

# Evaluation of tissue oxygen saturation with near-infrared spectroscopy during experimental acute hemorrhagic shock and resuscitation in dogs

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**Objective**—To evaluate tissue oxygen saturation ( $Sto_2$ ) by use of near-infrared spectroscopy in experimental acute hemorrhagic shock and resuscitation in dogs.

**Animals**—14 healthy adult purpose-bred Beagles.

**Procedures**—Dogs were anesthetized with isoflurane via facemask, anesthesia was maintained with propofol and rocuronium bromide, and dogs were mechanically ventilated to maintain normocapnia. Dogs were studied under normovolemia (baseline), hypovolemia with target mean arterial blood pressure < 40 mm Hg achieved and maintained steady for 10 minutes (hypovolemia T1), then 20 minutes later (hypovolemia T2), following resuscitation with shed blood (after transfusion), and after administration of 20 mL of hetastarch/kg (hypervolemia). Conditions were executed sequentially during a single anesthetic episode, allowing stabilization between states (10 minutes). Hemoglobin concentration, mean arterial blood pressure, arterial blood gas concentrations, cardiac index, oxygen delivery indexed to body surface area, and  $Sto_2$  were monitored.

**Results**—From baseline to hypovolemia T1, there was a significant reduction in mean  $\pm$  SD oxygen delivery index ( $619 \pm 257$  mL/min/m<sup>2</sup> to  $205 \pm 76$  mL/min/m<sup>2</sup>) and  $Sto_2$  ( $94 \pm 4.4\%$  to  $78 \pm 12.2\%$ ). Following resuscitation,  $Sto_2$  ( $80 \pm 8.5\%$  vs  $92 \pm 6.45\%$ ) and oxygen delivery index ( $211 \pm 73$  mL/min/m<sup>2</sup> vs  $717 \pm 221$  mL/min/m<sup>2</sup>) significantly increased, returning to baseline values. Hypervolemia had no effect on  $Sto_2$  or oxygen delivery index. A strong correlation ( $r = 0.97$ ) was detected between mean oxygen delivery index and  $Sto_2$  across all time points.

**Conclusions and Clinical Relevance**—Under the conditions of this study, there was a strong correlation between  $Sto_2$  and oxygen delivery, suggesting that  $Sto_2$  may be used to estimate oxygen delivery. (*Am J Vet Res* 2014;75:48–53)

Oxygen is a key component in the oxidative reactions that drive cell metabolism and therefore is essential to survival. For multicellular organisms with physical boundaries that exceed the time-distance constraints of diffusion, circulatory systems have evolved to deliver

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## ABBREVIATIONS

BE	Base excess
$CaO_2$	Arterial oxygen content
CI	Cardiac index
$C\bar{V}O_2$	Mixed venous oxygen concentration
CO	Cardiac output
CVP	Central venous pressure
$Do_2$	Oxygen delivery
$Do_2I$	Oxygen delivery index
$Eo_2$	Oxygen extraction ratio
$PETCO_2$	End-tidal partial pressure of $CO_2$
Hb	Hemoglobin
HR	Heart rate
MAP	Mean arterial blood pressure
NIRS	Near-infrared spectroscopy
PAP	Pulmonary artery pressure
$P\bar{V}O_2$	Mixed venous oxygen partial pressure
$SpO_2$	Oxygen saturation as measured by pulse oximetry
$Sto_2$	Tissue oxygen saturation
SVI	Stroke volume index
SVRI	Systemic vascular resistance index
THI	Tissue hemoglobin index
$\dot{V}O_2$	Oxygen consumption
$\dot{V}O_2I$	Oxygen consumption index

oxygen to tissues remote to the gas exchange surface. Under normal physiologic conditions,  $Do_2$  greatly exceeds the  $\dot{V}O_2$  in these tissues. However, during hypovolemic shock,  $Do_2$  may become sufficiently diminished so that  $\dot{V}O_2$  becomes linearly dependent on  $Do_2$ . As a linear relationship develops between  $\dot{V}O_2$  and  $Do_2$ ,  $Do_2$  becomes inadequate to maintain aerobic metabolism. Timely restoration of  $Do_2$  during hemorrhagic shock is associated with reduced morbidity and mortality rates in patients in hemorrhagic shock following traumatic injury.<sup>1</sup> As a result, hemodynamic monitoring in the intensive care unit has become the cornerstone in the evaluation and treatment of critically ill patients.<sup>2</sup>

Traditional noninvasive methods for indirectly monitoring oxygen delivery have focused on indices of end organ function, such as blood pressure, urine output, and changes in mentation.<sup>3</sup> Although these methods may be effective at identifying states of profound hypoperfusion, occult hypoperfusion may go undetected in some patients, leading to poor clinical outcomes.<sup>4,5</sup> Lactate concentration and base deficit are commonly used in intensive care units to identify hypoperfusion in critically ill and injured patients. However, changes in lactate concentration and base deficit require time to develop and do not reflect instantaneous changes in perfusion status.<sup>6</sup> Additionally, lactate concentration can be falsely increased in patients with insufficient hepatic clearance.<sup>7</sup> Use of the pulmonary artery catheter (ie, the Swan-Ganz catheter) has allowed for continuous monitoring of PAP and right atrial pressure in addition to determination of CO, thereby allowing calculation of  $Do_2$  in critically ill patients. Nevertheless, this technology is highly invasive, associated with a range of complications, cost-prohibitive, and not easily used in an emergency.<sup>8</sup>

Near-infrared spectroscopy has been developed out of a need for a more precise, responsive, minimally invasive method to assess tissue perfusion. Near-infrared spectroscopy exploits the differential absorption properties of deoxygenated and oxygenated Hb to determine the ratio of oxygenated Hb to total Hb in muscle. On the basis of this ratio,  $Sto_2$  is calculated and reported as a percentage. In veterinary and human clinical studies,  $Sto_2$  in muscle has proved to be a good surrogate for global tissue perfusion.<sup>9,10</sup> This is likely attributable to peripheral tissues being the first to develop hypoperfusion as blood is shunted toward the body's core and the last to reperfuse during resuscitation.<sup>11,12</sup>

The purpose of the study reported here was to evaluate  $Sto_2$  by use of NIRS in experimental acute hemorrhagic shock and resuscitation in dogs. We hypothesized that would correlate with whole organism  $Do_2$  during hemorrhagic shock and reperfusion.

## Materials and Methods

**Animals**—Fourteen healthy purpose-bred university-owned adult Beagles were enrolled in the study. Dogs were determined to be healthy on the basis of results of physical examination, CBC, and serum biochemical profile. Food was withheld for 12 hours prior to each experiment, but dogs had unrestricted access to water. Dogs were housed and cared

for according to the Association for Assessment and Accreditation of Laboratory Animal Care adopted guidelines. The Virginia Tech Animal Care and Use Committee approved this study.

**Instrumentation**—Following preoxygenation with 100% oxygen, anesthesia was induced with 5% isoflurane<sup>a</sup> delivered by facemask. An endotracheal tube was placed and connected to a circle breathing system. Dogs were positioned in dorsal recumbency, and anesthesia was maintained with 1.3% to 2% isoflurane in 100% oxygen during the instrumentation period. The cephalic vein and the right dorsal pedal artery were catheterized with 20-gauge 32-mm-long over-the-needle catheters. A 7F 20-cm double lumen catheter<sup>b</sup> was placed in the left jugular vein, and a 5F 8.5-cm hemostatic introducer<sup>c</sup> was placed in the right jugular vein. Dogs were then positioned in left lateral recumbency, and a thermodilution balloon catheter<sup>d</sup> with heparin coating was advanced to the pulmonary artery. Placement was confirmed by observation of the characteristic waveform.

Dogs were instrumented for continuous monitoring of respiratory rate,  $PETCO_2$ , bispectral index, HR, SAP, MAP, diastolic arterial blood pressure, CVP, and PAP.<sup>e</sup> Pressure transducers were calibrated with a calibration device,<sup>f</sup> then placed and zeroed at the level of the sternum. Bispectral index was continuously acquired and displayed by use of a proprietary bispectral index module in the monitor.<sup>e</sup> Stainless steel subdermal needle electrodes with a 3-lead reference montage were connected to a proprietary sensor<sup>g</sup> and arranged as described.<sup>13</sup> Briefly, the primary lead was placed on the midline over the frontal bone at the level of the zygomatic processes, the ground lead was placed rostral to the base of the left ear, and the secondary lead was placed over the temporal bone. Esophageal temperatures were continuously monitored<sup>e</sup> and maintained between 36° and 38°C by use of a forced-air patient warmer.<sup>h</sup> Arterial and mixed venous blood samples were obtained and immediately analyzed<sup>i</sup> for Hb,  $Pao_2$ , pH,  $P\bar{v}O_2$ , BE, and lactate concentration. Cardiac output measurements were obtained in triplicate by thermodilution by use of 3 mL of iced 5% dextrose injected into the proximal port of the Swan-Ganz catheter. Cardiac output was recorded as the mean of 3 measured values with < 10% variation. Pulmonary artery wedge pressure was measured after CO determination with the Swan-Ganz catheter. Cardiac index, SVI, SVRI,  $CaO_2$ ,  $C\bar{v}O_2$ ,  $\dot{V}O_2$ , and  $Eo_2$  were calculated with standard formulas.<sup>14</sup> Tissue oxygen saturation was determined with a  $Sto_2$  monitor.<sup>j</sup> The  $Sto_2$  probe was placed over the sartorius muscle of the left pelvic limb (dependent limb).<sup>j</sup> Prior to placement of the  $Sto_2$  probe, the site was shaved to minimize interference from the hair during signal acquisition. Adequate signal strength was determined by detection of a THI > 5. Tissue Hb index is a measure of Hb in the monitored tissue and an indicator of signal strength. In human patients, a THI > 5 indicates sufficient Hb to obtain an accurate  $Sto_2$  reading. The  $Sto_2$  was continuously monitored at 2-second intervals over 1 minute with the  $Sto_2$  monitor. The  $Sto_2$  recorded was the mean determined over a designated minute with a THI > 5.

**Experimental protocol**—Following instrumentation, anesthesia was transitioned from isoflurane to a constant rate infusion of propofol,<sup>a</sup> as part of an unrelated study, to facilitate mechanical ventilation with a specific ventilator. The constant rate infusion of propofol was adjusted to maintain anesthesia and a bispectral index < 65. Dogs were paralyzed with a loading dose of rocuronium bromide<sup>k</sup> (0.2 mg/kg, IV), followed by a constant rate infusion (0.8 mg/kg/h) to facilitate ventilation. Mechanical ventilation<sup>l</sup> with 100% oxygen was continued to maintain normocapnia (PETCO<sub>2</sub>, 35 to 45 mm Hg). Before proceeding with the experimental protocol, complete washout of isoflurane was confirmed by use of the gas analyzer.<sup>c</sup> Dogs were evaluated at 3 volumetric states: euvoemia, hypovolemia, and hypervolemia. After a 30-minute stabilization period, hypovolemic data were collected (baseline). Following this, a hypovolemic state was induced by removing blood through the double lumen catheter in the left jugular vein, until the MAP stabilized at 40 ± 5 mm Hg. The blood bag collection set, containing a citrate-phosphate-dextrose-adenine solution, was suspended from a hook on the top of a vacuum chamber placed on a scale to measure total blood drawn. In preparation for autotransfusion, blood was stored in an incubator at 37°C. Once the target MAP was achieved, dogs were maintained at a steady hemodynamic plane for a minimum of 10 minutes before data were collected (hypovolemia T1). If MAP increased to greater than the target value, additional blood was removed until the target MAP was restored. Following restoration of the target MAP, the 10-minute equilibration period was restarted prior to data collection. Dogs were maintained in a hypovolemic state for 20 minutes, and data were collected prior to resuscitation with the shed blood (hypovolemia T2). Shed blood was administered over 20 minutes, and data were collected immediately after to confirm restoration of euvoemia (after transfusion). Then hetastarch<sup>a</sup> was administered at 20 mL/kg over 20 minutes to achieve hypervolemia and immediately afterward data were collected (hypervolemia). Dogs were allowed to recover. A dose of buprenorphine<sup>m</sup> (0.02 mg/kg, IV) was administered during recovery. Dogs were monitored after surgery until they were walking without ataxia. If signs of hemorrhage were detected at the catheter sites, the dogs were transferred to the intensive care unit for 12 hours. The following day, a physical examination was performed, and PCV, total solids concentration, and BUN were checked. All dogs survived.

**Statistical analysis**—Main outcomes of interest for this study were StO<sub>2</sub> and Do<sub>2</sub>. Other outcomes included respiratory rate, PETCO<sub>2</sub>, HR, MAP, CVP, PAP, temperature (esophageal probe), Hb concentration, PaO<sub>2</sub>, PaCO<sub>2</sub>, pH, P $\bar{v}$ O<sub>2</sub>, BE, and lactate concentration. Normal probability plots revealed that all outcomes followed a normal distribution. Subsequently, data were summarized as mean ± SD values. Effects of time period (normovolemia [baseline], hypovolemia with target MAP < 40 mm Hg achieved and maintained steady for 10 minutes [hypovolemia T1], then 20 minutes later [hypovolemia T2], following resuscitation with shed blood [after transfusion] and after 20 mL of hetastarch/kg [hypervolemia]) on each outcome were assessed by use of mixed-model ANOVA followed by the Tukey procedure for multiple comparisons. The linear model specified time period as a fixed effect and dog as the random effect. To test the association between Do<sub>2</sub> and StO<sub>2</sub>, dog-level data for Do<sub>2</sub> and StO<sub>2</sub> were initially summarized (by use of a mean value) at each time period before generating the Pearson correlation coefficient. Significance was set at *P* < 0.05. All analyses were performed with statistical software.<sup>n</sup>

## Results

All 14 dogs (7 males and 7 females) used in the study recovered from anesthesia without complications. They were all 2 years of age and older, with a mean ± SD body weight of 10 ± 0.72 kg. Cardiopulmonary values were determined (Tables 1–3).

Mean ± SD duration for complete isoflurane washout was 50 ± 11 minutes. Dosage for the constant rate infusion of propofol ranged from 18 to 42 mg/kg/h. Mean time required to achieve the target MAP during hypovolemia was 26.7 ± 15.3 minutes. Blood volume removed from the dogs ranged from 297 to 519 mL, with a mean of 393.6 ± 62.3 mL. The 10-minute stabilization period had to be repeated in 6 dogs following the removal of additional blood. Following initiation of hypovolemia, there was a significant increase in HR, BE, and Eo<sub>2</sub>, compared with baseline values. These changes were accompanied by a significant decrease in MAP, CVP, CI, SVI, P $\bar{v}$ O<sub>2</sub>, and Cm $\bar{v}$ O<sub>2</sub> (Tables 1–3). From baseline to hypovolemia T1, there was a 67% reduction in Do<sub>2</sub>I (619 ± 257 mL/min/m<sup>2</sup> vs 205 ± 76 mL/min/m<sup>2</sup>; *P* < 0.001) and a 17% reduction in StO<sub>2</sub> (94 ± 4.4% vs 78 ± 12.2%; *P* < 0.001; Figure 1).

Table 1—Mean ± SD values for cardiovascular variables measured in 14 dogs during euvoemia (baseline), after hemorrhage (hypovolemia T1), 20 minutes later (hypovolemia T2), after transfusion, and after hetastarch administration (hypervolemia).

Variable	Baseline	Hypovolemia T1	Hypovolemia T2	After transfusion	Hypervolemia
HR (beats/min)	89 ± 20.29	125 ± 15.79*	131 ± 16.66*	127 ± 9.89*	123 ± 12.21*
MAP (mm Hg)	91 ± 15.02	32 ± 5.11*	41 ± 10.82*	93 ± 16.9†‡	109 ± 15.25*†‡§
CI (L/min/m <sup>2</sup> )	3.79 ± 1.47	1.29 ± 0.35*	1.57 ± 0.49*	4.67 ± 1.34†‡	5.63 ± 1.55*†‡§
SVI (mL/beat/kg)	1.94 ± 0.42	0.46 ± 0.14*	0.56 ± 0.21*	1.71 ± 0.50	2.08 ± 0.48
SVRI (dynes•s•cm <sup>-5</sup> /m <sup>2</sup> )	2,276 ± 582	2,290 ± 682	1,707 ± 323*	1,573 ± 361*	1,561 ± 286*
CVP (mm Hg)	4.69 ± 0.95	0.23 ± 0.95*	1.07 ± 0.95*	10.61 ± 0.95*†‡	11.8 ± 0.95*†‡

\*Significantly (*P* < 0.05) different from baseline. †Significantly (*P* < 0.05) different from hypovolemia T1. ‡Significantly (*P* < 0.05) different from hypovolemia T2. §Significantly (*P* < 0.05) different from after transfusion.

Table 2—Mean  $\pm$  SD arterial and mixed venous blood gas values measured in the same dogs as in Table 1.

Variable	Baseline	Hypovolemia T1	Hypovolemia T2	After transfusion	Hypervolemia
Pao <sub>2</sub> (mm Hg)	475 $\pm$ 39	452 $\pm$ 49	450 $\pm$ 51	482 $\pm$ 36	471 $\pm$ 36
BE (mmol/L)	-2.9 $\pm$ 2.18	-6.6 $\pm$ 2.06*	-8 $\pm$ 2.5*†	-7.3 $\pm$ 1.73*	-5.2 $\pm$ 1.72*††§
P $\bar{v}$ O <sub>2</sub> (mm Hg)	75 $\pm$ 21.42	37 $\pm$ 6.96*	43 $\pm$ 6.78*	84 $\pm$ 15.44††	90 $\pm$ 21.10*††
Hb (g/dL)	11 $\pm$ 0.97	10.74 $\pm$ 1.59	9.08 $\pm$ 1.34*†	10.32 $\pm$ 0.87†	8.16 $\pm$ 1.29*†§
Lactate (mmol/L)	0.77 $\pm$ 0.52	1.06 $\pm$ 0.69	1.24 $\pm$ 0.76*	1.08 $\pm$ 0.56	0.51 $\pm$ 0.30††§

See Table 1 for key.

Table 3—Mean  $\pm$  SD values for cardiopulmonary variables calculated in the same dogs as in Table 1.

Variable	Baseline	Hypovolemia T1	Hypovolemia T2	After transfusion	Hypervolemia
CaO <sub>2</sub> (mL/dL)	16.17 $\pm$ 1.33	15.74 $\pm$ 2.17	13.52 $\pm$ 1.84*	15.23 $\pm$ 1.14†	12.35 $\pm$ 1.69*†§
C $\bar{v}$ O <sub>2</sub> (mL/dL)	13.70 $\pm$ 1.48	8.29 $\pm$ 2.25*	7.83 $\pm$ 1.95*	12.97 $\pm$ 1.29††	10.54 $\pm$ 1.62*††§
VO <sub>2</sub> I (mL/min/m <sup>2</sup> )	89.08 $\pm$ 29.79	94.43 $\pm$ 41.49	84.22 $\pm$ 17.30	104.56 $\pm$ 21.64	98.75 $\pm$ 21.59
Eo <sub>2</sub> (%)	0.15 $\pm$ 0.04	0.47 $\pm$ 0.12*	0.42 $\pm$ 0.10*	0.15 $\pm$ 0.03††	0.15 $\pm$ 0.03††
THI	16 $\pm$ 2.91	14 $\pm$ 2.18*	14 $\pm$ 2.40*	16 $\pm$ 2.34††	15 $\pm$ 2.90††

See Table 1 for key.

Mean  $\pm$  SD duration of the hypovolemic period, from hypovolemia T1 to hypovolemia T2, was 37.8  $\pm$  10.9 minutes. During the hypovolemic period, there was a decrease in BE, SVRI, Hb, and Cao<sub>2</sub> from hypovolemia T1 to T2 (Tables 1–3). There was no significant change in HR, MAP, CI, SVI, P $\bar{v}$ O<sub>2</sub>, lactate concentration, and C $\bar{v}$ O<sub>2</sub>. However, there was a significant increase in lactate concentration at hypovolemia T2, compared with the euvoletic value (Table 2).

Dogs received a transfusion during a mean of 20  $\pm$  11 minutes. Upon completion of autotransfusion of shed blood, MAP, CVP, CI, SVI, P $\bar{v}$ O<sub>2</sub>, Hb, lactate concentration, C $\bar{v}$ O<sub>2</sub>, and Eo<sub>2</sub> returned to euvoletic values (Tables 1–3). Heart rate, BE, and SVRI failed to return to euvoletic values. In comparison to hypovolemia T2 values, Sto<sub>2</sub> (80  $\pm$  8.5% vs 92  $\pm$  6.45%;  $P < 0.001$ ) and Do<sub>2</sub>I (211  $\pm$  73 mL/min/m<sup>2</sup> vs 717  $\pm$  221 mL/min/m<sup>2</sup>;  $P < 0.001$ ) significantly increased, returning to euvoletic values (Figure 1).

Subsequent to the administration of hetastarch and induction of hypervolemia, MAP, CVP, HR, CI, and P $\bar{v}$ O<sub>2</sub> were significantly increased, compared with euvoletic values (Tables 1 and 2). There was a significant decrease in SVRI, Hb, BE, Cao<sub>2</sub>, and C $\bar{v}$ O<sub>2</sub>, compared with euvoletic values. No significant differences were observed with respect to SVI, lactate concentration, Do<sub>2</sub>I, Sto<sub>2</sub>, or the Eo<sub>2</sub>, compared with euvoletic values. Across all time points in the study, there was no significant change in Pao<sub>2</sub> or  $\dot{V}$ O<sub>2</sub>. Comparison of mean Do<sub>2</sub>I and Sto<sub>2</sub> across all time points yielded a strong relationship, with a correlation coefficient of 0.97 ( $P = 0.005$ ).

## Discussion

The present study was performed to evaluate Sto<sub>2</sub> by use of NIRS in experimental acute hemorrhagic shock and resuscitation in dogs. We sought to test the hypothesis that tissue-specific oxygenation as measured by Sto<sub>2</sub> would correlate with whole organism Do<sub>2</sub> during hemorrhagic shock and reperfusion.

Following induction of hemorrhagic shock, there was a significant decrease in Do<sub>2</sub>I and Sto<sub>2</sub>. Although

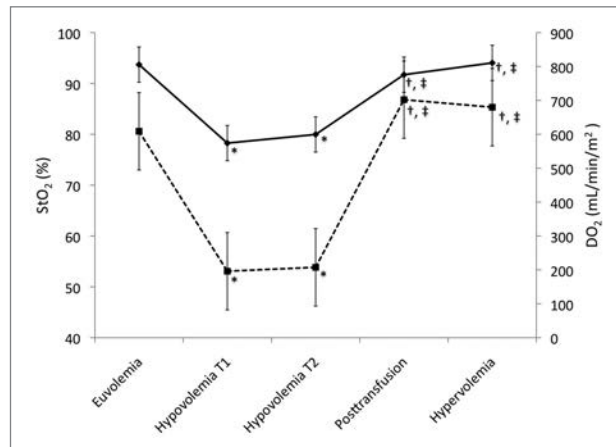


Figure 1—Mean  $\pm$  SD Do<sub>2</sub>I (squares) and Sto<sub>2</sub> (diamonds) values at euvolemia (baseline), after hemorrhage (Hypovolemia T1), 20 minutes later (Hypovolemia T2), after transfusion (posttransfusion), and after hetastarch administration (Hypervolemia) in 14 dogs. \*Significantly ( $P < 0.05$ ) different from baseline. †Significantly ( $P < 0.05$ ) different from hypovolemia T1. ‡Significantly ( $P < 0.05$ ) different from hypovolemia T2. §Significantly ( $P < 0.05$ ) different from hypovolemia T2.

the decrease in Do<sub>2</sub>I was greater than the decrease in Sto<sub>2</sub>, the data revealed a strong correlation between Sto<sub>2</sub> and Do<sub>2</sub>I during the period between baseline and hypovolemia T1. As dogs received the autotransfusion, leading to the restoration of euvolemia, Sto<sub>2</sub> and Do<sub>2</sub>I significantly increased toward baseline values and a strong correlation was again observed between Sto<sub>2</sub> and Do<sub>2</sub>I. These results were similar to those obtained in previous studies in other species. McKinley et al<sup>10</sup> monitored Sto<sub>2</sub> during resuscitation and for the first 24 hours following admission of human patients who had sustained severe abdominal trauma; Sto<sub>2</sub> correlated with changes in Do<sub>2</sub> and was useful in guiding restoration of euvolemia. In a study<sup>15</sup> of the relationship between Do<sub>2</sub> and Sto<sub>2</sub> during experimental acute hemorrhagic shock in splenectomized pigs, a target blood volume of 28% was removed. Similar to the present study, changes in Sto<sub>2</sub> induced by hemorrhage were not as profound as those observed in Do<sub>2</sub> and a strong correlation was evident between changes in Sto<sub>2</sub> and Do<sub>2</sub> during hem-

orrhage and reperfusion. The larger fluctuation in  $Do_2$ , compared with that in  $Sto_2$ , may be attributable to a buffering effect in the  $Do_2$ . There may be a critical point beyond which changes in  $Do_2$  have little effect on  $Sto_2$  and before which changes in  $Do_2$  significantly affect  $Sto_2$ , similar to the oxygen-Hb dissociation curve.

Changes in BE and lactate concentration, the traditional markers of perfusion, lagged behind changes in  $Do_2I$  and  $Sto_2$  following induction of hemorrhagic shock and were slower to return to baseline following fluid resuscitation. This finding was in accordance with clinical and laboratory studies,<sup>6,15</sup> in which changes in  $Sto_2$  precede changes in lactate concentration and base deficit. Following induction of hemorrhagic shock, statistical analysis indicated that the increase in lactate concentration was significant, but the increase was not of sufficient magnitude to be considered clinically important. This can be explained by the fact that  $Eo_2$  was increased in an attempt to maintain aerobic metabolism and the body reserves were not exhausted; therefore, critical  $Do_2$  was not achieved. Additionally,  $\dot{V}o_2$  did not change linearly with  $Do_2$ , as would be expected after an anaerobic threshold is reached. Conversely, the  $Sto_2$  monitor detected changes in regional tissue perfusion before changes in lactate concentration and BE occurred, suggesting that  $Sto_2$  may be a valuable tool in identifying patients in the initial stage of shock before critical changes in cellular metabolism occur.

Presently, the effects of volume overload on NIRS-acquired  $Sto_2$  are unknown. It has been speculated that volume overload may alter the reflectance by creating scatter, leading to falsely decreased measurements of  $Sto_2$ .<sup>16</sup> In the present study, hypervolemia had no effect on  $Sto_2$  or  $Do_2$ . However, the dogs in this study were not subject to extreme fluid overload and time was not allowed for fluid shift to occur. As fluid moves into the interstitial space, altering tissue density, the potential exists to affect the reflectance by creating scatter or decreasing tissue penetration by the near-infrared light. The data obtained in the present study indicated that  $Sto_2$  would not be an effective tool for assessing fluid overload. Additional studies are indicated to determine how fluid overload affects  $Sto_2$  over time.

Tissue hemoglobin index is an indicator of signal strength reported by the  $Sto_2$  monitor and is reported as a number in the range of 1 to 99. The THI corresponds to the amount of Hb present in the monitored tissue. A THI > 5.0 indicates sufficient Hb for the monitor to reliably measure  $Sto_2$  in human patients under most circumstances.<sup>17</sup> The relationship between THI and signal accuracy has not been verified in dogs, and on the basis of clinical experience, we believe THI needs to be > 5.0 to indicate a reliable signal. Tissue hemoglobin indices in this study were all > 5.0. The usefulness of THI is still under investigation, but in the present study, changes in THI were similar to those in  $Do_2$  and  $Sto_2$  across all volemic states. These changes were probably caused by extravascular and vascular Hb concentrations resulting from changes in the volume of the underlying vascular bed, as occur during hemorrhage and reperfusion.

It is important to distinguish the difference between  $Sto_2$  and another commonly used oxygen mea-

surement,  $Spo_2$ . Whereas pulse oximetry, measures oxygen saturation in arterial blood,  $Sto_2$  is a measure of oxygen saturation in the vascular bed of the muscle. The  $Sto_2$  signal is composed of not only the arterial oxygen but also the oxygen in the capillaries and venous network. Unlike  $Spo_2$  which reflects changes in oxygenation,  $Sto_2$  reflects changes in oxygen extraction at the tissue level.<sup>17</sup> Therefore, when local tissue conditions of supply and consumption change,  $Sto_2$  will change but  $Spo_2$  will not. This would be a typical finding in a patient with adequate ventilation but poor oxygen delivery from causes such as poor CO, anemia, or hypovolemia. In the present study, there were no changes in  $Spo_2$  with changes in volemic states (data not shown).

Problems associated with placement of the NIRS  $Sto_2$  probe and signal acquisition have been reported in human patients. Darker skin pigmentation, areas with large amounts of fat deposition, and interstitial edema have all been implicated in poor signal acquisition.<sup>18-20</sup> In humans, the NIRS  $Sto_2$  probe is placed over the deltoid muscle or more commonly the thenar eminence (the group of muscles on the palm at the base of the thumb). Use of these regions yields a reliable measurement of  $Sto_2$  as determined by use of the THI. The decision to place the NIRS  $Sto_2$  probe on the medial aspect of the thigh over the sartorius muscle in the present study was based on previous work by Hall et al.<sup>21</sup> In that study,<sup>21</sup> probe placement was evaluated at 4 areas (lower region of the back, forearm, lateral aspect of the thigh, and medial aspect of the thigh) and it was determined that the medial aspect of the thigh provided the most reliable data. In the present study, the dogs did not have a pigmented area in the thigh and had minimal fat deposition. However, the authors have had difficulty with signal acquisition in the clinical setting in patients with dark hair and pigmented skin, suggesting that melanin may interfere. In the present study, the major challenge was to secure the probe to the skin and still allow good contact. We found that using surgical skin staples around the body of the probe worked well for this purpose.

The present study had several limitations. Blood was removed through an intravascular catheter instead of creating a surgical lesion. Although this methodology allows for standardization among animals, it does not completely reflect the clinical situation and this factor has to be considered when interpreting the results. Furthermore, the study was conducted while dogs received general anesthesia with a fraction of inspired oxygen of 0.95, and resuscitation of trauma patients in the emergency room may occur at lower oxygen concentrations, leading to an inability of  $Do_2$  to meet oxygen demands and therefore a faster onset of a state of shock.

Additionally, these dogs were not splenectomized, which accounted for the variability in the time to achieve target MAP and total blood volume removed. Six of the dogs required removal of additional blood after compensation, which was characterized by tachycardia and an increase in MAP. Despite the variability attributed to the splenic contraction in these dogs, this condition more closely resembled a clinical scenario and allowed for better extrapolation of the data.

Despite NIRS becoming more commonly accepted in human medicine, several obstacles to the use of NIRS for the determination of  $Sto_2$  must be overcome before this technology can gain widespread clinical application in the veterinary field. The technology is cost-prohibitive for the veterinary profession, with the cost of a single-use, disposable NIRS  $Sto_2$  probe at approximately \$200. There is considerable debate on how best to use this technology. Presently, we do not know what specific  $Sto_2$  would warrant interventions and what specific interventions should be performed when  $Sto_2$  is low. However, under the experimental conditions of hemorrhagic shock and resuscitation in the study reported here, there was a strong correlation between  $Sto_2$  and  $Do_2I$ , suggesting that  $Sto_2$  may be used to estimate  $Do_2$ . Additionally, changes in  $Sto_2$  preceded those in BE and lactate concentration, indicating that  $Sto_2$  might be used as an early indicator of hypoperfusion.

- a. Abbott Laboratories, North Chicago, Ill.
- b. MILA International Inc, Erlanger, Ky.
- c. St. Jude Medical Inc, Saint Paul, Minn.
- d. Arrow International Inc, Reading, Pa.
- e. S/5 Anesthesia monitor, GE Healthcare Datex-Ohmeda, Waukesha, Wis.
- f. Delta-Cal, Utah Medical Products Inc, Midvale, Utah.
- g. Pediatric BIS sensor (tree electrode sensor), Aspect Medical Systems Inc, Newton, Mass.
- h. Bair hugger, Arizant Inc, Eden Prairie, Minn.
- i. I-STAT, Abbott Point of Care Inc, East Windsor, NJ.
- j. Hutchinson Technology Inc, Hutchinson, Minn.
- k. APP Pharmaceuticals LLC, Schaumburg, Ill.
- l. Newport Medical, Costa Mesa, Calif.
- m. Reckitt Benckiser Healthcare Ltd, Hull, England.
- n. JMP Pro, version 10, SAS Institute Inc, Cary, NC.

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## Appendix

Equations used in a study of  $Sto_2$  during experimental acute hemorrhagic shock and resuscitation in dogs.

$$BSA \text{ (in m}^2\text{)} = 0.0072 \cdot (\text{height [in cm]})^{0.725} \cdot (\text{weight [in kg]})^{0.425}$$

$$CI = CO/BSA$$

$$SVI = (CO/\text{Body weight})/HR$$

$$SVRI = (\text{Arterial blood pressure} - CVP) \cdot 79.92/CI$$

$$CaO_2 = (1.34 \cdot Hb \cdot Sao_2) + (0.003 \cdot PaO_2)$$

$$C\bar{V}O_2 = (1.34 \cdot Hb \cdot Svo_2) + (0.003 \cdot P\bar{v}O_2)$$

$$Do_2I = CaO_2 \cdot CI \cdot 10 \text{ dL/L}$$

$$\dot{V}O_2I = (CaO_2 - C\bar{m}\bar{v}O_2) \cdot CI \cdot 10 \text{ dL/L}$$

$$Eo_2 = Vo_2 / Do_2$$

BSA = Body surface area. Sao<sub>2</sub> = Arterial oxygen saturation.  
Svo<sub>2</sub> = Venous oxygen saturation.