A Prospective Single-Site Case-Controlled Study Comparing the Microcirculatory Stress Response in the Diabetic and Non-Diabetic Foot Using Near Infrared Imaging

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Introduction

- Throughout the last decade clinicians and researchers have gained a better understanding of the pathophysiologic processes leading to the impairment of the microcirculation in the diabetic foot.
- More recently, endothelial dysfunction along with derangements in numerous biochemical pathways has been implicated as the primary causes of microcirculation impairment.
- A reduction or absence of the nerve-axon reflex renders the neuropathic diabetic foot leading to the inability of the autonomic nervous system to mount a vasodilatory response under conditions of stress, such as injury or infection thus making the diabetic foot functionally ischemic even in the presence of satisfactory blood flow under normal conditions.
- Furthermore, these changes appear to be directly related to the presence and severity of diabetic neuropathy.
- Alterations in the diabetic microcirculation may precipitate the formation of diabetic foot ulcers and lead to poor wound healing commonly observed in diabetes.
- The purpose of this study was to compare the microcirculatory response seen via Near-infrared spectroscopy (NIRS) to various stresses in 10 patients without diabetes and neuropathy (controls) to 10 patients with diabetes and neuropathy.

Methods

- This was a prospective single-site case-controlled single visit study comparing the microcirculatory stress response in the diabetic and non-diabetic foot using near infrared imaging.
- N=20 with 1:1 diabetic to nondiabetic cohort ratio
- Subjects were >18 and had screening ABIs between 0.8 and 1.3
- All subjects with diabetes must have confirmed DPN based on the Michigan Neuropathy Screening Instrument (MNSI) and the Semmes-Weinstein *Monofilament* test (SWM)
- The right foot of all subjects was exposed to various stresses for a duration of 5 minutes to include heat, cold, elevation, dependency occurring in a controlled clinic environment.
- Baseline NIRS images were obtained from the dorsum and plantar right forefoot of each subject
- Additionally, dorsal and plantar NIRS images were obtained by each subject after the 5-minute duration of each stress had elapsed.

Results

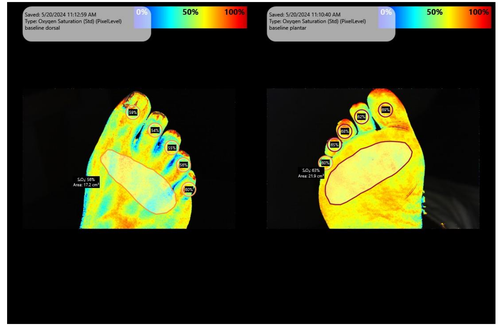

Figure 1: StO_2 images of the dorsal (left image) and plantar (right image) sides of the right foot of a subject as visualized in SnapshotNIR. These heat maps are generated such that blue/cooler regions correspond to lower StO_2 values and red/warmer regions correspond to higher StO_2 values. The values displayed inside the markers on the toes show the mean StO_2 of all the tissues within the marker. For the lasso drawn at the middle of the foot, the mean StO_2 value and area of the lasso are displayed on the black text boxes on the sides.

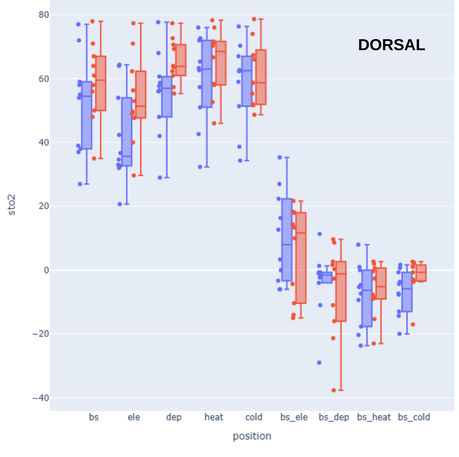

Figure 2: Box plots illustrating the mean StO_2 values measured at dorsal foot under various positions or stress conditions, along with their differences from baseline values. The blue plots (Group 1) represent subjects with diabetic peripheral neuropathy (DPN), while the red plots (Group 2) represent subjects without DPN.

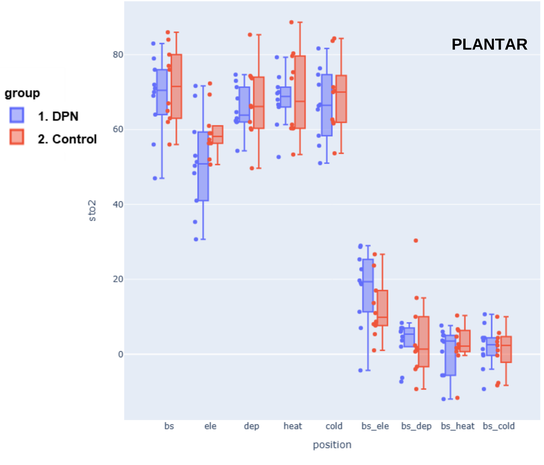

Figure 3: Box plots illustrating the mean StO_2 values measured at plantar foot under various positions or stress conditions, along with their differences from baseline values. The blue plots (Group 1) represent subjects with diabetic peripheral neuropathy (DPN), while the red plots (Group 2) represent subjects without DPN.

DATASET

- Markers were placed on both the dorsal and plantar images taken via SnapshotNIR (Figure 1). The tissue oxygen saturation (StO_2) values from the great toe *(1st)*, 5th toe *(5th)*, and middle of the foot *(mid)* were recorded. A fourth variable *mean* was calculated by averaging the StO_2 values from these 3 sites. Thus, 4 StO_2 values recorded from both dorsal and plantar (2 sides) NIRS images of the right foot of the subject taken at baseline and after 4 different stresses (elevated, dependent, heat, and cold) resulted in 40 (=4x2x5) variables to analyze.
- 4 additional parameters were defined by calculating the difference of the StO_2 values from baseline *(bs)* position to elevated *(ele)*, dependent *(dep)*, post heat treatment *(heat) and* post cold treatment *(cold)* respectively *(depicted as bs_ele, bs_dep, bs_heat* and *bs_cold)* resulting in 32 (=4x2x4) additional variables.

STATISTICAL ANALYSIS

- All variables were analyzed with a multivariate General Linear Model (GLM) to test for statistically significant difference of the values between the DPN subjects against controls.
- The results did not identify any variable to be significantly differentiating between the diabetic and non-diabetic groups.
- However, some trends in the values were found across the 2 groups of patients as shown in Figures 2 and 3.

OBSERVATIONS

- Figure 3 depicts that elevation causes the plantar StO_2 values to drop from the baseline values for subjects belonging to both groups. This effect is not as well clearly observed for the dorsal side in Figure 2.
- Both Figures 2 and 3 depict that there isn't any observable trend in StO_2 values from baseline for other stress factors such as dependent, heat or cold.
- Figure 3 depicts a higher difference of elevated StO_2 values from baseline in subjects with DPN than subjects without DPN.

*NIRS device -SnapshotNIR (Kent Imaging, Calgary, AB, Canada)

Conclusion

- Endothelial dysfunction and autonomic neuropathy are critical factors contributing to microcirculation issues in the diabetic neuropathic foot.
- These factors can lead to functional ischemia, even when blood flow seems adequate under normal circumstances.
- Near-Infrared Spectroscopy (NIRS) has emerged as a validated technology, effectively measuring functional tissue oxygen saturation in diabetic foot ulcer management.
- The trends observed in this pilot study further support the idea that NIRS is not only instrumental in monitoring oxygen levels but also serves as a powerful tool for identifying changes in the microcirculatory system of the diabetic foot.
- The variables used in this study didn't turn out to be statistically significant to differentiate subjects with DPN from healthy subjects due to limited sample size.
- The trends observed in the plots are consistent with previous studies* utilizing NIRS technology in patients with Peripheral Arterial Disease (PAD). It is recommended that this protocol be applied to a larger sample population for further validation.

References

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Special Appreciation for Statistical Analysis
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