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FORCE RELATED TISSUE DAMAGE

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"Force related tissue damage shifts the focus from something to be managed to something to be predicted and prevented."

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FORCE RELATED TISSUE DAMAGE: A WHITE PAPER

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Key words: pressure injury, force related tissue damage, tissue, manual handling, mechanical handling, patient care, ergonomic, biomechanical

Overview: The intention of this white paper is to challenge and explore existing thinking around force related tissue damage or pressure injury.

FORWARD

Damage to skin and tissue is an important and expensive issue for the NHS and other organisations providing care for those who are confined to their bed or chair for any period of time. The costs are not just financial; a lot of individual suffering and loss of quality of life occur when tissue breaks down. This white paper brings together existing research into skin and tissue damage associated with patient's being cared for in bed.

The latest term being used for this is pressure injury (NPUAP 2016). This term replaces previous terminology used such as; pressure ulcers, pressure sores, bed sores /ulcers and decubitus ulcers. However, with our extensive review of the literature into the internal and external influences, we believe a more accurate description is force related tissue damage.

This paper investigates the observations regarding unobvious causes of force related tissue damage and the events linking both biomechanical and biological processes at several organisational (pathological) levels together with external in bed events. Over 22 internal marginal influences are identified which, as countless Cochrane reviews demonstrate, wound care science struggles to diagnose and cure; mostly due to the underestimation of the complexity and processes involved regarding tissue homoeostasis, damage and regeneration.

The paper explains how there are two major causal factors connected with all in bed force related tissue damage. The patient's resting/support surface synergy and the way the person is moving/being moved and stabilised on that surface, regardless of whether this is by manual or mechanical means. We will explore how in bed force related tissue damage can be a direct result of both manual and/or mechanical handling and the incorrect synergetic interface layers of the resting/support surface with the patient's skin and tissues.

We strongly suggest the major causal factors involved with all in bed force related tissue damage are external and within our control. This paper proposes that a preventative trajectory is both desirable and achievable by adopting a combined ergonomic and biomechanical approach to remove the risks to both patients' skin/tissue and the carer's muscular-skeletal system associated with in bed care and positioning.

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SUMMARY

Current evidence suggests there are many contributing factors that work together to cause a pressure injury. These contributing factors in the underlying aetiology can more accurately be described as force related tissue damage. This is therefore the term adopted throughout the paper.

Force related tissue damage can occur at any point in the body, where the body is unable to maintain its innate tissue protection and homeostasis. These forces may affect the skin, but can also radiate and have an effect in the deeper tissue layers of the body and trigger many marginal contributing factors within the body, which when combined, can surpass a threshold beyond which cells die or tissues rupture.

Under normal healthy circumstances the body's tissues work jointly to manage both external and internal forces. The body protects and repairs its internal environment by using both physiological and biomechanical mechanisms (biotensegrity) to maintain homeostasis. Force related tissue damage occurs when the threshold of the tissue integrity is surpassed or reduced. This can be caused by forces, physiological events or behaviour which either surpass or reduce the tissue threshold for one or more parameters. This damage can occur from the micro level in the form of stress up to the level of a visible lesion.

This is an expansion of current thinking which relates to (internal) lesions due to a vessels collapse or tissue ruptures. It is necessary because it addresses the parameters needed for diagnosis, prognosis, treatment and prevention of force related damage. It allows a detailed description of the way a patient differs from a healthy subject who will not acquire force related lesions. Expanding from the description of the lesion towards a description of the biomechanical and physiological state of the tissue involved will make caregivers aware of the preventable causes and practical treatment options.

Attention to forces will raise awareness that instead of pressure, a force has dimensions of magnitude, direction and time. This can explain why a low magnitude force can be more damaging than a large magnitude force or vice versa depending on the time and direction it is applied to the body.

Attention to physiology will explain why it is incorrect to think of a lesion as being unavoidable and raise awareness to diagnostic and therapeutic approaches that have the ability to reduce the number of lesions that occur.

Attention to behaviour will reduce the generation of unnecessary external forces which surpass the body's innate protection mechanisms as a result of manual or mechanical handling of patients.

The diagnosis of factors related to the tissue threshold will help in discovering and managing individuals prone to acquiring a force related lesion. The type of forces that results from both manual and mechanical handling of patients can cause damage in tissue, when they are of an intensity and dissipation that cannot be handled by the body's homeostatic and biotensegrity mechanisms.

Therefore, this paper identifies that the major causes of force related tissue damage are twofold and results from a combination of the methods used to move patients and/or the way in which the patient is stabilised on resting/support-interfaces.

Both the major causative and the marginal contributing factors must be assessed at all organisational levels to predict and prevent the occurrence of force related tissue damage and resultant pathological lesions. This will allow for a desired safer trajectory for patients and their carers, by the adoption of preventative strategies that design out the major causes of force related tissue damage and induced lesions.

INTRODUCTION

Following NPUAP 2016 guidelines[1], pressure injuries are areas of localised damage to the skin and underlying tissue, caused by pressure, shear or friction. Pressure injuries are historically called pressure ulcers, pressure sores, bed sores/ulcers, decubitus ulcers and other names. With growing understanding of the aetiology underlying the damage to the tissue a more accurate description may be force related tissue damage.

Healthy individuals do not develop force related tissue damage; this results instead from a number of events caused by damaged or impaired tissues and/or systems. Force alone is not sufficient to explain the occurrence of the force related injury seen in current clinical practice. It therefore makes sense to have a deeper look into the aetiology of lesions commonly described as 'pressure injury", to allow for more tailored diagnostic, curative and preventive interventions. This allows for defining marginal factors, factors allowing for a lesion to occur and causing factors, which are the cause of the lesion. Usually marginal factors are a prerequisite for a causal factor to lead to a lesion.

Normally, tissues are continuously submitted to forces as a result of maintaining body posture, gravity and movement. Due to these forces, tissues and cells are frequently and recurrently damaged. So even in a healthy subject, homeostatic and regeneration processes are always active [2,3]. Living organisms maintain their homeostasis by handling forces and damage [4] by the continuous replacement or repair of cells and tissues[5,6].

> *"This applied force and the tissue involved are complex, dynamic and an interrelated phenomena."*

The amount of damage incurred depends on the way forces are applied and also on the cells, tissue and processes involved Damage occurs when the tissue involved is not able to withstand the applied force. Therefore, the amount of force any given tissue can handle, is defined by its specific characteristics; the tissue threshold. If the tissue threshold is surpassed, damage will occur. Initially there are only two parameters: the applied forces and included tissues. This applied force and the tissue involved are complex, dynamic and interrelated phenomena.

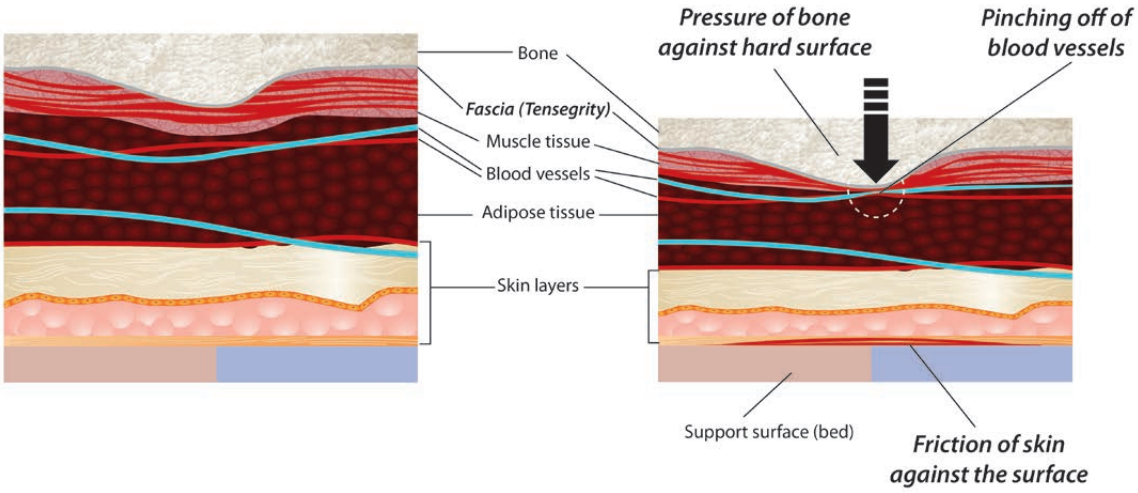

Figure 1: Classic representation of events related to force related tissue damage.

The common concept of pressure damage (pressure ulcers) states it results from vessel collapse and cell death due to compressing tissue between bone and a hard surface (figure 1). This is an oversimplification of the processes involved. It focuses on passing the tissue threshold whilst ignoring the reasons the threshold has been passed. Research on the subject is of high quantity and usually of low quality as highlighted in a recent review on support surfaces for pressure ulcer prevention, which revealed that few studies were of sufficient quality to be evaluated [7,8]. Most studies relate to pressure exerted on tissue; some address shear; few address tension and none address the interrelation and dynamics of force exerted on tissue. Also, most studies focus on lesions or necrosis, but prior to necrosis; cells will be stressed, injured and damaged. Forces exerted on tissue have several direct and indirect effects on all levels of organisation. Events may occur at molecular, cellular, tissue and/or body level [9] and may be of a chemical, physical, biological or mathematical nature or combination thereof. Since the main lesions occur due to biomechanical events, the effect of forces on tissue is relevant. It is important therefore to consider the direct and indirect way forces influence tissue and in what way the tissue threshold can be altered or lowered.

FORCE

External force (a major causal factor) acting on tissues has primary, secondary and tertiary effects. The primary effects of forces are compression, shear and tension leading to deformation, damage and possible rupture of cells and tissues.

The primary effects of external force on tissue cause problems in perfusion leading to secondary events such as hypoxia, lack of nutrients and waste accumulation. Usually, these effects then cascade into further events such as reperfusion injury, chronic immune response, nerve damage etc. which result from the effects of applying forces to tissues for a longer period of time.

Finally, significant loss of tissue and tissue integrity due to the combination of primary and secondary effects, usually triggers the formation of forces on other places in the tissue; a house-of-cards like tertiary effects which result in further spreading of damage. A telling example is the removal of skin, which decreases the shear threshold of skeletal muscle by 50% [10].

Pulling or pushing forces are usually expressed in pascal (1Pa= 1N/m2), describing how much force (newton) is applied per surface (m2). The amount of energy a cell or tissue can handle depends on the force applied and the tissue(s) involved. The way tissue responds to force depends on its resilience - part of this is described by its response to mechanical strain and stress by its elasticity or Young's modulus [11]. However, the resilience of tissue to withstand force depends on the combination of the tissues and structures involved. For several tissue types this has been established [12–14]. This means, for example, adipose tissue has a different response to forces applied than epidermal or muscle tissue. The structure and cooperation of cells and tissues form a complex system, allowing for the management of larger forces than a single cell could handle alone. Reversely, damage to one type of tissue will influence other tissues' threshold.

"The tissue threshold is defined by the amount of force, chemical events (including redox) and/or radiation (including temperature) any given tissue can handle."

If and when applied forces lead to a lesion depends upon the circumstances. Every type of cell or tissue has a certain amount of energy it can absorb; beyond this, it will be damaged to the extent that it fails. Fibrin networks are able to handle damage, but this ability can be compromised due to mechanical or metabolic events [15,16].

It is commonly known the skin has an inhomogeneous response to force applied[17]. Most cells and tissues are anisotropic; the ability to withstand compression, shear and tension is not the same in all directions and depends upon the angle at which it is applied[18]. Therefore, the amount of damage also depends on the angle of forces applied. This is usually not taken into account and this is illustrated by the way ulcers are classified: they are now called pressure injury a classification which tends to ignore other causative factors.

Damage also depends on the tissues involved and how much force they can withstand, i.e. the tissue threshold. The pathological damage may originally start in muscle, adipose tissue, the dermis or other tissue types and spread from there. Deep tissue damage is the common denominator for this group of pathological phenomena. The tissue threshold is defined by the amount of force, chemical events (including redox) and/or radiation (including temperature) any given tissue can handle. Generally, it makes sense to discern "normal force" – in other words, events surpassing the tissue threshold of healthy tissue causing trauma, but within the limits of normal homeostasis. The only way force related damage occurs in a healthy subject is when force is applied at abnormal magnitude, angle and/or time: i.e. trauma. Apart from trauma, pathological lesions develop when tissues and/or systems are compromised. Therefore, the characteristics of a force applied to tissue have three elements: the magnitude, the time and the angle to which it is applied.

DIRECT AND INDIRECT CELLULAR RESPONSE TO FORCES

Under normal circumstances, cells and tissues are constantly challenged and damaged, leading to not only mechanical stress but also to other kinds of stress such as regulatory and metabolic stress[19]. Tissues, and cells within tissues, co-operate to handle these stresses, strains and their secondary effects[20,21].

At cellular level, compressing, tension and/or shear will lead to deformation. Tissue damage therefore starts at the cytoskeletal level of a single cell[22,23]. Further deformation of cells leads to increased membrane permeability, which will cause intracellular metabolic stress[24]. Dermal and muscle cells, as well as neural cells, respond in this way to damage[25]. Damaging the cell membrane leads to an influx of extracellular Ca2+. This influx is regarded as an immediate danger signal for the cell, which will quickly repair the membrane[26] . But even limited pressure can lead to a breakdown of cell organelles[27], triggering programmed cell death or apoptosis. Even though large magnitude forces can lead to necrosis, apoptosis appears to be the main cause for tissue damage[28]. Cells also respond to other events resulting from applying force. For example, stiffness of the tissue, which increases under an applied force, has effect on the cells involved[29].

Oxygen depletion leads to changes in energy and redox potentials and causes cells to switch to different metabolic routes to maintain redox homeostasis[30]. A first step is that the mitochondria produce reactive-oxygen and -nitrogen species. This causes oxidation in the cell[31], leading to further damage and eventually apoptosis[32]. Prolonged hypoxia causes cells to produce stress signals leading to vasodilatation[33,34]. The same factors leading to vasodilatation also switch on angiogenesis[35], senescence, apoptosis and autophagy[36]. Depending on the type of cell involved, hypoxia also leads to different responses of, for example, stem cells[37,38].

Apart from hypoxia, the lack of nutrients can lead to reduced vitality and reduced mitogenic capacity. Eventually, it will lead to cell death, for instance by endoplasmic reticulum stress where the production of proteins is disturbed. This leads to the unfolded protein response (UPR), which entails several actions to restore homeostasis, and, if they fail, to apoptosis[39]. Accumulation of waste products also causes problems for individual cells[40,41].

Not only do hypoxia and lack of nutrients cause metabolic stress, the accumulation of waste and the accumulation of 'cell remains' in the tissue causes further problems in the mitochondrion and the endoplasmic reticulum[42,43]. Stress also makes cells more susceptible to other events such as reperfusion damage[44] and inflammation[45].

Regulatory signals can force a cell to proliferate or (partially) kill itself[46,47]. For example, increased or prolonged stress causes cells to reduce the need for oxygen and nutrients by apoptosis or autophagy.

At some point, the number of dying cells triggers an active immune response as a result of circulating stress signals and cell remains; damage associated molecular patterns (DAMPs)[48–50]. Damaged cells and molecular debris is considered a main trigger of the post-traumatic danger response[51]. Accumulating neutrophils may further increase local pressure leading to damage induced damage.

Generally, the preferred way of cells to die is by apoptosis because necrosis generates massive danger signals and the remains of the cell cannot be "recycled" efficiently[52–54]. Repair at the cellular level involves local cells, stem cells, macrophages[55] and fibroblasts[56]. Therefore at the level of the cell, even if there is no cell death, many complex events occur as a result of forces applied to tissue[57]. The resulting molecular and cellular events impact the threshold level of the tissue involved.

DIRECT AND INDIRECT TISSUE RESPONSE TO FORCES

Lesions usually develop in tissue between the body and a surface. Deformation of tissue can block vessels but also has an effect of other structures like fascia and nerves[58]. Typically, the tissue involved is organised in layers; dermis, subcutis, fat tissue, muscle tissue and bone. In and around these are fascia, blood vessels, lymph vessels and nerves. Tissues have an individual and an interdependent role in homoeostasis and regeneration[59].

Homeostasis handles primary and secondary effects in tissues[60,61] by monitoring tissue and systems quality and by replacing compromised cells and structures. Repair of damage as a result of "living"[62] is a straightforward well controlled process, involving vascular, lymphatic, immunologic, neural and endocrinological systems at local and systemic level[63]. In areas where more damage is to be expected, like the plantar regions, the metabolic speed is somewhat upregulated to allow the homeostatic process to resolve excess damage.

To prevent damage, the body has several ways to detect local deformation[64] and its symptoms[65,66]. The neural, fascial and vascular systems play a central role in detecting and responding to force, hypoxia, acidification, cell and/or tissue damage[67,68]. The usual response to force induced damage signals, is to reposition the body.

Mechanical force causes perfusion problems when compressing arterial, venous or lymphatic vessels[69]. Perfusion problems are wider than just preventing transport by compressing capillaries[70]. Collapsing of capillaries causes hypoxia[71] and leads to upregulation of hypoxia signals[66,72] and organelle dysfunction[73]. But the application of force on tissue also compromises the lymphatic system[74] were for instance, the lymph flow is reduced[75] due to and leading to oedema[76]. Compressed vessels have a recovery time in which they restore the original lumen. This means that after compression the perfusion is not fully restored immediately[77]. The time needed for recovery is a second parameter influencing damage[78]. Finally, the endothelial quality of the dilated vessel will dictate improvement of further damage as a result of pressure induced vasodilatation. In studies with spinal cord injury (SCI) patients it was observed that recovery time was necessary to prevent injury[79]. It seems that there is a sweet spot in recovery time to allow for pressure induced vasodilatation but prevent reperfusion injury. This could also explain tissue damage during repeated stress-compression cycles[80,81].

"Tissues have an individual and an interdependent role in homoeostasis and regeneration."

The combination of perfusion collapse and following reperfusion is, in itself, a cause of cell death as a result of reperfusion injury[44]. Refilling blocked blood vessels is not without consequences. Due to the lack of perfusion, the endothelium becomes very permeable[82]. The renewed influx of blood will cause significant leakage, which results in local oedema as well as an increased influx of neutrophils also due to the influence of the neural system[83].

The lymphatic system has a very complex role in handling forces in tissue. In general it depends on oscillating pressures in the tissue for its transport[84]. In adipose tissue it plays a role in initial force handling by allowing for interstitial fluid transport away from an area of high internal pressure[13]. It does so by opening up its lumen under a medium applied force, however, if the forces are larger, the vessel will collapse leading to oedema due to accumulating fluid consisting of metabolic waste products and other compounds [85].

Nerves have several important roles in tissue homeostasis and regeneration [86]; as understood from regeneration studies with SCI patients where wounds above the lesion heal better compared to wounds below the lesion. Nerves sense hypoxia[87], ischaemic pain and play a role in pressure induced vasodilatation [88]. Longer term effect of nerves comes from their role in maintaining the redox balance in tissue[89]. Aging also influences the sensory neurons leading to a decline in vasodilatory response upon hypoxia[90].

Despite its strength [91], the epidermis is usually the first place where the effects of the vessel collapse becomes visible [92]; in the form of skin reddening and blister formation [93]. Visible reddening of the skin is the result of vasodilatation due to the NOX (nitric oxide) generated[94]. This response is meant to increase the blood flow to ischemic areas and it starts at pressures above 32mmHg[95,96]. The integrity of the skin is also influenced by moisture, which causes increased friction and a reduced tissue quality. Being on the outer perimeter of the body the skin is susceptible to climatic events [97,98].

The dermis has a higher viscoelasticity compared to the epidermis [99] in that it can extend up to 25% and compress in a similar manner. This effect is caused by the adipose tissue in the subcutis. The role of adipose tissue, in relation to exerted force, is to absorb energy and redistribute lower forces to the surrounding tissue. Adipose tissue can suffer from damage due to direct strain and from damage due to hypoxia. However, the biomechanical properties of adipose tissue are different. It can deform much more than other tissue layers and has, like muscle [100], a anti-thixotropic effect. Under pressure it deforms but under prolonged pressure it stiffens [101]. In adipose tissue the fascia handles most of the force and as such it protects the vessels and cells in the tissue[102]. The connective tissue in the adipose tissue ensures that increased pressure is handled by a combination of fibres and adipose cells while the vessels and nerves are not compressed [103]. Apparently, if the pressure in one part is too high, more adipose cells are involved in the process. This is how the amount of force applied relates to the volume of adipose tissue with an increased pressure. This allows the adipose tissue to withstand higher pressures without damage. It is not clear what causes this effect. The mechanical function of adipose tissue can be impaired by prolonged exposure to NOX which leads to fibrosis [104].

The role of muscle in force related damage is well investigated [105]. It absorbs pressure by deforming whilst remaining able to function. Deformation has a negative impact on interstitial transport. This is one of the main reasons muscle tissue is more prone to compression-induced injury [106]. The impaired diffusion of large molecules in muscle tissue [107] not only hampers the oxygenation of individual cells but also disables the transport of metabolites in and out of the tissue and the surrounding blood and lymph vessels. So, there are two ways in which muscle tissue is damaged. Firstly, direct force causing tissue strain, which is greatest near a bony prominence and leads to fast occurring damage. Secondly, due to hypoxia, leading to anaerobic metabolism - which for a short period of time is well tolerated but during prolonged periods leads to tissue acidification and cell death.

All layers, from the epidermis to the muscles, are well able to handle forces. The bone functions as a hard structure to counterbalance powers from outside and as an anchor point for tissues.

> “It is clear that the fascia integrates the mechanical functionality of all tissues involved.”

Where bone delivers rigidity to the body mass, the dermis envelops and the fascia handles all the mechanical issues in between. Fascia has several, sometimes conflicting functions: to separate, to allow movement [108], to connect, to hold together and/or to transfer forces [109]. It consists of tissue sheets (fascia profunda), septa, capsules, the epimysium, skin fascia, endomysium, perimysium, periosteum, ligaments and tendons etc.

Fascia and connective tissue play a vital central role in force handling [110]. It forms a continuous network, connecting each individual cell to the entire body in a reciprocal way [111,112]. Every tissue type has its own specific type of fascia [113]. Its role extends beyond the level of the cell, as it forms a mechanical link between a cell nucleus and the entire body [114–116]. It is clear that the fascia integrates the mechanical functionality of all tissues involved [117]. In its specific role in the force distribution in and between tissues [105], it has a large impact on the Young’s modulus where it allows for the combination of tissues to handle far more force than each tissue type could in isolation. . It is not clear in what way fascia dysfunction [118] influences force transmission in tissue nor is its role clear in damage, regeneration [119] and wound healing[120]. General issues with fibrin and collagen however, directly impact the quality and function of the fascia.

Healthy tissue can normally withstand 2-4 hrs of static mechanical forces causing local reduced perfusion (occlusion). Sitting, for instance, causes non-pathological ischaemia in the subcutaneous tissue [121]. The reaction of tissue to pressure is not static but relies on the characteristics of the force applied. Brief periods of load relief during a 2 hour loading period did not have any significant effect on the damage progress [122]. It also appears that, over time, the relative softness of, for example, a sitting cushion becomes less important[123].

The integrated biomechanical and physiological properties of tissue allow the body to handle forces far beyond normal biological values.

BIOMECHANICS AND BIOTENSEGRITY

Each tissue type responds differently to force applied. Forces applied on a complex structure like a body, will not only compress tissue, but also cause shearing and even pulling forces. Shearing and pulling forces cause tension. Logically, shear and tension usually act at a different location than compression forces[124].

Tissue is not homogeneous[125]. The parts cooperate to absorb and/or handle energy from forces applied from outside of the body, by stretching, absorbing force and/or deformation. Complex processes are involved in transferring forces between tissues whilst maintaining homeostasis. The body needs to allow stretching of the skin, handle pressure increase in the adipose tissue and also allow free movement of the muscle whilst not obstructing perfusion of blood and lymph or hindering neural function[126].

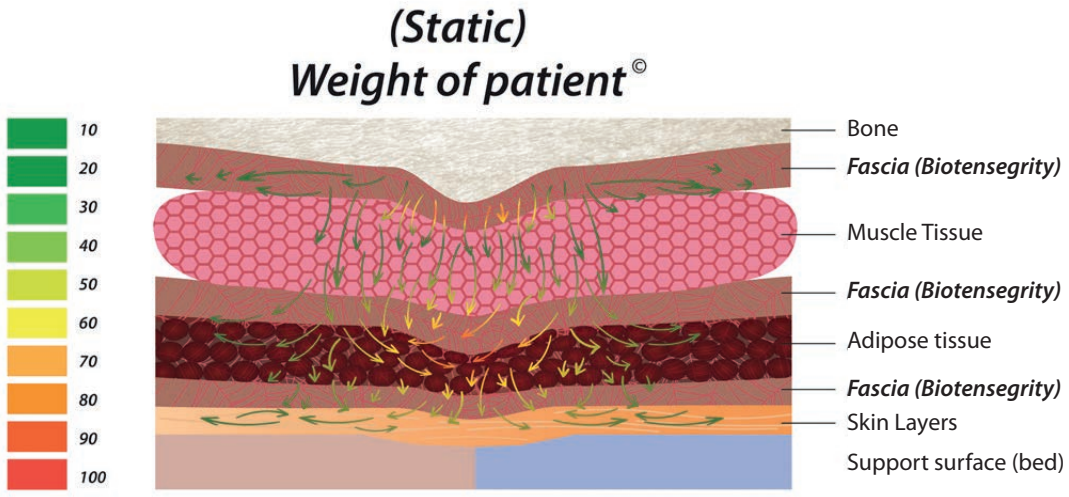

Figure 2: Schematic representation of force distribution in tissue under the influence of gravitational forces.

To be able to maintain tissue integrity and mechanical stability, fascia plays a pivotal role. It has a complex structure from macro to micro[127] and is very well adapted to sensing and transferring static and dynamic forces in the body[112]. This system functions in a continuum at the molecular[128], cellular, tissue[129] and body level[130]. Therefore, it can sense, transfer and withstand forces in a continuous way from the skin up to the atomic level of an individual cell nucleus and vice versa [131].

Tissue, bones and fascia cooperatively functions like a flexible pole and guy rope structure. This means that the combination of tension in the fascia and rigidity of the bones, combined provide a strong but flexible structure. This system, based upon tension to maintain tissue integrity, is called biotensegrity[132]. In this system, the muscles function as an actor, the bones as an anchor and the fascia as connecting rope. This system also exists at the level of tissue and cells. It enables the formation of compartments in, around and between tissues. The connective tissue then functions as a force handling structure (figure 2). Its function may be more than to act as a rope because it functions in a moist environment where hydraulic or hydrodynamic mechanisms come into play [133].

The biotensegrity system also implies that the ability to withstand external forces depends on the direction the forces are applied. The "design" of the human body is made for a "normal" and "self-supporting" life. This means that the tissue is anisotropic [134]. The ability to handle forces is not the same for all angles and starting points. There are indications that shear stress is more causative for tissue damage when compared to pressure stress [124,135]. Therefore, if force applied is too large or from an odd angle, it may cause ruptures in tissue[136]. Mostly due to changes in the collagen structure[137,138]. The Morel-Lavallée lesion, a posttraumatic haemolymphatic collection related to shearing injury and disruption of interfascial planes between subcutaneous soft tissue and muscle[139], is not a part of usual pressure damage theory, whilst it should be since 40% percent of these lesions are on the hip, gluteal or lumbosacral region [140]. Reversibly it is unclear how many deep tissue injuries are in reality a traumatic lesion with a very different aetiology (patient transfer)[141]. This also has implications for diagnosis and treatment [142].

Damage in tissue as a result of mechanical stresses can occur at several levels, from blistering of the skin if the dermo-epidermal junction [143] is damaged; to necrosis of the subcutis due to the adipose tissue; to necrosis of muscles because they have a small low threshold for mechanical stress; to local necrosis due to extreme high forces (Laplace law) near bony structures [144]. If and which type of tissue will fail will depend on the characteristics of the mechanical forces exerted and on the quality of the tissues or body systems involved [145]. This may involve more than one tissue type as damage to a tissue can affect the threshold of other tissues. The interdependent function of tissues in force handling means that events on one point have an impact on the entire system. Problems may not manifest at the site of origin. Even at a superficial ulcer, the microcirculation can be compromised at a depth of 10mm[146].

It is not unlikely that a structural problem in a tissue manifests itself at a different location, making it hard to discover exactly what is causing injury.

The amount of force is negatively correlated with the time it is applied in relation to damage. However, this is not the entire story. Thixotropy of tissue causes it to have a tissue response time, its deformation can only begin when the tissue has become more viscoelastic. In a very short time frame lesser force can cause damage due to the inert and, slightly thixotropic nature of tissue [147]. These properties are the reason tissue needs some time to respond to a force. Forces applied faster than the "tissue response time" cause trauma. This means tissue will need time to adapt to an incoming force. Logically, this means that pushing very fast will also cause bruises in the tissue. Similarly, pulling on a body may cause unanticipated tissue damage [148]. This is well in line with findings that deep tissue damage develops in a short time frame and ischemia is likely not the only causative factor [149].

This also explains why manual handling techniques for moving patients can cause Morel-Lavallée like trauma which later is categorised as pressure damage (pressure sore). So not only relatively low but prolonged forces may cause injury, also short but high forces damage tissues. Therefore, we must adapt the time-force graph in order to reflect trauma induced by short peak forces (figure 3).

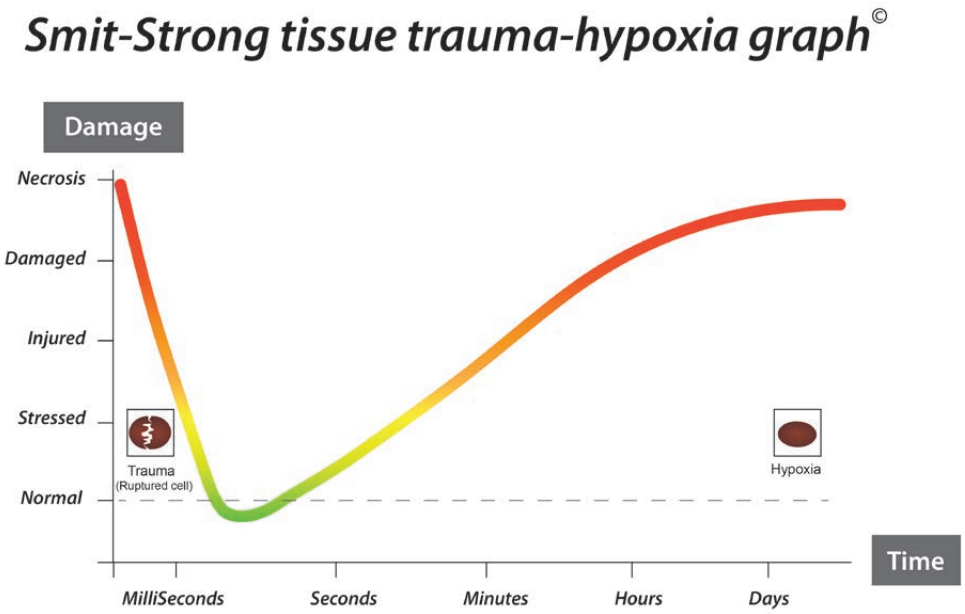

Figure 3. Representation of force over time, surpassing the tissue threshold in a very short or a long period

Any patient movement can be both intentional and unintentional. Similarly, any movement can be gross or micro movement. Some of the patients' movements can be made by themselves and other movements can be initiated by their carers manually (manual handling) or using mechanical aids. These types of movements when combined together with the identified complexities of the body's internal systems for preventing and repairing tissue damage, leads to a reasoned conclusion that, the most effective preventative trajectory to maintaining the patient's optimum tissue integrity is to control the two major factors that are within their external environment: Both the resting/support surface interface and ways that patients are rested/supported, moved and stabilised.

DIFFERENCES BETWEEN HEALTH AND DISEASE

In a healthy subject, lesions at the body-surface interface rarely develop. Lesions occur when the tissue involved is not able to withstand the force applied. In order to develop force-induced damage in patients, it is required that a) the forces cannot be evaded, b) the tissue quality is reduced and/or c) homeostatic and/or regeneration processes are impaired. Patients suffering from generic, structural or systemic issues may qualify by having less opportunity to counter, recover or bypass the effects of forces on or in the tissue compared to a healthy subject.

General risk factors for acquiring pressure ulcers are summed up in the Braden scale: which addresses both causative external factors: pressure and friction and disabling factors (tissue threshold reducing): sensory perception, activity, mobility, nutrition, skin moisture. Table 1 provides more detail and examples in which the tissue threshold may be impaired by factors in the entire body, its systems, its structures and/or local factors.

The fastest source of damage is trauma, which results from extreme forces on tissue – for instance, due to pulling the body to reposition a patient, or non-suitable contact surfaces (shoes). Connective tissue and interfaces between tissue types are especially prone to this type of injury. If the connective tissue or collagen structures are compromised, even a light force can cause pathological ruptures[150,151]. However vigilant patient carers are, manually handling a patient generates peak forces that easily lead to the rupture of compromised tissue. Laplace Law dictates the generated force will maximise at bone-tissue interfaces, causing deep tissue injury.

The quality of the dermis can be influenced by moisture - changes in its collagen and elastin and flattening of the dermal-epidermal junction - all leading to a decrease in its energy absorbing capacity and increasing the chances of force related damage [93,152]. The same applies for a degradation of the epidermal-dermal junction.

Adipose and muscle tissue have thixotropic properties; if it is not moved, it becomes stiff. This can be understood by the combined effect of adipose cells and the fascia. However, this means that abrupt application of force on static tissue has an effect on muscle and adipose tissue that may cause microscopic ruptures in the compromised tissue [102]. Generally, collagen will not deteriorate gradually but it is more likely to rupture. The mechanical integrity of the tissue can be further reduced by lipid position in fascia [153] and stiffening [154,155].

Behavioural issues, the position of the body in time and space, are usually summarised as mobility problems. Immobility causes vessels to be occluded for a longer period than the tissue can handle. Lack of oxygen causes cells to die. Normally, hypoxic signalling leads to repositioning of the body. Repositioning is compromised when the body cannot be timely repositioned. This is usually caused by an inability to move – as in the case of very ill or weak persons, or co-morbidity due to spinal cord injury. There is a trade-off in surface type – in terms of the positioning is easy on a relatively hard surface whilst a high conforming surface may increase the energy needed to reposition the body. This becomes even more important when it is understood that aged muscle in itself is "stuck in gear", and is not able to produce the force needed to reposition the body [176]. Another possibility is that the body is not detecting forces and/or hypoxia, usually as a result of neural pathology. Damage can also occur without obvious ischaemia, which makes it hard for the body to detect.

Immobility for longer than a few days causes numerous changes such as increased skin temperature, hyperaemia and increased transepidermal water loss[177] of which reduced bone density and muscle atrophy[178] are the most well-known[179]. Tissue deformation can be macro: muscle deformation[180] and micro: thinning, stiffening, deformation of several tissue types and changes in collagen and elastine type and function[181,182]. Micro changes in tissue, especially stiffening, alter the cellular response. In as little as fourteen days of bed rest, a healthy middle-aged subject will develop significant muscle damage[183]. Apart from immobility, there are more marginal factors for reduced tissue quality. Atrophy compromises the force handling ability of muscle tissue184. Impaired force handling ability of muscle and other tissues may lead to numerous small, sublytic lesions. Repair will lead to a gradual fibrosis and further loss of tissue quality[185]. Ageing also impacts the ability to regenerate injured tissue like muscle[186]. The main cause for this is tissue fibroblast and macrophage senescence.

The role of the arterial system in force related injuries has been discussed above. However, any age or disease-related change to the vascular system will have an immediate effect on the reaction to force and the ability to handle hypoxia, due to issues such as reduced elasticity and or endothelial dysfunction[187]. Different pathologies require different measures, where the quality of the vessel wall is compromised [188]. Reduced vessel quality can dramatically increase the time needed for recovery from minutes to days. The key factor is to prevent indentation and maximise recovery time. For example, in spinal cord injured patients, the vessel walls are not compromised and here, alternating pressure has a better outcome[189].

Table 1: Possible causes for reduction of tissue threshold©

Generic factors	
1.	Mobility issues which compromise the ability to reposition the body.
2.	Ageing [156–158]
3.	Co-morbity (diabetes, spinal cord injury)
4.	Nutritional problems, patients can be cachexic which means that they simply do not have the energy available to run the necessary processes[159, 160].
5.	Endocrinological issues like diabetes[161]
6.	Slow metabolic processes leading to slower cell generation[159].
7.	Stress [158,163]
Systemic factors	
8.	Sensory disability due to neural system impairment. Compromising detection of local pressure and/or ischaemia.
9.	Neural problems reducing the homoeostatic capacity of the tissue.
10.	Metabolic problems which hamper the homoeostatic capacity of the tissue[159,164,165].
11.	Endothelial disability; due to endothelial problems, the exchange of metabolites in the tissue is impaired, local energy balance is disturbed and oedema can occur.
12.	Non-resolving inflammation is not a primary cause, but it contributes significantly to the pathogenesis[166].
13.	Vasopressors [cox]
Structural factors	
14.	Atrophy functionally compromising tissue[167].
15.	Tissue stiffening, which also leads to problems in force distribution[168].
16.	Lymphatic sclerosis[169].
17.	Perfusion problems like vascular disease where vessels easily collapse or have impaired recovery ability[170,171].
18.	Fascial dysfunction[150,172,173].
19.	Local metabolic capacity, wounds in areas with a high metabolic activity like hands and face usually heal faster than wounds in areas with a lower metabolic rate
20.	Biotensegrity issues
Local factors	
21.	Moisture[174,175].
22.	Time issues (See figure 3).

If the tissue reperfusion is not optimal, tissue will be hypoxic for a longer period. Adipose, muscular, dermal and neural tissues are not equally sensitive to hypoxia. This may be another explanation why damage does not always occur at the location of the highest force, notwithstanding better resistance to hypoxia. The short-term and the mechanical properties of adipose tissue are negatively influenced by fibrosis as a result of long-term hypoxia[190], which is another cause of connective tissue degradation reducing tear resistance.

A prominent issue in tissue damage is inappropriate inflammation. In essence, this is damage-induced damage. It is conceivable that a small number of dead cells, combined with failing inflammation or sensory failure, triggers a snowball effect[191], leading to larger defects to which a response does not necessarily solve problems [192].

This is because the inflammatory response in itself can be a cause of nervous and muscular damage, eventually leading to nerve damage and rhabdomyolysis[193]. Further, immune senescence[194] can lead to a reduced immune response and this inflammation[195] is considered a major cause of age-related events.

Apart from the obvious hardship to reposition, the paraplegic person also faces the direct and indirect results of the spinal lesion[196,197] which impacts movement, but also tissue (including bone) itself [198,199]. Nerve fibres degrade over time, compromising the pivotal role that the neural system plays in tissue homeostasis and repair. Skin/tissue failure might be misdiagnosed as being force related tissue damage. Critically ill patients may develop acute skin/tissue failure[200,201], which appears as force related tissue damage but has a different aetiology[202]. Failing skin loses normal temperature control and cannot prevent transdermal loss of fluid, electrolyte and protein[203]. It is an indicator of body system failure.

The body uses complex systems of cells for homeostasis and repair. The impact/effect that forces have on the biotensegrity system at one point may manifest elsewhere in the system. The many ways that forces can exceed thresholds, and tissues comprised, makes typing ulcerations difficult[204]. Critically ill patients suffer from serious system malfunction where the neural and muscular system are deteriorating[205].

Patients may help us to not only distinguish between skin/tissue failure that is due to body system failure of both critically ill and end of life patients (last 5 days approx.) and that of force related tissue damage (pressure injury), but also help discover what is age-related and what is disease-related marginal factors in pressure related tissue damage. So not only factors related to force and tissue threshold but also behavioural factors play a role in force related tissue damage.

CONCLUSION AND RECOMMENDATIONS

There is a common concept that force related tissue damage (presently referred to as pressure injury, historically called pressure ulcers etc.) results from vessel collapse and cell death due to compressing (pressure theory) tissue between bone and a hard surface (figure 1). This is an oversimplification of the processes involved as it focuses on passing the static tissue pressure threshold. However, it ignores the interrelation and dynamics of many forces exerted on tissue and the reasons why tissue thresholds have been passed.

Force related tissue damage occurs when events lead to stress and damage at a molecular, cellular, tissue, organ and organism level, well in advance of the skin being broken. Sublytic damage at one point can cascade via mechanical, physiologic, chemical or systemic pathways into pathological lesions. Present wound care science struggles to diagnose and cure lesions due to the complexity and processes involved regarding tissue homoeostasis, damage and regeneration. This paper identifies in table 1 over 22 internal marginal influencing factors. These include generic (such as stress), systematic, structural and local factors, that can contribute to the loss of optimum tissue integrity (i.e. that can cause/contribute to both a reduction in the tissue resistance threshold and/or a reduction in tissue recovery).

“Over 22 internal marginal influencing factors. These include generic (such as stress), systematic, structural and local factors, that can contribute to the loss of optimum tissue integrity.”

A predictive approach will require a greater use of available standard medical procedures which are applicable for wound care and would include current diagnostic tools for assessing and grading deep tissue injury (DTI), endothelial status and reperfusion injury. Incorporating the use of classical diagnostic tools such as medication screening[206,207], laboratory values[208,209], biomarkers[210,211], tissue sampling[212,213] and imaging[106,123] guidelines. Together with available advanced diagnostic tools such as (epi) genetic[212,214–216], proteomic[217] and metabolomic[218,219] screening they will allow us to predict, prevent and treat individuals at risk in the near future.

Some patients are more prone and of a higher risk to tissue damage, screening tools can overlook patients who don’t show tell-tale signs but are nevertheless prone and are at risk to tissue damage when the body’s threshold of resistance and/or ability to recover from damage, is reduced and/ or surpassed. Unnecessary external forces can be

generated by the practices used to rest the patient, by how they are moved and how they are re-stabilised, during and after their body mass has been re-orientated. They are an undesirable result from having to work against gravity and can be directly linked to the manual and/or mechanical handling practices being used to overcome the downward gravitational forces that are keeping the patient stable.

Any patient movement and stability should be controlled in a way, which requires working with gravity. Allowing the body to move and be re-orientated safely, further compliments and supports the body's innate homeostasis to keep the patients skin and tissues within its natural threshold of resistance and repair. Thereby, maintaining its optimum tissue integrity. Ideally a patient should be rested, repositioned and stabilised by using gravity without the need for manual and/or mechanical handling. It should allow repositioning and stabilising to be at a sufficiently slow controlled rate and allowing the bodies homeostatic and biotensegrity processes to safely dissipate any potential related tissue damaging forces.

This paper proposes a future trajectory that is both desirable and achievable and would bring wound care prevention, diagnosis and assessment up to date. A trajectory that consigns statements such as: ***"Off-loading the area still offers the best chance for tissue that is ischemic or injured, but not infarcted"*** [220] to be logical at first sight but in reality non-sufficient for practical application. The evidence base for this approach to safer care demonstrates that force related tissue damage prediction and prevention, rather than treatment, is always the preferred approach to maintaining the patient's optimum tissue integrity.

Categorising force related tissue damage using terms like inflammation, amount of tissue lost or necrosis does not fully address events leading to force related tissue damage. Recognising parameters of force, behaviour and tissue threshold in the events leading to ulceration may impact the way we prevent and treat force related tissue damage. Clearer guidelines are required that not only recognise, identify, and incorporate the exact tissues and systems involved but also make sure the latest up to date options for prevention, diagnosis, assessment and treatment are available and used.

Statement regarding conflict of interest:

Phil Strong: designer and supplier of related health care products
Harm Smit: none

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"Force-related tissue damage shifts the focus from something to be managed to something to be predicted and prevented."

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