Simultaneous *in-situ* NIRS of liver and bowel during septic shock

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**Abstract.** We wished to use near infrared spectroscopy (NIRS) to evaluate changes in blood perfusion in the liver and small bowel. However, conventional clinical NIRS probes use adhesive light shielding appliqués that fail in direct contact with the wetness and softness of the liver and small bowel surfaces. We describe our development and testing of customized NIRS probe holders.

**Methods:** Studies were conducted in 11 juvenile (9–17 kg) anesthetized Yorkshire piglets, with intact liver and bowel exposed during experimental septic shock induced by infusion of Escherichia coli. Internally, the emitter and detector of one NIRO-300 channel were sheathed, directed towards each other, and affixed to the opposite arms of a long-jawed ratchet clamp applied directly to the liver. The emitter and detector of the NIRO-300’s second channel were applied, facing each other, on opposite inner surfaces of a semicircular, semi-rigid, reinforced rubber tube through which a loop of the small bowel was drawn. Externally, optodes from a NIRO-500 were applied to the skin over the liver. NIRS data were collected at 1second intervals for 180 minutes. **Results:** A wide range of optical neutral density filters was required to attenuate the emissions because of the diversity of tissue density between subjects. There were no complications with the liver clamp, and the initial tendency for the bowel to slip from the NIRS holder was solved by securing it with surgical ribbon. **Conclusion:** Since the NIRO-300 control algorithm did not halt monitoring; the NIRO-300 data correlated with the NIRO-500 data ($r^2 = 0.292$ to 0.659) and both were correlated with the mean arterial blood pressure (range: $r^2 = 0.309$ to 0.918, $p < 0.05$ for $r^2 > 0.105$), our modifications were deemed successful.

1. **Introduction**

Septic shock occurs when an overwhelming infection leads to low blood pressure and low blood flow. Vital organs, such as the brain, heart, kidneys, and liver may be injured or may fail. In children, monitoring the progress of treatment is indirect, being based on organ function such as mental status and urine output, and by global parameters such as lactate level and blood pH. Previous near infrared spectrophotometry (NIRS) studies of septic muscle and brain tissues indicated the usefulness of NIRS in evaluating tissue oxygenation status [1,2]. We hypothesized that NIRS would also be useful in evaluating blood perfusion in the liver and small bowel.

Conventional clinical NIRS devices sample transcutaneously via adhesive light shield appliqués that serve to hold the emitter/detector arrays in place, but these are inappropriate for direct contact *in situ* sampling because of the wetness and softness of the liver and small bowel surfaces. Also, these soft
organs tend to change shape for physiologic reasons, and during changes in body position. A rigid means of holding the NIRS probes in place around the organs was required, and since no commercially available product existed, we designed our own probe holders intended for our specific NIRS septic shock experiment. The device solution we developed may be useful for other NIRS applications.

In the clinical setting, NIRS devices are intended for cerebral monitoring and monitor absolute change in the concentrations of oxygenated hemoglobin (HbO₂), and de-oxygenated hemoglobin (Hb) present in the tissue [3]. Such devices have a standard emitter/detector separation to ensure quality control of signal penetration and facilitate ease of use. This standard separation is inappropriate for either the liver or bowel, and if applied, the NIRS manufacturer’s control algorithms report a tissue density error preventing further operations. To avoid this error, signal attenuation is needed. To enable our experimental protocol to include NIRS monitoring of liver and small bowel (separately), we investigated novel solutions for optode attachment using a customized probe holder; the signal attenuation required; and the need for light-shielding.

Our hypothesis was that our technique could be deemed successful if the NIRS device’s control algorithm did not halt data collection, and the NIRS data logically corresponded to that of separate indwelling blood pressure measurement.

2. Methods

Subjects were 11 healthy juvenile (9–17 kg) Yorkshire piglets with septic shock induced by infusion of *Escherichia coli* LPS O55:B5 (Sigma-Aldrich Inc., USA). The experimental protocol was approved by the Animal Care Committee of the University of British Columbia.

Following anesthesia, the liver and small bowel were surgically exposed but left intact. An indwelling catheter was installed to continuously record blood pressure changes.

The fiber-optic emitter and photodiode arrays of a dual channel NIRO-300 (Hamamatsu Photonics KK, Japan) spectrophotometer were sheathed in the cut off tips of common latex surgical gloves (Fig. 1). This was done to prevent the non-waterproof photodiode’s micro circuitry short circuiting when exposed to the abdominal cavity’s electrolytic body fluids.

For use on the liver, the emitter and detector were affixed, facing each other, approximately 25 mm apart, on opposite arms of a long reach, ratcheted, jaw clamp (Fig. 2). The jaw clamp bracketed the right hepatic lobe of the liver (Fig. 3). The clamp was made of light-weight polycarbonate and was sold in small and large versions as a multipurpose utility clamp by a national automotive and home hardware retail store. We tested both versions as well as similar standard surgical stainless steel clamps.

A second emitter and photodiode array of the NIRO-300 were affixed, facing each other, 15 mm apart on opposite inner surfaces of a semicircular 40 mm segment of reinforced rubberized tubing (Fig. 4). A loop of the small bowel was drawn through the semi-tube such that both the standing and returning parts of the loop were enclosed in the semi-tube. The semi-tube was cut from standard automotive hot water hose.

Optical neutral density filters are available from Hamamatsu for its NIRO-300 to attenuate the emitted light when interrogating low tissue densities. Although ungraded, these are supplied as a set of three incremental filters that can be used separately or in combination. We had two such sets available for each channel, 12 filters in total.

For comparison, with the NIRO-300 customized probe holders, the fiber-optic emitter and fiber-optic collector of a photomultiplier tube based NIRO-500 (Hamamatsu Photonics KK, Japan) were placed in
Fig. 1. A NIRO-300 photodiode array is shown sheathed in the excised tip of a common thin latex surgical glove. Standard cloth adhesive tape is used to seal the sheath to the interface cable.

Fig. 2. NIRO-300 emitter optode and photodiode array, sheathed and taped in place on a common utility grade light-weight resin ratcheting jaw clamp.
Fig. 3. The same jaw clamp as seen in Fig. 2, applied to the post-experiment excised liver. The placement location and tissue mass are typical of the experiment.

reflection mode, 40 mm apart, transcutaneously on the intact skin over the left lobe of the unexposed portion of liver. Signal attenuators were not required for this device. The NIRO-500 optodes were held in place by the device’s standard rubberized light shield appliqué.

Changes in the concentration of HbO2 and Hb were monitored at 1 second intervals for 180 minutes after the start of the endotoxin infusion.

3. Results

To attenuate the light emission in each animal a different number of optical neutral density filters were required and different attenuation was also required for both liver and bowel. The exact filter value(s) could not be predicted in advance and was arrived at empirically through iteration. The NIRO-300 control algorithm would indicate either insufficient, excessive, or adequate detected light and the filters would be added or subtracted accordingly. A suitable attenuation was always found, but the time required for these iterations did prolong the start of each experiment by approximately 25 minutes.

Light-shielding for the optodes proved unnecessary as we were able to reduce ambient light sufficiently in the operating room for no interference to occur.

The liver clamp designed worked without complication except in a preliminary trial when a short-armed version of the clamp was used. This smaller short armed version eventually slipped from the tapered edge of the liver, whereas when the larger long armed version was used, the clamp was able to reach onto the main flattened body of the liver and did not slip. The standard stainless steel surgical tools
we evaluated proved unsuitable, being too heavy and having a tendency to rotate and deform the liver as
they settled due to gravity.

In early trials, the isolated loop of bowel had a tendency to slip out of the semi-tube jig midway
through a trial. This was resolved by suspending the loop with surgical ribbon tied to the cone mounted
on the outside of the jig.

With the standard transcutaneous placement of the NIRO-500 optodes, no difficulties were encoun-
tered.

Post experiment, the cloth adhesive tape binding the emitters and detectors to the clamp and jig was
easily released by running them under hot tap water.

The NIRO-300 data correlated with the NIRO-500 data ($r^2 = 0.292$ to 0.659) and all but HbO₂ in
the bowel were significant ($p < 0.05$ for $r^2 > 0.3056$). Liver and bowel NIRS data were significantly
correlated with blood pressure (range: $r^2 = 0.309$ to 0.918, $p < 0.05$ for $r^2 > 0.105$). The mean HbO₂
and Hb patterns of change for all subjects are given in Figs 5 and 6 respectively.

4. Discussion

The adaptation of NIRS from its standard cerebral monitoring to novel in situ liver and bowel mon-
itoring was easily accomplished with our customized probe holders. However, achieving the necessary
degree of light attenuation to account for different tissue density was time consuming. The cost of our
Fig. 5. Patterns of change in oxygenated hemoglobin (HbO$_2$) during endotoxicity. “Bowel” and “Liver” measurements are by NIRS in situ. “Skin” is by NIRS of the liver transcutaneously. Each trend line is the mean of 11 trials.

Fig. 6. Pattern of change in de-oxygenated hemoglobin (Hb) collected simultaneously with, and in the same manner, as that of HbO$_2$ given in Fig. 5. Each trend line is the mean of 11 trials.

probe holder solution was negligible. Whereas the time taken to achieve appropriate attenuation was costly in terms of facility use charges, and the time commitment for the surgeon and technologist. In this context, commercial NIRS devices would be improved by incorporating an “optical potentiometer” that automatically samples a continuous gradation of attenuation filter to self-select the correct light detection level.
Our NIRS physiology results of septic shock in swine liver alone, using this technique, are given elsewhere and indicate that there were significant correlations ($p < 0.05$ for $r^2 > 0.11$) between the HbO$_2$ readings and liver oxygen delivery ($r^2 = 0.58$), liver blood flow ($r^2 = 0.73$) and cardiac output ($r^2 = 0.80$) [4]. Similarly, we also show that Hb readings are highly correlated ($p < 0.05$ for $r^2 > 0.11$) with mixed venous lactate ($r^2 = 0.87$) and with hepatic vein lactate ($r^2 = 0.82$) [4]. Others have used NIRS to sample septic shock in humans [5] but using NIRS in the conventional manner [3] to sample the forearm, which is easier to access and less pliable than the liver or bowel. They have shown that NIRS related changes are two times greater in patients suffering septic shock than in healthy subjects [5].

Since our in situ NIRO-300 data collection was significantly correlated with the transcutaneous NIRO-500 data set, and the NIRS data was also significantly correlated with the independent blood pressure measurements, we conclude that the use of our novel probe holder and attenuation solution was successful. Our solution may be of interest to other investigators seeking novel applications of NIRS in the animal model.

References

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