INTRODUCTION

Pressure ulcers (PUs) are defined as “a localised injury to skin and/or underlying tissue, usually over a bony prominence, as a result of prolonged mechanical loading in the form of pressure, or pressure in combination with shear”.¹ PUs represent a major burden to populations worldwide and have been attributed with the highest disability index in comparison with other dermatological conditions.² Despite increased awareness and interventions to improve the effectiveness of preventative strategies, the incidence in both the acute and community settings has remained unacceptably high, contributing to an estimated chronic wound care burden of £5 billion p.a. in the UK.³

An evaluation of dermal microcirculatory occlusion under repeated mechanical loads: Implication of lymphatic impairment in pressure ulcers

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Abstract

Objective: Pressure ulcers are caused by prolonged mechanical loads deforming the underlying soft tissues. However, the mechanical loads for microcirculatory occlusion are unknown. The present study was designed to characterize the simultaneous response of microvascular and lymphatic structures under repeated mechanical loading.

Methods: The effects of two distinct loading/unloading cycles involving (a) incremental pressures 30, 60, and 90 mmHg and (b) three repeated cycles of 30 mmHg were evaluated on a cohort of able-bodied volunteers. Microvascular response involved the monitoring of transcutaneous gas tensions, while dermal lymphatic activity was estimated from near-infrared imaging. Responses were compared during each load and recovery cycle.

Results: Changes in microvascular response were dependent on the load magnitudes, with 30 mmHg resulting in a reduction in oxygen tension only, while 90 mmHg affected both oxygen and carbon dioxide values in most cases (54%). By contrast, lymphatics revealed near total occlusion at 30 mmHg. Although there were intersubject differences, temporal trends consistently revealed partial or full impairment under load, with recovery during off-loading.

Conclusions: The pressure required to cause microcirculatory occlusion differed between individuals, with lymphatic impairment occurring at a lower pressure to that of microvascular vessels. This highlights the need for personalized care strategies and regular off-loading of vulnerable tissues.
The sustained external pressure and shear forces experienced by immobile individuals in the lying and sitting postures can result in internal tissue deformations, causing two major damage mechanisms. First, ischemic damage from the occlusion of blood and lymph vessels, which occurs at relatively low internal tissue strains. The resulting deficit of vital nutrients and accumulation of toxic metabolites lead to tissue damage, a process that can take several hours to develop. Alternatively, direct cell damage resulting from high internal strains can occur within tens of minutes. Seminal research in the field identified an association between tissue damage and both the magnitude and duration of tissue deformations, which reflects that tissue damage is possible at high deformations for short periods of loading and at lower pressures applied for prolonged periods. This relationship inevitably depends on the health status of the individual and their respective tissue tolerance, which is influenced by age, comorbidities, and nutritional status.

To date, an international team of bioengineers have investigated the etiology of pressure ulcers creating a framework of understanding for the mechanisms, which lead to skin and subdermal tissue damage. Such research encompasses a hierarchical approach, involving cell models, tissue-engineered constructs, and evaluations of specific subpopulations at risk of developing PUs. Several studies have assessed the effects of large strains in subdermal tissues involving muscle and fat, by evaluating the biomechanical and physiological response of the tissues employing imaging and biomarker analysis. However, this approach does not account for the damage mechanisms associated with the majority of PUs involving small tissue strains in superficial dermal tissues. Indeed, in this case, researchers have used biophysical and imaging techniques to assess the response of superficial skin tissues under representative loads. These studies revealed that due to microvascular compromise, tissue ischemia can occur in both able-bodied and patient cohorts during periods of lying and sitting postures. In addition, specialized imaging techniques adopted in the host laboratory have enabled the quantification of dermal lymphatic vessel occlusion under applied loads.

With the advent of state-of-the-art imaging and biophysical modalities, it is now possible to simultaneously assess microvascular and lymphatic changes during periods of loading and subsequent recovery. Therefore, the present study aimed to determine thresholds of dermal vessel occlusion and recovery following representative loading using a customized biophysical and imaging experimental design protocol.

2 | METHODS

2.1 | Participants

Participants between the ages of 18 and 65 years were recruited via poster advertisement. Ethics Approval for the study was granted by the Local Institutional Committee at the University of Southampton (REC ID: 19378). Each participant was provided with an information sheet, which detailed any risks associated with the protocol. Exclusion criteria included a history of skin damage or disease and contraindications for fluorophore injections.

2.2 | Methodology

The experiments were performed in an environmentally controlled laboratory, with an ambient temperature of 22 ± 1°C and relative humidity of 42 ± 6%. For each participant, the dominant arm was positioned on a foam-based structure at the level of the heart, designed to ensure that the arm remained as still as possible during testing (Figure 1). This position ensured minimal contribution of passive mechanisms to lymphatic clearance and reduced potential movement artefacts during imaging.

Figure 1  A, Test setup involving the dominant arm of participants resting on a foam surface. The indenter has a specially designed interface to house the transcutaneous gas electrode, and the lymphatic imaging was conducted proximal to the loading site. B, Image of delineated dermal lymphatic image using ICG injection and near-infrared imaging.
Indocyanine green (ICG) injections of 50 µL 0.05% w/v at a shallow intradermal depth were administrated to delineate dermal lymphatic vessels. Single injections were delivered into the two interdigital spaces between the thumb and the second finger by a registered practitioner (PW), constituting a total microdose of 0.05 mg. To encourage rapid uptake of ICG into lymphatic vessels, each participant was instructed to clench their fists 20 times following injection. Dermal lymphatic video sequences were captured using a Near-Infrared Fluoroscopy Lymphatic Imaging (NIRFLI) system, with a commercial camera (Fluobeam R 800) and associated software (Fluobeam v3.1.1, Fluoptics, France). The system incorporates an integrated laser (780 nm) and CCD sensor, with appropriate filters to isolate fluorescence of ICG (peak 830 nm). Frame acquisition was captured at frequencies of between 3 and 4 Hz, individually optimized to maximize detection of vessels and minimize grayscale saturation. The imaging system was used initially to identify antecubital delineation of lymphatic vessels, to provide a suitable focal point for loading on an active dermal lymphatic vessel.

A transcutaneous gas monitor (TCMS, Radiometer) with a combined gas electrode set at a local temperature of 43.5°C was then attached to the selected test site. A special 3D printed case was placed on top of the electrode to produce a curved loading surface and minimize stress concentrations at the edges of the indenter. The electrode was calibrated and attached to the skin in an unloaded state for 20 minutes. Following the equilibrium phase, a baseline lymphatic video sequence was recorded for 20 minutes to accommodate the effects of local heating induced by the electrode.

### 2.3 | Loading protocol

To investigate the effects of repeated loading on lymphatic activity and transcutaneous gas tensions, two distinct loading regimes were employed. The first involved incremental repeating loading with pressures of 30, 60, and 90 mmHg applied to the test site with the 38-mm-diameter indenter (Figure 1). Each load was maintained for a 20-minute period followed by 20 minutes of unloading (recovery phase). During these loading and unloading periods, video sequences with the NIRFLI were recorded. In addition, transcutaneous tissue gas tensions (TcPO2 and TcPCO2) were continuously monitored at 0.5 Hz, with changes in loading conditions identified at each interval.

On a separate day separated by a minimum of 48 hours, six participants returned to the laboratory for a further test session. This involved three repeated loads each at a constant pressure of 30 mmHg applied to the identical test site. Identical time periods, each of 20 minutes, were employed for loading and unloading, with continuous monitoring of transcutaneous gas data and NIRFLI capture at each test condition. This was performed to assess the cumulative effects of repetitive loading, in comparison with that of the incremental pressures, previously described.

### 2.4 | Data and statistical analysis

Robust parameters of lymphatic function from the imaging sequences were identified using a customized software application (MATLAB, The MathWorks), described in previous publications. To review briefly, the features were established using a droplet morphometry and velocimetry (DMV) tracking approach. Here, image subtraction, binary conversion, and centroid tracking provided the basis to identify and measure each transient lymph packet event captured within the 20-minute video sequences. Lymph packets are related to contractile propulsion events, associated with the lymph "pump", where lymph fluid transitions toward collecting nodes. Each transient event was analyzed to provide x and y coordinates of the centroid of the packet, whereby the resultant displacements could be estimated. An extended Kalman filter (EKF) was applied to ensure the centroid axes from distinct packets were isolated between the video frames. The primary output parameter involved the frequency of transient lymph packets. Participant data sets were presented to describe transient lymph behavior across each of the test phases involving both loading and unloading periods. Data regarding transient lymphatic events were nonparametric in distribution, and appropriate descriptors of median and interquartile ranges were used. Subsequent analysis of the effects of incremental pressures (30, 60, or 90 mmHg) and repeated pressures (30, 30, and 30 mmHg) was conducted using a Friedman test. Comparisons between post-loading data and baseline values were conducted using Wilcoxon signed-rank tests.

The transcutaneous gas data were normalized to baseline unloaded values, then categorized according to the established characteristic responses during the applied loads: Category 1—minimal changes in both TcPO2 and TcPCO2 values; Category 2—>25% decrease in TcPO2 with minimal change in TcPCO2; and Category 3—>25% decrease in TcPO2 associated with a >25% increase in TcPCO2. The resultant categorical responses are described as a percentage of the number of participants. Oxygen deficit was estimated by calculating the integral between TcPO2 values and time, with respect to the basal TcPO2 levels.

### 3 | RESULTS

#### 3.1 | Participants

A total of twelve participants (7 male and 5 female) were recruited with a mean age of 26 years (range 22-37 years), mean height of 1.66 ± 0.11 m, mean weight of 65.3 ± 10.8 kg, and their corresponding BMI of 21.15 ± 3.4 kg/m². These were subjected to the incremental loading protocol (30, 60, 90 mmHg). In addition, six participants (3 male and 3 female) were subsequently subjected to repeated constant loading (30, 30, and 30 mmHg). Their mean height was 1.71 ± 0.11 m, mean weight was 68.3 ± 8.3 kg, and their corresponding BMI was 23.2 ± 4.1 kg/m².
3.2 | Effects of incremental pressures of 30, 60, and 90 mmHg

At baseline, the number of lymph packages revealed a large intersubject variation, with a median value of $n = 9$ transient events (quartile range 6-12). During the incremental loading regimen, the number of transient lymphatic events reduced during the loading periods but then increased in the subsequent recovery periods. Indeed, for each pressure, there were very few cases of transient through flow events, with median values of between 2 and 3 (Figure 2). During the subsequent recovery periods, the number of transient events increased from baseline, reflecting a full recovery. There were no significant differences ($P > .05$) between the number of transient lymphatic packets at each of incremental loading periods.

There were contrasting changes in transcutaneous gas response depending on the magnitude of applied pressures (Figure 3). Indeed, for a pressure of 30 mmHg, there was generally a reduction in $T_cPO_2$ and no corresponding changes in $T_cPCO_2$; that is, 67% of participants exhibited a Category 2. With an increased pressure of 60 mmHg, a number of individuals (44%) exhibited both a reduction in $T_cPO_2$ and an increase in $T_cPCO_2$, denoted by a Category 3 response. At the third load cycle corresponding to an applied pressure of 90 mmHg, a Category 3 response was evident in over half of the participants (56%), indicative of an ischemic state in the underlying tissues. The temporal trend in the transcutaneous gas data reveals the cyclic changes in $T_cPO_2$ during periods of loading and recovery. Figure 3 provides a typical example for one participant (#P4), demonstrating that at the highest pressure (90 mmHg), there is a sharp decline in $T_cPO_2$, to a point at which oxygen is depleted. The corresponding $T_cPCO_2$ values are observed to accumulate over this loaded period, reaching values of $>80$ mmHg, representing a 100% increase from basal values (Figure 3). With the subsequent removal of load, full recovery to basal levels for both $T_cPO_2$ and $T_cPCO_2$ was observed.

3.3 | Effects of repeated pressures of 30 mmHg

A similar intersubject variation was observed during the repeated loading test phase, as illustrated in Figure 4. The median number of transient lymph packets at baselines was $n = 5$, with an interquartile range of 4-7. During the applied loading, the number of transient events was reduced with median values ranging from 0 to 2 across each of the three loading cycles. During each unloading cycle, the lymphatic...
activity increased with median values of transient events ranging between 12 and 15. This represented a significant increase ($P < .05$) of more than twofold compared with baseline values. The results were indicative of significant occlusion during loading and full recovery in the subsequent unloading periods, for each of the three loading cycles.

There were no significant differences ($P > .05$) between the number of transient lymphatic packets during each loading cycle.

Changes in transcutaneous gas data were also observed during the loading period, with tissue gas deviations corresponding to loading and unloading phases, as illustrated with one participant (#4) (Figure 5). Indeed, there was a decrease in $T_{PCO2}$ during 30 mmHg loading with a recovery during the unloaded phases. In each cycle, oxygen was reduced while carbon dioxide remained at basal levels, indicative of a Category 2 response. This was consistent across the test participants, with full recovery of $T_{PO2}$ levels observed during each period of unloaded recovery (Figure 5).

### 3.4 Associations between lymphatic occlusion and transcutaneous changes

The effects of the incremental loading regime on both the perfusion, in the form of the oxygen debt parameter, and the lymphatic activity for two participants are illustrated in Figure 6. There is a clear increase in oxygen debt with a corresponding reduction in lymphatic activity during the periods of incremental loading. At each unloading cycle, full recovery of perfusion and an associated increase in lymphatic activity were observed (Figure 6A). These temporal trends were apparent in the vast majority of participants ($n = 10$). In a small number of participants ($n = 2$), the responses were less evident with minimal changes in both lymphatic activity and perfusion during the loading cycles (Figure 6B).

### 4 DISCUSSION

This study represents for the first time a simultaneous evaluation of both dermal microvascular and lymphatic compromise as a direct result of mechanical loading of the skin. The combination of biophysical sensing and NIRFLI provided a unique opportunity to assess compromise to skin microcirculation, with a focus on two key mechanisms of pressure ulcer development, namely ischemia and impaired lymphatic drainage.9 The results of this study on an able-bodied cohort revealed that even under relatively low pressures (30 mmHg), the dermal lymphatic vessels were occluded with little or no transient events observed. By contrast, when subjected to repeated constant pressures, changes in the transcutaneous gas tensions generally revealed some reduction in partial pressures of oxygen associated with carbon dioxide remaining at basal values. The most significant changes in transcutaneous gas data were observed at the third cycle of incremental loading corresponding to a pressure of 90 mmHg, where the majority of participants exhibited a large reduction in $T_{PO2}$ with an associated increase in $T_{PCO2}$, indicative of local ischemia.

The results of the study have demonstrated that an applied pressure of 30 mmHg can compromise dermal lymphatic vessels. This pressure was smaller than the 60 mmHg used in a previous study, which resulted in impaired valve function and backflow events in some of the able-bodied participants.13 In both studies, however, there was considerable variability in both the basal lymphatic activity levels and the individual responses to mechanical loading. In addition, each study revealed a full recovery of lymphatic activity during the unloaded recovery phases (Figures 2 and 4). The present study design includes the advantage of imaging during the loading period, which was not available during the previous study.16 With reference to the seminal animal study, which used radioisotope tracers to monitor the clearance of deeper lymphatic vessels, critical uniaxial pressures of between 60 mmHg (8 kPa) and 75 mmHg (10 kPa) were reported.17 However, direct comparisons between this and the present study must be treated with caution due to the differences in lymphatic anatomy and physiology between species under...
investigation. It is of note that lymphatic vessel function characterized in the present study may not be related to lymphatic capillary exchange occurring distally, although similar pressures were shown to cause distinct changes in interstitial flow, causing local halo patterns of ICG dispersion.12

The changes in transcutaneous gas data revealed that moderate compromise was observed at 30 mmHg, representing a Category 2 response. Repeating this pressure resulted in a similar response. By contrast, when pressure was incrementally increased, changes in both TcPO2 and TcPCO2 were observed (Category 3), indicative of an ischemic state in over half the able-bodied cohort. Previous studies have shown that to achieve a 50% reduction in TcPO2 from unloaded resting value in an able-bodied cohort, applied pressures ranged from 22 to 92 mmHg.16 These findings highlight the individual nature of the tissue response, in terms of tolerance to mechanical-induced impairment of the microcirculation. This was also reported using biophysical measures to assess the physiological response to prolonged lying and sitting postures.15,18,19 Here, a proportion of individuals, typically 15%-30% of the total, demonstrated ischemic responses during common postures, that is, supine, lateral lying and high sitting, with corresponding interface pressure values ranging between 30 and 90 mmHg.9 This could be due to differences in soft tissue structure and geometry, underlying changes in physiology, such as preclinical changes in microcirculation or nutrition factors.8

It is clear that the blood and lymphatic vessels demonstrate different sensitivities to mechanical-induced occlusion, which could be attributed to their unique anatomy and physiology. For example, the lumen of lymphatic vessels is wider and more irregular than in blood vessels, and under normal conditions, the lymphatic capillaries are maintained in a collapsed state.20 By

**FIGURE 6** The profile of oxygen debt and the number of transient lymphatic events from two participants for each period of incremental loading and recovery. (A) #P6 and (B) #P5
contrast, a relationship is known to exist between cutaneous mechanosensitivity and vasodilation, referred to as pressure-induced vasodilation (PIV).\textsuperscript{21} When an external pressure is applied on the skin, the cutaneous microautoregulation vasodilate to prevent ischemia. The present study has shown that under relatively low pressures of 30 mmHg, microcirculation remained functional with only small changes in $T_{cPO2}$, which often showed some recovery during loading indicative of PIV (Figures 3 and 5). However, at the higher loads of 60 and 90 mmHg, there appears to be greater compromise in a number of individuals, with elevated $T_{cPCO2}$ levels corresponding to complete microcirculation occlusion (Figure 3). The changes in microcirculation values should be put into the context of normative capillary pressures, which range from 10.5 to 22.5 mmHg at the apex of the capillary loop.\textsuperscript{22} Hence, our loading regimes were above that of the normative values. However, PIV by vascular smooth muscle tone appears to compensate for loads up to a threshold between 60 and 90 mmHg in most cases, a finding that has also been demonstrated in the microvascular response in animal models, for example, threshold of 70 mmHg in murine model.\textsuperscript{23} Similar pressures have been reported to cause local ischemia and inflammation,\textsuperscript{5,24} with an accumulation of metabolites associated with a change from aerobic to anaerobic cellular respiration.\textsuperscript{5,25}

The present study clearly examines the response of a relatively small cohort of young able-bodied participants, limiting its generalizability to cohorts of patients at risk of pressure ulcers, such as those with comorbidities including diabetes or the spinal cord injured. Demographic factors such as body fat, blood pressure, and hydration status may have influenced the individual responses. However, our sample of young healthy individuals within a limited BMI range (21.15 ± 3.4 kg/m$^2$) provided limited scope to adopt any form of multifactorial analysis. The loading periods were restricted to 20 minutes, whereas in the clinical setting, patients are supported in prolonged postures for periods in excess of 4 hours. The heated transcutaneous gas electrode could have influenced the underlying tissue physiology, although this condition was standardized across all test participants, ensuring both lymphatic and microcirculation measures reflected the relative changes in the vessel patency as a result of mechanical loading.

In clinical practice, carers and healthcare professionals advise vulnerable patients to regularly reposition to allow recovery of previously compromised tissues.\textsuperscript{1} The present study has highlighted the importance of tissue recovery within an able-bodied cohort. However, individuals with microvascular compromise and reduced tissue tolerance may require an extended period to recover.\textsuperscript{26} In addition, the pressure required to cause local ischemia and lymphatic occlusion appears to differ between individuals, even within an able-bodied cohort. This highlights the need for personalized care strategies, where patients are assessed and monitored depending on their individual tolerance to prolonged postures. Further studies are required on specific patient subpopulations who may have underlying comorbidities, which affect their microcirculation and the dermal tissue tolerance to applied loading.

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**REFERENCES**

1. National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel, and Pan Pacific Pressure Injury Alliance, Prevention and Treatment of Pressure Ulcers: Quick Reference Guide., ed. E. Haesler. Osborne Park, Australia: Cambridge Media; 2014.

2. Hay RJ, Johns NE, Williams HC, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. J. Invest. Dermatol. 2014;134(6):1527-1534.

3. Guest JF, Ayoub N, McIlwraith T, et al. Health economic burden that wounds impose on the National Health Service in the UK. BMJ Open. 2015;5(12):e009283.

4. Bouten CV, Oomens CW, Baaijens FP, Bader DL. The etiology of pressure ulcers: skin deep or muscle bound? Arch Phys Med Rehabil. 2003;84:616-619.

5. Soetens J, Worsley PR, Herniman JM, Langley GJ, Bader DL, Oomens C. The expression of anaerobic metabolites in sweat and sebum from human skin subjected to intermittent and continuous mechanical loading. J Tissue Viability. 2019;28(4):186-193.

6. Reswick JB, Rogers JE. Experience at ranch los amigos hospital with devices and techniques to prevent pressure sores, In: Kenedi RM, Cowden JM, eds. Bed sore biomechanics: Proceedings of a seminar on tissue viability and clinical applications organised in association with the department of biomedical engineering, Glasgow, in August, 1975, Macmillan Education UK: London; 1976: 301-310.

7. Gefen A, van Nierop B, Bader DL, Oomens CW. Strain-time cell-death threshold for skeletal muscle in a tissue-engineered model system for deep tissue injury. J. Biomech. 2008;41(9):2003-2012.

8. Coleman S, Nixon J, Keen J, et al. A new pressure ulcer conceptual framework. J. Adv. Nurs. 2014;70(10):2222-2234.

9. Bader DL, Worsley PR. Technologies to monitor the health of loaded skin tissues. Biomed Eng Online. 2018;17(1):40.

10. Traa WA, van Turnhout MC, Nelissen JL, Strijkers GJ, Bader DL, Oomens CWJ. There is an individual tolerance to mechanical loading in compression induced deep tissue injury. Clin Biomech Elsevier Ltd. 2019;63:153-160.

11. Loerakker S, Manders E, Strijkers GJ, et al. The effects of deformation, ischemia, and reperfusion on the development of muscle damage during prolonged loading. J Appl Physiol. 2011;111(4):1168-1177.

12. Gray RJ, Voegeli D, Bader DL. Features of lymphatic dysfunction in compressed skin tissues - Implications in pressure ulcer aetiology. J Tissue Viability. 2016;25(1):26-31.

13. Gray RJ, Worsley PR, Voegeli D, Bader DL. Monitoring contractile dermal lymphatic activity following uniaxial mechanical loading. Med Eng Phys. 2016;38(9):895-903.

14. Loper C, Worsley PR, Bader DL, Fenlon D. Investigating the short-term effects of manual lymphatic drainage and compression garment therapies on lymphatic function using near-infrared imaging. Lymphat Res Biol. 2017;15(3):235-240.

15. Chai CY, Bader DL. The physiological response of skin tissues to alternating support pressures in able-bodied subjects. J Mech Behav Biomed Mater. 2013;28:427-435.

16. Bader DL, Gant CA. Changes in transcutaneous oxygen tension as a result of prolonged pressures at the sacrum. Clin Physiol Meas. 1988;9(1):33-40.
17. Miller GE, Seale J. Lymphatic clearance during compressive loading. Lymphology. 1981;14(4):161-166.
18. Woodhouse M, Worsley PR, Voegeli D, Schoenhoven L, Bader DL. The physiological response of soft tissue to periodic repositioning as a strategy for pressure ulcer prevention. Clin Biomech. 2015;30(2):166-174.
19. Worsley PR, Parsons B, Bader DL. An evaluation of fluid immersion therapy for the prevention of pressure ulcers. Clin Biomech. 2016;40:27-32.
20. Skobe M, Detmar M. Structure, Function, and Molecular Control of the Skin Lymphatic System. J Invest Derm Symp P. 2000;5(1):14-19.
21. Fromy B, Abraham P, Saumet J-L. Progressive calibrated pressure device to measure cutaneous blood flow changes to external pressure strain. Brain Res Protoc. 2000;5(2):198-203.
22. Shore AC. Capillaroscopy and the measurement of capillary pressure. Br J Clin Pharmacol. 2000;50(6):501-513.
23. Tsuji S, Ichioka S, Sekiya N, Nakatsuka T. Analysis of ischemia-reperfusion injury in a microcirculatory model of pressure ulcers. Wound Repair Regen. 2005;13(2):209-215.
24. Soetens J, Worsley PR, Bader DL, Oomens C. Investigating the influence of intermittent and continuous mechanical loading on skin through non-invasive sampling of IL-1α. J Tissue Viability. 2019;28(1):1-6.
25. Knight S, Taylor RP, Polliack AA, Bader DL. Establishing predictive indicators for the status of loaded soft tissues. J Appl Physiol. 2001;90:2231-2237.
26. Bogie KM, Nuseibeh I, Bader DL. Early progressive changes in tissue viability in the seated spinal cord injured subject. Spinal Cord. 1995;33(3):141-147.

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