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Assessment of skin blood content and oxygenation in spinal cord injured subjects during reactive hyperemia

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Abstract—This study was undertaken to determine whether the reactive hyperemia response following ischemia in spinal cord injured (SCI) individuals is different from that which occurs in able-bodied (AB) individuals. The reactive hyperemia response was produced by applying a pressure of 150 mmHg for 300 s, 600 s, and 900 s to the skin over the greater trochanter in 10 SCI and 10 AB subjects using a computer-controlled pneumatic indentation system. The changes in blood content and oxygenation in the superficial vessels of the skin, associated with indentation, were monitored using reflectance spectrophotometry. A brief pressure of 80 mmHg, to simulate finger pressing (blanching), was applied to the same site to detect changes in reflow behavior during the hyperemic period. The results indicate that the reactive hyperemia response in SCI group was not substantially different from AB group although the reflow rate after load release was slower in the SCI group compared with the AB group.

Key words: *pressure sores, reactive hyperemia, reflectance spectrophotometry, skin, spinal cord injury.*

INTRODUCTION

Pressure sores remain one of the most serious complications in patients with spinal cord injury (SCI). Prevention is the best strategy for managing this problem, but once the condition does occur, it often progresses to produce destructive tissue damage. Early identification of tissue distress caused by pressure application is clinically important because early intervention can significantly reduce the severity of tissue damage and the associated myriad of social, economic, and medical implications.

The most commonly used technique to detect tissue distress in clinical settings is inspection of the skin for color, hardness, and warmth. The earliest clinical indicator of tissue distress is localized redness. Clinicians often palpate the area and observe the blanching response of the reddened area to light finger pressure. This is done to confirm that there is a patent blood supply to the skin and to differentiate the normal reactive hyperemia response from persistent redness that indicates an early inflammatory response. In cases of persistent redness, there is faster reflow following blanching than there is in reactive hyperemia. Unfortunately, these observations neither allow quantitative description of such tissue responses nor are they effective for many patients with deeply pigmented skin (1).

Animal experiments by Groth (2), Nola and Vistnes (3), and Daniel, et al. (4) indicate that initial pathologic changes occur in the muscle, and subsequently progress toward the skin. Skeletal muscle has higher metabolic demands than the skin, and it is more sensitive to ischemia (5). In addition, because the muscle is close to the bone and enclosed by fascia, pressure is thought to be more concentrated in the deeper tissues (6). However, it is difficult to simulate clinical conditions for pressure sores in animal models; therefore, it is difficult to interpret animal experiment results in terms of human pressure sore etiology. The precise relation-

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ship between skin redness and deeper tissue damage during the early stages pressure sores development is still unclear.

When tissue is exposed to pressure, it usually reacts in a predictable way, depending upon whether damage has occurred to the tissue. Most external stimuli to the skin, including mechanical forces, cause skin redness.

After short periods of ischemia, skin redness develops as a result of increased vascular perfusion in the upper dermis. The capillaries and venules are greatly dilated during this response (7) that is described as "reactive hyperemia" and is a normal physiological response to correct a local metabolic debt accumulated during ischemia. Usually, it resolves in less than 30 minutes after pressure release. If this response is impaired, it may suggest that tissue metabolic recovery will be delayed and the tissues may become toxic following repeated sequences of ischemia. After a period of prolonged ischemia, persistent redness, usually defined as an area that fails to resolve after one hour, may occur and is thought to be an inflammatory response. Persistent redness may be sustained for several days before resolving or progressing to frank skin breakdown.

If pressure-induced ischemia produces more severe damage, "non-blanchable" erythema often results. It is recognized by dark-reddened skin that remains red during blanching with light finger pressure. Under these conditions, vascular engorgement, plasma leakage from blood vessels into the interstitial tissues, and then hemorrhage occur (7).

There is little information available about the circulatory response to pressure-induced ischemia in spinal cord injured (SCI) skin. Although it has been shown that lower pressure is required for the occlusion of skin blood flow in SCI patients (8,9), only a few studies have been carried out on the reactive hyperemia response in SCI patients, and the results are not consistent. Bidart and Maury (10), who used water plethysmography, and Mahanty, et al. (11), who used skin temperature measurement, note that there is no difference in response between SCI and able-bodied (AB) subjects. In contrast, Schubert and Fagrell (9), who used laser Doppler flowmetry, report reduced reactive hyperemia response following ischemia in paralyzed skin of SCI patients.

Recently, tissue reflectance spectrophotometry instrumentation has become commercially available providing information on blood content and oxygenation in the upper dermis where vessels involved in reactive hyperemia are located. With this technique, dynamic changes in blood content and oxygenation following mechanically induced ischemia of varying durations were used to characterize the reactive hyperemia response after ischemia in SCI and AB individuals.

MATERIALS AND METHODS

Subjects

The study consisted of two groups: SCI and AB subjects. Subjects were selected from the population of in- and outpatients associated with Helen Hayes Hospital. Age and sex-matched AB subjects were recruited from hospital staff. Informed consent approved by the hospital's Institutional Review Board was obtained from each subject.

Ten SCI subjects and 10 sex- and age-matched AB subjects for each group participated in testing for reactive hyperemia. Prior to testing, all subjects were carefully screened according to the subject criteria described below.

The following exclusion criteria were applied to all potential participants: less than 20 years and over 50 years of age; tobacco, alcohol, or drug abuse; anemia; diabetes mellitus; hypertension; hypotension; cardiovascular disease; pulmonary disease/deficiency; or dermatological pathology. For subjects with SCI, inclusion criteria were: spinal cord injury with the neurological level of injury between C-5 and T-12; 1 year or more postinjury; complete injury with both motor and sensory loss.

The basic demographic information for subjects participating in this study is summarized in **Tables 1** and **2**. The test was usually performed 2 hours after a meal.

Postischemic Reactive Hyperemia Measurement

To investigate the reactive hyperemia response following ischemia, the methods listed below were used for force application and blood content and oxygenation measurement.

Site. The skin over the greater trochanter was used as a testing site to produce reactive hyperemia. This area is usually at risk for pressure sore formation, but for individuals who use wheelchairs, it is usually free from pressure prior to testing.

Table 1.
Characterisics of the subject tested (SCI).

Subject	Age	Sex	BP	Level of Injury	Post Injury*	Spasticity	History of PS**
1	36	M	120/77	T3-4	15	Y	0
2	27	M	104/58	C5-7	9	Y	1
3	46	M	110/72	T6	22	Y	2
4	50	M	127/82	T5-6	8	Y	1
5	28	F	112/74	T7	13	Y	1
6	27	M	98/66	C4-5	9	Y	2
7	31	M	110/70	T12	2	N	1
8	38	M	120/86	T6	10	Y	1
9	33	M	110/66	T6-7	13	Y	0
10	30	M	118/72	C6-7	8	Y	1
Mean	30.6		113/72		10.9		

BP = blood pressure
PS = pressure sores
Y = presence of spasticity
N = absence of spasticity
*time in years
**number of times subject developed pressure sores in the past.

Table 2.
Characterisics of the subject tested (able-bodied).

AB	Age	Sex	BP
1	36	M	124/76
2	26	M	115/61
3	43	M	130/71
4	45	M	109/66
5	30	F	113/62
6	24	M	116/74
7	31	M	115/64
8	36	M	118/71
9	31	M	128/80
10	28	M	112/58
Mean	33		118/68

AB = able-bodied
BP = blood pressure

Tissue Indentation. A load of 4 N applied to the probe of the spectrophotometer (area: 2.0×10^{ms4} m^2, corresponding to a pressure of 150 mmHg) was used for 300 s, 600 s, and 900 s to produce reactive hyperemia following indentation. This amount of pressure was sufficient to occlude arterial circulation (12) and also corresponded to the pressure levels frequently encountered in clinical settings. In addition, a load of 2.1 N (corresponding to a pressure of 80 mmHg) was used to produce blanching during the hyperemic period (13,14). The combination of this amplitude and duration of pressure was not expected to cause any tissue damage even in insensate skin (11).

A pneumatically controlled bellows indentation system was used for force application to the greater trochanter. The details of this system are described elsewhere in this issue (see pp. 15–19). To produce a convex surface for minimizing the edge effects of the indentor at the indentor/soft tissue interface and to eliminate the blood from the measured area allowing complete ischemia, the probe was milled at about 13°.

Tissue Reflectance Spectrophotometry. A tissue reflectance spectrophotometer (TS-200, Sumitomo Electric, Japan) was used for this study (**Figure 1**). This instrument emits light from a white light source to the skin through a fiber optic probe attached to

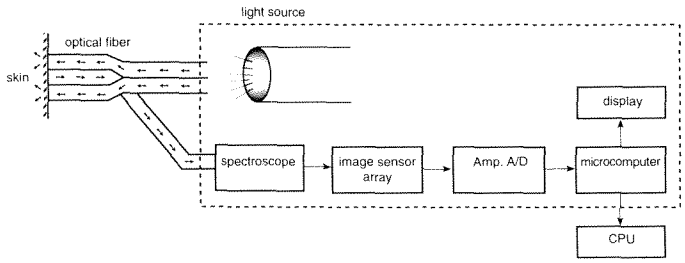

Figure 1.
Block diagram of the TS-200 used for this study.

the skin surface. The light back-scattered from the skin is collected and analyzed in a spectrometer. By comparing the back-scattered spectrum to that obtained from a standard white diffuse surface, it is possible to determine blood content (IHB) and oxygenation of blood (IOX) in the upper dermis. The full-spectrum data were output from the TS-200 to a PC 386 workstation using a GPIB interface (National Instruments Corp., TX). The absorption values for each wavelength increment of 1 nm between 450 and 650 nm were then stored on floppy disk for further processing.

Because the normal sampling speed for data acquisition of a full-spectrum from the TS-200 was 0.66 Hz, which was not sufficient to monitor postblanching reflow behavior (3–4 s), during the postblanching period, the mode of the spectrophotometer was changed from graphic to numeric mode (output: specHB), which increases the sampling rate to 3 Hz. SpecHB is the blood content index provided directly by the instrument. During *in vitro* calibration, this output was found to have some cross-talk between blood content and oxygenation. Since the oxygenation level did not vary substantially during blanching, this parameter was used for monitoring blood content during blanching.

Procedures. Prior to the measurement, the subject, appropriately draped, exposed the skin over the greater trochanter and remained in a supine position with flexed knees on the examination couch for 900 s to acclimate to the temperature of the room (25–26°C) and to stabilize the circulation of the site. Support was placed below the knees to stabilize the position of lower extremities.

During the stabilization period, blood pressure was measured at the brachial artery using a conventional sphygmomanometer. The probe of spectrophotometer was placed on the skin surface of the trochanter with double-sided adhesive tape (Electrode Washers E401, In Vivo Metric). Careful alignment of the experimental system was assessed by applying a short test load to ensure that loading was perpendicular to the surface of the skin and to avoid shear forces. The probe and all equipment used in this experiment were kept at room temperature to reduce interference with skin microcirculation. For SCI subjects, a 0.1-m wide strap with Velcro™ was provided around the abdominal area for safety purposes.

After the resting period, the trochanteric area was indented for a prescribed period of time with the pneumatic indentor through the probe of spectrophotometer (**Figure 2**). The postischemic reactive hyperemia response was monitored for the same period as the duration of indentation. During the postischemic period, a blanching pressure of 80 mmHg was applied to the hyperemic site for 3–4 s every 120 s to measure postblanching reflow behavior. This test was repeated three consecutive times for 300 s, 600 s, and 900 s durations of indentation. Between any two test sessions a 48-hour period was provided to prevent carryover between tests.

Data Processing. After data acquisition, the binary data were converted to ASCII, and the indices of IHB and IOX were calculated using a method described by Feather, et al. (15). Minor modifications to this method were made based on our *in vivo* tests[1].

[1]Unpublished observations.

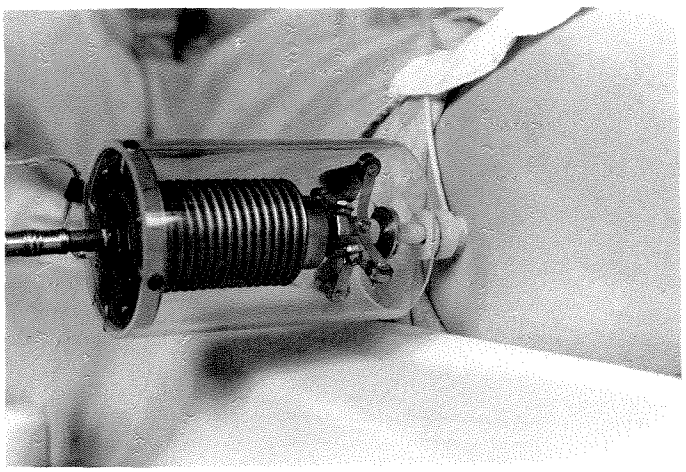

Figure 2.
Indentation of skin over the greater trochanter.

The load, IHB, IOX and specHB were then plotted graphically against time, using ILS software version 6.1 (Signal Technology, CA), which also provided a convenient method for applying simple smoothing algorithms, feature extraction and analysis.

DATA ANALYSIS

Analysis of Reactive Hyperemia

A typical data set of load, IHB, and IOX obtained from an AB subject is indicated in **Figure 3**. Reactive hyperemia was characterized by using the parameters defined below, many of which have been used in previous studies (16,17,18).

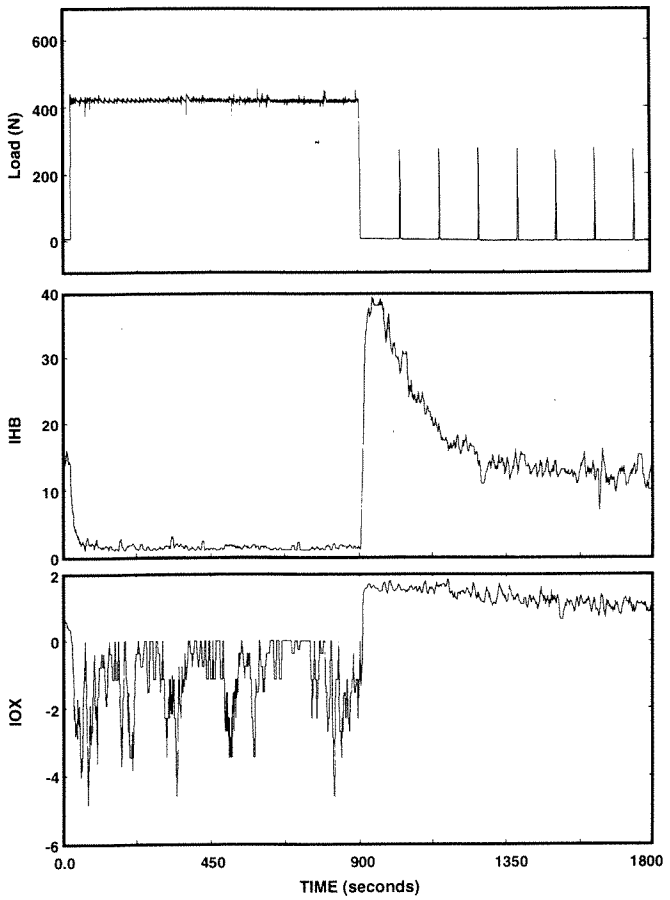

Figure 3.
Typical results of reactive hyperemia response obtained from an able-bodied subject following 900 s indentation. *Upper:* Load (N); *middle:* IHB; *lower:* IOX.

Smoothing. For calculation of most of the parameters used in this study, 5-point moving window averaging was used. However, for λ_{1HB}, λ_{2HB}, A_1, A_2, and λ_{OX}, 15-point averaging was used to smooth the curve for linear regression without modifying the original trend of the response curve. This analysis was performed by using the ILS software version 6.1 (Signal Technology, CA).

Parameters for the Characterizing of Reactive Hyperemia:

a. **Resting IHB and IOX**—the average value before indentation, calculated by averaging the absorption of the first 15 spectra;
b. **Peak IHB**—maximum value of IHB following indentation;
c. **Time to peak IHB**—defined as the time interval (s) between the starting point and the peak point in IHB after load release;
d. λ_{pHB} **and** λ_{pOX}—defined as the gradients to peak IHB and mean peak IOX (IHB/s and IOX/s) calculated by linear regression between the starting point and the point that the linearity is lost after load release;
e. **Half-life of IHB**—defined as the time interval (s) between the peak point of IHB and half of its value during hyperemia;
f. λ_{1HB}—defined as the decay constant of IHB (IHB/s) for the first decay exponential after the peak **(Figure 4)**;
g. λ_{2HB}—defined as the decay constant of IHB (IHB/s) for the second decay exponential **(Figure 4)**;
h. A_1—defined as the amplitude of IHB at the start of first decay period **(Figure 4)**;
i. GA_2—defined as the amplitude of IHB at the start of second decay period (extrapolated to start of first decay period) **(Figure 4)**;
j. **Total area of IHB and IOX**—defined as the area between the hyperemic curve and the resting level ($\Delta IHB \times time$ and $\Delta IOX \times time$) during monitoring period excluding the blanching period;
k. **Peak IOX**—the value of peak IOX averaged for the first 30 seconds after stabilizing following indentation;
l. **Plateau period for IOX**—defined as the time interval (s) between the beginning of the peak plateau and the onset of the decline in decay IOX **(Figure 4)**; and

m. λ_{OX}—defined as the gradient of IOX (IOX/s) calculated by linear regression between the onset of the decline in IOX and the end of measurement **(Figure 4)**.

Analysis of Blanching Response

Figure 5 shows a typical example of postblanching behavior of specHB associated with a step load.

Blanching response parameters:

a. **ΔHB**—defined as the difference between averaged maximum value of specHB following blanching and averaged minimum value of specHB during momentum loading **(Figure 6)**;

b. **Recovery time**—defined as the time interval (s) between the crossing points of regression line with minimum and maximum line **(Figure 6)**.

c. λ_b—defined as a reflow gradient (specHB/s) calculated by linear regression between the onset of reflow and the point of full recovery **(Figure 6)**.

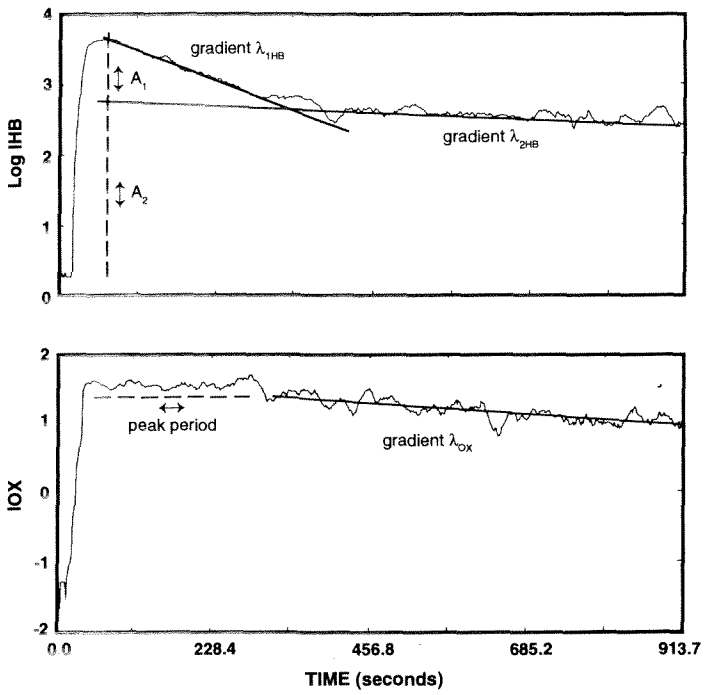

Figure 4.
Determination of λ_{1HB}, λ_{2HB}, A_1, A_2, plateau period for IOX and λ_{OX}.

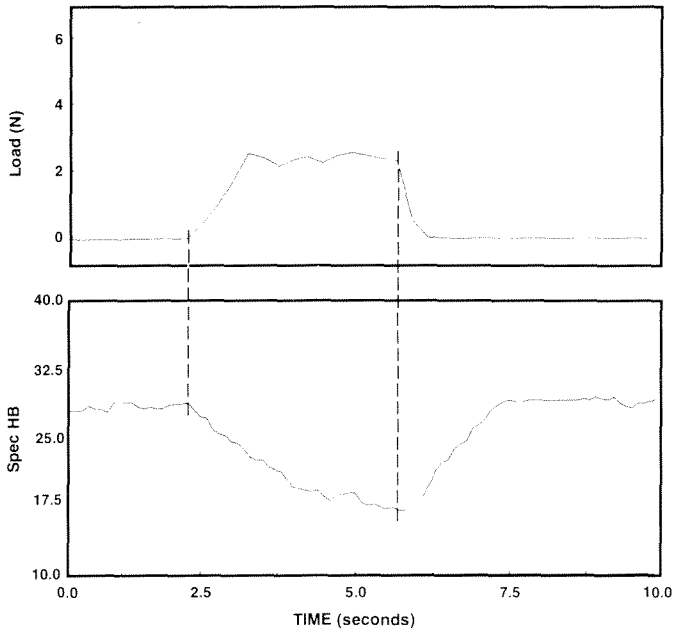

Figure 5.
Typical example of blanching response for approximate step load of 3–4 s. *Upper:* Load (N); *lower:* SpecHB.

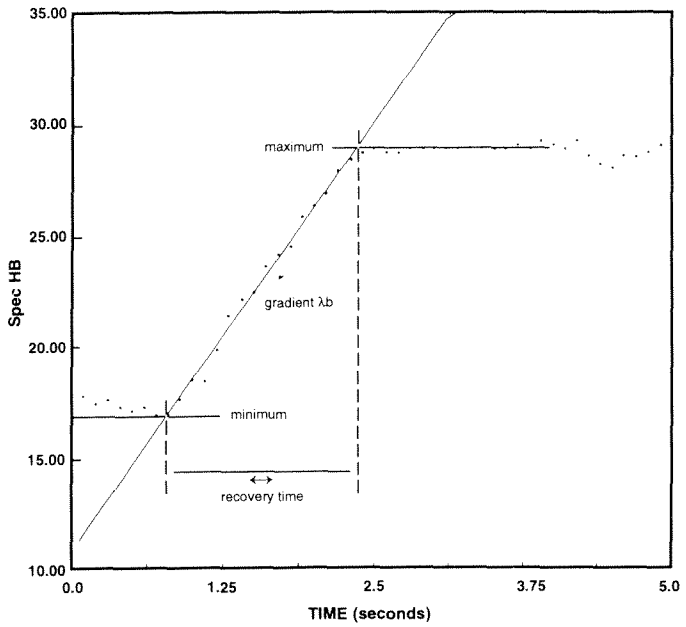

Figure 6.
Determination of ΔHB, λ_b, and recovery time during postblanching.

Statistical Analysis

To determine the statistical significance of the differences in response between SCI and AB groups,

statistical tests provided by Statistical Package for Social Science software version 4.0 (SPSS Inc., Chicago, IL) were used. Prior to the analysis, the data were screened with box plot and normal probability plot to determine whether the data were normally distributed. In addition, spread and level plots coupled with the Levene test were used to check for homogeneity of variance. Where necessary, a power transformation was used to stabilize variances. If the data passed these tests, a multiple regression test was performed. The significance level was defined as $p<0.05$. If the data failed any of the tests, a non-parametric test (Kolmogorov-Smirnov) was used (significance level $p<0.05$).

To determine whether the duration of ischemia causes significant differences in each dependent variable in a combined (AB+SCI) group and whether the effect is different between the AB and SCI groups, repeated measures multivariate analysis of variance (MANOVA) was used. This method has been designed for analysis when the same variable is measured on several occasions for each subject.

Table 3.
Statistical results of repeated measures MANOVA used to determine the effect of duration of ischemia on parameters measured.

Parameters	Significance Within (AB+SCI)	Significance Between AB and SCI
peak IHB	0.002	0.175
time to peak IHB	<0.001	0.612
half life	0.023	0.615
λ_{1HB}	<0.001	0.102
λ_{2HB}	<0.001*	0.208
A_1	<0.001*	0.010
A_2	0.007*	0.565
total area of IHB	<0.001	0.436
plateau period for IOX	<0.001	0.681
λ_{OX}	0.003*	0.955
total area of IOX	<0.001	0.020

*Test for normality and homogeneity indicate either non-normally distributed or inhomogeneous data. However, high level of significance suggests that the parameters are correlated with duration of ischemia.

RESULTS

Effect of Duration of Indentation

Table 3 summarizes the results of the repeated measures MANOVA. There were significant increases in the peak value of IHB ($p<0.01$), time to peak IHB ($p<0.001$), half-life ($p<0.05$), A1 ($p<0.001$), total area of IHB ($p<0.001$), plateau period for IOX ($p<0.001$), and total area of IOX ($p<0.001$) with the increase in duration of indentation in AB+SCI group. The changes in A_1 associated with duration of indentation was significantly different in the SCI group from AB group ($p<0.01$).

In contrast, with increased duration of indentation, the λ_{1HB} ($p<0.001$), λ_{2HB} ($p<0.001$) and λ_{OX} ($p<0.005$) and the A_2 ($p<0.01$) were decreased significantly. The relationship between λ_{OX} and duration of indentation in the SCI group was significantly different from the AB group ($p<0.05$).

Reactive Hyperemia Response

Table 4 shows the results of the reactive hyperemia response following three different durations of indentation. During the resting period, there was no difference in IHB between the AB and SCI groups. Following indentation, the IHB value rapidly increased toward the peak. The λ_{pHB} was significantly smaller in the SCI group compared with the AB group for the 300 s and 900 s protocols ($p<0.05$); however, the peak IHB did not differ between the two groups. After the peak, the IHB value started to decrease gradually to the baseline. The λ_{1HB} was significantly greater in the SCI group than that in the AB group for the 300 s protocol (Non-parametric test: $p<0.05$). A significant difference in the λ_{2HB} was also observed between the AB and SCI groups for the 600 s protocol ($p<0.05$). The A_1 parameter was significantly lower in the SCI group for the 900 s protocol compared with the AB group ($p<0.05$). As a consequence, the total area of IHB did not differ between the AB and SCI groups.

The IOX parameters did not show significant differences in response between AB and SCI groups. Only the λ_{OX} was significantly greater in the SCI group compared with the AB group for the 600 s protocol ($p<0.05$).

The blanching response during reactive hyperemia is shown in Table 5.

Table 4.
Reactive hyperemia response following three different durations of indentation.

		300 s		600 s		900 s	
Parameters		**Mean**	**S.D.**	**Mean**	**S.D.**	**Mean**	**S.D.**
IHB							
Rest IHB	AB	10	2	13	3	11	3
	SCI	9	2	10	4	9	3
Peak IHB	AB	33	5	36	4	37	5
	SCI	29	6	34	8	32	7
Time to peak IHB	AB	27	10	31	13	42	15
	SCI	22	8	34	8	40	6
Gradient to	AB	3.4	0.5	3.5	0.6	3.8	0.7
peak IHB	SCI	2.9	0.4	3.2	1.0	3.0	0.8
Half life	AB	135	57	167	43	181	73
	SCI	120	52	153	64	166	38
First decay	AB	−12.3	4.8	−10.3	4.2	−10.1	3.3
constant (x E−03)	SCI	−23.1	8.5	−13.8	6.2	−10.8	4.2
Second decay	AB	−1.6	0.7	−0.3	0.3	−0.3	0.2
constant (x E−03)	SCI	−2.6	1.6	−0.7	0.5	−0.4	0.2
Amplitude of	AB	13	3	19	4	23	7
first decay	SCI	10	4	19	3	17	6
Amplitude of	AB	20	6	15	4	14	4
second decay	SCI	16	6	15	6	13	4
Total area of IHB	AB	2.6	0.9	3.4	1.2	5.7	1.9
(x E+03)	SCI	2.1	0.5	3.4	1.3	4.9	2.4
IOX							
Rest IOX	AB	1.1	0.4	1.3	0.3	1.1	0.4
	SCI	1.3	0.6	0.9	0.8	1.4	0.4
Peak IOX	AB	2.0	0.2	2.0	0.2	2.0	0.2
	SCI	2.1	0.3	2.0	0.3	2.0	0.2
Gradient to	AB	0.29	0.10	0.32	0.10	0.28	0.08
peak IOX	SCI	0.24	0.06	0.27	0.08	0.25	0.06
Plateau period	AB	75	19	184	72	343	101
	SCI	80	34	159	64	258	104
Gradient of decay	AB	−1.9	1.0	−0.7	0.6	−1.5	2.0
IOX (x E−03)	SCI	−2.7	1.3	−1.7	0.8	−1.1	0.6
Total area of IOX	AB	2.18	0.73	4.04	1.17	7.55	2.43
(x E+02)	SCI	1.95	0.96	5.33	3.09	7.36	2.74

AB: able-bodied subjects, SCI: spinal cord injured subjects.

Postblanching Response

For the postblanching response, ΔHB, recovery time and reflow gradient (λ_b) were evaluated. With increased postischemic period, the values of ΔHB and λ_b decreased. However, the rate of decrease was slower in the AB group following the 900 s protocol compared with the SCI group although the differences were not statistically significant. Only λ_b at blanching 5 was significantly smaller in the SCI group compared with the AB group for the 900 s protocol.

DISCUSSION

In general, blood flow or flux is determined by blood volume and flow rate, both of which are well controlled under normal conditions. In this study, blood content (IHB) and blood oxygenation (IOX), which may be influenced by flow rate, were measured to characterize the reactive hyperemia following ischemia.

For the IHB parameters analyzed in this study, the time to peak IHB, the peak value of IHB and

Table 5.
Blanching response during reactive hyperemia.

		300 s		600 s		900 s	
Parameters		**Mean**	**S.D.**	**Mean**	**S.D.**	**Mean**	**S.D.**
Blanch 1							
△HB	AB	12	6	13	6	11	4
	SCI	11	6	12	5	12	6
Recovery time	AB	2.2	0.7	1.9	0.5	1.5	0.4
	SCI	2.2	0.4	1.9	0.6	1.6	0.6
Reflow gradient	AB	6.0	4.0	6.5	3.5	6.8	2.1
	SCI	5.4	3.2	7.3	4.6	8.3	4.0
Blanch 2							
△HB	AB	10	5	9	3	11	3
	SCI	10	5	10	3	10	4
Recovery time	AB	2.3	0.4	2.2	0.7	1.7	0.4
	SCI	2.6	0.7	2.3	0.8	1.5	0.3
Reflow gradient	AB	4.7	2.7	5.8	3.2	5.6	1.4
	SCI	3.9	2.2	4.8	2.4	5.8	3.3
Blanch 3							
△HB	AB			11	5	10	3
	SCI			9	2	9	4
Recovery time	AB			2.3	0.9	1.8	0.6
	SCI			2.2	0.7	2.2	0.6
Reflow gradient	AB			4.6	2.8	5.6	1.7
	SCI			4.6	2.1	4.1	2.6
Blanch 4							
△HB	AB			11	5	10	3
	SCI			8	3	8	4
Recovery time	AB			2.2	0.5	1.8	0.3
	SCI			2.3	0.5	2	0.4
Reflow gradient	AB			4.8	2.7	5.5	1.7
	SCI			3.9	1.7	4.2	1.5
Blanch 5							
△HB	AB					11	4
	SCI					8	4
Recovery time	AB					1.8	0.3
	SCI					2.2	0.8
Reflow gradient	AB					6.4	2.3
	SCI					3.9	2.1
Blanch 6							
△HB	AB					10	3
	SCI					7	4
Recovery time	AB					2.3	0.6
	SCI					2.0	0.5
Reflow gradient	AB					5.0	2.1
	SCI					3.6	2.1
Blanch 7							
△HB	AB					10	3
	SCI					8	3
Recovery time	AB					2.2	0.6
	SCI					2.3	0.7
Reflow gradient	AB					4.6	1.7
	SCI					3.7	2.6

AB: able-bodies subjects, SCI: spinal cord injured subjects.

consequently A_1 represents how fast and how extensively the vessels react to ischemia. The λ_{pHB} represents the rate of increase in blood content following load release and depends upon vascular distensibility and the perfusion pressure gradient acting across the papillary microvessels. Under pathological conditions, as observed in patients with arterial insufficiency and systemic sclerosis, a longer time to peak and lower peak are noted (19,20).

Nevertheless, the λ_{1HB}, λ_{2HB}, and half-life may represent gradual vascular constriction after peak hyperemia and are likely to be affected by tissue metabolism, vasoconstriction, and environmental temperature (22,22).

As a consequence, the total area between the time versus IHB curve and the resting IHB represent the total additional blood content produced by reactive hyperemia.

The parameter IOX represents blood oxygenation mostly in the papillary and subpapillary plexus, depending on vasodilation, tissue oxygen consumption and blood flow rate. It is also influenced by the efficiency of pulmonary gas exchange. The duration of vasodilation following ischemia increases with increased duration of ischemia to allow tissue metabolic recovery, and consequently the period of peak plateau for IOX may last longer in response to metabolic needs and the λ_{OX} after the plateau may be smaller.

Effect of Duration of Ischemia

Some of the parameters measured were found to be affected by the duration of ischemia in a combined AB and SCI group. For this protocol, where 150 mmHg of pressure was applied to the trochanteric area and the IHB and IOX are measured using reflectance spectrophotometry, the peak IHB, time to peak IHB, half-life, A_1, total area of IHB, total area of IOX, plateau period for IOX, λ_{1HB}, λ_{2HB}, and A_2 are sensitive to ischemia/metabolic debt, whereas λ_{pHB}, peak IOX, and λ_{pOX} are less sensitive.

The λ_{pHB} did not change with increasing duration of indentation in both groups. Thus, the vascular dilation immediately after load release may be caused by a myogenic factor resulting from changes in intravascular pressure rather than a metabolic factor. After the sharp initial rise of λ_{pHB}, a slower increase in IHB was observed to reach a maximum value. This suggests that metabolic satiation may begin to moderate the rate of the increase in hyperemia. The peak IHB increased with increasing duration of indentation; however, the rate of increase in peak IHB varied and probably depends upon the maximum capacity of the vessels to dilate. After reaching the peak, IHB values decreased, gradually returning to the resting level. The constants λ_{1HB} and λ_{2HB} were inversely related to increasing duration of ischemia. According to a study by Mahanty and Roemer (23) who measured skin temperature as an indicator of hyperemia at the trochanteric area, with changing duration and amount of pressure, the rate of decay increased with the increase in duration of ischemia. The difference in the findings between present study and that of Mahanty and Roemer (23) may be due to the techniques used. Skin temperature measurement, especially for longer durations and intense pressure, is indirect and has a slow response which probably reflects not only superficial but also deeper tissue blood flow. Spectrophotometry is a real-time, more specific measurement of superficial blood content.

The total area of IHB increased with increasing duration of ischemia; however, the rate of increase was not proportional to the duration of ischemia as described by Imms, et al. (17). The total area of IHB produced for "repayment" (total area of IHB between the IHB curve and resting level during hyperemia) of oxygen debt was compared with total area of "debt" (total area of IHB between the IHB line and resting level during ischemia), according to Bar's study (24). He calculated the ratio of (R/D = area for Recovery/area for Debt) from skin temperature measurements and reported that with increasing intensity of pressure, the ratio decreased. He defined the $R/D > 5.0$ as a mild tissue response, $5.0 > R/D > 1.0$ as a moderate tissue response and $R/D < 1.0$ as severe tissue response. The calculated values of the ratio in the present study were much smaller than his, placing the results of this study in the "severe" category of his scale in the AB and SCI group even for 300 s indentation. In this study, the R/D ratio was slightly decreased with increasing duration of ischemia, but this difference was not significant in either AB or SCI group. The values for total area for recovery and debt are greatly influenced by the resting value. For example, if the resting value is higher, there is a bigger area for debt and smaller area for recovery. Consequently, the value of the ratio becomes smaller. Because the

maximum capacity of vessels to dilate is limited, the value of the ratio may not change relative to changes in duration of ischemia.

Thus, the R/D ratio provides a conceptual model but is not applicable for quantitative assessment of the reactive hyperemia response.

Differences in Response between AB and SCI Subjects

The resting IHB showed no significant difference between AB and SCI groups. The resting value indicates some diagnostic significance for some pathological conditions, such as hypertension (25) and peripheral vascular disease (26). However, most previous studies on reactive hyperemia note that there is no significant difference in the pre-occlusive value between experimental and control groups although they demonstrate significant differences in the postischemic reactive hyperemia response (19,27,28).

According to Ewald (29), the correlation coefficient between the resting value and peak value of transcutaneous pO_2 in postischemic reactive hyperemia was 0.07 for measurements in 101 healthy subjects. This indicates independence between these two variables. In the present study, the coefficient of determination (r^2) between resting IHB and peak IHB in each group of each protocol ranged from 0.2120 (SCI, 900 s) to 0.3781 (AB, 300 s), and supported Ewald's findings.

Seifert, et al. (19) pointed out in a study of reactive hyperemia, that the time to peak and time to appearance of vasomotion following ischemia were reliable parameters for characterizing skin hyperemia rather than the resting flux in patients with peripheral arterial occlusive disease. Aikawa (30) also noted similar findings for skin blood flow in SCI patients who showed "pretended normal" behavior under resting conditions, although vascular reactivity to external stimuli was greatly diminished.

It can be postulated that the resting value is less informative from a diagnostic point of view than dynamic vascular responses to external stimuli, such as the postischemic reactive hyperemia response. Therefore, it was determined that because the correlation between resting IHB and peak IHB in this study was weak, the reactive hyperemia response following ischemia was evaluated independently of resting values.

After load release, the reflow starts from zero. No significant difference in peak IHB between the AB and SCI groups was observed in this study. This may suggest that the maximum capacity of the vessels to dilate is not reduced in the SCI group. However, in the SCI group the A_1, which is considered to represent the additional increase in blood content produced by reactive hyperemia, was significantly lower ($p<0.05$) than the AB group for the 900 s protocol and marginally lower for the 300 s protocol ($p=0.0616$). This result indicates that the vascular capacity for dilation in the SCI group may be smaller than the AB group but should be confirmed with a larger number of subjects.

The results of the present study concur with studies by Bidart and Maury (10) and Mahanty, et al. (11), but not Schubert and Fagrell (9) who reported a significant difference in percent increase of flux during hyperemia between SCI and AB subjects. This discrepancy may result from the different techniques used: water plethysmography for Bidart and Maury, skin temperature for Mahanty, et al., and laser Doppler flowmetry for Schubert and Fagrell. However, the calculated percent increase of flux in a study by Schubert and Fagrell (9) greatly depends on the resting value. If the absolute peak values in SCI subjects are compared with AB subjects in their study (9), there is no significant difference between both groups.

Because the peak IHB was not significantly different between the two groups, the smaller λ_{pHB} observed in the SCI group suggests that the immediate response to load release is slower in the SCI group. It may be due to reduced vascular tone (31) and increased venous pressure (32). If the venous pressure is increased, the perfusion pressure gradient (difference between local arterial and venous pressures) is decreased resulting in slower flow rate. The muscle pumping action, which usually facilitates venous return, does not function following SCI due to loss of vasomotor control (32,33). This may explain our result of a slower reflow rate following load release in the SCI group.

After reaching the peak, the λ_{1HB} for the 300 s protocol and λ_{2HB} for the 600 s protocol in the SCI group were greater than that of AB group. This suggests that the vascular constriction after the peak might be different in SCI subjects compared to AB subjects. However, this tendency was not consistent for each protocol. Further studies are needed to

determine the factors contributing to the changes in vascular constriction following peak IHB associated with duration of ischemia.

Overall, the total area of IHB did not show a difference between the AB and SCI groups for each protocol. This may suggest that the metabolic repayment during reactive hyperemia in the SCI group does not differ from AB group.

There was no difference in the resting IOX between two groups; however, the value of one of SCI subjects was extremely low (-0.44 to -0.49). No reason for this extremely low value was evident upon examination of the clinical chart.

Abramson, et al. (34) calculated oxygen uptake during reactive hyperemia from the changes in the arteriovenous oxygen difference in the forearm. For varying periods of arterial occlusion, there was consistently an initial rise in oxygen uptake for the first 4 s to 25 s following ischemia, achieving a peak followed by a rapid fall to the base line. This suggests that oxygen uptake in the tissue takes place at an early stage of postischemic reactive hyperemia. The time intervals between onset of response and a stable peak level of IOX in this study were 11 s to 13 s in AB and SCI group regardless of the duration of ischemia. The onset of response was also similar to that of IHB.

The peak IOX did not differ between the AB and SCI groups even when the duration of indentation was changed. This suggests that the circulatory function for blood oxygen transportation to the capillaries in the SCI group does not differ from the AB group. It also suggests that at the peak, the vessels from arterioles to venules are dilated to facilitate blood flow in both the AB and SCI group, probably with a high flow rate. The amount of oxygenated blood passing through the vessels exceeds that of deoxygenated blood even if the tissue expends some oxygen. If it is assumed that the tissue oxygen debt is the same between two groups following ischemia under the same protocol, the duration of plateau period for IOX may represent the efficiency of nutrient and metabolic exchange during reactive hyperemia influenced by the duration of vasodilation and the flow rate. The greater λ_{OX} in the SCI group for the 600 s protocol suggests that vasoconstriction following ischemia may start earlier and/or flow rate decreases earlier in the SCI group than the AB group. The results of the λ_{OX} greatly varied among the data, which was probably caused by the limited sensitivity of the TS-200 output.

The reason why a less significant difference between AB and SCI groups was found in the 600 s indentation protocol compared with 300 s and 900 s indentation protocol is unclear, as there was no apparent difference in the indentation technique.

The postblanching response was also evaluated to determine whether there is a difference in response between the AB and SCI groups during the postischemic hyperemia. The λ_b essentially represented how fast the blood returns following blanching and is related to recovery time and ΔHB. Although there were no statistically significant differences in blanching response and A_2 between the AB and SCI group, ΔHB was relatively constant regardless of the intensity of reactive hyperemia in the AB group whereas in the SCI group it was decreased with increasing postischemic period for the 900 s protocol. This difference may relate to increased vasoconstriction in the SCI group. The λ_b following blanching was decreased with increasing postischemic period in both groups for the 900 s protocol, but the λ_b in the SCI group was more "intensity of hyperemia-dependent" compared with AB group. This phenomenon seems to be affected by vascular constriction, vascular tone, and venous pressure. The responses observed in blanching should be confirmed with a larger number of subjects.

In conclusion, there are a number of possible explanations for the findings of this study that demonstrate that the reactive hyperemia response in SCI subjects was not substantially different from AB subjects.

1. In individuals with SCI, the vascular response to pressure may be influenced by the effect of denervation and a secondary effect due to long-term paralysis and disuse. The reactive hyperemia response is a local response caused by myogenic and metabolic mechanism occurring even in denervated skin (35). During reactive hyperemia, capillary flow is markedly increased, whereas A-VA flow is unchanged in sympathectomized legs according to Cronenwett and Lindenauer (36). It is assumed that during reactive hyperemia the capillary plays an important role in controlling blood flow rather than the A-VA and arterioles, both of which

are greatly affected by innervation. According to Brown (37) who used vital skin capillary microscopy, sympathetic denervation did not induce dilation of cutaneous capillaries and did not affect the capillary size and number. These studies suggest that the sympathetic denervation itself does not affect capillary size, number and capillary flow during reactive hyperemia. The results of the present study suggest that even in the chronic stage of SCI, the reactive hyperemia response is not altered. However, the immediate response to load release (λ_{pHB}) was slower in the SCI group than in the AB group. This may be attributable to a decrease in the rate of reflow rather than a decrease in overall blood content.

2. Findings may be influenced by a limited population size. This study is not definitive, having only ten subjects for each group. The resting IHB, peak IHB, λ_{1HB} and plateau period for IOX are potential parameters which may provide significant difference between the AB and SCI groups with increased sample size. In addition, the characteristics of the population we studied may be different from more sedentary subjects (38).
3. The amount and duration of pressure were not sufficient to produce significant differences in hyperemia response between AB and SCI subjects. The threshold level for tissue tolerance to pressure is known to be decreased in SCI subjects. Our indentation protocol, pressure application with a 150 mmHg for maximum 900 s, was within widely used "acceptable" range of pressure-duration guideline (39). If the duration and/or amount of pressure are increased to approach more closely the threshold of tissue tolerance to pressure, then some differences in the capacity of vessels to react, or limitations in the reservoir capacity to accommodate these conditions, may become apparent.
4. Some neurological recovery (22), or reestablishment of vascular tone (22,40) exists although a mechanism is still unclear.

This study describes the characteristics of the reactive hyperemia response for SCI subjects in detail by providing a baseline normal response in AB and SCI group. We anticipate that based on this work an objective technique for differentiation of persistent redness from reactive hyperemia will provide a means to quantify and objectively identify early tissue distress.

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