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Near Infrared Spectroscopy and Lower Extremity Acute Compartment Syndrome: A Review of the Literature

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Abstract

Similar to pulse-oximetry, near infrared spectroscopy (NIRS) uses the proportionate differential in reflection and absorption of different wavelengths of light to estimate the proportion of hemoglobin saturated with oxygen approximately 2-3 cm below the sensor. The depth of readings is based on the separation between the light source (s) and the receptor (s); the farther the receptor and source are separated, the deeper the arc of penetration. This technology is currently FDA approved for the noninvasive, continuous monitoring of cerebral and somatic tissue regional perfusion. This makes NIRS an ideal technology to consider when seeking a best means for diagnosing acute compartment syndrome (ACS), which is a condition that is physiologically defined as a regional hypoperfused/ischemic states due to excessive pressure within a muscle compartment.

Introduction

Similar to pulse-oximetry, Near Infrared Spectroscopy (NIRS) uses the proportionate differential in reflection and absorption of different wavelengths of light (Beer-Lambert Law) to estimate the proportion of hemoglobin saturated with oxygen approximately 2-3 cm below the sensor. The depth of readings is based on the separation between the light source (s) and the receptor (s); the farther the receptor and source are separated, the deeper the arc of penetration. With NIRS, light travels in a banana shaped pathway coming out on the same side of the tissue in order to sample deep tissue without the need of traveling straight through an extremity. This effect allows NIRS to be used on a broader array of tissues other than just fingers, toes and ear lobes as in the case of pulse-oximetry. This technology is currently FDA approved for the non-invasive, continuous monitoring of cerebral and somatic tissue regional perfusion. This makes NIRS an ideal technology to consider when seeking a best means for diagnosing Acute Compartment Syndrome (ACS), which is a condition that is physiologically defined as a regional hypoperfused/ischemic state due to excessive pressure within a muscle compartment.

Recent advancements in devices using NIRS technology have made them better suited for use in patients at risk for ACS. Newer devices utilize standardized calibration settings, so timely calibration prior to each use is unnecessary. Smaller, flatter sensors provide easier application and are more maneuverable around dressings and splints. Deeper penetration of light (2-3 cm) permits measurement of oxygen saturation in anatomic locations which were previously much more difficult to isolate. Additionally, by utilizing multiple wavelengths, some NIRS devices have been able to minimize the effects of skin pigment on NIRS values.

Over the past decade, studies using NIRS have consistently supported its use as a diagnostic tool for ACS. While certain clinical factors still require further research, these studies, combined with the recent advancements in NIRS-based monitoring, make NIRS a promising candidate for the next generation of diagnostic tools for ACS.

Discussion

Over the last 20 years ongoing research in both animal models and human participants has reinforced the usefulness of this technology in the trauma setting. The series of support begins with validation of its ability to identify changes in perfusion pressure in the leg [1-5] and then, more specifically, ischemic state in a porcine model [6]. This laid the groundwork for validation in humans [7], superiority over perfusion pressure [8] and establishing normal NIRS values [9]. We have now entered a stage of identifying potential sources of error in the technique and responding with relevant research [10,11].

In 1999, Garr et al. induced compartment syndrome in 9 anesthetized landrace swine to test the hypothesis that NIRS was a superior predictor of neuromuscular dysfunction than intra-compartment pressure [5]. Both hind legs of each pig were monitored using pressure transducers to record intra-compartment pressures and a Hutchinson NIRS probe (Hutchinson, Minnesota) to measure regional oxyhemoglobin saturation (rSO_2). Compartment syndrome was induced via albumin infusion. A nerve stimulator attached to the peroneal nerve caused dorsiflexion of the lower limb, and compartment syndrome was defined as complete loss of twitch. Perfusion Pressure (PP) was calculated as Mean Arterial Pressure (MAP) Minus Intra-Compartmental Pressure (ICP). Loss of dorsiflexion was observed at mean compartment pressures of 43.1 mmHg, mean PP of 13.6 mmHg, and mean rSO_2 of 19.8%. Within 10 minutes of fasciotomy, pressures and rSO_2 values returned to 75% of baseline values. The authors found that rSO_2 values were significantly correlated with both ICP and PP, suggesting that NIRS can correctly identify changes in perfusion

in a leg with compartment syndrome. Incidentally, this study also demonstrates that NIRS may be able to detect the appropriateness of a fasciotomy, as there was a significant increase in rSO_2 following successful fasciotomy in the state of critical hypoperfusion with resultant neuromuscular dysfunction (i.e. ACS).

Arbabi et al. tested the ability of NIRS to differentiate between hypotension/hypoxia and ACS in a follow-up study, using the same compartment syndrome model and NIRS device described previously [6]. Hypotension (MAP at 60% of baseline) was induced in 9 landrace swine for 30 minutes, followed by the addition of hypoxia for 30 minutes, after which compartment syndrome was added by incrementally increasing compartment pressures with albumin infusion until a compartment syndrome ensued (loss of dorsiflexion twitch). Fasciotomies were performed and measurements were repeated.

All conditions (hypotension, hypotension + hypoxemia, hypotension + hypoxemia + compartment syndrome) produced significant decreases in rSO_2 values from baseline; however, mean rSO_2 values during compartment syndrome in hypotensive, hypoxemic animals were significantly lower, compared to values observed during hypotension + hypoxemia without ACS (p<0.0001), as well as hypotension alone (p<0.0001). The authors found that hypotension and hypoxia did result in small decreases in NIRS values; however, ACS was easily differentiated and had a significantly more profound effect on NIRS values. Compared to mean rSO_2 values of the control leg, values of the test leg only differed significantly once compartment syndrome was induced (p=0.0002). This study suggests that NIRS is capable of discriminating between regional ischemic changes caused by compartment syndrome and global changes observed in a severe shock state. Additionally, this study shows the potential value of a control site, which ideally is the contra-lateral like compartment, to differentiate the two conditions in an injured subject. Control leg values when compared in both uninjured and injured subjects have shown high correlation [9,12,13]. Injured extremities typically demonstrate elevated values compared to uninjured contralateral extremities. With the development of ACS, the increase seen in injured extremities is diminished or falls below the control indicating impaired perfusion [9,13].

In a 2000 study, Giannotti et al. used NIRS to monitor 9 trauma patients with a clinical diagnosis of lower extremity ACS, as well as 33 randomly selected trauma patients without evidence of ACS [7]. From the 33 control patients, 9 patients were matched based on injury to the patients with ACS. Among compartment syndrome patients, rSO_2 was measured using a NIRS device (Hutchinson Technology, Hutchinson, MN) pre and post fasciotomy in the affected lower extremity and compared to control readings taken from the deltoid, the contralateral leg, and matched controls. Mean rSO_2 values of affected compartments were significantly lower when compared to both the uninjured contralateral leg (p=0.015) and the matched extremity of control patients (p=0.002). In addition, mean rSO_2 values of the affected compartments before fasciotomy were significantly lower when compared to the same compartment following fasciotomy (p=0.017). This clinical study redemonstrated the previous results that a predictable increase in oxygenation occurs after fasciotomy is performed in patients with ACS.

Although the sample size was small, this study was the first to demonstrate successful use of NIRS in a clinical trauma setting, and it corroborated results observed in previous animal studies. Mean rSO_2 values accurately reflected ischemic changes in ACS patients compared

to controls, as well as reperfusion following fasciotomy. However, as the authors note, the study population consisted wholly of patients with definitive ACS, so further study is needed to investigate the ability of NIRS to detect the early evolution of ACS. Additionally, the study was inconclusive regarding ideal control sites, as values observed in the deltoid and contralateral lower extremity were observed to be variable and were not consistent across all subjects, relative to the limb with ACS.

In 2001, Gentilello and colleagues used a cuff compression model to investigate the relationship between NIRS, ICP, and perfusion pressures (PP) [8]. Using a 21-cm wide blood pressure cuff placed around the leg, a compartment syndrome was simulated in the lower extremity of 15 volunteers. A NIRS sensor (Hutchinson Technology, Hutchinson, MN) was placed over the anterior compartment and cuff pressures were increased until rSO_2 decreased to 60%, at which point rSO_2 was further decreased at 30 minute intervals until reaching 40%, 20% and <10%. rSO_2 was maintained at <10% for 30 minutes before the cuff was released and measures were repeated after a recovery period. ICP was calculated from cuff pressure using a validated formula and PP was calculated as MAP minus ICP. Ischemia was defined using changes in neuromuscular function measured by deep peroneal nerve conduction studies, monofilament sensitivity, and visual analog pain scale.

In regression modeling, the authors observed a significant association between rSO_2 values and PP for all ischemia measures. Moreover, when plotting various cutoff values of rSO_2 and PP using receiver operating characteristic (ROC) curves, rSO_2 demonstrated higher sensitivity for detecting ischemia measures at all cutoff values. These results suggest that NIRS is not only a useful tool for detecting ischemia, but that it may be superior to PP, which provides only an indirect measure of ischemia, and in common use PP is obtained only as a painful spot check, making it difficult and/or painful to evaluate the evolution of this process over time.

In order to interpret data in the setting of ACS, a complete understanding of normal NIRS values in both uninjured and injured patients without ACS is required. Shuler et al. published a study in 2009, which evaluated 26 patients with unilateral tibial fractures that did not progress to ACS and 25 healthy volunteers [9]. rSO_2 values were collected using an INVOS cerebral oximeter (Somanetics, Troy, MI) from the anterior, lateral, deep and superficial posterior compartments of each lower extremity. rSO_2 values obtained from like compartments of alternate legs among uninjured subjects were found to be extremely well correlated. In linear regression modeling, fracture status combined with rSO_2 values from the contralateral limb explained a large proportion of the variance observed among the test limbs (R^2=0.74 to 0.80), suggesting that the contralateral uninjured lower extremity provides a useful internal control against which rSO_2 values of injured extremities can be compared.

Furthermore, a repeated measures model used to evaluate the effect of trauma on NIRS values revealed that rSO_2 values of injured extremities were an estimated 15.4 percentage points higher compared to those of uninjured extremities, supporting the hypothesis of a hyperemic response to injury. The model controlled for rSO_2 of the contralateral limb as well as race, which was found to be a significant covariate with this particular device.

This study provides important insight into NIRS, the pathophysiology of ACS, and the hyperemic response to trauma, which

the authors suggest may play a protective role against the development of ACS. Giannotti et al. observed that, among some ACS patients, rSO_2 values of the affected leg were nearly equal to those of the uninjured contralateral leg [7]. This study suggests that this lack of a hyperemic response may be indicative of an impending compartment syndrome, not a shortcoming of the NIRS device. Shuler et al. also observed significant differences between mean rSO_2 values obtained from black compared to white subjects. The authors surmise that differences in melanin concentration, a chromophore, can explain the lower values seen in more pigmented individuals. However, when using a control within the same subject, such as a contralateral leg, the affects of pigment are removed as pigment levels are similar throughout these sites.

In 2010, a subsequent study was published by Shuler and colleagues, using the same NIRS device as previously mentioned and consisting of 14 patients with clinically diagnosed ACS [13]. rSO_2 and ICP values were collected from each subject. PP was calculated as diastolic blood pressure minus ICP. All rSO_2 values were normalized based on values from the contralateral uninjured side (rSO_2 of the injured leg minus rSO_2 of the contralateral leg).

Compared to the previous study, in which rSO_2 values of injured legs were approximately 14 to 17 percentage points higher, on average, than the contralateral uninjured leg [9], rSO_2 values of legs with ACS were an average of 9 to 16 percentage points lower than the contralateral uninjured leg, indicating a perfusion deficit. The authors also observed significant positive correlations between rSO_2 and PP values.

In 2011, Bariteau et al. reported a study in which 7 patients with clinically diagnosed ACS had rSO_2 (using the InSpectra Tissue Spectrometer [Hutchinson Technology, Hutchinson, MN]) and ICP values collected from each compartment of the affected lower extremity prior to fasciotomy [14]. Mixed linear growth modeling was used to test for associations between rSO_2 and ICP and rSO_2 and PP in the affected lower extremity. In both models, no statistically significant association was observed between rSO_2 and each explanatory variable. A simple linear regression model was also constructed to calculate R^2 values for these associations. The model, which contained all observations from all compartments, yielded an $R^2 = 0.2452$ for the model of $rSO_2 = ICP$ and $R^2 = 0.0233$ for the model of $rSO_2 = PP$.

This study shows that the use of NIRS in ACS is not straight-forward. The negative results from this study may stem from differences between commercially available NIRS devices. The device used in this study is limited in its depth and is commercially available to monitor superficial muscles such as the thenar eminence. Additionally, several design flaws can explain the negative findings. Raw NIRS values were correlated with ICP and PP. Based on the hyperemia associated with trauma, elevated NIRS values would be expected up until approximately 10 mmHg of perfusion pressure. A linear correlation between absolute ICP and NIRS would not be expected. Additionally, no control data was obtained to interpret the raw NIRS values obtained in this study.

A case report published in 2011 outlined the longitudinal use of NIRS in 3 cases of lower extremity ACS [15]. Although NIRS monitoring over time requires study in larger samples prior to being generalized to clinical use, the report provided important insight into NIRS' ability as a monitor for ACS in various situations. First, NIRS successfully differentiated between adequately perfused lateral compartment and poorly perfused deep posterior compartments of an individual with ACS. rSO_2 values reflected hyperperfusion followed by

gradual decreases in perfusion pressure over time within the affected compartment. Furthermore, NIRS was able to detect perfusion deficits in an unresponsive, hypotensive patient, who was unable to provide clinical feedback. In an additional patient, NIRS' response to changes in perfusion due to induction was seen within seconds. In all three patients, NIRS changes were observed well before permanent muscle damage or necrosis occurred. This study demonstrated the potential power of NIRS as a continual, noninvasive monitoring device that detects perfusion changes in real time.

These positive results were also seen in a 2013 porcine-model study correlating NIRS and tibial intra-compartmental perfusion pressure (TIPP) in two groups of landrace swine with induced ACS [16]. Tibial Intra-Compartmental Pressure (TICP) was increased via albumin infusion in both groups, which was recorded alongside blood pressures and percent oxygenation in each leg. One group also received blunt trauma to the monitored site. NIRS was able to accurately reflect decreases in TIPP over time (decreased oxygenation) and increases in TIPP after fasciotomy (rebound in oxygenation) in both groups. These results provide another illustration of the responsiveness of NIRS to changes in perfusion. Additionally, this is the first ACS study to attempt to reproduce the actual trauma setting by traumatizing the porcine leg prior to infusion. NIRS was able to record oxygenation without difficulty in the setting of trauma.

Some criticism has been raised regarding anatomic sensor placement of NIRS sensors, particularly in the deep posterior compartment. In order to provide a useful solution for ACS monitoring, anatomic pad placement must be validated to ensure that rSO_2 values are specific to the intended compartment. This was done for the upper extremity in a 2012 study published in the Journal of Hand Surgery [10]. 63 volunteers were asked to perform exercises to sequentially isolate muscle groups of each compartment of the forearm. Significant decreases in rSO_2 in compartments being activated by exercise were observed, while neighboring compartments showed no clinically relevant changes. These findings suggest that NIRS can provide a sensitive and specific measure of tissue oxygenation for the upper extremity. Similar studies are planned to validate anatomic placement of the lower extremity; however, the ability to accurately differentiate between the smaller structures and spaces in the forearm, bodes well for the capabilities of this technology in the larger compartments of the leg and this has borne out in clinical experience with NIRS in evaluating ACS in legs.

Concerns of have been raised about possible limitations inherent to NIRS. Those limitations include the effects of skin pigmentation, subcutaneous fat and hematomas. Skin pigmentation does affect raw values in some devices, while others can overcome this confounding variable. However, by using an uninjured control site such as the contralateral leg or forearm, which has shown high correlation as well, any pigment affects can be removed. A control of some sort, will likely be needed in all cases to differentiate perfusion changes based on systemic factors (hypotension / hypoxia) and local changes such as ACS.

Subcutaneous fat was thought to be a limiting factor in the severely obese; however, a recent study of 50 patients with traumatic leg injuries found that symptoms commonly associated with these injuries do not affect the mean subcutaneous adipose tissue thickness (ATT) [11]. The distance from skin to fascia was never more than 2.5 cm, regardless of the presence of swelling, edema, or high body mass index. This study showed that while leg circumference increases in the traumatize leg,

this occurs within the compartment and not superficial too it, which is intuitive, since it is the swelling that produces ACS.

Lastly, hematomas can in some instances block the signal of NIRS. Hematomas are so concentrated with hemoglobin that they act as light sinks, absorbing the emitted light; thereby, reducing the amount of light that is reflected back to the sensor to thresholds that are below the specified parameters for the device. While this fact seems to be a limiting factor, it may be a strength. If a signal is lost due to an expanding hematoma, this loss of signal can be a warning for the clinician of an expanding hematoma. Additionally, the inability to read through a hematoma, prevents NIRS from inadvertently monitoring a hematoma instead of the desired muscle and masking a potential developing ACS.

There has been some evidence to also suggest in some settings increase perfusion or blood flow due to trauma can potentially absorb enough light to prevent readings. These challenges in traumatized tissue are currently being examined.

Evidence in the literature up to this point (summarized in Table 1) supports the consideration of NIRS for the diagnosis of ACS in the trauma setting; however, several factors necessitate further study and as a result this technology is not currently ready for wide-spread use. Current understanding indicates that the lack of hyperemia when comparing an injured extremity to an uninjured extremity may indicate a compartment syndrome [15]. Additionally, a change in values over

First Author	Year	Aim/hypothesis	Setting	Study Population	Device Manufacturer	Findings
Garr et al. [5]	1999	NIRS can detect changes in venous oxyhemoglobin levels attributable to compartment syndrome.	Infusion model for ACS	9 landrace swine	Hutchinson Technology, Hutchinson, MN	rSO_2 was significantly inversely correlated with ICP and significantly positively correlated with PP; no significant changes in rSO_2 or ICP observed in control legs
Arbabi et al. [6]	1999	NIRS can differentiate between ischemia due to severe shock and ischemia due to compartment syndrome.	Infusion model for ACS	8 landrace swine	Hutchinson Technology, Hutchinson, MN	Mean rSO_2 during compartment syndrome + shock was significantly lower compared to both hypotension and hypotension + hypoxia, suggesting that NIRS is capable of differentiating between ischemia due to ACS and severe shock.
Giannotti et al. [7]	2000	Describe characteristics NIRS findings in patients with compartment syndrome to better understand the usefulness of NIRS	Trauma center	9 ACS patients + 33 trauma patients without ACS	Hutchinson Technology, Hutchinson, MN	Mean pre-fasciotomy rSO_2 of legs with ACS were significantly lower than both mean rSO_2 in limbs of matched controls and post-fasciotomy measurements
Gentilello et al. [8]	2001	NIRS is more accurate than perfusion pressure at detecting ischemia.	Cuff ischemia model	15 uninjured volunteers	Hutchinson Technology, Hutchinson, MN	rSO_2 and PP were significantly correlated with all ischemia measures; in ROC curves, rSO_2 was a more sensitive measure of ischemia than PP when specificity was the same.
Shuler et al. [9]	2009	Describe the expected alteration of normal tissue oxygenation in the lower leg in the setting of ACS without compartment syndrome and examine the utility of the contralateral leg as a control.	Trauma center	25 tibia fractures without ACS + 26 uninjured volunteers	Somanetics, Troy, MI	rSO_2 values of injured legs were an estimate 15.4 percentage points higher than uninjured legs, indicating a hyperemic response to injury; Together, controlling for fracture status and the contralateral uninjured leg explained an extremely high proportion of variation in rSO_2.
Shuler et al. [13]	2010	Decreased in muscle oxygenation measured with NIRS will be correlated with PP among patients with ACS.	Trauma center	14 ACS patients	Somanetics, Troy, MI	rSO_2 and PP were significantly correlated; mean rSO_2 in legs with ACS were 9 to 16 percentage points lower than the contralateral uninjured leg.
Bariteau et al. [14]	2011	Assess the association between NIRS and compartment pressure in patients with lower extremity compartment syndrome.	Trauma center	7 ACS subjects	Hutchinson Technology, Hutchinson, MN	No significant associations observed between rSO_2 and ICP or rSO_2 and PP. Limited depth of measurement, no control used for NIRS. Hyperemia not accounted for in analysis
Shuler et al. [15]	2011	Describe the longitudinal use of NIRS for monitoring 3 cases of ACS.	Case report	3 ACS subjects	Somanetics, Troy, MI	NIRS differentiated between adequately perfused and poorly perfused compartments within the same leg; NIRS demonstrated real-time changes in perfusion; NIRS detected perfusion deficits in unresponsive, intubated patient.

Jackson et al. [12]	2013	Describe correlation in rSO$_2$ between varying extremity control sites in lower extremity trauma	Trauma Center	44 uninjured volunteers	Somanetics, Troy, MI	Correlations in rSO$_2$ suggest corresponding compartments of the contralateral leg serve as the best control sites for one another; As an upper extremity control, the volar forearm displayed the highest correlation
Cathcart et al. [16]	2013	Correlate NIRS and TIPP in ACS	Infusion model for ACS	31 Landrace swine	Nonin, Plymouth, MN	NIRS accurately detected increases in TICP and decreases in TIPP in both the blunt trauma+infusion and infusion only models

Abbreviations: NIRS: Near Infrared Spectroscopy; ACS: Acute Compartment Syndrome; ICP: Intracompartmental Pressure; PP: Perfusion Pressure; ROC: Receiver Operating Characteristics; TIPP: Tibial Intra-Compartmental Perfusion Pressure; TICP: Tibial Intracompartmental Pressure

Table 1: Summary of current literature on near infrared spectroscopy and lower extremity acute compartment syndrome.

time of roughly 10 percentage points indicates a significant change in perfusion. Still, this change needs to be examined in conjunction with a control sensor to determine if this change is a systemic versus local change in perfusion.

Large-scale longitudinal observational studies are currently underway to better delineate clinical guidelines for the use of NIRS in the setting of ACS. A fully validated diagnostic device that could accurately detect ACS could lead to a dramatic reduction in the number of unneeded/prophylactic fasciotomies, in addition to reducing morbidity due to missed or delayed diagnosis. Additionally, this device could reduce the burden on medical staff who are monitoring trauma patients for a condition that could develop over a course of hours or even days. NIRS has the potential to offer a continual, noninvasive monitoring system in real time that more accurately estimates tissue perfusion than intracompartmental pressures which do not account for other factors such as hemoglobin concentration, cardiac output, vasospasm and cellular metabolism which can all play a part in tissue perfusion and ischemia.

Conclusions

The evidence to date shows that the physiological principles behind NIRS are sound and can be feasibly applied, but on-going work is needed to validate a specific technology for this task. Additionally, the parameters with which to interpret the data need to be validated. The tremendous potential NIRS portends as a non-painful, non-invasive continuous measure of the parameter that matters most in ACS (perfusion), means that we must devote the further research needed to vet and translate this technology into common use.

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