NEW SENSOR DESIGN MADE TO DISCRIMINATE BETWEEN TISSUE BLOOD FLOW AT DIFFERENT TISSUE DEPTHS AT THE SACRAL AREA

Annika Jonsson

Department of Computer Science and Electronics, Mälardalen University, Västerås

ABSTRACT

Evaluation of antidecubitus mattresses is to a large extent based on interface pressure and pressure distribution measurements. These measurements do not give an answer to the effect on the tissue microcirculation cause by the external loading. A better and more direct parameter on the properties' of the mattress would be to measure blood flow in the tissue under loading. This paper presents a new optical sensor probe for blood flow measurement that combines the two methods laser Doppler and photoplethysmography, PPG. With use of two methods, multiple light wavelengths and combinations of the distances between light sources and photodetector in the PPG, the blood flow at several different tissue depths can be assessed. However, interference problems between the two methods occurred with the present sensor design. The preliminary result presented in this paper, shows differences in blood flow response at the different measurement depths.

INTRODUCTION

Pressure sores occurs in tissue that has experienced prolonged ischemia due to external forces (EK, 1987; KOSIAK, 1959) and are a major problem in today's medical care. Persons with pressure sores describe both physiological and psychological suffering (GIBSON, 2002; LANGEMO et al., 2000). In addition to this, the cost for prevention and treatment of pressure sores is extensive (LINDHOLM et al., 1999; SEVERENS et al., 2002). For prevention and treatment it is common to use antidecubitus mattresses to better distribute the pressure over the tissue or periodically relive the tissue from loading. A large number of different types of mattresses and manufactures exist on the market. The problem is that the efficiency of these mattresses is not always evaluated. Most evaluations of mattresses performed are based on pressure and pressure distribution measurements. However, since the skin is not a frictionless surface and the external force is not always applied perpendicular to the skin, the loading of the tissue is a combination of pressure and shear stress. Therefore it is incomplete to only measure the external pressure applied to the tissue, when the loading also includes shear stress. Measuring the tissue blood flow would render the tissue's response to loading and a thus be a more direct indication on the mattresses properties of distributing or relieving of pressure (JONSSON et al., 2005).

The etiology behind pressure sores is not fully understood and there are two theories about the development of pressure sores. One theory implies that the sore starts superficially and develops downwards, called top-to-bottom, and the other states that the sore starts next to the bone prominence and develop upwards, bottom-to-top (BRIDEL, 1993; DANIEL et al., 1981; SALCIDO et al., 1994; WITKOWSKI and PARISH, 1982). Due to the two theories about pressure sore development it is not clear where it is of most interest to measure the blood flow when evaluating the efficiency of antidecubitus mattresses.

The aim of this study was to develop a sensor with the possibility to discriminate between blood flow at different tissue depths under compression of the tissue at the sacral area. The approach has been to use two different optical methods for assessment of the skin blood flow and to see at which tissue depth or depths, the blood flow first and primarily is occluded. Blood flow measurements in tissue under loading can help to understand the etiology behind and the development of pressure sores and also improve the evaluation of antidecubitus mattresses.

MATERIAL AND METHODS

Light sent into the skin is scattered, absorbed, and reflected by the static structures in the tissue and the red blood cells. How light interacts optically with the skin and blood is complex and depends on several factors (ANDERSON and PARRISH, 1981). The penetration of light into the tissue increases with increasing wavelength (ANDERSON and PARRISH, 1981; GILTVEDT and SURA, 1984; LINDBERG and ÖBERG, 1991). The optical methods for blood flow measurements use different light wavelengths and, different distance between light source and photodetector to achieve desired measurement depths (FRIDOLIN and LINDBERG, 2000; JAKOBSSON and NILSSON, 1993). The measurement depth increases with the distance between light source and photodetector. Laser Doppler flowmetry and photoplethysmography, PPG, are both established and noninvasive optical methods for measuring changes in skin blood flow. Through usage of both these methods, the tissue blood flow in different tissue layers can be measured; laser Doppler flowmetry to study the more superficial blood flow (HOLLOWAY and WATKINS, 1977; STERN, 1975) and PPG to assess the blood flow deeper in the soft tissue and also the muscle blood flow (ZHANG et al., 2004; ZHANG et al., 2001).

Laser Doppler flowmetry
With laser Doppler flowmetry the superficial capillary flow is assessed with the use of monochromatic light (HOLLOWAY and WATKINS, 1977; NILSSON et al., 1980; STERN, 1975). The measurement principle is based on the Doppler shift and with the broadening of the frequency spectra an estimation of the blood flow in the tissue can be made. The perfusion value is calculated from the frequency broadening and is defined as the product of average velocity of the red blood cells and the concentration of moving blood cells in the illuminated tissue volume. Laser Doppler flowmeters are available with different wavelengths and together with different geometry of the sending and receiving optical fibers, different penetration depths can be assessed.

Photoplethysmography
PPG was introduced in the 1930's by Hertzman and Spealman, and Mattheus and Hauss (HERTZMAN and SPEALMAN, 1937; MATTHES and HAUSS, 1938). They described that changes in the amount of blood could be assessed with variations in the light transmission of a finger or an ear lobe. The principle of PPG is that light sent into the tissue is attenuated due to reflection, scattering and absorption of light and that variations in the attenuation occur due to the amount of blood in the tissue under observation. Blood has a light absorption coefficient that is higher than that of the surrounding tissue, thus an increase in the amount of blood in the measured tissue volume causes a corresponding decrease in the intensity of light detected (ANDERSON and PARRISH, 1981; MATTHES and HAUSS, 1938).

To mimic the pressure pulse and simplify the interpretation, the PPG signal is always presented inverted. During systole, the blood volume in the tissue increases and more light is absorbed.

Therefore less light is detected by the photodetector and a lower voltage is presented – corresponding to an increased signal due to the inversion, Figure 1. During diastole the blood volume decreases, more light is detected and the signal increases, presented as a lowering in the inverted PPG signal. The light attenuation, and thus the signal, is also effected from the orientation by the erythrocytes (FUJII et al., 1999; LINDBERG and ÖBERG, 1993). The second top in the signal in figure 1, is called the incisura and is caused by the elastic recoil of the aorta and other large arteries and follows systole.
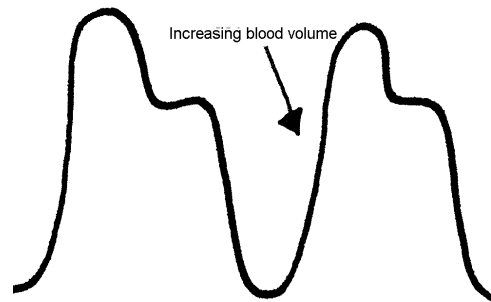

Figure1. The inverted pulsative PPG signal.

The PPG signal can be divided into two parts, a DC component and an AC component. The amplitude of the DC level is related to the attenuation due to the static structures in the tissue and corresponds to the blood volume (HERTZMAN and SPEALMAN, 1937). The AC component's pulsative pattern is directly correlated to flow rate (D'AGROSA and HERTZMAN, 1967; ZWEIFLER et al., 1967).

There are two types of photoplethysmography; transmission mode and reflection mode, referring to how the light is exiting the tissue and is detected. In transmission mode, also called "transillumination photoplethysmography", the light source and detector are on opposite side of the extremity. In reflection mode or "absorption photoplethysmography", the light source and detector are placed adjacent to each other on the skin.

Several measurement depths can be achieved with PPG using a multiple of wavelengths and combinations of different distances between light source and photodetector. To render the superficial blood flow, PPG with green light can be used and to assess the deeper flow, IR light is suggested (HALES et al., 1993).

Optical probe

Since it is uncertain at what tissue level the pressure sores start to develop, not one implicit measurement depth can be specified for etiology studies or for evaluation of antidecubitus mattresses. With a combination of laser Doppler flowmeter and PPG it might be possible to measure the superficial and deeper skin blood flow, and also the muscle blood flow. To be able to assess the tissue perfusion at different tissue depths at the sacral area, a custom-design optical probe with a reflection mode PPG and laser Doppler instrumentation, was designed and constructed. The PPG instrument used had three channels. The first channel constituted of two green light emitting diodes (LEDs) (CR 10 SG, 560 nm) symmetrically placed around a photodetector (BPW348 Photodiode, Farnell) at a distance of 5 mm for reflecting the superficial blood flow, figure 2. For reflecting the deeper skin and the muscle blood flow, the other two channels were constituted of four infrared (IR) LEDs (810-05AU, 810 nm), placed at distances of 10 mm and 25 mm, respectively, at each side of the photodetector. With the combinations of light wavelengths and probe geometry, we assume measure depths of approximately 2 mm with the green LEDs and approximately 8 mm and 20 mm, respectively, with the IR light. The lights from the LEDs were pulsed at 60 Hz so the same photodetector could be used to sample the three pairs of LEDs. This also minimized excessive heating of the tissue under the probe.

Inserted in the same probe was one optic fiber connected to a Laser Doppler flowmeter (PeriFlux Pf2b, 632.8 nm, Perimed, Järfälla, Sweden) with a wavelength of 632.8 nm. The optical components were embedded in silicon and the optical probe was inserted in a wooden plate. The wooden plate, 10 cm x 10 cm, was constructed so that it could be inserted in the measurement bunk. With this construction blood flow in compressed tissue could be assessed.
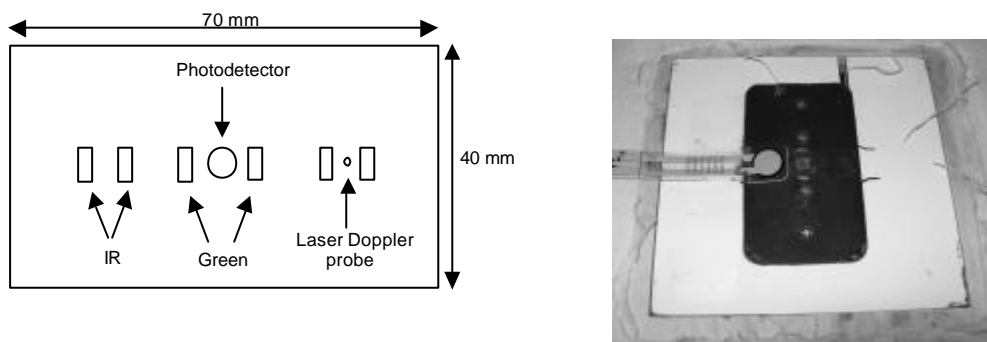

Figure 2. Design of the optical probe that combines the two methods: PPG and laser Doppler. The photo shows the optical probe and the pressure sensor inserted in the bunk.

To be able to relate the blood flow signal to the pressure applied to the tissue, the interface pressure was measured next to the probe using a flexible pressure sensor (Flexscan OEM 400N, CA Mätsystem, Täby, Sweden). The pressure signal, the PPG signals (AC and DC), and the perfusion signal from the laser Doppler flowmeter were A/D converted and recorded (DAQ-card 6062E, National Instruments, Sweden) at a sampling frequency of 60 Hz using an in-house developed LabView program, (LabView, version 6.1, National instrument, Sweden).

With the laser Doppler probe inserted in-between the two IR LEDs, backscattered IR light from the tissue was detected by the laser Doppler flowmeter. The intensity of the light detected by the laser Doppler flowmeter, when the IR LEDs were on, was so high that the instrument presented a false high calculation of the perfusion or in some cases came out of range, Figure

8. This problem was solved through switching the IR LEDs on and off in sequences of 30 seconds so the laser Doppler flowmeter could present a correct perfusion value when the IR LEDs were switched off. With this solution, the green PPG could record the superficial blood flow continuously, and sequential measurements with the laser Doppler flowmeter and IR PPG were performed.

The signals recorded by the PPG and the laser Doppler flowmeter from each individual, were individually analyzed in respect to the relative change in blood flow during the loading sequences. With the use of the relative change in blood flow signals, also comparison between the signal from the laser Doppler flowmeter and the PPG can be performed.

Measurement procedure

In the first preliminary measurements performed with the optical sensor probe, four healthy female test subjects were included. The test subjects rested in prone position on a hard bunk for 15 minutes before blood pressure, pulse, and skin and body temperature were measured, Figure 3.
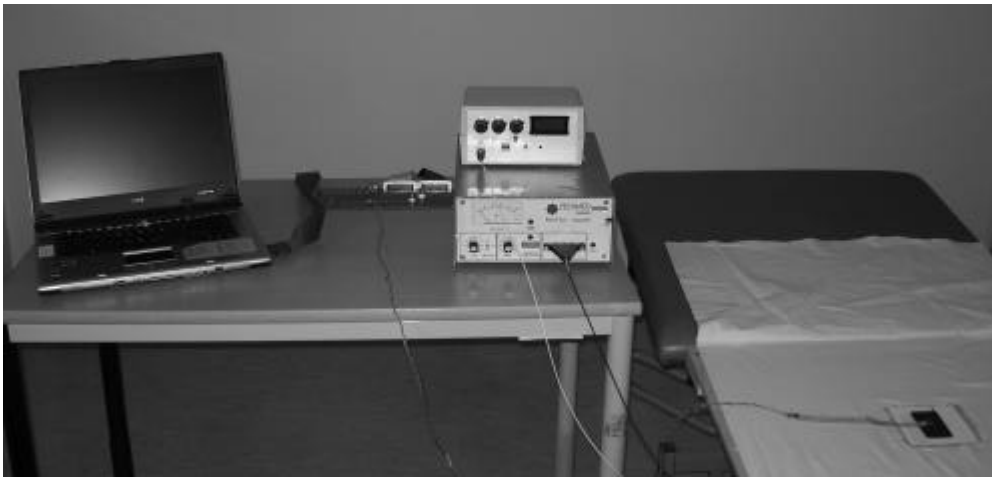

Figure 3. Instrument and measurement bunk with inserted optical probe.

To assess the effect on the blood flow during external loading of the tissue, the individuals were placed in supine position and weights were placed at the sacral area to compress the tissue, Figure 4. First a baseline measurement of 5 minutes without loading was performed, followed by 5 minutes of loading, first with 4 kg and then with 7 kg. Ten minutes of unloading for tissue recovery was inserted in-between the two loading sequences and after the unloading of 7 kg, the blood flow was recorded for 5 minutes to assess the reactive hyperaemia. The total time for the procedure was about one hour.

Figure 4. Loading of the tissue at sacrum.

The loading of 4 kg and 7 kg represent pressure application of approximately 30 mmHg and 50 mmHg, respectively. The loading application did involve both pressure, and shear stress since the weight was not placed parallel to the bunk due to the shape of the soft tissue over sacrum. The loads applied were cylindrical and placed on the rigid wooden backside of the probe, 10 cm x 10 cm. An advantage with the larger application area of the loading is that the pressure on the tissue becomes more evenly distributed and the pressure gradients in the sacral area were minimized. The loading situation used in this study mimics the loading situation of the sacral area when the subject is laid in bed with the head end of the bed is elevated. This position involves loading of the sacrum and shear stress that stretch the skin at the sacral area towards the lower back.

RESULTS

Technical problems

In addition to the problem with the IR light detected by the laser Doppler flowmeter which was solved through switching off the IR LEDs every 30 seconds. During the preliminary measurements another interference problem was observed. A light contribution from the laser was given to all three channels of the PPG and was easily observed in the signals recorded from the IR channels when the IR LEDs were switched off, Figure 7. The laser light contribution consisted of an additional false pulsative PPG. This results in that it is unclear from which tissue depths the signals from the PPG instrument originate, since the signals are a mixture of light with different penetrating wavelengths.

The first 30 seconds of every new sequence of loading or unloading, started with the IR LEDs switched on and recording of all three PPG channels. Under these 30 seconds analyze of the perfusion signal from the laser Doppler flowmeter was no possible.

Measurement results

In this preliminary analyze of the PPG signals, only the pulsative PPG signals from the three channels have been analyzed. The top-to-top value of the pulsative PPG signal is interpreted as the blood flow. In the figures 5-8, the blood flow response during loading of the tissue can be seen between the time of 5-10 minutes (4 kg) and between the time of 20-25 minutes (7 kg).

The result shows large differences in blood flow response between the four individuals and also large difference in the blood flow response to the external loading between the different measurement depths. In three of the individuals a decreased blood flow was seen during loading, in one or several of the three pulsative PPG signals originating from different measurements depths. In one of the individual an increased blood flow was recorded from all three channels and thereby, from all three measurements depths. In the three individuals who experienced an impaired blood flow during loading, the signal from the green PPG (superficial blood flow) was decreased in all individuals, Figure 5. In two of the individuals, also the signal from the deeper penetrating IR channel decreased. Whereas the signal from the less penetrating IR channel increased in all four individuals, indicating increased blood flow at this tissue depth. The "spikes" seen in figure 5 during the loading sequences are due to the switching of the IR LEDs.
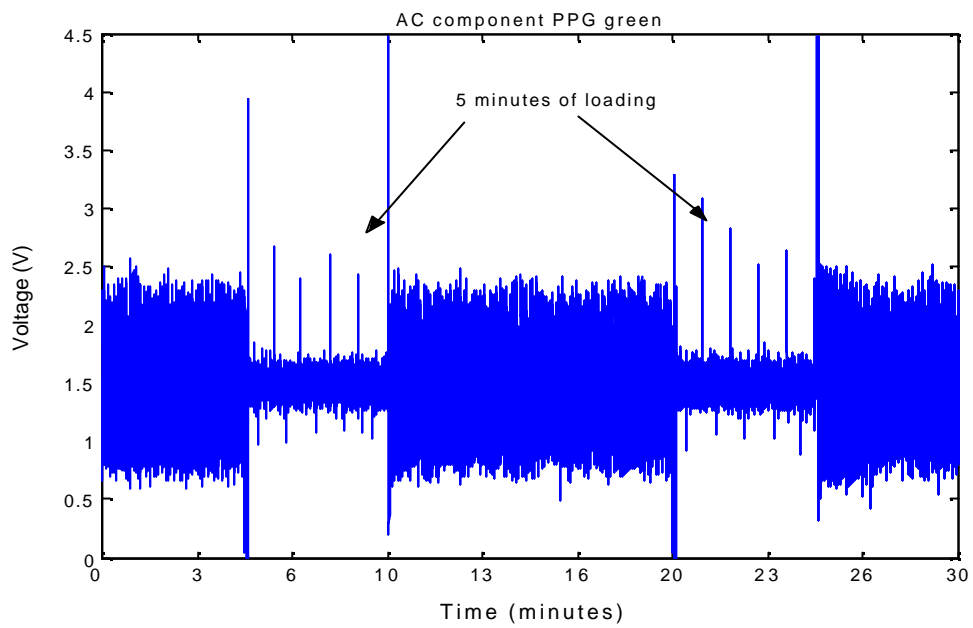
Figure 5. The green PPG signal recorded in one of the individuals representing a decrease in blood flow during external loading with 4 kg and 7 kg, respectively.

A compensation with an increased blood flow during external loading could be seen in all individuals, Figure 6 and Figure 7. As mentioned, in one of the individuals this increased blood flow was recorded from all measurement depths. For the other individuals, this compensation could be seen in one or two of the three recorded PPG signals.
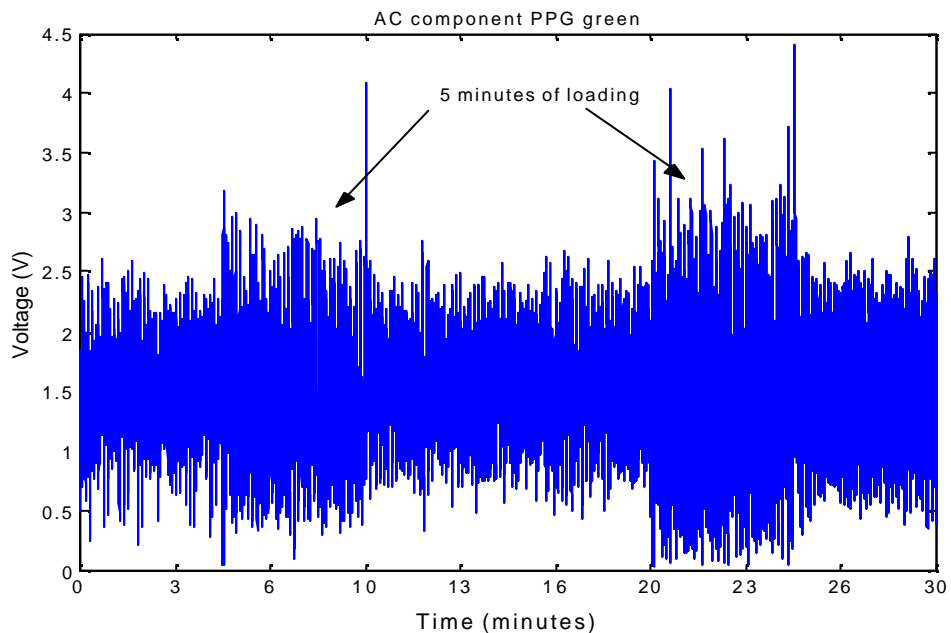

Figure 6. Increase in blood flow during external loading in one of the individuals, assessed by the green PPG signal.

When studying the signals from the IR PPG, the IR LEDs are switched on during the first time sequence and therefore the signal shall be studied during these sequences. The constant light contribution from the laser, detected by the photodetector in the PPG instrument, can be seen at some occasions when the IR LEDs are switched off, Figure 7.
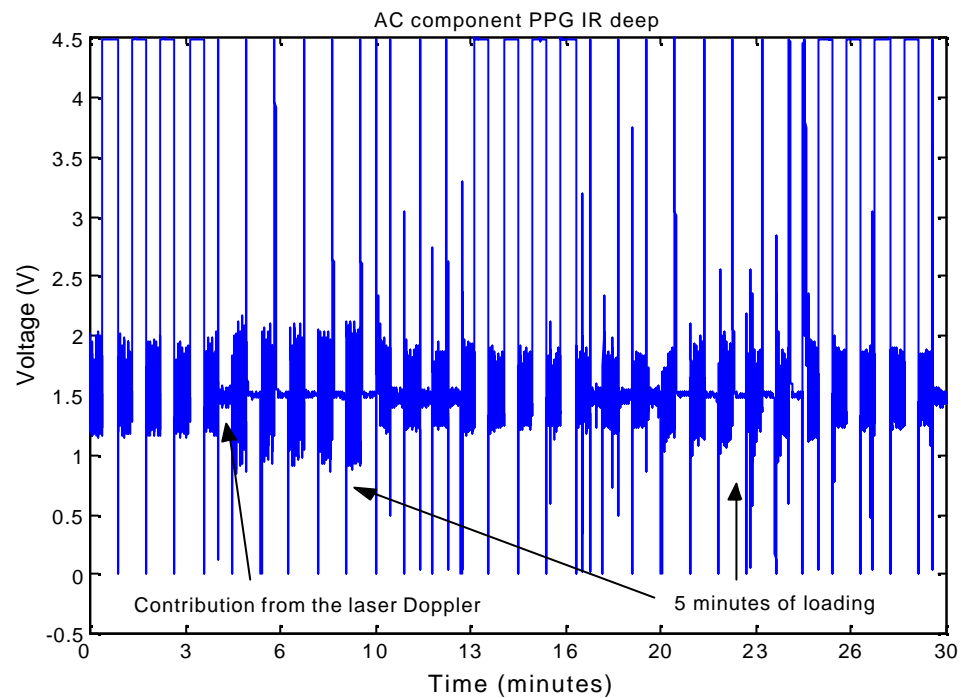

Figure 7. Compensation with increased blood flow during external loading recorded with the signal from the channel of IR LEDs that penetrate deeper into the tissue. In the figure, the contribution from the laser can be recognized when the IR LEDs are switched off.

The laser Doppler signal from three of the individuals could be analyzed and the blood flow signal show the same pattern as with the pulsative PPG signal; one of the individuals experienced a decreased superficial skin blood flow followed by a clear reactive hyperaemia. The other two individuals responded to the external loading with of an increased blood flow, Figure 8. Probably due to poor contact between the optical fiber and the tissue in the fourth individuals, the signal could not be analyzed.

The contribution from the IR LEDs detected by the laser Doppler flowmeter, can be seen when the IR LEDs were switched on and the IR light contributes to the calculation of the perfusion value. In figure 8 the lower perfusion signal level, under the line, is recoded with the IR LEDs switched off and corresponds to the correct perfusion signal.
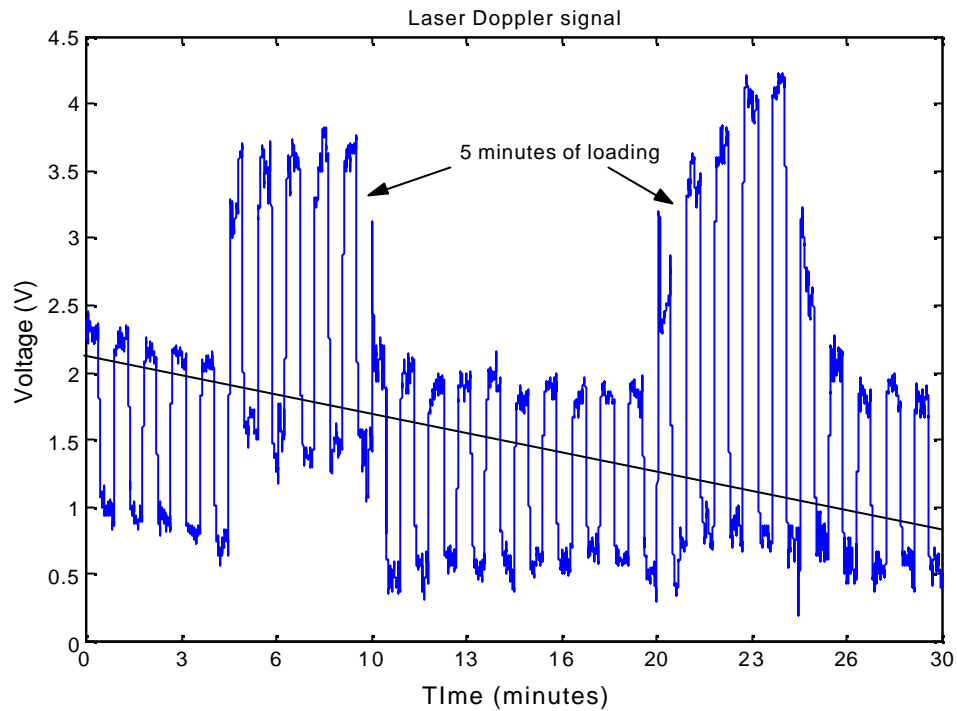
Figure 8. The true laser Doppler signal was recorded when the IR LEDs were switched off and can be seen under the line.

A summery of the four individuals' blood flow response at the four measurement depths is seen in Table 1. The response for each individual was the same with loading of the 4kg weigh and the 7 kg weigh. Occurrence of reactive hyperaemia in the tissue when unloading is also noted in the table.

Table 1. Blood flow response in the different tissue depths during the measurement procedure.

	Person 1	Person 2	Person 3	Person 4
PPG green	Decrease	Decrease + reactive hyperaemia	Increase + reactive hyperaemia	Decrease + reactive hyperaemia
PPG IR deep	Increase	Increase	Increase	Increase + reactive hyperaemia
PPG IR deeper	Decrease	Increases	Increase	Decrease + reactive hyperaemia
Laser Doppler flowmeter	Increase	Decrease + reactive hyperaemia	Increase + reactive hyperaemia	-

DISCUSSION

The blood flow response at different tissue depths can be obtained with this new optical sensor that combines the two methods laser Doppler flowmetry and PPG. The preliminary result from this study indicates that the tissue blood flow at the sacral area in healthy individuals can be negatively affected with application of as low pressure as 30 mmHg and 50 mmHg. Earlier studies performed have reported that 120 mmHg was needed to impair the blood flow at the ischial tuberosities in seated healthy persons (BENNETT et al., 1981). The corresponding value for some of the geriatric hospitalized patients included in the same study was 20 mmHg. External pressure in the range of 11-50 mmHg has been shown to impair the blood flow in geriatric hospitalized persons with partial of total hemiplegic (EK et al., 1987).

Increase of the blood flow in the tissue exposed to external loading was also seen in all four individuals included in the study. This is a phenomena described by other researchers in earlier performed studies (FRANTZ and XAKELLIS, 1989; FRANTZ et al., 1993; HERRMAN et al., 1999; PATEL et al., 1999; XAKELLIS et al., 1993). The results obtained are even more interesting, since they shown that the blood flow at different tissue depths, might react differently to the same external loading in the same individual. The two methods, laser Doppler flowmetry and PPG and also the use of the different measurement depths of the three PPG channels, seem to complement each other when studying the effect from external loading.

However, two interference problems occurred and simultaneous measurement of the blood flows in all four intended tissue depths could not be performed with the present instrumentation and design of the optical probe. Since interference between the two measurement methods was recognized with this design of the probe, no extensive analyze regarding the external pressure effect on blood flow at different tissue depths has been performed. A drawback with the switching of the IR LEDs is that the first 30 seconds at loading or unloading is not assessed by the laser Doppler flowmeter.

The next step in the development will be to solve the interference problems with optical filters and to move the laser Doppler fiber further from the IR LEDs. This will allow simultaneous measurements without interference between the two methods.

In future studies with the optical sensor, an extensive number of subjects will be included for rendering of possible differences in the blood flow response in the sacral area between young and elderly healthy. In these studies also monitoring of the tissue thickness over sacrum in connection to the blood flow measurements is desired. This can be made through a 25 mm thick Plexiglas inserted to the bunk at the same place as the optical probe. To get an idea about the thickness of compressed soft tissue, experimental testing with ultrasound (Philips HDI5000, 12MHz, a linear probe L12-5) was performed in one subject, Figure 9.
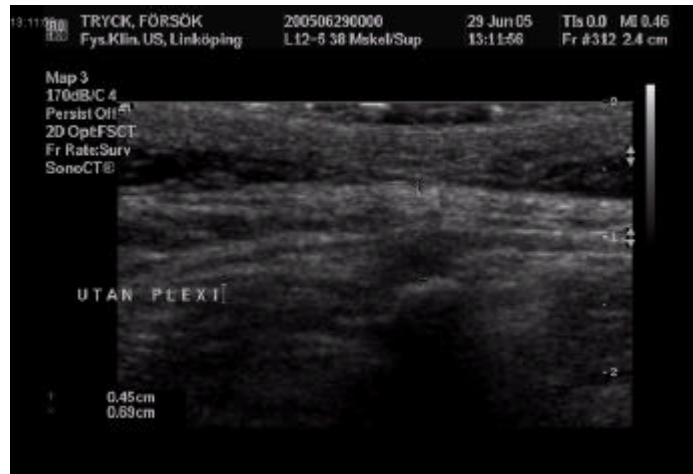
Figure 9. Ultrasound picture of the compression of the soft tissue.

Today, laser Doppler flowmeters with a wavelength of 780 nm are available. With this wavelength the penetration depth of the light is increase compared to 632.8 nm (ANDERSON and PARRISH, 1981). It would be of interest to compare measurements performed with lasers with 780 nm and 632.8 nm, and also investigate if the 780 nm laser Doppler flowmeter do render the same tissue depth as the green PPG.

This new developed optical sensor is believed to be very useful in studies regarding the pressure sore etiology and in the long run in evaluation of antidecubitus mattresses. To perform a good evaluation also the mattress's thermal properties and pressure distributing or pressure relieving ability should be assessed. The interface pressure measurement is with advantage performed with a pressure sensitive mat.

When to finally develop a measurement system for evaluation of antidecubitus mattresses, there are many aspects that need to be regarded for performance of good evaluations. The measurement systems used must fulfill the criteria regarding flexibility, and smallness since it is of very high importance that the measurement system do not affect or change the mattress pressure distribution or pressure relieving ability. It is also important to regard that the measurement system does not solely affect the mattress's properties but also the blood flow. The advantages with our blood flow sensor is that it is small and flexible and the LEDs are pulsed to minimize the heating that occurs from the light illumination of the tissue.

REFERENCES

ANDERSON, R. R. and PARRISH, J. A. (1981): 'The optics of human skin', *J. Invest. Dermatol.*, 77, pp. 13-19

BENNETT, L., KAVNER, D., LEE, B. Y., TRAINOR, F. S. and LEWIS, J. M. (1981): 'Skin blood flow in seated geriatric patients', *Arch. Phys. Med. Rehabil.*, 62, pp. 392-398

BRIDEL, J. (1993): 'The aetiology of pressure sores', *J. Wound Care*, 2, pp. 230-238

D'AGROSA, L. S. and HERTZMAN, A. B. (1967): 'Opacity pulse of individual minute arteries', *Journal of Applied Physiology*, 23, pp. 613-620

DANIEL, R. K., PRIEST, D. L. and WHEATLEY, D. C. (1981): 'Etiologic factors in pressure sores: An experimental model', *Arch. Phys. Med. Rehabil.*, 62, pp. 492-498

EK, A.-C. (1987): 'Prevention, treatment and healing of pressure sores in long-term care patients', *Scand. J. Caring Sci.*, 1, pp. 7-13

EK, A.-C., GUSTAVSSON, G. and LEWIS, D. H. (1987): 'Skin blood flow in relation to external pressure and temperature in the supine position on a standard hospital mattress', *Scand. J. Rehabil. Med.*, 19, pp. 121-126

FRANTZ, R. and XAKELLIS, G. C. (1989): 'Characteristics of skin blood flow over the trochanter under constant, prolonged pressure', *Am. Journal of Phys. Med. Rehabil.*, 68, pp. 272-276

FRANTZ, R., XAKELLIS, G. C. and ARTEAGA, M. (1993): 'The effects of prolonged pressure on skin blood flow in elderly patients at risk for pressure ulcers', *Decubitus*, 6, pp. 16-20

FRIDOLIN, I. and LINDBERG, L.-G. (2000): 'Optical non-invasive technique for vessel imaging: I. Experimental results', *Phys. Med. Biol.*, 45, pp. 3765-3778

FUJII, M., NAKAJIMA, K., SAKAMOTO, K. and KANAI, H. (1999): 'Orientation and deformation of erythrocytes in flowing blood', *Annals New York Academy of Sciences*, 873, pp. 245-261

GIBSON, L. (2002): 'Perceptions of pressure ulcers among young men with a spinal injury', *Br. J. Community Nurs.*, 7, pp. 451-60

GILTVEDT, J. and SURA, A. (1984): 'Pulsed multifrequency photoplethysmograph', *Med. Biol. Eng. Comput.*, 22, pp. 212-215

HALES, J. R. S., ROBERTS, R. G. D., WESTERMAN, R. A., STEPHENS, F. R. N. and FAWCETT, A. A. (1993): 'Evidence for skin microvascular compartmentalization by laser-Doppler and photoplethysmographic techniques', *Int J Microcirc: Clin Exp*, 12, pp. 99-104

HERRMAN, E. C., KNAPP, C. F., DONOFRIO, J. C. and SALCIDO, R. (1999): 'Skin perfusion responses to surface pressure-induced ischemia: Implication for the developing pressure ulcer', *J. Rehabil. Res. Dev.*, 36,

HERTZMAN, A. B. and SPEALMAN, C. R. (1937): 'Observations on the finger voulme pulse recorded photo-electrically', *Am. J. Physiol.*, 119, pp. 334-335

HOLLOWAY, G. A. and WATKINS, D. W. (1977): 'Laser Doppler measurement of cutaneous blood flow', *J Invest Dermatol*, 69, pp. 306-309

JAKOBSSON, A. and NILSSON, G. E. (1993): 'Prediction of sampling depth and photon pathlength in laser Doppler flowmetry', *Med. Biol. Eng. Comput.*, 31, pp. 301-307

JONSSON, A., LINDÉN, M., LINDGREN, M., MALMQVIST, L.-Å. and BÄCKLUND, Y. (2005): 'Evaluation of antidecubitus mattresses', *Med. Biol. Eng. Comput.*, 43, pp. 541-547

KOSIAK, M. (1959): 'Etiology and pathology of ischemic ulcers', *Arch. Phys. Med. Rehabil.*, pp. 62-69

LANGEMO, D. K., MELLAND, H., HANSON, D., OLSON, B. and HUNTER, S. (2000): 'The lived experience of having a pressure ulcer: A qualitative analysis', *Adv. Skin Wound Care*, 13, pp. 225-235

LINDBERG, L.-G. and ÖBERG, P. Å. (1991): 'Photoplethysmography Part 2. Influence of light source wavelength', *Med. Biol. Eng. Comput.*, 29, pp. 48-54

LINDBERG, L.-G. and ÖBERG, P. Å. (1993): 'Optical properties of blood in motion', *Optical Engineering*, 32, pp. 253-257

LINDHOLM, C., BERGSTEN, A. and BERGLUND, E. (1999): 'Chronic wounds and nursing care', *J. Wound Care*, 8, pp. 5-10

MATTHES, K. and HAUSS, W. (1938): 'Lichtelektrische plethysmogramme', *Klinische Wochenschrift*, 17, pp. 1211-1213

NILSSON, G. E., TENLAND, T. and ÖBERG, P. Å. (1980): 'A new instrument for continuous measurement of tissue blood flow by light beating spectroscopy', *IEEE Trans. Biomed. Eng.*, BME-27, pp. 12-19

PATEL, S., KNAPP, C. F., DONOFRIO, J. C. and SALCIDO, R. (1999): 'Temperature effects on surface pressure-induced changes in rat skin perfusion: Implications in pressure ulcer development', *J. Rehabil. Res. Dev.*, 36, pp. 189-201

SALCIDO, R., DONOFRIO, J. C., FISHER, S. B., LEGRAND, E. K., DICKEY, K., CARNEY, J. M., SCHOSSER, R. and LIANG, R. (1994): 'Histopathology of pressure ulcers as a result of sequential computer-controlled pressure sessions in a fuzzy rat model', *Advances in Wound Care*, 7, pp. 23-40

SEVERENS, J. L., HABRAKEN, J. M., DUIVENVOORDEN, S. and FREDERIKS, C. M. A. (2002): 'The cost of illness of pressure ulcers in the Netherlands', *Advances in Skin & Wound Care*, 15, pp. 72-77

STERN, M. D. (1975): 'In vivo evaluation of microcirculation by coherent light scattering', *Nature*, 254, pp. 56-58

WITKOWSKI, J. A. and PARISH, L. C. (1982): 'Histopathology of the decubitus ulcer', *J. Am. Acad. Dermatol.*, 6, pp. 1014-1021

XAKELLIS, G. C., FRANTZ, R. A., ARTEAGA, M. and MELETIOU, S. (1993): 'Dermal blood flow response to constant pressure in healthy older and younger subjects', *J. Gerontol.*, 48, pp. M6-M9

ZHANG, Q., ANDERSSON, G., LINDBERG, L. G. and STYF, J. (2004): 'Muscle blood flow in response to concentric muscular activity vs. passive venous compression', *Acta. Physiol. Scand.*, 180, pp. 57-62

ZHANG, Q., LINDBERG, L., 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*, pp. 448-452

ZWEIFLER, A. J., CUSHING, G. and CONWAY, J. (1967): 'The relationship between pulse volume and blood flow in the finger', *Angiology*, 18, pp. 591-598