Official Title: Quantifying the Venous Congestion Curve of a Tissue Oximetry Device
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Background, Rationale, and Context

Transcutaneous oximetry monitoring, which utilizes near infrared spectroscopy (NIRS) technology, is one of many modalities in existence to monitor the post-operative circulatory status of microvascular skin flap reconstruction[1]. Specifically NIRS devices such as the ViOptix T.Ox Tissue Oximeter (Newark CA.) have the ability to detect vascular compromise in microsurgical flaps prior to gold standard techniques such as serial clinical exam and handheld doppler[2]. The ViOptix T.Ox machine utilizes NIRS to measure the oxygenation of composite tissue. The technology is able to assess the oxygenation of a piece of tissue with chromophore – this reads a percent tissue oxygenation (StO_2).

Success rates of microsurgical procedures has increased in recent years but complications still exist. The most common reason for flap failure is vascular thrombosis, and venous thrombosis occurs three times more often in free flaps than arterial occlusion[3,4]. Additionally the success rate of flap salvage is higher for venous congestive problems when compared to arterial complications[3]. Larger scale studies have also been conducted which demonstrate the use of ViOptix monitoring can improve flap salvage rates and decrease the rate of total flap loss [2,5,6]. Although technique improvements have decreased complications, microvascular complications such as venous congestion still routinely occur post operatively in free flap procedures. Most free flap microvascular complications occur within the

first 48 hours [3]. These complications often result in surgical re-exploration and increased expense to the subject[7].

Close monitoring remains essential to free tissue transfer success, and timing of intervention increases chance of successful salvage if problems arise. Previous studies in the plastic surgery literature have retrospectively analyzed data and determined certain tissue oxygenation patterns may exist in compromised skin flaps[2]. However, these samples of data are in a very limited number of patients. Keller suggests that an absolute drop of StO_2 of 20% in an hour or an absolute StO_2 reading below 30% indicates flap compromise [2]. This criteria may still produce false positives leading to patients returning to the OR without microvascular complication [6].

The body of research on NIRS and non-invasive free flap monitoring has grown significantly in recent years. To our knowledge these studies have not been able to describe an inflection point or a specific pattern which characterizes the venous congestion curve. Identifying these specific patterns will help to establish an evidence-based approach in recognizing specific problems and patterns associated with tissue compromise that can guide physicians to consider earlier flap salvage measures.

Objectives

We hypothesize the rate of decline and pattern seen in tissue oxygenation as quantified by a NIRS device (ViOptiox T.Ox) can be quantified and described by a mathematical model which will allow earlier detection and identification of venous congestion in tissue. The vascular occlusion test has been established as a safe and accurate model to induce various states of vascular insufficiency and occlusion [8–15]. Specifically the vascular occlusion test has been demonstrated to be an accurate model for inducing venous insufficiency on awake and aware patients [14]. This study will aim to analyze the StO_2 data output of the ViOptix in order to establish the earliest signs of tissue failure in various states of vascular compromise.

Methods and Measures

Design:

Subjects will be recruited through convenience sampling. Subjects will be given a study number at the initiation of the study and will not be identified through any identifying information throughout the study.

First, participants included will enter an examination room in the Department of Plastic and Reconstructive Surgery clinic. Subjects will be acclimatized for a minimum of 10 minutes before commencing the study. After 10 minutes of acclimatization, subjects will have their baseline vitals measured and recorded, including heart rate, temperature, blood pressure, height, weight, and BMI. Their blood pressure will be taken once on each arm to determine the baseline blood pressure. The variables to be measured and recorded will be pulse oximetry (SpO_2), transcutaneous oximetry (StO_2), demographic information, and past medical history.

The ViOptix machine has the capability to measure two StO_2 values simultaneously. Two ViOptix sensor probes will be secured to the subject, one over the volar forearm and one on the volar hand. The recording process on the ViOptix machine will begin, and obtain baseline StO_2 levels for 5 minutes. After 5 minutes of baseline measurements the vascular occlusion test will be initiated. A blood pressure cuff will be inflated on one upper extremity in order to occlude venous outflow from the extremity. Venous

flow is reasonable occluded 20mmHg below systolic blood pressure. The cuff will thus not be inflated past the systolic pressure. This blood pressure cuff will be left inflated at a constant pressure for 10-20 minutes or as long as the subject can tolerate. Every 2 minutes a pulse check or doppler exam will be performed at the radial artery to ensure the arterial flow is present. For the duration of the vascular occlusion test the desired variables of SpO_2, StO_2 will be measured and recorded. The ViOptix machine continuously records StO_2 data. Every 2 minutes during the vascular occlusion test SpO_2 will be recorded. The cuff will be deflated and the subject will be free to leave the study room.

Setting:

The study will be conducted in a clinic room of the Department of Plastic and Reconstructive surgery. Subjects will include volunteers who meet inclusion/exclusion criteria and provide written informed consent for application of upper extremity tourniquet and monitoring by near infrared spectroscopy.

Subjects Selection Criteria

To be included in this study it is required that human subject participants are between 18 and 65 years of age and meet the following inclusion/exclusion criteria.

Inclusion Criteria

- Age 18 – 65 volunteers

Exclusion Criteria

- Subjects with a history of major cardiac disease, peripheral vascular disease including (vascular insufficiency), Raynaud syndrome, blood dyscrasias, pain syndromes, neurologic conditions, major upper extremity soft tissue trauma or previous vascular injury,

Sample Size

To ensure the study is adequately powered, we aim to include 40 subjects in the study. We will terminate data collection if 100 subjects undergo data collection process.

The number of subjects recruited has been determined by an a priori sample size calculation using the statistical software G*Power. Alpha will be set at 5% and beta at 20%. The necessary sample size will be determined based on previously collected data regarding the means and standard deviations of the measured variables, transcutaneous oximetry number in experimental and control conditions. Based on a previous pilot study we anticipate a large effect size in our data gathering. Given these previously researched values and effect size an early statistical sample size estimate using G*Power suggests a sample size of 32 subjects achieve statistical significance, however we will plan to enroll up to 40 subjects.

Interventions and Interactions

1. All identifying information will be removed from subject data collection forms
2. Anticipated data collection measures include but are not limited to age, gender, height, weight, BMI, vitals, O2 saturation, TCOM, and past medical history.

The T.Ox™ device has 2 small monitors at the end of fiber optic cables that are placed on the skin of a patient. It is normally used after surgery to be placed on a patient directly on or near their surgical area to remain there for 48 hours post-operatively. For that intended use, The T.Ox™ sensor is packaged as a sterile device and is intended for single-use in a sterile environment. For this study however, the monitors are being placed on the wrists of patients with no surgical interventions. The monitors will remain on for only the length of the study visit (~35min) as opposed to 48 hours after a surgery.

Because this is a non-significant risk study for non-invasive data collection only, we plan to re-use the sterile T.Ox™ sensor on multiple subjects with appropriate cleaning (Sani Cloth AF3 wipe) between uses as with any non-sterile device used on multiple subjects. The device will be allowed to dry for 3 minutes per instructions. This wipe has shown effectiveness against SARS-CoV-2.

Outcome Measures

We will collect de-identified data including age, gender, BMI. WE will collect vital signs prior to initiation of vascular occlusion test. Additionally, we will collect tissue oxygenation values from the ViOptix terminal, and oxygen saturation via pulse oximetry. The main outcome measure will be the change in StO2 over time of vascular occlusion test.

Analytical Plan

We will initially use descriptive statistics to quantify and describe the results. We will aim to analyze the rate of change of tissue oxygenation across time to better define the aggregate rate of change. We will use descriptive statistics to compare subject demographic data.

Human Subjects Protection

There will be no identifying subject information included in data collection. Informed consent will be required prior to enrollment and initiation of the study. Subjects will be provided informed consent and given the option to participate in the study or decline. All data will be de-identified and there will be no way to link data collection to specific subject. Subjects and characteristics will be identified by a generated code for database codification.

Subject Recruitment Methods

Subjects for the study will be recruited via convenience sampling. A minimum of 32 subjects at WFBMC will be recruited for the study. A face to face interaction will occur in the exam room where the potential subject will have the opportunity undergo the informed consent process and decide to participate in the study. If they agree to participate the subject will be enrolled and will proceed with data collection after informed consent is obtained.

Informed Consent

Signed informed consent will be obtained from each subject. Informed consent will be obtained after the study has been fully explained to each subject and all questions and concerns have been properly addressed. The investigators or a member of the study team will obtain informed consent. Informed consent will take place in a private examination area of Plastic and Reconstructive Surgery clinical areas. After signing the ICF, the subject will be given a signed copy.

Confidentiality and Privacy

Confidentiality will be protected by collecting only de-identified information needed to assess study outcomes, thus any information that could directly identify subjects. The de-identified database will be kept in a secure excel file on the Plastic Surgery Drive on the WFBMC network. Identities will not be saved on data collection forms. We will be producing an producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study. The planned data to be collected will not include any of the 18 personal identifiers set forth by HIPAA.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Reporting Unanticipated Problems, Adverse, Events, or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

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