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Existence of tissue blood flow in response to external pressure in the sacral region of elderly individuals – Using an optical probe prototype

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Running head: Blood flow in response to external pressure

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Abstract

Objective: The aim was to investigate the existence of sacral tissue blood flow at different depths in response to external pressure and compression in elderly individuals using a newly developed optical probe prototype.

Methods: The tissue blood flow and tissue thickness in the sacral area were measured during load in 17 individuals using laser Doppler flowmetry and photoplethysmography in a combined probe, and digital ultrasound.

Results: The mean age was 68.6 ± 7.0 years. While loading, the mean compression was $60.3 \pm 11.9\%$. The number of participants with existing blood flow while loading increased with increased measurement depth. None had enclosed blood flow deep in the tissue and at the same time an existing more superficial blood flow. Correlation between tissue thickness and BMI in unloaded and loaded sacral tissue was shown: r = 0.68 (p=0.003) and r = 0.68 (p=0.003).

Conclusions: Sacral tissue is highly compressed by external load. There seems to be a difference in responses to load in the different tissue layers, as occluded blood flow in deeper tissue layers do not occur unless the blood flow in the superficial tissue layers is occluded.

Key words: Pressure ulcer, photoplethysmography, laser Doppler flowmetry, non-invasive, tissue blood flow

Introduction

Pressure ulcerations, e.g. in the sacral region, are a common phenomenon in disabled patients that entail high costs for the health care system (27, 37, 42) and suffering for the individual (43). The etiology is complex and not fully understood, although tissue ischemia may be of importance (11, 14). Furthermore, no consensus has been reached regarding the depth at which pressure ulcer formation starts. Based on histological changes in the vessels of the papillary dermis, some studies favor the skin surface with progression down to deep tissue and muscle, i.e. top-to-bottom ulcer formation (47). Others have found initial changes in the deeper lying muscle or tissue over bony prominences, indicating that the ulcerations grow in a bottom-to-top fashion (10, 39). The theories seem contradictory, but may depend on factors such as tissue location and/or the individuals studied.

Recently, computer simulation models as well as magnetic resonance imaging (MRI) in rat models have been used to explore deep tissue changes (22-23, 44). Further, from a biomechanical perspective, the relationship between interface pressure and the mechanics of compressed tissue has been studied (36). However, despite the fact that ischemia may be an important factor in the development of pressure ulceration, very few studies have focused on tissue perfusion and compression of the tissue. There are studies that focus on the circulatory changes (using laser Doppler techniques) when tissues prone to pressure ulcer development are exposed to pressure, such as microvascular heel skin perfusion (29) and sacral skin blood flow (17, 35, 38), as well as characterizations of post-pressure blood flow responses in different populations such as diabetics (16), subjects with spinal cord injury (38) and smokers (35). If these types of studies are developed further to include techniques for exploring tissue blood flow simultaneously at different depths, there will be new improved opportunities to explore circulatory changes and pressure ulcer etiology.

The aim of this study was to investigate the existence of sacral tissue blood flow at different depths in response to external pressure and compression in elderly individuals using a newly developed optical blood flow measurement probe prototype.

Materials and methods

To be able to observe blood flow at different depths simultaneously, a system combining laser Doppler flowmetry (LDF) and photoplethysmography (PPG) was recently developed and was used in this study (5).

Optical methods

A HeNe laser (PeriFlux Pf2b, Perimed, Järfälla, Sweden), wavelength 632.8nm, was used to measure skin perfusion with a measurement depth of a few hundred μ m (46). The LDF technology is based on the principle that monochromatic light incident on the tissue is scattered and, if reflected by a moving scatterer, Doppler broadened. This frequency shift is detected and presented in arbitrary units (Volt) as an estimate of the perfusion. The perfusion scales linearly with the velocity (v_{RBC}) and the concentration of moving red blood cells (c_{RBC}) provided a low blood cell concentration to avoid multiple scattering (32-34).

A three-channel PPG instrument was used in this study (Department of Biomedical Engineering, Linköping University, Sweden). In short, the PPG signal consists of two components: an AC signal and a DC signal. The AC signal reflects the arterial/pulsatile part of the blood flow (20) in the vascular bed and depends on pulsatile blood volume and pressure variations as well as the orientation of the red blood cells during each heart beat (21, 31). The DC signal is a slowly varying baseline, reflecting, e.g., total blood volume changes, but was not used in this study (20). The ability to measure blood flow from shallow and deeper vascular beds is based on an appropriate combination of optical wavelengths and the distance between the light source(s) and the photodetector(s). It has been demonstrated that PPG can discriminate between skin and muscle blood flow, e.g. over the tibial anterior and trapezius

and supraspinatus muscles using 560nm and a source-to-detector separation of 3.5mm and 806 or 880nm at a source-to-detector distance of 20 or 25mm (40-41, 49).

The optical probe was developed for blood flow measurements in both superficial and deeper lying vascular beds in the sacral tissue combining the LDF and PPG techniques described above. Three pairs of light emitting diodes (LEDs) were placed in line, symmetrically on both sides around the photo detector and the components were integrated into a silicon plate and a laser Doppler fiber optic probe was inserted between the IR LEDs (Figure 1). The light source-to-detector separation was 5mm in the case of green LEDs and 10mm and 25mm for the IR LEDs, respectively. It was assumed that the different combinations of wavelengths and distances using LDF and PPG corresponded to approximate measurements depths of a few hundred µm, 2mm, 8mm and 20mm. The probe had one detector each for PPG and LDF, resulting in single point measurements, and was fixed in a 10*10cm stiff plate and integrated into the test bench to avoid any influence on the tissue during the measurements.



Figure 1. The optical probe with LEDs, placed around a photodetector and an optic fiber placed between.

Other methods

A digital ultrasound system (HDI 5000, Philips Medical Systems, ATL Ultrasound, Bothell, WA, USA) equipped with a linear transducer (L7-4) was used for scanning the sacral skin and subcutaneous tissue down to the bone. A pressure mapping system consisting of an underlay (45cm × 45cm) of integrated pressure sensors (Xensor Pressure Mapping System X236, Anatomic Sitt, Norrköping, Sweden, range 10-220mmHg, 4 sensor/square inch) was used to measure pressure distribution and contact area in the sacral area. The following background data was collected: weight (electronic balance scale with the individuals wearing light clothes on), height (to the nearest 0.5 in standing position), blood pressure (Speidel & Keller, Jungingen, Germany), heart rate (manually checked), body temperature (ThermoScan 6022, Braun, Kronberg, Germany) and skin temperature (IR thermometer, Raytek Raynger ST, Santa Cruz, CA, USA).

Subjects and procedures

Seventeen individuals (six males and 11 females) were recruited to participate in this study. All lived an active life and managed their daily life independently without assistance. They all experienced themselves as healthy, although some had cardiovascular diagnoses. Sub-analysis of the material in the study was therefore performed, and there were no significant differences between the individuals who had diagnoses and those who did not. The results are therefore presented as applying to one group.

The medial sacral crest of the individual was located, and a point 2-3cm above this was marked as the point of measurement. The sacral tissue consists of skin and subcutaneous tissue over the large wedged-shaped sacrum bone. The large intrinsic back muscles and gluteus maximus attach to the bone but in the middle area there is no muscle, only possibly some fascia that are low perfused.

The blood flow and ultrasound measurements were performed on a bench consisting of a wooden plate with a 10*10cm hole at the area of sacrum. When the blood flow measurements were performed in the unloaded tissue (used as a reference), the individuals were placed in prone position; all other measurements were performed with them in supine position. A board of Plexiglas or the prototype probe was fixed in the bench hole in line with the surface of the bench for measurements of tissue thickness and blood flow, respectively, in the loaded tissue. The blood flow measurements in each position were preceded by at least 25 minutes of rest. Blood pressure, heart rate, body temperature and room temperature were noted after 15 minutes of rest. Skin temperature was noted pre- and post-blood flow measurement.

The LDF device was calibrated in accordance with the manufacturer's manual and published guidelines (6, 15)

Approval for this study was granted by the Research ethical committee in Linköping, Sweden, Dnr M166-06. The study was performed according to the World Medical Association Declaration of Helsiki of 1989.

Data collection and analysis

The tissue thickness was assessed and calculated directly in the digital ultrasound system. All measurements were performed by a highly experienced technician, and the mean value of three separate measurements was calculated and registered (Figure 2). The measurements with deep IR light (at a depth of approximately 20mm) are not presented in the study as only two individuals had a tissue thickness of approximately 20mm or more while loading, thus deep IR light will be of no interest to this study (Table 3).

The blood flow was recorded continuously on a computer for a session of five minutes on both unloaded and loaded tissue (Labview 6.1, National Instruments, Kista, Sweden) at a sampling frequency of 75 Hz. The amplitudes of the AC signal and laser

Doppler signal were analyzed using a program developed in-house (IMT, Linköping University, Linköping, Sweden). When the pulsations in the AC signal ceased, the blood flow was assessed as occluded (Figure 3), in accordance with previous studies (18-19). When the laser Doppler signal decreased to a certain calibrated flux value, the blood flow was assessed as occluded.



Figure 2. Picture from the ultrasound measurements of the sacral tissue thickness in unloaded (A) and loaded tissue (B) in one individual.

The mean arterial pressure (MAP) was calculated as a function of diastolic pressure (DP) and systolic pressure (SP): MAP = DP + (SP-DP)/3. The body mass index was calculated as BMI = weight in kilograms / (height in meters)². The WHO BMI classification of underweight is BMI < 18.5; normal range of BMI is between 18.5-24.99; and overweight is BMI \ge 25 (1).



Figure 3. An example of tissue blood flow responses in one individual during load. The AC signals at the two PPG channels are recorded simultaneously. Blood flow was present and measured using IR light (A). The pulsations in the AC signal using green light had ceased, and the blood flow was therefore assessed as closed (B).

Statistics

Background variables tested for skewness and kurtosis showed normal distribution and are therefore presented in terms of mean \pm standard deviation. Paired sample t-test was used to compare differences in skin temperature pre- and post-measurement and differences in unloaded and loaded tissue thickness.

The variable blood flow was dichotomized into existing blood flow (1) and non-

existing blood flow (0). For comparing existing blood flow in unloaded and loaded tissue, the

McNemar chi squared test was used. A correlation matrix including age, BMI, tissue

thickness, tissue thickness while loading, compression and contact area was set up and the correlation coefficients were analyzed using Pearson's Correlation. P< 0.05 was considered to be significant. All statistical analysis were performed using SPSS® for Windows, version 15.0 (Statistical Package of Social Sciences, SPSS Inc., Chicago, IL).

Results

The mean age of the participants was 68.6 ± 7.0 years. The participants' mean weight was 72.0 ± 8.6 kg and mean BMI was 25.2 ± 2.6 . All participants had a normal heart rate of 67 ± 7 b/min, SP 129.1 \pm 13.6mmHg, DP 74.4 \pm 8.8mmHg and a body temperature of 36.3 ± 0.4 °C (Table 1). No significant differences were found between the genders regarding background characteristics. Five participants had cardiovascular diagnoses and took medication, and one participant used tobacco (Table 2).

	All (n=17)
Age (years)	68.5 ± 7.1
Weight (kg)	72.0 ± 8.6
Body mass index (kg7m ²)	25.2 ± 2.6
Heart rate (beats/minute)	66 ±7
Systolic pressure (mmHg)	129.1 ± 13.6
Diastolic pressure (mmHg)	74.4 ± 8.8
Mean arterial pressure (mmHg)	92.6 ± 9.3
Ambient temperature (°C)	23.1 ± 0.6
Body temperature (°C)	36.4 ± 0.4
Skin temperature prior to measurements (°C)	32.3 ± 1.8
Skin temperature after measurements (°C)	32.7 ± 0.8

Table 1: Mean and SD in the individuals' conditions relevant to microcirculation observed before blood flow measurements were performed.

Subject	Sex/Age	Pulse	Systolic	Diastolic	Vascular Diseases	Medication
			blood	blood		
			pressure	pressure		
			(mmHg)	(mmHg)		
7	Female/65	62	135	80	hypertension	1
8	Male/79	48*	140	70	atrial fibrillation,	2, 3, 4
					hypertension	
9	Female/62	66	120	80	parox. atrial fibrillation	2
15	Female/65	64	120	70	hypertension	2
16	Female/87	66	135	65	hypertension,	3, 5, 6
					post-cardiac infarction,	
					heart valve insuff.	

Table 2: Overview of the individuals' vascular diseases and medications.

1=ACE inhibitor, $2=\beta_1$ receptor-selective antagonist, 3=calcium antagonist, 4=anticoagulant (warfarin), 5=ASA, 6=loop diuretic * irregular pulse

The mean sacral tissue thickness (TT_{unload}) of the participants was 26 ± 12.7 mm. While loading, the tissue thickness (TT_{load}) was reduced to 10 ± 5.3 mm (p < 0.0005); the mean compression was $60.3 \pm 11.9\%$ and the sacral contact area was 188.0 ± 72.0 cm². No differences were found between the genders in TT_{unload} , TT_{load} , compression or sacral contact area. The interface pressure in the sacral area in supine position attained values of at least 220mmHg in 14 participants.

The number of participants with existing blood flow while loading (BF_{load}) increased with increased depth: Two of 16 participants had existing BF_{load} at a depth of maximum 1mm (LDF); five of 16 participants had existing BF_{load} at a depth of approximately 2mm (green PPG); and 11 of 17 participants had existing BF_{load} at a depth of approximately 8mm (infrared PPG) (Table 3). Compared with the blood flow in the unloaded tissue (BF_{unload}), the differences are significant at all three depths (p < 0.0005 at 1mm, p = 0.001 at 2mm and p = 0.031 at 8mm) (Figure 4).

Sex/Age		Compression	BF at <1mm BF at 2mm		BF at 8mm
	(mm)	(%)	depth	depth	depth
			(LDF)	(green PPG)	(IR PPG)
M / 67	4	66.5	0	0	1
M / 62	5	68.0	0	0	0
M / 75	5	59.6	0	0	0
F / 65	5	27.3	0	0	1
F / 65	6	72.3	0	0	1
F / 72	7	69.9	0	0	0
M / 79	8	57.4	0	0	0
F / 65	8	71.6	0	0	1
F / 62	9	77.4	0	0	0
F / 66	10	64.1	0	1	1
F / 63	11	58.7	1	-	1
M / 77	13	59.5	-	0	0
F / 68	13	51.3	0	1	1
M / 62	13	45.1	1	1	1
F / 65	15	62.3	0	0	1
F / 87	19	52.3	0	1	1
F / 65	22	61.3	0	1	1

Table 3: Overview of the individual's sex (M = male, F = female), age, sacral tissue thickness (TT_{load}), compression and dichotomized blood flow (0 = non-existing blood flow and 1 = existing blood flow) at approximately 1mm, 2mm and 8mm while loading.

There were no differences between the participants who had existing BF_{load} and those who had non-existing BF_{load} during measurements at a depth of maximum 1mm regarding MAP, TT_{unload} or sacral contact area (Table 3). Participants who had non-existing BF_{load} measured at a depth of approximately 2mm had less sacral contact area (p=0.009) and less TT_{load} (p=0.002) than those who had existing BF_{load} . Participants who had non-existing BF_{load} at a depth of approximately 8mm had less sacral contact area (p=0.028) than those who had existing BF_{load} . Comparisons with regard to age, BMI and compression showed no differences between individuals with existing BF_{load} and those with non-existing BF_{load} at any of the three depths (Table 4).



Existence of blood flow at different depths

Figure 4. Percentage of participants with existing blood flow at different depths for loaded tissue. At all depths (approximately < 1mm, 2mm and 8mm), the differences between unloaded and loaded tissue are significant (* p < 0.05 and *** p < 0.001).

There was a positive correlation between BMI and: $TT_{unload} r = 0.68$ (p=0.003), $TT_{load} r = 0.68$ (p=0.003) and sacral contact area r = 0.60 (p=0.011). There was also a positive correlation between TT_{load} and: $TT_{unload} r = 0.88$ (p<0.0005) and sacral contact area r = 0.58 (p=0.014). A positive correlation was found between the TT_{unload} and sacral contact area r = 0.50 (p=0.043). No correlation between compression or age and any of the variables, BMI, TT_{load} or TT_{unload} was detected.

Discussion

The main findings in this study were that skin and subcutaneous tissue in the sacral region in elderly individuals are compressed by approximately 60%, in line with others (25). The sacral region is a sensitive area, prone to pressure ulcer development (26). Strong forces are involved, 270mmHg (mean pressure) in the seat area in sitting healthy individuals (45),

Depth of measurements	TT _{unload} , mm	TT _{load} , mm	Compression,%	Sacral contact area,
				cm ²
<1mm (LDF)				
BF+ (n=2)	26±2	12 ± 1	51.9±9.6	171.0±13.7
BF- (n=14)	26 ±14	10 ± 6	61.5±12.4	189.0±79.2
Р	0.970	0.540	0.316	0.761
2mm (Green PPG)				
BF+ (n=5)	35 ± 14	16 ± 5	54.8±7.4	256.5±92.2
BF- (n=11)	22 ± 11	8 ± 4	62.9±13.4	159.4±39.7
Р	0.060	0.002	0.237	0.009
8mm (IR PPG)				
BF+ (n=11)	28±14	11 ± 6	57.5±13.1	211.5±79.4
BF- (n=6)	23±10	8 ± 3	65.3±7.8	137.6±12.7
Р	0.429	0.148	0.208	0.028

Table 4: Comparison between the two groups: those with existing (BF+) and those with non-existing (BF-) blood flow at different depths while loading with regard to unloaded tissue thickness (TT_{unload}), tissue thickness while loading (TT_{load}), compression and sacral contact area.

similar to the present study with at least 220mmHg in supine position. The skin and the subcutaneous tissue serve as an important protective cover in order to resist mechanical forces. The sacral tissue thickness was only about 1-3cm in the study, and the thickness is probably even less in patients (9). This study showed a relationship between BMI and tissue thickness, in accordance with other studies of total body fat (28, 30) as well as subcutaneous abdominal adipose tissue (8). Patients with pressure ulcer have lower BMI than do patients with no ulcer and are often malnourished (13). This might be explained by the present findings that individuals with non-existing BF_{load} had a smaller total contact area and TT_{load} than those who had existing BF_{load} at 2 and/or 8mm depth.

The influence of compression on human tissue is an object of interest in the biomechanical field concerning exploring deep tissue changes. This is due to a special kind of pressure ulcer, i.e. deep tissue injury (7). This ulcer is said to develop deep in the tissue and to start in the muscle tissue over a bony prominence. Studies with MR and finite element models in sitting human buttocks have shown that the different tissue layers are affected very differently by internal compression strains and stresses (24-25). The maximum compressive stress in the fat layer was located 1-3mm distally from the muscle-fat interface (24). This heterogeneity in local tissue strains and stresses could be an explanation for why the compression variable in the present study did not differentiate in any of the performed analysis, as the total compression of the tissue over the sacrum was measured instead of locally in the different tissue layers. Previous results using a computer model show that the load distribution over the buttocks in sitting humans depends on individual body shape (36), indicating that the individual's condition and character are of great importance.

Decreased/occluded blood flow during load was found in the superficial tissue layer in the majority of the individuals, but in deeper tissue layers as well in some cases (Table 2), and could be an important factor in pressure ulcer formation. These findings support the most established theory regarding the development of tissue damage, i.e. mechanically induced occlusion of the capillaries leading to tissue ischemia and oxygen deprivation. Further, the findings show that the system is able to discriminate between blood flow in different tissue layers. There seems to be a difference in sensitivity to interface pressure in the different tissue layers, whereby the blood flow deeper in the tissue is not occluded unless the blood flow in the superficial layer is: None of the participants had occluded blood flow deep in the tissue with simultaneous existing blood flow in the more superficial layers.

The interaction between blood perfusion and interface pressure is complex and affects individuals differently. Young, healthy people are less affected by loading (12) than are the old and/or disabled, who are more likely to have deteriorated skin blood flow (3-4). This study combined LDF and PPG, non-invasive and separately well evaluated methods, to measure tissue blood flow with the ability to observe the blood flow simultaneously at different depths in the tissue (2, 5, 48). Limitations can be identified and related to the design of the prototype probe: It was integrated into the test bench due to its stiffness and thickness, resulting in a test situation with very high interface pressure, and the pressure mapping system reached its maximum value. The pressure map showed low interface pressure in two individuals due to their body constitution, with the buttocks unloading the sacral area. These individuals were presumably exposed to much lower interface pressure at the point of measurement than the other individuals were, and they were the only ones with existing blood flow at the skin surface. Due to the design, there was no possibility to relate the blood flow values before and during load, leading to an uncertainty of the level of blood flow above calibration level, and the variable was therefore dichotomized into existing and non-existing blood flow. However, the endpoint non-existing blood flow is of high relevance in the field of pressure ulcer etiology.

Further development into a thin, flexible probe is ongoing and will make it possible to characterize humans with impaired blood flow while loading and to compare different groups with regard to tissue blood flow responses before, during and after tissue load.

Conclusions

Sacral tissue in elderly individuals is highly compressed by external load of at least 220mmHg. At all three examined tissue depths, blood flow was affected severely on several occasions during load. None of the participants in the study had occluded blood flow deep in the tissue with simultaneous existing blood flow in the more superficial layers; there thus seems to be a difference in response to external pressure in the different tissue layers.

However, there are some limitations of the probe prototype that will be handled in further development of the system.

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References

1. (2004). Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 363: 157-163.

2. Allen J. (2007). Photoplethysmography and its application in clinical physiological measurement. *Physiol Meas* 28: R1-39.

3. Bennett L, Kavner D, Lee BY, Trainor FS, and Lewis JM. (1981). Skin Blood Flow in Seated Geriatric Patients. *Arch Phys Med Rehabil* 62: 392-398.

4. Bennett L, Kavner D, Lee BY, Trainor FS, and Lewis JM. (1984). Skin stress and Bood Flow in Sitting Paraplegic Patients. *Arch Phys Med Rehabil* 65: 186-190.

5. Bergstrand S, Lindberg LG, Ek AC, Linden M, and Lindgren M. (2009). Blood flow measurements at different depths using photoplethysmography and laser Doppler techniques. *Skin Res Technol* 15: 139-147.

 Bircher A, de Boer EM, Agner T, Wahlberg JE, and Serup J. (1994). Guidelines for measurement of cutaneous blood flow by laser Doppler flowmetry. A report from the Standardization Group of the European Society of Contact Dermatitis. *Contact Dermatitis* 30: 65-72.

7. Black JM. (2005). Moving toward consensus on deep tissue injury and pressure ulcer staging. *Adv Skin Wound Care* 18: 415-416, 418, 420-411.

8. Bonora E, Micciolo R, Ghiatas AA, Lancaster JL, Alyassin A, Muggeo M, and DeFronzo RA. (1995). Is it possible to derive a reliable estimate of human visceral and subcutaneous abdominal adipose tissue from simple anthropometric measurements? *Metabolism* 44: 1617-1625.

9. Clark M, Rowland LB, Wood HA, and Crow RA. (1988). Measurement of tissue thickness over the sacrum of elderly hospital patients using B-mode ultrasound. 11: 200-202.

10. Daniel RK, Priest DL, and Wheatley DC. (1981). Etiologic Factors in Pressure Sores: An Experimental Model. *Arch Phys Med Rehabil* 62: 492-498.

11. Dinsdale SM. (1973). Decubitus ulcers in swine: Light and electron microscopy study of pathogenesis. *Arch Phys Med Rehabil* 54: 51-56.

12. Ek A-C, Gustavsson G, and Lewis DH. (1987). Skin blood flow in relation to external pressure and temperature in the supine position on a standard mattress. *Scandinavian Journal of Rehab Medicine* 19: 121-126.

13. Ek A-C, Unosson M, Larsson J, Von Schenck H, and Bjurulf P. (1991). The
development and healing of pressure sores related to the nutritional state. *Clinical Nutrition*10: 245-250.

14. Eriksson E. Etiology: microcirculatory effects of Pressure. In: *Pressure ulcers: principles and techniques of management*, edited by Constantian MB: Little Brown & Co., 1980, p. 7-14.

15. Fullerton A, Stucker M, Wilhelm KP, Wardell K, Anderson C, Fischer T, Nilsson GE, and Serup J. (2002). Guidelines for visualization of cutaneous blood flow by laser Doppler perfusion imaging. A report from the Standardization Group of the European Society of Contact Dermatitis based upon the HIRELADO European community project. *Contact Dermatitis* 46: 129-140.

16. Humeau A, Koitka A, Abraham P, Saumet JL, and L'Huillier JP. (2004). Spectral components of laser Doppler flowmetry signals recorded in healthy and type 1 diabetic subjects at rest and during a local and progressive cutaneous pressure application: scalogram analyses. *Phys Med Biol* 49: 3957-3970.

17. Jan YK, Brienza DM, Geyer MJ, and Karg P. (2008). Wavelet-based spectrum analysis of sacral skin blood flow response to alternating pressure. *Arch Phys Med Rehabil* 89: 137-145.

Jonsson B, Laurent C, Skau T, and Lindberg LG. (2005). A new probe for ankle
 systolic pressure measurement using photoplethysmography (PPG). *Ann Biomed Eng* 33: 232-239.

19. Laurent C, Jonsson B, Vegfors M, and Lindberg LG. (2005). Non-invasive measurement of systolic blood pressure on the arm utilising photoplethysmography: development of the methodology. *Med Biol Eng Comput* 43: 131-135.

20. Lindberg LG and Oberg PA. (1991). Photoplethysmography. Part 2. Influence of light source wavelength. *Med Biol Eng Comput* 29: 48-54.

21. Lindberg LG and Öberg PÅ. (1993). Optical properties of blood in motion. *Optical Engineering* 32: 253-257.

22. Linder-Ganz E, Engelberg S, Scheinowitz M, and Gefen A. (2006). Pressure-time cell death threshold for albino rat skeletal muscles as related to pressure sore biomechanics. *J Biomech* 39: 2725-2732.

23. Linder-Ganz E and Gefen A. (2004). Mechanical compression-induced pressure
sores in rat hindlimb: muscle stiffness, histology, and computational models. *J Appl Physiol*96: 2034-2049.

24. Linder-Ganz E, Shabshin N, Itzchak Y, and Gefen A. (2007). Assessment of mechanical conditions in sub-dermal tissues during sitting: a combined experimental-MRI and finite element approach. *J Biomech* 40: 1443-1454.

25. Linder-Ganz E, Shabshin N, Itzchak Y, Yizhar Z, Siev-Ner I, and Gefen A. (2008). Strains and stresses in sub-dermal tissues of the buttocks are greater in paraplegics than in healthy during sitting. *J Biomech* 41: 567-580.

26. Lindgren M, Unosson M, and Ek A-C. (2000). Pressure sore prevalence within a public health services area. *International Journal of Nursing Practice* 6: 333-337.

27. Lindholm C, Bergsten A, and Berglund E. (1999). Chronic wounds and nursing care. *Journal of Wound Care* 8: 5-10.

28. Ludescher B, Machann J, Eschweiler GW, Vanhofen S, Maenz C, Thamer C, Claussen CD, and Schick F. (2009). Correlation of fat distribution in whole body MRI with generally used anthropometric data. *Invest Radiol* 44: 712-719.

29. Mayrovitz HN and Smith J. (1998). Heel-skin microvascular blood perfusion responses to sustained pressure loading and unloading. *Microcirculation* 5: 227-233.

30. Mei Z, Grummer-Strawn LM, Pietrobelli A, Goulding A, Goran MI, and Dietz WH.
(2002). Validity of body mass index compared with other body-composition screening
indexes for the assessment of body fatness in children and adolescents. *Am J Clin Nutr* 75:
978-985.

31. Naslund J, Pettersson J, Lundeberg T, Linnarsson D, and Lindberg LG. (2006). Noninvasive continuous estimation of blood flow changes in human patellar bone. *Med Biol Eng Comput* 44: 501-509.

32. Nilsson GE, Salerud EG, Strömberg NOT, and Wårdell K. Laser Doppler perfusion Monitoring and Imaging. In: *Biomedical photonics handbook*, edited by Vo-Dinh IT. Boca Raton, Florida: CRC Press, 2003, p. 1-24. 33. Nilsson GE, Tenland T, and Öberg PÅ. (1980). Evaluation of a Laser Doppler Flowmeter for Measurement of Tissue Blood Flow. *IEEE Transactions on Biomedical Engineering* BME-27: 597-604.

34. Nilsson GE, Tenland T, and Öberg PÅ. (1980). A new instrument for continous measurement of tissue blood flow by light beating spectroscopy. *IEEE Transactions on Biomedical Engineering* 21: 12-19a.

35. Noble M, Voegeli D, and Clough GF. (2003). A comparison of cutaneous vascular responses to transient pressure loading in smokers and nonsmokers. *J Rehabil Res Dev* 40: 283-288.

36. Oomens CWJ, Bressers OFJT, Bosboom EMH, Bouten C, and Bader D, L. (2003). Can loaded interface characteristics influence strain distributions in muscle adjacent to bony prominences? *Computer Methods in Biomechanical Engineering* 6: 171-180.

37. Posnett J and Franks PJ. (2008). The burden of chronic wounds in the UK. *Nurs Times* 104: 44-45.

38. Sae-Sia W, Wipke-Tevis DD, and Williams DA. (2007). The effect of clinically relevant pressure duration on sacral skin blood flow and temperature in patients after acute spinal cord injury. *Arch Phys Med Rehabil* 88: 1673-1680.

39. Saldico R, Donfiro JC, Fisher SB, LeGrand EK, Dickey K, Carney JM, Schosser R, and Liang R. (1994). Histopathogy of Pressure Ulcers as a Result of Sequential Computer-Controlled Pressure Sessions in a Fuzzy Rat Model. *Advances in Wound Care* 7: 23-40.

40. Sandberg M, Larsson B, Lindberg LG, and Gerdle B. (2005). Different patterns of blood flow response in the trapezius muscle following needle stimulation (acupuncture) between healthy subjects and patients with fibromyalgia and work-related trapezius myalgia. *Eur J Pain* 9: 497-510.

41. Sandberg M, Zhang Q, Styf J, Gerdle B, and Lindberg L-G. (2005). Non-invasive monitoring of muscle blood perfusion by photopletysmography: evaluation of a new application. *Acta Physiol Scand* 183: 335-343.

42. Severens JL, Habraken JM, Duivenvoorden S, and Frederiks CM. (2002). The cost of illness of pressure ulcers in The Netherlands. *Adv Skin Wound Care* 15: 72-77.

43. Spilsbury K, Nelson A, Cullum N, Iglesias C, Nixon J, and Mason S. (2006). Pressure ulcers and their treatment and effects on quality of life: hospital inpatient perspecives. *Journal of Advanced Nursing* 57: 494-504.

44. Stekelenburg A, Oomens CW, Strijkers GJ, Nicolay K, and Bader DL. (2006). Compression-induced deep tissue injury examined with magnetic resonance imaging and histology. *J Appl Physiol* 100: 1946-1954.

45. Thorfinn J, Sjöberg F, and Lidman D. (2002). Sitting pressure and perfusion of buttock skin in paraplegic and tetraplegic patients, and in healthy subjects: A comparative study. *Scand J Plast Reconstr Surg Hand Surg* 36: 279-283.

46. Wardell K, Jakobsson A, and Nilsson GE. (1993). Laser Doppler perfusion imaging by dynamic light scattering. *IEEE Trans Biomed Eng* 40: 309-316.

47. Witkowski JA and Parish LC. (1982). Histopathology of the decubitus ulcer. *J Am Acad Dermatol* 6: 1014-1021.

48. Wright CI, Kroner CI, and Draijer R. (2006). Non-invasive methods and stimuli for evaluating the skin's microcirculation. *J Pharmacol Toxicol Methods* 54: 1-25.

49. Zhang Q, Lindberg L-G, Kadefors R, and Styf J. (2001). A non-invasive measure of changes in blood flow in the human anterior tibial muscle. *Eur J Appl Physiol* 84: 448-452.