THE ETIOLOGY OF PRESSURE SORES: SKIN DEEP OR MUSCLE BOUND?

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Pressure sore etiology

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Abstract

Pressure sores are areas of soft tissue breakdown resulting from sustained mechanical loading of the skin and underlying tissues that affect the quality of life of many individuals. Despite considerable efforts to prevent pressure sores, prevalence figures are unacceptably high. This can at least partly be attributed to limited knowledge of the aetiology of the clinical condition and the fact that identification and prevention of pressure sores mainly focus on skin tissue, even though the underlying muscle tissue may be more susceptible to mechanical loading.

The present paper proposes a new, hierarchical research approach to obtain improved insights into the basic pathways whereby mechanical loading leads to soft tissue breakdown. This approach investigates the relationships between 1) global mechanical loading at skin level, 2) the resulting local internal mechanical conditions within the soft tissue layers extending from skin to muscle tissue, and 3) the pathophysiological response to loading. The latter response should be assessed from the various functional tissue units involved in soft tissue breakdown, being the cells, the interstitial space, and blood and lymph vessels. It is foreseen that the proposed strategy will provide new fundamental knowledge about the etiology of pressure sores that can serve as a sound basis for effective clinical identification and prevention.

Key words
Pressure ulcers, soft tissues, mechanical loading, pathophysiology

Introduction

Pressure sores are localized areas of tissue breakdown in skin and/or underlying tissues. They can occur in all situations where people are subjected to sustained mechanical loads, but are particularly common in subjects who are bedridden, wheelchair bound or wearing a prosthesis or orthosis. The sores are painful, difficult to treat, and represent a burden to the community in terms of health care and money. Consequently, they may affect the quality of life of many young and elderly individuals. To date, attempts to prevent pressure sores have not led to a significant reduction of the problem. Prevalence figures remain unacceptably high, ranging between 8% and 23% depending on the severity of wounds included and the subject group under investigation. In our view this is at least partly due to the limited fundamental knowledge related to the etiology of the clinical condition. Thus, the design and application of preventive aids and risk assessment techniques are dominated by subjective measures or, at best, based on a relatively small amount of data focusing on skin, which are largely outdated or misinterpreted.

A striking example is the traditionally quoted value for capillary closure pressure of 32 mm Hg (4.27 kPa) that is still frequently used as a threshold for tissue damage. Interface pressures at the contact area between skin and supporting surfaces (such as mattresses or cushions) in excess of this value are assumed to produce a degree of ischaemia, which, if applied for a sufficient period of time, may lead to tissue breakdown. Leaving aside the discussion of whether ischaemia is the principal factor for tissue breakdown in pressure sores, capillary closure depends on local pressure gradients across the vessel wall and not just on interface pressures at skin level. Hence interface pressures well above capillary pressures can be supported by the soft tissues before blood flow is seriously impaired. An interesting observation reported by Husain in 1953 was that localized interface pressures obliterated more vessels in the skin and subcutaneous tissue than in the muscle, while the latter was severely damaged and the skin and subcutis were not. Later studies also demonstrated that muscle
tissue is more susceptible to mechanical loading than skin\textsuperscript{6,11,12}.

In order to be able to reduce the prevalence of pressure sores it is essential to improve and expand our knowledge of the etiology in terms of both basic science and clinical experience. In terms of the former we propose a more rigorous analysis of existing data, followed by a hierarchical research approach in which the effects of mechanical loading on the different functional units of soft tissue are studied.

Deep versus superficial sores

As a guide to pressure sore prevention, research has focused on determining the minimal degree of loading that will consistently lead to tissue damage. Typically, such physical conditions are derived from animal experiments\textsuperscript{6,8,13,14} with some degree of variable control, and, more rarely, from occasional human studies, the most prominent of which is often quoted\textsuperscript{15}. In the animal studies soft tissues are loaded externally via prescribed pressures or shear stresses applied to the skin, whereas the onset of tissue breakdown is generally observed from histological examinations after predetermined periods of time. Despite large variations in absolute measures these studies all demonstrate an inverse relationship between the magnitude and duration of loading, indicating that the higher loads require less time to initiate tissue breakdown. More importantly, they suggest that pressure sores can develop either superficially or from within the deep tissue depending on the nature of the surface loading. The superficial type forms in the skin with maceration and detachment of superficial skin layers and is predominantly caused by shear stresses within the skin layers. If allowed to progress the damage may form an ulcer, which is easily detected\textsuperscript{13,16}. Deep sores on the other hand arise in deep muscle layers covering bony prominences and are mainly caused by sustained compression of the tissue\textsuperscript{6,8,10,12,17}. These sores are very harmful, developing at a faster rate than superficial sores and yielding more extensive ulceration\textsuperscript{18}. The damage progresses towards the surface, so that considerable necrosis of muscle, fascia, and subcutaneous tissue may occur even at a stage when the skin shows only minor signs of tissue breakdown. Hence the initial pathological changes which lead to the most severe sores are in the deep tissues and therefore are difficult to identify with techniques currently available. Although this is recognized in clinical practice where tactile examinations are prescribed to screen the tissue for deep pressure sores\textsuperscript{19,20,21}, this fact is frequently overlooked by objective risk assessment techniques, clinical classification schemes and techniques for prevention, most of which focus on the skin and ignore the underlying tissues. Although these approaches have relevance in clinical practice because the skin is easily accessible, it should be realized that by the time a deep pressure ulcer becomes visible clinical intervention is too late and prognosis is variable.

Pathways of tissue breakdown

Although is well acknowledged that pressure sores are primarily caused by sustained mechanical loading of the soft tissues of the body, prevention of the sores by reducing the degree of loading alone remains difficult. This is mainly due to the fact that the underlying pathways whereby mechanical loading leads to tissue breakdown are poorly understood. It is not clear how global, external loading conditions are transferred to local stresses and strains inside the tissues and how these internal conditions may ultimately lead to tissue breakdown.

Considerable efforts have been made to determine the most effective way of measuring and reducing surface pressures at skin level\textsuperscript{22,23}. However, surface pressures are not representative of the internal mechanical conditions inside the tissue, which are most relevant for tissue
breakdown. This is especially the case when tissue geometry and composition are complex and surface pressures result in highly inhomogeneous internal mechanical conditions, as is the case adjacent to bony prominences. Nonetheless, in order to study the response of various tissue layers to mechanical loading the local mechanical environment within these layers needs to be known. The transition from global external loads to local internal stresses and strains requires the use of computer models, typically unfamiliar to experimentalists and clinical and nursing staff. Although not yet clinically validated these models may provide better insights into the mechanical conditions of separate tissue layers, extending from skin to muscle tissue. As an example Figure 1 shows a simplified computer model of the mechanical response of the separate soft tissue layers in the human buttock during sitting on a foam cushion. The ischial tuberosity is simulated by an undeformable bony indenter, whereas representative visco-elastic mechanical properties are incorporated for the individual tissue layers and the cushion material. Using the finite element approach detailed information on the magnitude and location of internal stresses and strains as a result of external loading can be obtained. Figure 1 clearly shows the inhomogeneous mechanical condition of the various tissue layers and areas of high internal stresses in the deeper fat and muscle layers. Combining such models with experimental data on the load bearing capacity of the individual tissue layers will provide predictive measures of when and where tissue damage is likely to occur. This is, however, not straightforward since the load bearing capacity of the biological tissues is influenced by many systemic and local factors, such as temperature and nutritional status.

Figure 1

Although computer models will provide insight in the internal mechanical conditions relevant for tissue damage, experimental research is required to explain how these conditions eventually lead to tissue breakdown. There is surprisingly little consensus about the pathophysiological response to mechanical loading that triggers soft tissue breakdown. Theories involve localized ischaemia, impaired interstitial fluid flow and lymphatic drainage, reperfusion injury, and sustained deformation of cells. Traditionally, these theories have been proposed following experimental observations limited to the depth of skin layers determined by the physical characteristics of such measurement techniques involving blood flow and oxygen tension. However, with the development of new techniques, including magnetic resonance imaging (MRI), it is certainly possible to relate mechanical loading to pathophysiological phenomena within deeper tissues.

Theories focusing on ischaemia and impaired lymphatic drainage have been studied in-vivo and generally confirm that sustained tissue loading will influence tissue perfusion and/or lymph flow, thereby affecting the transport of nutrients to and metabolic waste products away from cells within the tissue. Although this is appropriate for muscle tissue, which is metabolically more active than skin, these theories can only partly explain the onset of pressure sores and have to date not been fully verified. The same argument also applies to reperfusion injury mediated through oxygen free radicals. This theory states that it is the restoration of blood flow after load removal rather than impaired blood flow during loading per se, which exacerbates the compromise to the tissue viability. Although described for other postischaemic pathologies, such as cardiac infarction, the specific role of reperfusion injury in the causation of pressure sores remains to be defined. However, if reperfusion injury is indeed an important factor in promoting pressure sores, many traditional clinical practices involving patient turning and pressure relieving systems need to be carefully evaluated.
Existing histopathological data suggest a cellular origin to pressure sore development and it has been hypothesized that cellular damage is caused by sustained cell deformation. Indeed cell deformation triggers a variety of effects, such as volume changes and cytoskeletal reorganization, which may be involved in early tissue breakdown. As it is impossible to examine the cellular response to loading in-vivo independently of other factors, in-vitro models of cultured cells under compressive or shear loading have been employed. Recent studies by our group demonstrate that such models are useful in studying the damaging effects of well-controlled compressive loading regimens on living cells (Table 1). For this purpose skeletal muscle cells are seeded and cultured in agarose constructs, representing a form of extracellular matrix. A specially designed loading apparatus inside an incubator is used to subject the cell-seeded constructs to clinically relevant loading regimens, whereas cell damage is assessed from evidence of nuclear or membrane damage. The results indicate that cell damage increases with both the magnitude and duration of compression. Although in-vitro models may prove to be an important tool in defining thresholds for cell damage they are, as yet, difficult to relate to patient studies.

Table 1

Overall the theories focus on different functional units of soft tissue, involving cells, the interstitial space with extracellular matrix, and blood and lymph vessels. These units are affected by mechanical loading to varying degrees and hence have different relevance for tissue breakdown. Most probably each of them contributes to the causation of pressure sores, although their individual and combined role in tissue breakdown will undoubtedly vary depending on the nature of the mechanical insult and patient characteristics such as illness or age, which affect soft tissue properties and hence the liability to tissue breakdown.

Hierarchical approach

To investigate the differential response of the various tissue functional units to mechanical loading and their relative contributions to the etiology of pressure sores a hybrid methodology involving a combination of computer and experimental studies must be adopted. The experimental studies should aim at elucidating the relationships between mechanical loading, the pathophysiological response to loading and tissue breakdown in testing hypotheses on the etiology of pressure sores. The computer studies should aim at predicting the association between external and internal mechanical conditions within soft tissues and their functional units. This methodology must incorporate all soft tissue layers involved in pressure sores, extending from superficial skin layers, to subcutaneous fat, fascia, and deep muscle layers. Moreover, a hierarchical approach is proposed, in which the effects of loading are studied in different, yet complementary, model systems with increasing complexity and length scale and incorporating one or more functional tissue units. Thus, in-vitro models, ranging from the single cell (μm scale) to cell-matrix constructs (mm scale) and individual tissue layers (mm-cm scale) might be used to study the relationship between cell deformation and cell damage as well as the influence of the surrounding extracellular matrix and three-dimensional tissue architecture on this relationship. The role of tissue (re)perfusion and lymph flow as well as the interaction between tissue layers in bulk tissue might further be assessed using in-vivo studies with animal models or human subjects. The different length scales of these models can be coupled by multi-scale computer calculations that enable the prediction of the internal microscopic mechanical environment within a given model from global, macroscopic loading conditions, such as interface pressures (and vice-versa). In this way relationships between, for
instance, cell deformation and cell damage can be extrapolated to the level of bulk tissue to give clinically relevant predictions on tissue breakdown.

This approach can strongly benefit from new technologies such as cell and tissue engineering and vital imaging techniques like MRI or vital microscopy. Cell and tissue engineering strategies enable the fabrication of in-vitro model systems with well-defined, controllable properties, which are designed to test specific hypotheses independently of predisposing factors associated with the onset of pressure sores. Vital imaging techniques allow to follow the pathophysiological response to loading in real-time with much less ethical considerations than histological examination of loaded tissue in animal studies. Moreover, these techniques offer the potential of both examining the effects of mechanical loading in human subjects and ultimately as predictive tools for the screening of tissues for superficial or deep pressure sores in a clinical setting.

Despite the considerable amount of existing clinical experience, it is our opinion that the proposed approach will provide better fundamental knowledge about the etiology of pressure sores that can serve as a sound basis for effective clinical identification and prevention. The hierarchy of model systems can be used to establish well-defined thresholds for tissue damage, which can provide new guidelines for pressure sore prevention and to redirect available pressure relieve strategies. In addition, the established thresholds can be related to biochemical markers for the identification of early, reversible tissue damage. Adequate guidelines for damage prevention and early identification of damage will lead to a reduction of medical costs and time of hospitalization, as well as a more efficient and economic use of available support systems.

References


Table 1: Percentage cell damage in time in compressed and uncompressed muscle cell seeded agarose constructs. Degrees of compression are clinically relevant. For example the local deformations of muscle tissue during sitting (Fig. 1) range between 0 and 40%.

<table>
<thead>
<tr>
<th>Time of compression (h)</th>
<th>Uncompressed</th>
<th>10% Compression</th>
<th>20% Compression</th>
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<tbody>
<tr>
<td>0</td>
<td>29</td>
<td>30</td>
<td>28</td>
</tr>
<tr>
<td>1</td>
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<td>42</td>
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<tr>
<td>12</td>
<td>29</td>
<td>42</td>
<td>74</td>
</tr>
</tbody>
</table>

*Assessed from evidence of membrane disruption or nuclear breakdown in a minimum sample of 200 cells.

Figure 1: Simplified computer model of deformed buttock (top right) demonstrating the differential response of the separate soft tissue layers (left) during sitting of a 80 kg male subject on a foam cushion. Because of assumed symmetry only half a buttock is used for calculations. Values indicate Von Mises stresses, representing distortional energy. Note the areas of high stress in the subcutaneous fat and muscle layers (arrows).