840.61 | 5499.54 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 14.99 | 15.01 | 51.53 | 32.62 |
| Standard Deviation (Unit) | 1.89 | 2.93 | 0.71 | 0.7 |
| Standard Error (Unit) | 0.03 | 0.05 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 2954.92 | 2958.87 | 10157.22 | 6430.27 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 17.76 | 11.82 | 51.37 | 32.11 |
| Standard Deviation (Unit) | 5.01 | 2.05 | 0.69 | 0.68 |
| Standard Error (Unit) | 0.09 | 0.04 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 3241.05 | 2157.53 | 9375.34 | 5860.34 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 16.83 | 16.81 | 51.45 | 33.53 |
| Standard Deviation (Unit) | 1.75 | 4.54 | 1.03 | 0.7 |
| Standard Error (Unit) | 0.03 | 0.08 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 3808.88 | 3805.03 | 11644.76 | 7589.4 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 17.34 | 16.89 | 47.43 | 32.54 |
| Standard Deviation (Unit) | 1.34 | 2.78 | 0.91 | 0.58 |
| Standard Error (Unit) | 0.02 | 0.05 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 3545.38 | 3452.11 | 9695.11 | 6652.54 |

Patient ID: 112

placebo - Holofiber

| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 16.01 | 40.53 | 57.54 | 61.8 |
| Standard Deviation (Unit) | 2.99 | 13.56 | 0.35 | 0.51 |
| Standard Error (Unit) | 0.11 | 0.48 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 795.15 | 2012.84 | 2857.73 | 3069 |
| Slope (Unit/sec.) | 0.08 | 0.76 | 0.02 | 0.03 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 19.81 | 65.83 | 54.54 | 62.38 |
| Standard Deviation (Unit) | 6.77 | 7.89 | 0.6 | 0.68 |
| Standard Error (Unit) | 0.24 | 0.28 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 992.65 | 3298.75 | 2732.23 | 3125.17 |
| Slope (Unit/sec.) | 0 | -0.03 | -0.04 | -0.05 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 14.44 | 49.46 | 55.21 | 63.29 |
| Standard Deviation (Unit) | 3.32 | 18.21 | 0.07 | 0.09 |
| Standard Error (Unit) | 0.12 | 0.65 | 0 | 0 |
| Area under curve (Unit*sec.) | 712.62 | 2441.15 | 2724.49 | 3123.51 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 11.53 | 39.22 | 57.25 | 64.08 |
| Standard Deviation (Unit) | 0.75 | 6.95 | 0 | 0.04 |
| Standard Error (Unit) | 0.03 | 0.24 | 0 | 0 |
| Area under curve (Unit*sec.) | 577.31 | 1964.84 | 2868.05 | 3210.11 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 14.72 | 36.98 | 56.43 | 62.96 |
| Standard Deviation (Unit) | 3.19 | 4.27 | 0.08 | 0.07 |
| Standard Error (Unit) | 0.11 | 0.15 | 0 | 0 |
| Area under curve (Unit*sec.) | 744.55 | 1871.41 | 2854.91 | 3185.09 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.29 | 16.18 | 56.11 | 62.44 |
| Standard Deviation (Unit) | 2.71 | 9.12 | 0.15 | 0.2 |
| Standard Error (Unit) | 0.1 | 0.32 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 670.14 | 815.61 | 2828.5 | 3147.15 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 14.82 | 24.93 | 57.97 | 62.27 |
| Standard Deviation (Unit) | 4.36 | 2.89 | 0.61 | 0.14 |
| Standard Error (Unit) | 0.15 | 0.1 | 0.02 | 0 |
| Area under curve (Unit*sec.) | 750.88 | 1262.79 | 2936.45 | 3154.07 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.27 | 37.71 | 63 | 67.08 |
| Standard Deviation (Unit) | 2.12 | 5.25 | 0.26 | 0.27 |
| Standard Error (Unit) | 0.07 | 0.19 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 658.29 | 1870.75 | 3125.01 | 3327.29 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 15.16 | 29.61 | 59.56 | 64.89 |
| Standard Deviation (Unit) | 3.71 | 7.88 | 0.04 | 0.13 |

| | | | | |
|------------------------------|--------|---------|---------|---------|
| Standard Error (Unit) | 0.13 | 0.28 | 0 | 0 |
| Area under curve (Unit*sec.) | 759.79 | 1484.62 | 2983.51 | 3250.59 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 15.61 | 24.5 | 60.51 | 65 |
| Standard Deviation (Unit) | 2.6 | 4.56 | 0.75 | 0.51 |
| Standard Error (Unit) | 0.09 | 0.16 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 781.98 | 1227.67 | 3031.34 | 3256.38 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.91 | 28.46 | 60.96 | 65.65 |
| Standard Deviation (Unit) | 3 | 5.51 | 0.19 | 0.19 |
| Standard Error (Unit) | 0.11 | 0.19 | 0.01 | 0.01 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 17.37 | 27.45 | 63.52 | 67.55 |
| Standard Deviation (Unit) | 6.72 | 4.78 | 1.02 | 0.72 |
| Standard Error (Unit) | 0.24 | 0.17 | 0.04 | 0.03 |
| Area under curve (Unit*sec.) | 871.64 | 1377.42 | 3186.25 | 3388.11 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 14.3 | 28.04 | 60.31 | 64.34 |
| Standard Deviation (Unit) | 2.5 | 5.69 | 0.08 | 0.11 |
| Standard Error (Unit) | 0.09 | 0.2 | 0 | 0 |
| Area under curve (Unit*sec.) | 718.24 | 1408.51 | 3029.02 | 3231.07 |

Patient ID: 113

placebo - Holofiber

| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|---------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 11.73 | 37.11 | 44.18 | 53.16 |
| Standard Deviation (Unit) | 0.6 | 14.89 | 0.26 | 0.23 |
| Standard Error (Unit) | 0.02 | 0.6 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 443.53 | 1405.21 | 1670.88 | 2010.66 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.38 | 11.77 | 37.79 | 49.16 |
| Standard Deviation (Unit) | 0.98 | 3.31 | 0.62 | 0.86 |
| Standard Error (Unit) | 0.04 | 0.13 | 0.03 | 0.03 |
| 20M MIN PLACEBO | | | | |
| Mean value (Unit) | 12.79 | 31.57 | 36.21 | 47.2 |
| Standard Deviation (Unit) | 0.76 | 30.34 | 0.29 | 0.1 |
| Standard Error (Unit) | 0.03 | 1.25 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 464.56 | 1147.38 | 1315.59 | 1714.9 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.68 | 10.83 | 42.7 | 49.34 |
| Standard Deviation (Unit) | 1.25 | 4.02 | 0.09 | 0.16 |
| Standard Error (Unit) | 0.05 | 0.16 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 522.46 | 413.97 | 1630.78 | 1884.25 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.56 | 23.89 | 41.05 | 46.79 |
| Standard Deviation (Unit) | 0.94 | 32.39 | 0.4 | 0.5 |
| Standard Error (Unit) | 0.04 | 1.31 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 514.29 | 907.18 | 1557.78 | 1775.61 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.11 | 11.39 | 44.02 | 47.54 |
| Standard Deviation (Unit) | 0.66 | 8.92 | 0.34 | 0.22 |
| Standard Error (Unit) | 0.03 | 0.36 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 502.26 | 436.37 | 1686.68 | 1821.62 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 13.22 | 26.59 | 45.05 | 49.64 |
| Standard Deviation (Unit) | 1.47 | 17.24 | 0.15 | 0.21 |
| Standard Error (Unit) | 0.06 | 0.7 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 502.46 | 1011.3 | 1712.09 | 1886.64 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 15.03 | 15.44 | 42.68 | 44.94 |
| Standard Deviation (Unit) | 1.05 | 5.91 | 0.19 | 0.59 |
| Standard Error (Unit) | 0.04 | 0.24 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 559.9 | 575.51 | 1590.17 | 1674.57 |
| 20 MIN HOLOFIBER | | | | |

| | | | | |
|---------------------------------|--------|---------|---------|---------|
| Mean value (Unit) | 14.3 | 26.8 | 46.36 | 49.38 |
| Standard Deviation (Unit) | 3.32 | 44.74 | 0.09 | 0.59 |
| Standard Error (Unit) | 0.13 | 1.81 | 0 | 0.02 |
| Area under curve (Unit*sec.) | 539.98 | 1010.99 | 1750.52 | 1864.47 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 14.98 | 17.83 | 49.69 | 60.29 |
| Standard Deviation (Unit) | 1.81 | 7.41 | 1 | 0.66 |
| Standard Error (Unit) | 0.07 | 0.3 | 0.04 | 0.03 |
| Area under curve (Unit*sec.) | 565.73 | 673.1 | 1876.23 | 2276.41 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 14.24 | 13.77 | 53.91 | 59.06 |
| Standard Deviation (Unit) | 1.67 | 13.84 | 0.14 | 2.54 |
| Standard Error (Unit) | 0.07 | 0.56 | 0.01 | 0.1 |
| Area under curve (Unit*sec.) | 536.5 | 519.01 | 2032.21 | 2226.07 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 15.09 | 19.44 | 55.61 | 61.52 |
| Standard Deviation (Unit) | 2.35 | 14.84 | 0.29 | 0.18 |
| Standard Error (Unit) | 0.1 | 0.6 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 570.79 | 735.48 | 2103.19 | 2326.66 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 14.49 | 12.54 | 52.19 | 52.64 |
| Standard Deviation (Unit) | 1.29 | 3.37 | 0.44 | 0.6 |
| Standard Error (Unit) | 0.05 | 0.14 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 551.5 | 476.94 | 1986.72 | 2003.69 |

| Patient ID: 114 | Holofiber - placebo | | | |
|------------------------------|---------------------|------------|-----------|------------|
| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| Mean value (Unit) | 16.16 | 29.8 | 53.82 | 26.28 |
| Standard Deviation (Unit) | 1.21 | 5.2 | 0.88 | 0.25 |
| Standard Error (Unit) | 0.05 | 0.22 | 0.04 | 0.01 |
| Area under curve (Unit*sec.) | 569.29 | 1049.13 | 1895.28 | 925.65 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 28.72 | 47.2 | 49.62 | 48.58 |
| Standard Deviation (Unit) | 1.08 | 30.98 | 0.23 | 0.3 |
| Standard Error (Unit) | 0.04 | 1.26 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 1066.78 | 1753.81 | 1842.96 | 1804.27 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 23.56 | 21.1 | 53.96 | 49.08 |
| Standard Deviation (Unit) | 1.88 | 8.68 | 0.38 | 0.23 |
| Standard Error (Unit) | 0.08 | 0.35 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 885.25 | 792.98 | 2027.29 | 1844.15 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 24.46 | 23.72 | 53.66 | 51.29 |
| Standard Deviation (Unit) | 5.94 | 3.84 | 0.21 | 0.12 |
| Standard Error (Unit) | 0.28 | 0.18 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 684.21 | 663.36 | 1500.47 | 1434.21 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 22.82 | 25.35 | 55.94 | 52.34 |
| Standard Deviation (Unit) | 1.23 | 4.94 | 0.12 | 0.12 |
| Standard Error (Unit) | 0.06 | 0.22 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 697.48 | 774.94 | 1709.74 | 1599.74 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 23.18 | 22.17 | 58.83 | 55.01 |
| Standard Deviation (Unit) | 1.78 | 2.96 | 1.58 | 0.46 |
| Standard Error (Unit) | 0.07 | 0.12 | 0.06 | 0.02 |
| Area under curve (Unit*sec.) | 865.23 | 827.2 | 2195.65 | 2053.21 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 23.22 | 34.93 | 61.01 | 59.54 |
| Standard Deviation (Unit) | 1.79 | 36.16 | 0.4 | 0.19 |
| Standard Error (Unit) | 0.07 | 1.47 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 865.21 | 1302.78 | 2273.16 | 2218.5 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 25.53 | 18.31 | 57.44 | 61.32 |
| Standard Deviation (Unit) | 2 | 2.59 | 0.56 | 0.69 |
| Standard Error (Unit) | 0.08 | 0.11 | 0.02 | 0.03 |
| Area under curve (Unit*sec.) | 925.79 | 664.25 | 2083.34 | 2223.99 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 23.72 | 23.8 | 58.36 | 63.01 |
| Standard Deviation (Unit) | 1.47 | 3.55 | 0.06 | 0.13 |
| Standard Error (Unit) | 0.06 | 0.15 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 776.45 | 778.68 | 1910.64 | 2062.73 |

| | | | | |
|------------------------------|---------|--------|---------|---------|
| Slope (Unit/sec.) | 0.04 | 0.04 | 0 | 0.01 |
| 30M MIN PLACEBO | | | | |
| Mean value (Unit) | 23.61 | 22.49 | 59.07 | 61.56 |
| Standard Deviation (Unit) | 1.49 | 4.2 | 0.41 | 0.16 |
| Standard Error (Unit) | 0.06 | 0.18 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 834.35 | 794.72 | 2087.6 | 2175.4 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 27.04 | 22.16 | 64.38 | 65.88 |
| Standard Deviation (Unit) | 2.05 | 3.85 | 0.67 | 0.18 |
| Standard Error (Unit) | 0.08 | 0.16 | 0.03 | 0.01 |
| Area under curve (Unit*sec.) | 1009.22 | 826.95 | 2402.88 | 2459.07 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 26.4 | 25.38 | 61.35 | 62.59 |
| Standard Deviation (Unit) | 1.85 | 6.67 | 0.14 | 0.09 |
| Standard Error (Unit) | 0.08 | 0.28 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 959.01 | 922.03 | 2228.99 | 2273.99 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 28 | 22.28 | 62.41 | 60.32 |
| Standard Deviation (Unit) | 1.61 | 2.87 | 0.58 | 0.11 |
| Standard Error (Unit) | 0.07 | 0.12 | 0.02 | 0 |
| Area under curve (Unit*sec.) | 973.76 | 775.08 | 2170.64 | 2098.21 |

| Patient ID:115 | Holoiber - placebo | | | |
|------------------------------|--------------------|------------|-----------|------------|
| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| Mean value (Unit) | 8.01 | 74 | 59.65 | 61.72 |
| Standard Deviation (Unit) | 1.56 | 7.98 | 0.33 | 0.52 |
| Standard Error (Unit) | 0.07 | 0.34 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 273.12 | 2523.81 | 2034.05 | 2104.71 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 8.98 | 97.65 | 50.25 | 52.22 |
| Standard Deviation (Unit) | 1.26 | 7.4 | 0.17 | 0.13 |
| Standard Error (Unit) | 0.04 | 0.26 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 457.48 | 4976.38 | 2560.96 | 2661.17 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 9.42 | 96.64 | 49.54 | 51.55 |
| Standard Deviation (Unit) | 1.21 | 6.74 | 0.05 | 0.1 |
| Standard Error (Unit) | 0.05 | 0.26 | 0 | 0 |
| Area under curve (Unit*sec.) | 402.27 | 4128.6 | 2116.07 | 2202.22 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.03 | 103.33 | 49.93 | 51.77 |
| Standard Deviation (Unit) | 12.79 | 7.62 | 0.19 | 0.16 |
| Standard Error (Unit) | 0.41 | 0.25 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 774.99 | 6143.45 | 2968.93 | 3078.16 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 12.19 | 104.22 | 52.59 | 54.61 |
| Standard Deviation (Unit) | 2.28 | 10.22 | 0.45 | 0.51 |
| Standard Error (Unit) | 0.07 | 0.31 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 797.03 | 6816.43 | 3439.7 | 3571.91 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.19 | 108.65 | 53.26 | 55.23 |
| Standard Deviation (Unit) | 2.2 | 10.52 | 0.29 | 0.29 |
| Standard Error (Unit) | 0.07 | 0.33 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 836.74 | 6891.66 | 3378.19 | 3503.05 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 14.97 | 107.18 | 55.44 | 58.77 |
| Standard Deviation (Unit) | 3.1 | 10.43 | 0.32 | 0.22 |
| Standard Error (Unit) | 0.09 | 0.32 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 1010.21 | 7234.09 | 3742.32 | 3967.38 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 21.3 | 100.68 | 58.51 | 62 |
| Standard Deviation (Unit) | 4.84 | 33.08 | 0.29 | 0.51 |
| Standard Error (Unit) | 0.15 | 1.05 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 1308.59 | 6185.51 | 3595.11 | 3809.65 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 21.82 | 110.34 | 57.2 | 59.93 |
| Standard Deviation (Unit) | 4.03 | 22.22 | 0.3 | 0.3 |
| Standard Error (Unit) | 0.13 | 0.69 | 0.01 | 0.01 |

| | | | | |
|------------------------------|---------|---------|---------|---------|
| Area under curve (Unit*sec.) | 1383.84 | 6998.02 | 3627.8 | 3801.03 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 24.02 | 119.21 | 57.44 | 59.5 |
| Standard Deviation (Unit) | 4.86 | 29.74 | 0.22 | 0.28 |
| Standard Error (Unit) | 0.16 | 0.96 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 1427.97 | 7087.93 | 3415.21 | 3537.56 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 26.29 | 102.83 | 57.06 | 59.07 |
| Standard Deviation (Unit) | 5.46 | 17.63 | 0.23 | 0.25 |
| Standard Error (Unit) | 0.17 | 0.54 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 1719.79 | 6726.44 | 3732.44 | 3863.84 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 24.5 | 112.79 | 56.39 | 58.63 |
| Standard Deviation (Unit) | 5.63 | 38.24 | 0.25 | 0.41 |
| Standard Error (Unit) | 0.18 | 1.21 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 1506.26 | 6934.67 | 3466.66 | 3604.71 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 25.4 | 94.83 | 58.13 | 60.06 |
| Standard Deviation (Unit) | 5.18 | 23.13 | 0.48 | 0.6 |
| Standard Error (Unit) | 0.15 | 0.68 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 1816.98 | 6780.63 | 4158.57 | 4296.31 |

Patient ID:116

placebo - HoloFiber

| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 7.41 | 8.01 | 87.64 | 3.96 |
| Standard Deviation (Unit) | 6.55 | 0.79 | 0.44 | 0.19 |
| Standard Error (Unit) | 0.16 | 0.02 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 764.23 | 825.69 | 9036.03 | 408.23 |
| GENERAL CALCULATIONS : | | | | |
| AREA 2 | | | | |
| Mean value (Unit) | 6.4 | 27.82 | 83 | 7.83 |
| Standard Deviation (Unit) | 7.08 | 13.25 | 1.09 | 0.21 |
| Standard Error (Unit) | 0.25 | 0.46 | 0.04 | 0.01 |
| Area under curve (Unit*sec.) | 323.81 | 1406.45 | 4193.85 | 395.74 |
| GENERAL CALCULATIONS : | | | | |
| AREA 3 | | | | |
| Mean value (Unit) | 10.5 | 35.26 | 80.84 | 8.39 |
| Standard Deviation (Unit) | 17.81 | 5.49 | 0.4 | 0.38 |
| Standard Error (Unit) | 0.63 | 0.19 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 515.83 | 1731.63 | 3969.49 | 412.08 |
| GENERAL CALCULATIONS : | | | | |
| AREA 4 | | | | |
| Mean value (Unit) | 5.47 | 28.88 | 78.47 | 6.85 |
| Standard Deviation (Unit) | 0.7 | 12.07 | 0.27 | 1.34 |
| Standard Error (Unit) | 0.02 | 0.42 | 0.01 | 0.05 |
| Area under curve (Unit*sec.) | 279.74 | 1476.97 | 4013.99 | 350.46 |
| GENERAL CALCULATIONS : | | | | |
| AREA 5 | | | | |
| Mean value (Unit) | 6.3 | 21.09 | 85.28 | 3.87 |
| Standard Deviation (Unit) | 0.48 | 13.81 | 1.99 | 0.57 |
| Standard Error (Unit) | 0.02 | 0.48 | 0.07 | 0.02 |
| Area under curve (Unit*sec.) | 321.65 | 1077.17 | 4356.58 | 197.95 |
| GENERAL CALCULATIONS : | | | | |
| AREA 6 | | | | |
| Mean value (Unit) | 6.13 | 29.34 | 77.64 | 6.47 |
| Standard Deviation (Unit) | 0.96 | 10.12 | 0.35 | 0.71 |
| Standard Error (Unit) | 0.03 | 0.36 | 0.01 | 0.03 |
| Area under curve (Unit*sec.) | 291.96 | 1397.47 | 3696.87 | 308.07 |
| GENERAL CALCULATIONS : | | | | |
| AREA 7 | | | | |
| Mean value (Unit) | 6.2 | 40.39 | 85.05 | 2.62 |
| Standard Deviation (Unit) | 3.4 | 32.59 | 1.12 | 0.11 |
| Standard Error (Unit) | 0.12 | 1.17 | 0.04 | 0 |
| Area under curve (Unit*sec.) | 296.25 | 1927.41 | 4060.2 | 124.92 |
| Mean value (Unit) | 5.65 | 36.77 | 77.14 | 4.02 |
| Standard Deviation (Unit) | 0.47 | 16.61 | 0.93 | 0.12 |
| Standard Error (Unit) | 0.02 | 0.75 | 0.04 | 0.01 |
| Area under curve (Unit*sec.) | 172.76 | 1123.05 | 2358.01 | 122.96 |
| GENERAL CALCULATIONS : | | | | |
| AREA 9 | | | | |
| Mean value (Unit) | 5.84 | 55.19 | 80.92 | 4.04 |

| | | | | |
|------------------------------|--------|---------|---------|--------|
| Standard Deviation (Unit) | 0.85 | 19.91 | 0.55 | 0.73 |
| Standard Error (Unit) | 0.02 | 0.45 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 695.29 | 6574.94 | 9637.78 | 481.01 |

GENERAL CALCULATIONS : AREA 10

| | | | | |
|------------------------------|--------|---------|---------|--------|
| Mean value (Unit) | 6.23 | 65.39 | 90.3 | 4.12 |
| Standard Deviation (Unit) | 2.01 | 50.18 | 0.41 | 0.45 |
| Standard Error (Unit) | 0.07 | 1.75 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 318.79 | 3345.68 | 4618.86 | 210.69 |

GENERAL CALCULATIONS : AREA 11

| | | | | |
|------------------------------|--------|---------|---------|--------|
| Mean value (Unit) | 6.05 | 40.51 | 93.24 | 3.9 |
| Standard Deviation (Unit) | 0.79 | 17.22 | 0.16 | 0.33 |
| Standard Error (Unit) | 0.03 | 0.61 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 297.11 | 1989.82 | 4578.62 | 191.71 |

GENERAL CALCULATIONS : AREA 12

| | | | | |
|------------------------------|--------|---------|---------|--------|
| Mean value (Unit) | 6.1 | 25.81 | 98.14 | 6.4 |
| Standard Deviation (Unit) | 1.02 | 22.14 | 0.25 | 0.48 |
| Standard Error (Unit) | 0.04 | 0.77 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 311.99 | 1321.22 | 5019.89 | 327.57 |

GENERAL CALCULATIONS : AREA 13

| | | | | |
|------------------------------|--------|---------|---------|--------|
| Mean value (Unit) | 5.98 | 30.97 | 94.84 | 6.38 |
| Standard Deviation (Unit) | 0.95 | 20.91 | 0.48 | 0.24 |
| Standard Error (Unit) | 0.03 | 0.73 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 305.18 | 1580.65 | 4839.29 | 325.37 |

GENERAL CALCULATIONS : AREA 14

| | | | | |
|------------------------------|--------|---------|---------|--------|
| Mean value (Unit) | 6.11 | 33.9 | 92.84 | 4.68 |
| Standard Deviation (Unit) | 0.67 | 11.63 | 1.54 | 0.35 |
| Standard Error (Unit) | 0.02 | 0.4 | 0.05 | 0.01 |
| Area under curve (Unit*sec.) | 312.45 | 1733.61 | 4748.48 | 239.43 |

Patient ID:117

Holofiber - placebo

| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 16.44 | 56.95 | 52.26 | 11.02 |
| Standard Deviation (Unit) | 2.73 | 5.94 | 0.32 | 0.08 |
| Standard Error (Unit) | 0.13 | 0.28 | 0.02 | 0 |
| Area under curve (Unit*sec.) | 449.51 | 1557.22 | 1428.92 | 301.3 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 28.09 | 57.14 | 45.32 | 8.1 |
| Standard Deviation (Unit) | 2.3 | 5.74 | 0.1 | 0.12 |
| Standard Error (Unit) | 0.1 | 0.26 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 879.4 | 1789.04 | 1418.89 | 253.64 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 32.55 | 62.1 | 45.13 | 6.71 |
| Standard Deviation (Unit) | 2.98 | 10.82 | 0.13 | 0.01 |
| Standard Error (Unit) | 0.12 | 0.45 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 1168.61 | 2229.22 | 1620.09 | 241.01 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 31.87 | 63.74 | 44.1 | 7.75 |
| Standard Deviation (Unit) | 2.61 | 6.48 | 0.14 | 0 |
| Standard Error (Unit) | 0.12 | 0.29 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 983.99 | 1968.15 | 1361.57 | 239.33 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 31.84 | 59.1 | 42.44 | 5.46 |
| Standard Deviation (Unit) | 2.28 | 6.92 | 0.06 | 0.16 |
| Standard Error (Unit) | 0.1 | 0.3 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 1026.69 | 1905.51 | 1368.12 | 176.01 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 24.35 | 68.6 | 43.17 | 3.88 |
| Standard Deviation (Unit) | 1.3 | 4.9 | 0.44 | 0.12 |
| Standard Error (Unit) | 0.06 | 0.21 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 795.71 | 2241.93 | 1410.59 | 126.72 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 28.58 | 77.73 | 43.03 | 4.14 |
| Standard Deviation (Unit) | 3.11 | 4.23 | 0.32 | 0.14 |
| Standard Error (Unit) | 0.14 | 0.18 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 934.08 | 2539.68 | 1405.82 | 135.37 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 26.63 | 67.56 | 39.01 | 5.79 |
| Standard Deviation (Unit) | 1.2 | 90.84 | 0.39 | 0.12 |
| Standard Error (Unit) | 0.06 | 4.33 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 726.47 | 1845.6 | 1064.31 | 157.92 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 29.83 | 26.3 | 39.28 | 5.85 |
| Standard Deviation (Unit) | 1.74 | 2.51 | 0.12 | 0.19 |
| Standard Error (Unit) | 0.07 | 0.1 | 0 | 0.01 |
| Area under curve (Unit*sec.) | 1083.71 | 955.64 | 1427.11 | 212.48 |

| | | | | |
|------------------------------|--------|---------|---------|--------|
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 23.12 | 34.13 | 41.55 | 1.77 |
| Standard Deviation (Unit) | 2.09 | 7.75 | 0.5 | 0.11 |
| Standard Error (Unit) | 0.09 | 0.33 | 0.02 | 0 |
| Area under curve (Unit*sec.) | 789.82 | 1165.97 | 1419.51 | 60.42 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 12.47 | 22.62 | 42.59 | 2.24 |
| Standard Deviation (Unit) | 2.26 | 2.81 | 0.32 | 0.1 |
| Standard Error (Unit) | 0.1 | 0.13 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 368.78 | 668.97 | 1259.43 | 66.17 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 11.83 | 22.53 | 44.05 | 2.84 |
| Standard Deviation (Unit) | 5.63 | 2.79 | 0.7 | 0.12 |
| Standard Error (Unit) | 0.23 | 0.11 | 0.03 | 0 |
| Area under curve (Unit*sec.) | 440.22 | 838.4 | 1638.59 | 105.76 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 10.76 | 25.18 | 42.46 | 1.95 |
| Standard Deviation (Unit) | 1.46 | 1.86 | 0.22 | 0 |
| Standard Error (Unit) | 0.06 | 0.08 | 0.01 | 0 |
| Area under curve (Unit*sec.) | 380.94 | 891.19 | 1503.29 | 69.14 |

| Patient ID:118 | placebo - Holofiber | | | |
|------------------------------|---------------------|------------|-----------|------------|
| RECORDING INFORMATION | | | | |
| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| Mean value (Unit) | 15.59 | 41.17 | 31.08 | 49.12 |
| Standard Deviation (Unit) | 1.53 | 6.23 | 1.44 | 1.37 |
| Standard Error (Unit) | 0.03 | 0.14 | 0.03 | 0.03 |
| Area under curve (Unit*sec.) | 1918.73 | 5067.54 | 3825.09 | 6045.28 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 17.21 | 52.38 | 14.69 | 45.45 |
| Standard Deviation (Unit) | 1.45 | 4.66 | 0.96 | 0.47 |
| Standard Error (Unit) | 0.03 | 0.09 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 2596.41 | 7900.42 | 2216.16 | 6855.66 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 16.38 | 48.01 | 11.81 | 47.41 |
| Standard Deviation (Unit) | 1.49 | 10.4 | 0.77 | 0.74 |
| Standard Error (Unit) | 0.03 | 0.19 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 2991.91 | 8767.94 | 2155.54 | 8657.17 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 24.19 | 49.18 | 13.06 | 48.14 |
| Standard Deviation (Unit) | 29.59 | 9.07 | 0.79 | 0.3 |
| Standard Error (Unit) | 0.55 | 0.17 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 4418.24 | 8979.26 | 2384.3 | 8789.47 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 21.59 | 50.58 | 14.66 | 50.69 |
| Standard Deviation (Unit) | 17.23 | 8.07 | 1.27 | 0.38 |
| Standard Error (Unit) | 0.32 | 0.15 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 3941.82 | 9234.92 | 2677.09 | 9255.53 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 22.26 | 48.09 | 14.69 | 51.32 |
| Standard Deviation (Unit) | 9.22 | 11.02 | 1.23 | 0.77 |
| Standard Error (Unit) | 0.17 | 0.21 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 3887.79 | 8400.42 | 2564.92 | 8963.13 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 32.42 | 45.58 | 20.07 | 53.5 |
| Standard Deviation (Unit) | 41.87 | 11.34 | 0.85 | 0.67 |
| Standard Error (Unit) | 0.73 | 0.2 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 6693.43 | 9409.93 | 4142.42 | 11043.63 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 64.13 | 32.45 | 33.81 | 56.45 |
| Standard Deviation (Unit) | 64.22 | 19.46 | 1.25 | 1.88 |
| Standard Error (Unit) | 1.18 | 0.36 | 0.02 | 0.03 |
| Area under curve (Unit*sec.) | 11726.08 | 5933.78 | 6182.08 | 10322.27 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 40.82 | 37.76 | 29.93 | 54.97 |
| Standard Deviation (Unit) | 3.67 | 9.1 | 1.88 | 0.75 |
| Standard Error (Unit) | 0.07 | 0.17 | 0.03 | 0.01 |

| | | | | |
|------------------------------|---------|---------|---------|----------|
| Area under curve (Unit*sec.) | 7464.39 | 6904.57 | 5473.22 | 10050.86 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 37.24 | 40.67 | 30.64 | 57.15 |
| Standard Deviation (Unit) | 3.53 | 9.68 | 1.01 | 0.45 |
| Standard Error (Unit) | 0.06 | 0.17 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 7400.81 | 8084.58 | 6090.49 | 11358.87 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 38.26 | 40.09 | 31.63 | 55.42 |
| Standard Deviation (Unit) | 7.69 | 7.08 | 1.44 | 0.69 |
| Standard Error (Unit) | 0.13 | 0.12 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 7908.95 | 8286.38 | 6537.93 | 11454.59 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 42.18 | 47.87 | 47.79 | 60.48 |
| Standard Deviation (Unit) | 4.38 | 4.97 | 3.93 | 2.58 |
| Standard Error (Unit) | 0.08 | 0.09 | 0.07 | 0.05 |
| Area under curve (Unit*sec.) | 8383.18 | 9514.03 | 9498.73 | 12020.27 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 41.98 | 47.64 | 44.73 | 63.55 |
| Standard Deviation (Unit) | 4.23 | 4.51 | 1.47 | 1.12 |
| Standard Error (Unit) | 0.09 | 0.09 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 6006.76 | 6815.94 | 6400.53 | 9092.94 |

Patient ID:119

placebo - Holofiber

| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
|------------------------------|-----------|------------|-----------|------------|
| Mean value (Unit) | 23.52 | 50.95 | 54.36 | 50.72 |
| Standard Deviation (Unit) | 2.67 | 21.02 | 1.12 | 0.64 |
| Standard Error (Unit) | 0.21 | 1.62 | 0.09 | 0.05 |
| Area under curve (Unit*sec.) | 243.36 | 528.2 | 562.72 | 525.14 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 35.19 | 76.8 | 57.98 | 67.63 |
| Standard Deviation (Unit) | 12.13 | 29.13 | 0.29 | 0.29 |
| Standard Error (Unit) | 0.39 | 0.92 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 2162.32 | 4714.42 | 3562.3 | 4155.21 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 33.85 | 126.84 | 62.51 | 71.14 |
| Standard Deviation (Unit) | 15.21 | 114.56 | 1.14 | 1.61 |
| Standard Error (Unit) | 0.47 | 3.55 | 0.04 | 0.05 |
| Area under curve (Unit*sec.) | 2180.64 | 8174.5 | 4026.65 | 4582.78 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 28.81 | 108.01 | 64.33 | 71.53 |
| Standard Deviation (Unit) | 9.77 | 54.75 | 0.52 | 0.81 |
| Standard Error (Unit) | 0.31 | 1.75 | 0.02 | 0.03 |
| Area under curve (Unit*sec.) | 1740.39 | 6528.88 | 3889.06 | 4323.97 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 23.71 | 81.12 | 66.85 | 72.59 |
| Standard Deviation (Unit) | 6.25 | 22.46 | 0.93 | 0.97 |
| Standard Error (Unit) | 0.2 | 0.71 | 0.03 | 0.03 |
| Area under curve (Unit*sec.) | 1457.23 | 4984.26 | 4107.54 | 4460.26 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 24.28 | 95.78 | 69.06 | 74.7 |
| Standard Deviation (Unit) | 7.34 | 15.73 | 0.26 | 0.24 |
| Standard Error (Unit) | 0.23 | 0.5 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 1467.4 | 5790.62 | 4174.97 | 4515.4 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 22.5 | 94.75 | 71.84 | 77 |
| Standard Deviation (Unit) | 4.97 | 24.66 | 0.72 | 0.72 |
| Standard Error (Unit) | 0.14 | 0.69 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 1784.94 | 7516.97 | 5699.41 | 6108.26 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 33.48 | 61.25 | 67.14 | 71.64 |
| Standard Deviation (Unit) | 11.29 | 18.59 | 0.64 | 0.5 |
| Standard Error (Unit) | 0.29 | 0.47 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 3185.63 | 5829.21 | 6389.25 | 6817.88 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 30.18 | 62.35 | 67.26 | 70.47 |
| Standard Deviation (Unit) | 5.45 | 30.2 | 0.91 | 1.13 |
| Standard Error (Unit) | 0.14 | 0.77 | 0.02 | 0.03 |
| Area under curve (Unit*sec.) | 2872.32 | 5934.04 | 6400.84 | 6706.8 |

| | | | | |
|------------------------------|---------|---------|---------|---------|
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 29.91 | 57.79 | 68.55 | 69.18 |
| Standard Deviation (Unit) | 6.75 | 33.9 | 1.78 | 1.21 |
| Standard Error (Unit) | 0.17 | 0.85 | 0.04 | 0.03 |
| Area under curve (Unit*sec.) | 2965.03 | 5729.62 | 6796.24 | 6858.19 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 28.85 | 53.47 | 68.73 | 71.72 |
| Standard Deviation (Unit) | 5.15 | 18.13 | 0.69 | 0.66 |
| Standard Error (Unit) | 0.13 | 0.46 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 2746.16 | 5088.82 | 6541.54 | 6825.3 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 31.32 | 53.98 | 71.36 | 75.16 |
| Standard Deviation (Unit) | 6.79 | 16.96 | 1.66 | 1.59 |
| Standard Error (Unit) | 0.15 | 0.37 | 0.04 | 0.04 |
| Area under curve (Unit*sec.) | 3974.71 | 6850.74 | 9056.87 | 9539.52 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 31.51 | 68.69 | 70.75 | 75.65 |
| Standard Deviation (Unit) | 5.98 | 50.86 | 1.25 | 1.4 |
| Standard Error (Unit) | 0.16 | 1.36 | 0.03 | 0.04 |
| Area under curve (Unit*sec.) | 2748.83 | 5993.38 | 6171.57 | 6599.18 |

| Patient ID:120 | Holofiber - placebo | | | |
|------------------------------|---------------------|------------|-----------|------------|
| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| Mean value (Unit) | 14.62 | 40.18 | 48.51 | 40.05 |
| Standard Deviation (Unit) | 7.77 | 7.89 | 0.77 | 1.08 |
| Standard Error (Unit) | 0.16 | 0.16 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 2102.7 | 5779.24 | 6977.14 | 5760.26 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 28.53 | 83.34 | 39.28 | 36.6 |
| Standard Deviation (Unit) | 9.34 | 68.95 | 2.18 | 0.93 |
| Standard Error (Unit) | 0.3 | 2.21 | 0.07 | 0.03 |
| Area under curve (Unit*sec.) | 1724.87 | 5038.3 | 2374.32 | 2212.52 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 28.54 | 82.1 | 39.04 | 36.32 |
| Standard Deviation (Unit) | 9.1 | 67.49 | 2.08 | 1.13 |
| Standard Error (Unit) | 0.28 | 2.11 | 0.06 | 0.04 |
| Area under curve (Unit*sec.) | 1815.85 | 5224.97 | 2483.45 | 2310.99 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 27.55 | 83.06 | 38.51 | 36.63 |
| Standard Deviation (Unit) | 9.97 | 19.27 | 0.95 | 0.75 |
| Standard Error (Unit) | 0.18 | 0.35 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 5284.65 | 15934.12 | 7388.58 | 7027.39 |
| 40 MIN HOLOFIBER | | | | |
| Item | 1 PU #1 | 2 PU #2 | 3 pO2 #3 | 4 pO2 #4 |
| Mean value (Unit) | 27.13 | 84.15 | 34.32 | 36.2 |
| Standard Deviation (Unit) | 2.22 | 36.99 | 3.67 | 1.08 |
| Standard Error (Unit) | 0.07 | 1.13 | 0.11 | 0.03 |
| Area under curve (Unit*sec.) | 1801.68 | 5589.37 | 2278.5 | 2403.35 |
| 50 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 27.7 | 65.54 | 42.87 | 40.44 |
| Standard Deviation (Unit) | 2 | 15.21 | 0.86 | 0.5 |
| Standard Error (Unit) | 0.06 | 0.48 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 1729.84 | 4092.9 | 2676.46 | 2524.83 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 24.58 | 60.17 | 47.49 | 41.93 |
| Standard Deviation (Unit) | 2.96 | 13.07 | 1.14 | 0.57 |
| Standard Error (Unit) | 0.09 | 0.42 | 0.04 | 0.02 |
| Area under curve (Unit*sec.) | 1510.02 | 3697.49 | 2918.27 | 2576.28 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 24.48 | 64.62 | 50.15 | 51.08 |
| Standard Deviation (Unit) | 6.45 | 15.49 | 1.36 | 0.54 |
| Standard Error (Unit) | 0.13 | 0.32 | 0.03 | 0.01 |
| Area under curve (Unit*sec.) | 3501.99 | 9244.51 | 7174.09 | 7308.01 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 37.31 | 70.95 | 47.86 | 48.42 |
| Standard Deviation (Unit) | 6.23 | 12.9 | 0.58 | 0.71 |
| Standard Error (Unit) | 0.16 | 0.33 | 0.01 | 0.02 |

| | | | | |
|------------------------------|---------|----------|---------|---------|
| Area under curve (Unit*sec.) | 3557.69 | 6764.93 | 4564.05 | 4617.4 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 28.94 | 71.24 | 50.17 | 51.49 |
| Standard Deviation (Unit) | 3.82 | 13.74 | 0.96 | 0.6 |
| Standard Error (Unit) | 0.12 | 0.44 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 1720.64 | 4236.42 | 2983.25 | 3061.49 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 21.87 | 90.2 | 48.61 | 50.33 |
| Standard Deviation (Unit) | 3.35 | 38.99 | 1.45 | 0.69 |
| Standard Error (Unit) | 0.09 | 0.99 | 0.04 | 0.02 |
| Area under curve (Unit*sec.) | 2085.7 | 8600.74 | 4635.14 | 4799.81 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 22.24 | 106.75 | 45.99 | 49.16 |
| Standard Deviation (Unit) | 16.45 | 56.96 | 1.19 | 0.87 |
| Standard Error (Unit) | 0.39 | 1.34 | 0.03 | 0.02 |
| Area under curve (Unit*sec.) | 2475.36 | 11878.13 | 5116.7 | 5469.06 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 27.65 | 79.06 | 52.92 | 53.02 |
| Standard Deviation (Unit) | 3.82 | 26.67 | 1.56 | 1.19 |
| Standard Error (Unit) | 0.09 | 0.65 | 0.04 | 0.03 |
| Area under curve (Unit*sec.) | 2850.9 | 8150.63 | 5456.89 | 5466.49 |

| Patient ID:121 | placebo - HoloFiber | | | |
|------------------------------|------------------------|---------------|-----------|------------|
| BASELINE | TCOM HAND | LASER HAND | TCOM FOOT | LASER FOOT |
| Mean value (Unit) | 11.2 | 23.97 | 25.16 | 45.37 |
| Standard Deviation (Unit) | 0.62 | 6.12 | 0.46 | 0.6 |
| Standard Error (Unit) | 0.02 | 0.21 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 575.41 | 1231.86 | 1293.08 | 2331.88 |
| 10 MIN PLACEBO | | | | |
| Mean value (Unit) | 14.15 | 43.08 | 8.53 | 43.96 |
| Standard Deviation (Unit) | 1.06 | 10.11 | 0.52 | 0.19 |
| Standard Error (Unit) | 0.04 | 0.35 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 729.86 | 2222.08 | 439.98 | 2267.62 |
| 20 MIN PLACEBO | | | | |
| Mean value (Unit) | 15.19 | 43.84 | 10.26 | 43.44 |
| Standard Deviation (Unit) | 0.88 | 11.52 | 0.37 | 0.2 |
| Standard Error (Unit) | 0.03 | 0.4 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 776.75 | 2242.17 | 524.63 | 2221.79 |
| 30 MIN PLACEBO | | | | |
| Mean value (Unit) | 16.14 | 43.41 | 8.78 | 44.06 |
| Standard Deviation (Unit) | 1.5 | 12.34 | 0.32 | 0.48 |
| Standard Error (Unit) | 0.05 | 0.43 | 0.01 | 0.02 |
| Area under curve (Unit*sec.) | 828.42 | 2228.4 | 450.51 | 2261.66 |
| 40 MIN PLACEBO | | | | |
| Mean value (Unit) | 15.29 | 30.9 | 12.72 | 46.69 |
| Standard Deviation (Unit) | 1.08 | 8.39 | 0.45 | 0.27 |
| Standard Error (Unit) | 0.04 | 0.29 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 782.91 | 1582.83 | 651.3 | 2390.91 |
| 50 MIN PLACEBO | | | | |
| Mean value (Unit) | 14.57 | 36.58 | 13.13 | 45.82 |
| Standard Deviation (Unit) | 0.97 | 8.63 | 0.41 | 0.25 |
| Standard Error (Unit) | 0.03 | 0.3 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 746.08 | 1873.17 | 672.37 | 2346.38 |
| 60 MIN PLACEBO | | | | |
| Mean value (Unit) | 14.54 | 35.88 | 14.19 | 47.4 |
| Standard Deviation (Unit) | 0.89 | 7.21 | 0.44 | 0.24 |
| Standard Error (Unit) | 0.03 | 0.25 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 745.38 | 1840.17 | 727.38 | 2430.56 |
| 10 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 16.17 | 40.79 | 21.14 | 50.58 |
| Standard Deviation (Unit) | 5.23 | 9.34 | 0.19 | 0.38 |
| Standard Error (Unit) | 0.18 | 0.33 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 825.03 | 2080.56 | 1078.75 | 2581.12 |
| 20 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.3 | 39.1 | 25.39 | 56.38 |
| Standard Deviation (Unit) | 2.09 | 8.46 | 0.25 | 0.25 |
| Standard Error (Unit) | 0.07 | 0.29 | 0.01 | 0.01 |

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|------------------------------|--------|---------|---------|---------|
| Area under curve (Unit*sec.) | 680.17 | 2001.13 | 1298.74 | 2884 |
| 30 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.04 | 39.02 | 21.29 | 55.7 |
| Standard Deviation (Unit) | 1.34 | 9.15 | 0.46 | 0.37 |
| Standard Error (Unit) | 0.05 | 0.32 | 0.02 | 0.01 |
| Area under curve (Unit*sec.) | 663.75 | 1986.12 | 1083.94 | 2835.31 |
| 40 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 11.87 | 43.98 | 24.71 | 56.22 |
| Standard Deviation (Unit) | 0.99 | 7.03 | 0.29 | 0.43 |
| Standard Error (Unit) | 0.03 | 0.24 | 0.01 | 0.01 |
| Area under curve (Unit*sec.) | 604.74 | 2241.77 | 1259.2 | 2865.29 |
| 50 MIN HOL | | | | |
| Mean value (Unit) | 11.76 | 47.1 | 26.25 | 58.05 |
| Standard Deviation (Unit) | 0.77 | 6.1 | 0.5 | 0.51 |
| Standard Error (Unit) | 0.03 | 0.21 | 0.02 | 0.02 |
| Area under curve (Unit*sec.) | 604.95 | 2423.57 | 1350.99 | 2987.11 |
| 60 MIN HOLOFIBER | | | | |
| Mean value (Unit) | 13.53 | 36.17 | 26.13 | 60.84 |
| Standard Deviation (Unit) | 2.45 | 10.83 | 0.24 | 0.94 |
| Standard Error (Unit) | 0.09 | 0.39 | 0.01 | 0.03 |
| Area under curve (Unit*sec.) | 631.06 | 1685.51 | 1218.38 | 2836.52 |