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# Autonomic Dysreflexia in Spinal Cord Injury: Its Role in Altering Skin Perfusion and Oxygenation

*Jessica Ramella-Roman, Ali Basiri, Joseph Hidler, Inger Ljungberg, and Suzanne L. Groah*

Autonomic dysreflexia (AD) is a condition unique to people with spinal cord injury (SCI) at and cephalic to T6. In these individuals, a noxious stimulus may cause a predominant sympathetic response of the autonomic nervous system characterized by extreme elevations in blood pressure, headache, vision changes, facial flushing, and sweating above the level of injury. In this study, we aimed to describe the tissue changes that occur in skin during an episode of AD. Because of the severe vasoconstriction that occurs with AD, we hypothesized that even minor episodes can lead to other problems, such as tissue ischemia. We describe the development and preliminary testing of a fiber optic-based system, which can be used to quantitatively and noninvasively assess skin changes, including oxygen levels, blood flow, and blood volume fraction, during normal rest and during an AD event. Seven subjects with tetraplegia and a history of AD were assessed. AD was induced by filling the subjects' bladders with saline. Systolic and diastolic blood pressure was monitored, and the subjects provided continual feedback as to AD symptoms. Six of the 7 individuals developed AD. All individuals who developed AD also showed a reduction in blood volume fraction below the level of injury. Five individuals also showed a reduction in superficial skin oxygenation, and 4 demonstrated a reduction in skin perfusion. In this small pilot study on 7 individuals with SCI, we demonstrate that AD is associated with changes in superficial skin hemodynamics. As this fiber optic system is further developed, these preliminary findings could impact preventive recommendations for pressure ulcer prevention in people with SCI. **Key words:** *autonomic dysreflexia, skin oxygenation, skin perfusion*

**A**utonomic dysreflexia (AD) is a potentially life-threatening condition of exaggerated sympathetic output that occurs in patients with spinal cord injury (SCI) at or above the sixth thoracic (T6) neurologic level. AD is triggered by any noxious stimulation that occurs below the level of

injury such as a bladder or bowel distention, an ingrown toenail, or a pressure sore, among others. It is characterized by headache, facial flushing, sweating of the head and neck, mucous membrane congestion, conjunctivitis, blurred vision, and lid retraction above the level of injury. Pallor, pilomotor erection,

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increased spasticity, and penile erection are symptoms that can be observed below the lesion level.<sup>1-4</sup> Elevated blood pressure (BP) is the hallmark of AD and, when severe, can lead to stroke, seizure, or even death.

As the elevated BP characteristic of AD is a medical emergency (an increase in systolic BP above 20 mmHg from rest is a recognized sign of AD), little attention has been focused on other detrimental effects of AD. While the headache, flushing, and sweating in the head and neck region are thought to be direct symptoms of parasympathetically mediated vasodilation,<sup>5</sup> vasoconstriction below the level of injury is sympathetically mediated. During AD, patients experience vasoconstriction below the level of lesion. This results in a reduction of capillary flow and blood volume possibly leading to skin deoxygenation.<sup>6</sup>

During AD episodes, reductions in the amount of circulating blood in the skin below the level of injury<sup>5,6</sup> can be measured with Doppler or plethysmography techniques. Ramella-Roman et al<sup>6</sup> have demonstrated that this vasoconstriction results in a measurable reduction in perfusion of the skin in an individual experiencing AD as a result of bladder stimulation. Similarly, Brown et al<sup>7</sup> measured several metrics related to AD including cutaneous blood flow and arterial pressure following penile vibratory stimulation-induced AD and found cutaneous vasoconstriction below the level of lesion.

Hence, in this study we aim to utilize non-invasive optical instrumentation to assess and quantify the effect of AD on the skin. We hypothesize that tissue oxygenation and blood flow are reduced during episodes of AD and that these reductions can be readily and noninvasively measurable utilizing a fiber optic-based system.

## Material and Methods

### Development of the skin probe

Measurements of skin perfusion and oxygenation in individuals with SCI undergoing AD events were obtained with a system that combined laser Doppler flowmetry (LDF) and reflectance spectroscopy (R). The spectral reflectance measurement was accomplished with a spectrophotometer (Ocean Optics, Dunedin, Florida), and a tungsten halogen lamp (Ocean Optics, Dunedin, Florida), while an LDF (Moor Instruments Ltd., United Kingdom) was used for the perfusion measurement. In the clinical setting, 3 different types of fiber probes were used: LDF factory-made probes (Moor Instruments Ltd, United Kingdom), custom-made reflectance spectroscopy fiber probes, and a custom-made combined spectral and Doppler probe. All devices and the controlling laptop were assembled on a cart for the purpose of maneuverability inside the hospital during the clinical trial (see **Figure 1**).

Two types of fiber optic probes were fabricated for this study. The first probe was made with 2 multimode 0.6 mm fibers (0.39 NA; Thorlabs, Newton, New Jersey), one source and one detector, 200 mm long with a Sub-Miniature version A adapter (SMA-905) at one side for connection to a spectrophotometer. An aluminum-coated 1 mm right-angle prism (Tower Optical Corporation, Boynton Beach, Florida) was attached to the polished side of each fiber using an ultraviolet (UV) curing index-matched adhesive (Norland Products Inc, Cranbury, New Jersey). The fibers and prisms were then positioned inside a machined Delrin disk (2 mm thick, 25 mm diameter). This geometry allowed a redirection of light to 90° from the fiber axis. The fibers' distance center to center was 2.5 mm



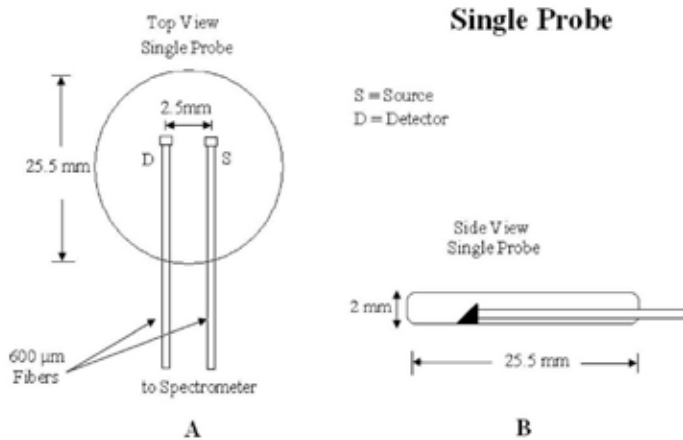
**Figure 1.** The clinical monitoring system, consisted of a laser Doppler unit, a spectrophotometer system, DAC board connected to pressure sensor, and a laptop computer controlling all the instrumentation.

as shown in **Figure 2**. A small amount of clear epoxy was applied to secure the fibers inside the Delrin support. The top surface of the probe support was painted black to block light penetration from outside sources.

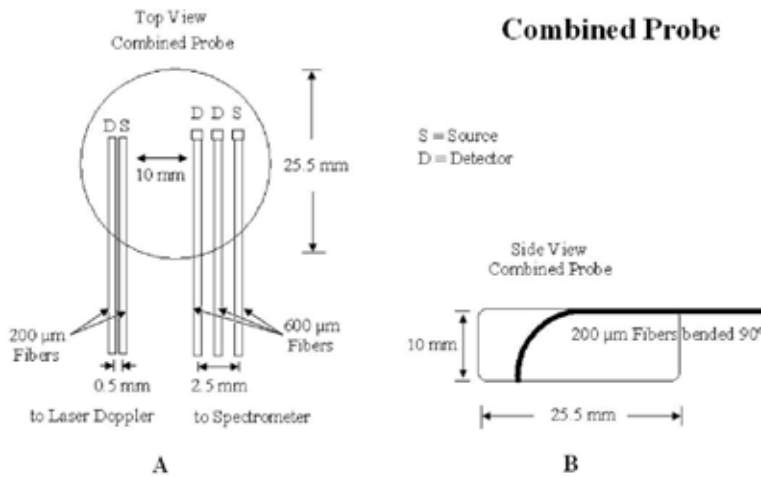
The second probe consisted of 3 multimode 0.6 mm fibers (1 source and 2 detectors) for R measurements and 2 multimode 0.2 mm fibers for LDF measurement as shown in **Figure 3**. We will refer to this probe as the *combined probe*. The 0.6 mm fibers were combined with the same 1 mm prisms as previously described, whereas the flexible 0.2 mm fibers were bent close to 90° to channel light directly to the skin surface. A Delrin disk (diameter 25.5 mm, thickness 10 mm) was used to support all the fibers. A pressure sensor (Trossen Robotics, Westchester, Illinois) was attached to the top of the combined probe to monitor applied pressure to the skin.

**Influence of AD on skin perfusion and oxygenation**

The developed probes were such that only the top 1 mm in the skin was monitored;



**Figure 2.** Reflectance spectroscopy single probe.



**Figure 3.** Combined spectral and perfusion probe.

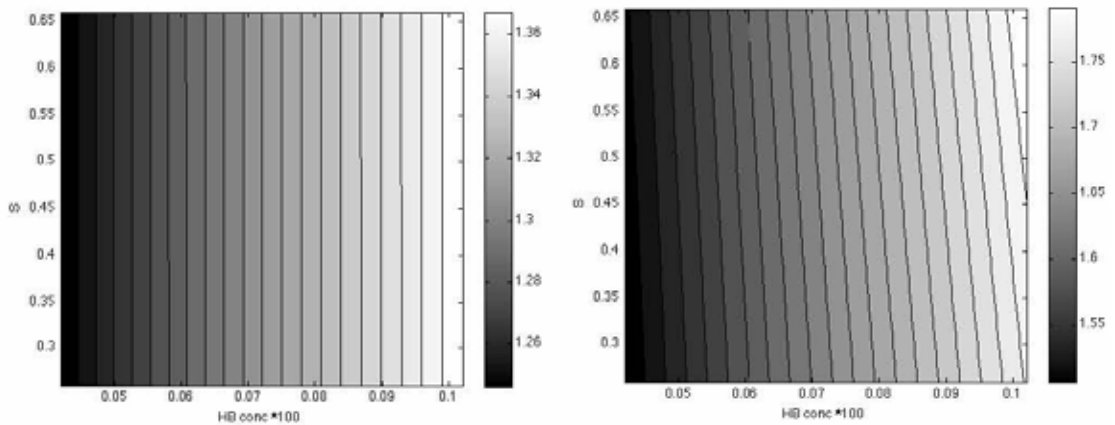
hence no information regarding deeper tissue and muscle oxygenation was obtained during this study. Wavelength-dependent diffused reflectance optical spectra were ultimately obtained. The extrapolation of oxygen saturation from such spectra have been achieved in the past<sup>8-10</sup> and generally rely on one or more isosbestic points.<sup>11</sup> This is done in part to limit the influence of blood volume fraction in the quantification of oxygen saturation.

Assessment of blood volume fraction was achieved using spectroscopic techniques based on the isosbestic points as shown in **Figure 4**. Simulated curves of skin reflectance were manipulated using a method previously described by Bargo et al<sup>9,10</sup> based on the Farrel's model.<sup>12</sup> In our simulation, the value of blood volume fraction (Hb Conc) and oxygen saturation (SO<sub>2</sub>) was allowed to vary ( $0.0005 < \text{Hb Conc} < 0.001$ , and  $0.3 < \text{SO}_2 < 0.7$ ). Realistic limits for AD were chosen in this study where blood volume fraction as well as SO<sub>2</sub> did not reach a zero value (complete ischemia). **Figure 4**

shows the results of such simulations when 2 isosbestic wavelengths (587 nm and 568 nm) were used. The figure gray-scale map is directly related to the ratio of the reflectance values (R) at the chosen values for increasing values of blood volume fraction and SO<sub>2</sub>.

By using the ratio of tissue diffused reflectance at 2 isosbestic wavelengths, we can obtain a parameter that is related to tissue blood volume fraction and is completely independent from the status of oxygenation in the skin.

Calculations of SO<sub>2</sub> are more complex as the blood volume fraction biases the measured diffused reflectance at different wavelengths. This effect is shown in **Figure 4** (right-hand side), where the pixel value was calculated using one isosbestic wavelength and one non-isosbestic wavelength (587 nm and 650 nm, at 650 nm curves of oxygenated and deoxygenated hemoglobin exhibit a large difference for all values of SO<sub>2</sub>). Recently Kollias et al<sup>8</sup> have proposed a model that minimizes the impact of blood volume fraction when using fiber optic probes; the model has been used by our



**Figure 4.** Each pixel in the images represent the ratio of reflectance values obtained at 2 isosbestic wavelengths,  $I=R(587)/R(568)$  (left-hand side), or one isosbestic and one nonisosbestic wavelength,  $I=R(650)/R(568)$  (right-hand side). The image on the left shows that the calculation of Hb Conc is completely independent of  $SO_2$  (which is expected since at isosbestic wavelengths the oxy and deoxy extinction coefficient is equal). In fact, different values of Hb Conc yield equal values of  $SO_2$  (straight up and down lines). The same cannot be said when using nonisosbestic wavelengths ratio, as shown in the image on the right-hand side.

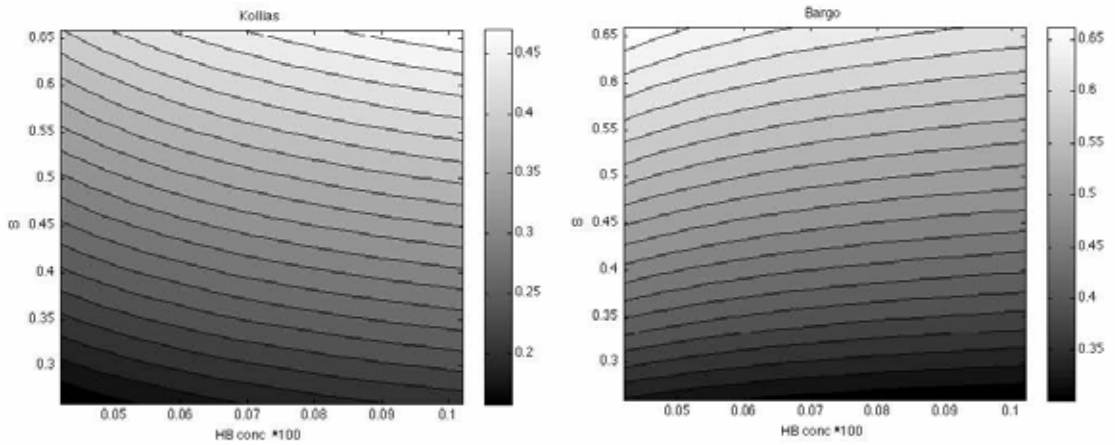
group in previous work.<sup>7</sup> Kollias' algorithm uses the curve of absorbance of skin, which is simply the logarithm of the ratio of the skin reflectance to standard reflectance (Spectralon standard 99% reflectance). The total absorbance curve of skin is corrected for melanin absorption by subtracting its contribution from the general data. Skin pigmentation is approximated as the slope of a fitted straight line between the values of absorbance at 620 and 720 nm, with the absorbance curve of melanin decreasing monotonically between 600 and 750 nm. Oxygen saturation is calculated by using tabulated absorption curves of oxygenated and deoxygenated hemoglobin to fit the experimental data in the range 550 to 580 nm. In this range, both curves exhibit local maxima.<sup>11</sup>

Using the same simulated data as utilized in **Figure 4** and applying the Kollias model,

we are able to obtain a better separation between  $SO_2$  and blood volume fraction (see **Figure 5**, left-hand side). The image shows the desired horizontal lines structure (constant  $SO_2$  for varying HB Conc) at high values of HB Conc (above 0.0007) but fails at low values. Bargo et al have proposed a correction to Kollias model that focuses the analysis on wavelength between 530 and 630 nm.<sup>13</sup> The results obtained with their algorithm shown in **Figure 5** (right-hand side) are successful in the separation of the 2 variables of interest at values of HB Conc above 0.0005.

### Procedure

This was a cross-sectional pilot trial of 7 men with SCI of at least 1 year duration. The study was conducted at the National



**Figure 5.** Analysis of simulated data with Kollias model (left-hand side) and Bargo model (right-hand side). Bargo's model is clearly superior in extrapolating correct values of  $SO_2$ . In this study we used this later model to calculate  $SO_2$  skin values.

Rehabilitation Hospital in Washington, DC, and was approved by the MedStar Research Institute Institutional Review Board (IRB). Participants were identified through database and medical record queries and via newsletter advertisements, flyers, and Web site announcements. Individuals were screened for study inclusion according to the following criteria: T6 or cephalic SCI, American Spinal Injury Association (ASIA) Impairment scale (AIS) A or B, history of

AD, at least 18 years of age, and at least 1 year since injury (see **Table 1**).

The morning of the assessment, subjects were instructed to not drink water for at least 3 hours prior to the test and to empty their bladder prior to their appointment. The subjects were positioned in their wheelchair during the test in a room with controlled comfortable temperature. Utilizing the probes described previously, 3 different locations of the subjects' skin were monitored. The

**Table 1.** Patient population statistics

Age	SCI level	ASIA classification	Time since injury (years)
47	C7	A	10
26	C4	B	6
50	C6	B	1
36	C5	B	13
39	C5	A	13
22	C4	A	3
36	T4	A	18

fiber probes were positioned on the patients' skin, grossly over the lateral aspect of the gastrocnemius (bilaterally; left limb had one LDF and one R measurement and the right limb had one LDF and two R measurements) and right deltoid with surgical tape. The measurement above the level of injury (on the arm, one LDF and one R measurement) was used as a reference since skin hemodynamics was not expected to change at that location.

Measurements of perfusion, oxygenation, and blood volume fraction were obtained continuously with the custom fiber probes. The patients' right arm was also fitted with an automatic BP monitor (Omron Comfit, Novi, Michigan) so that BP could be measured at short intervals (every 1 minute). Skin temperature was also monitored using the LDF fiber probes containing an embedded thermocouple. Skin humidity was measured using a skin moisture sensor (MoistSense; Moritex Inc, San Jose, California).

To induce AD, 20 cc of room temperature sterile saline (0.9% sodium chloride) was injected into each subject's bladder over 30 second intervals by a physician via a urethral or suprapubic catheter. If the subject's vital signs were normal and he did not report AD symptoms, saline was added. Maximal volume was limited to 500 mL to avoid bladder injury. This volume is routinely used in urodynamics studies with limited risk to the subject. If at any time the systolic BP exceeded 160 mm Hg, the diastolic pressure exceeded 100 mm Hg, or the clinician or subject did not feel comfortable with the subject's condition, the bladder was drained and the experiment was stopped. All the collected data related to skin hemodynamics was stored automatically on the computer

hard drive and analyzed in post processing. Finally the data were analyzed with the algorithm described in the previous section (Bargo model).

## Results

All fiber probes were tested on able-bodied individuals before the start of the clinical trial. In order to simulate the AD event and its impact on the skin, a pressure cuff was used to block blood flow to a volunteer forearm for several minutes. The probe was placed on the individual's skin and a transparent gel was added at the skin-probe interface for index matching, with a test length of 10 minutes. During the first 90 seconds, baseline values of blood flow and skin oxygenation were measured. The pressure cuff was then inflated for 2 minutes. Finally the pressure cuff was released and oxygenated blood was allowed to return to the area. Contemporaneous measurements of perfusion and oxygenation were conducted, and probe pressure on the arm and skin temperature were also continuously monitored but are not shown here.

In this trial, 6 of the 7 subjects experienced clear signs of AD (including an increase of systolic BP higher than 20 mm Hg), as well as headache, sweating, piloerection, and general sense of malaise. The summary of the study results is shown in **Table 2**. Systolic and diastolic BP increased by 23 to 74 mm Hg across the group; the time interval associated with the first sign of increased BP and to the release of the stimulus is noted in the last column. Relative changes in SO<sub>2</sub> varied from 0 to 0.42, and perfusion (as measured with LD) also varied in 4 of the 7 individuals by 0 to 0.41. Finally blood volume fraction changed in

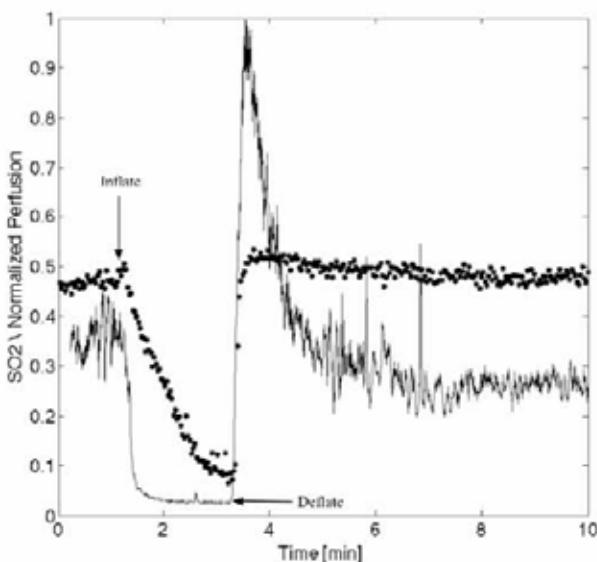
**Table 2.** Study summary

Patient no.	$\Delta$ Blood pressure, systolic mmH	$\Delta$ Blood pressure, diastolic mmHg	$\Delta$ SO <sub>2</sub> (-)	$\Delta$ Hb Conc (-)	$\Delta$ perfusion (-)	Amount of saline injected, mL	SCI level	Time, min
1	25	-21	0.37	0.15	0.41	360	C7	7
2	41	23	0.00	0.06	0.00	220	C4	5
3	70	36	0.42	0.08	0.21	120	C6	2
4	74	36	0.30	0.10	0.00	120	C5	3
5	20	27	0.00	0.06	0.14	120	C5	6
6	44	35	0.00	0.06	0.33	100	C4	3
7	5	2	0.00	0.00	0.00	500	T6	0

all subjects by 0.06 to 0.15. SO<sub>2</sub>, Hb Conc, and LD measurements were normalized by the patient baseline values.

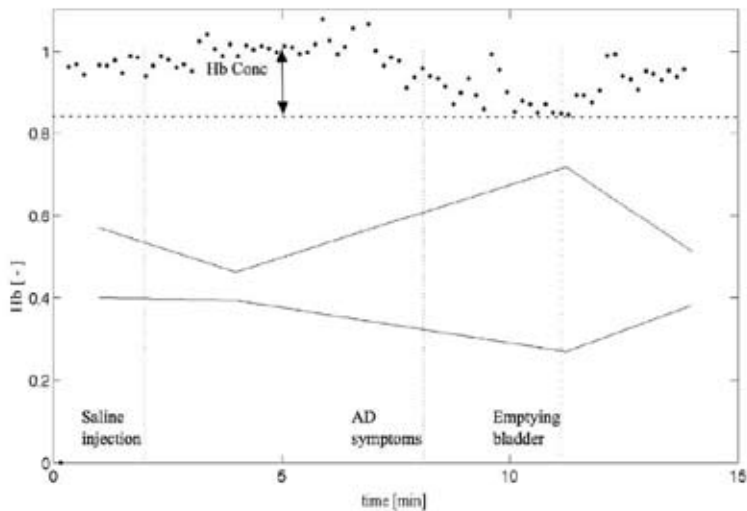
**Figures 7, 8, and 9** show the results for Subject 1. The patient's bladder was filled with 350 mL of saline before first symptoms of AD were reported (around minute 7-8). No change in perfusion, blood volume fraction, or oxygen saturation was noted above the level of injury. SO<sub>2</sub>, Hb Conc,

and LD declined to varying degrees during the episode of AD. Upon removal of the saline, all parameters showed slow recovery to normal values. Temperature and skin moisture remained unchanged above and below the level of injury. Several deviations in the signal can be seen in **Figures 8 and 9** and are due to movement artifacts, whereas the calculation of Hb Conc appears more consistent.

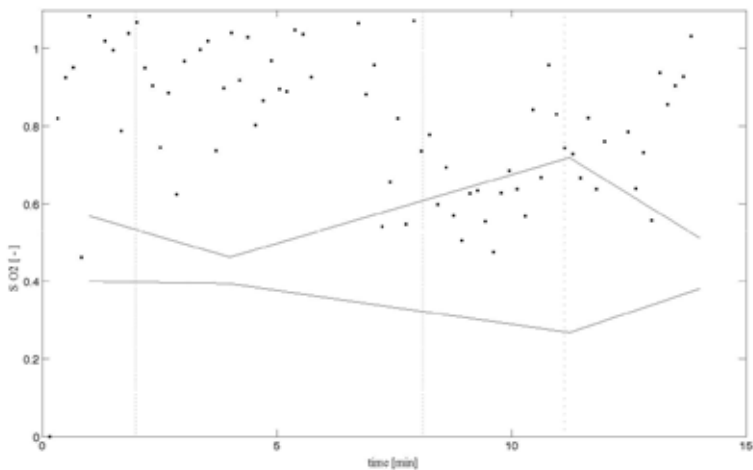


**Figure 6.** Combined oxygen saturation measurement (filled circles) and laser Doppler (line) measurement.

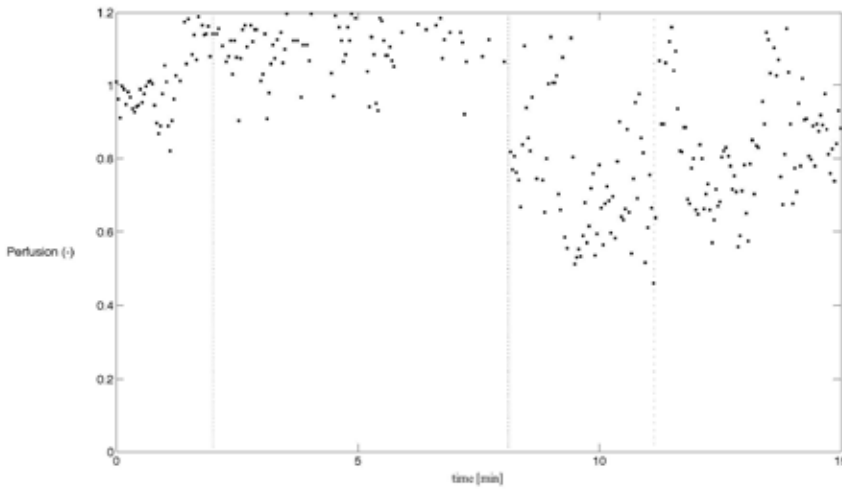




**Figure 7.** Blood volume fraction calculated with the algorithm described in the Methods section and normalized by the value obtained at rest. Vertical lines represent, from left to right, first injection of saline solution in patient bladder, acknowledgment from patient of AD symptoms, and patient’s bladder emptied. Systolic and diastolic blood pressure (BP) are also shown (solid line); the values of BP were divided by a constant  $c=160$  to fit the  $SO_2$  graph. The dashed line below the Hb conc value represents rest conditions.



**Figure 8.** Oxygen saturation calculated with Bargo’s algorithm normalized by the value obtained at rest. Vertical lines represent, from left to right, first injection of saline solution in patient bladder, acknowledgment from patient of AD symptoms, and patient’s bladder emptied. Systolic and diastolic blood pressure (BP) are also shown (solid lines); the values of BP were divided by a constant  $c=160$  to fit the  $SO_2$  graph.



**Figure 9.** Values of skin perfusion obtained with a laser Doppler system and normalized by the value obtained at rest. Vertical lines represent, from left to right, first injection of saline solution in patient bladder, acknowledgment from patient of AD symptoms, and patient's bladder emptied.

## Discussion

Bladder stimulation by injection of saline caused AD symptoms in 6 out of 7 of the individuals enrolled in this study. All patients who developed AD also experienced a reduction in blood volume fraction in the skin; a decrease of  $SO_2$  and perfusion also occurred in 3 and 4 individuals, respectively. This result may be due to the large variability that biases the 2 metrics, caused by movement artifacts and probe pressure on the skin. Very minor changes in skin moisture and temperature were noticed in all patients; this was possibly due to the brevity of the measurement and the fact that the study was interrupted as soon as severe signs of AD were reported by the test subjects. Recovery of baseline BP and skin optical properties was generally achieved less than 5 minutes after the release of the stimulus. All fiber-based

measurements were subjected to interference due to patient movement artifacts; LDF in particular proved to be extremely sensitive to such movement. Similarly, extrapolation of oxygen saturation from spectroscopic data proved to be complicated and largely impacted by the patient's movement. Of all metrics, measurements of blood volume fraction seem to be the most consistent and less prone to error. This parameter is proportional to the amount of blood present in the area of interest, both moving and stagnant, thereby differentiating it from the Doppler measurement.

To our knowledge, there has been only one other study examining the microvascular properties of skin during episodes of AD. Brown et al<sup>7</sup> examined cutaneous blood flow and sweating during AD caused by penile vibratory stimulation. In this study, skin blood volume was measured by photoelectric pleth-

ysmography on the pads of the index finger and big toe. Nine of 10 subjects experienced AD, and cutaneous vasoconstriction was evident in the toes in these patients. Decreases in perfusion reported ranged from 13% to 49%. Our study provides further evidence of cutaneous vasoconstriction during AD in people with SCI. This study provides greater detail on the physiologic properties of skin during AD. Using the optical fiber-based system, we showed that Hb concentration is the most reliable and consistent indicator of vasoconstriction, with skin perfusion by laser Doppler and SO<sub>2</sub> measurements demonstrating changes but with greater instability.

## Conclusions

Many individuals with SCI suffer from AD. This condition can be triggered by a full bladder, an ingrown toenail, or a pressure sore. We have constructed a system based on fiber optic probes to monitor blood flow and oxygen saturation in the skin of SCI individuals experiencing AD. We have

shown that the probes can accurately monitor ischemia and hyperemia in real-time. The results of this small clinical trial showed a consistent reduction in skin perfusion, oxygenation, and volume fraction below the level of injury during AD, confirming the presence of vasoconstriction. In contrast, no changes were noted above the level of injury. This preliminary evidence suggests that recurrent AD may be a risk factor for skin breakdown below the level of injury and that additional preventive actions may need to be taken in persons experiencing recurrent or chronic AD. These techniques will be further developed to increase our understanding of skin changes that could potentially lead to pressure-related skin breakdown.

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