Medical device-related pressure ulcers and the COVID-19 pandemic: from aetiology to prevention

KEY WORDS
- Bioengineering
- Computer model
- Medical device-related pressure ulcer (MDRPU)
- Pressure ulcer
- Pressure injury
- Pathophysiology
- Prevention

This article describes the aetiology of medical device-related pressure ulcers (MDRPU) and the vicious cycle that leads to these (typically, hospital-acquired) injuries. In this cycle, the primary, deformation-inflicted cell damage leads to a secondary inflammatory oedema-related damage and then to tertiary ischaemic cell and tissue damage. These three damage factors act cumulatively, and, once the first deformation-inflicted massive cell death initiates in the distorted tissues, each of these factors escalates the cell death and tissue damage further, under and near the applied medical device. The primary pathophysiological factors of the COVID-19 pandemic — including the cytokine storm, hypoxia and hyper-coagulation, which are typical to seriously ill patients who require life-support (skin-contacting) medical devices — can fuel the damage spiral of pressure injury. A continuous positive airway pressure (CPAP) mask is a classic example of a commonly used medical device (especially in treating patients with COVID-19 virus who present with breathing problems), which is often the cause of a MDRPU, as it applies intense, localised mechanical loads onto the facial skin and within underlying soft tissues. Moreover, the affected facial soft tissues cannot swell in response to the inflammatory oedema that typically develops under the mask, as they are sandwiched between the device and the skull. It is possible to lower the risk of a CPAP-caused MDRPU, particularly through appropriate selection and application of prophylactic dressings under the CPAP mask, primarily in order to alleviate and disperse the localised soft tissue loads. Other than alleviating the sustained, localised mechanical loads in the affected tissues (i.e. the tissue stress concentrations), such prophylactic interventions must minimise the heat accumulation on and within skin and reduce the exposure of skin to shearing forces. Understanding the aetiology of MDRPUs targets and focuses effective clinical interventions. An informed selection of a prophylactic dressing technology, based on bioengineering testing, is different from making non-evidence-based choices, such as selection of hydrocolloid materials, which are relatively stiff and are not conducive to tissue load alleviation.

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Medical device-related pressure ulcers (MDRPUs) are caused by sustained, external forces that are applied by skin-contacting medical devices (Gefen et al, 2020a; Gefen, 2021a). A recent systematic review article reported that the incidence and prevalence of MDRPUs are 12% and 10%, respectively (Jackson et al, 2019), indicating that MDRPUs occur frequently in the hospital setting. The suffering of patients affected by MDRPUs may continue for years or even a lifetime: for example, due to the injuries becoming hard-to-heal or as a result of permanent facial scarring. In addition, these wounds impose a considerable financial burden, both in terms of direct treatment

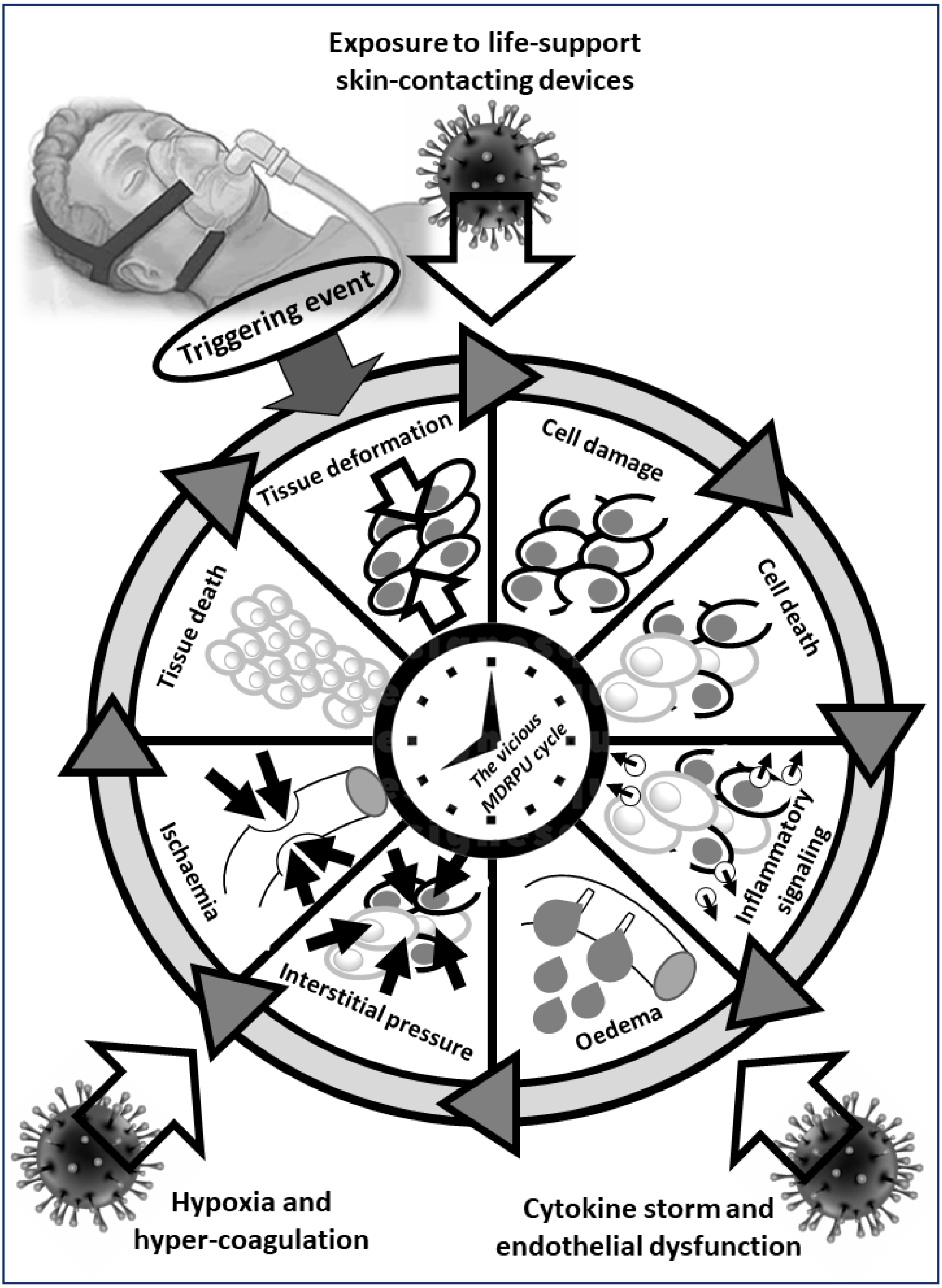

Figure 1. The vicious medical device-related pressure ulcer (MDRPU) cycle and the links with the pathophysiology of the coronavirus disease 2019 (COVID-19)

(material and labour) costs (Gefen et al, 2020b), and due to resulting litigation as, in the majority of cases, MDRPUs are, by definition, a hospital-acquired injury (associated with equipment that is primarily used in a hospital).

Similarly to the distorting influence of sustained bodyweight forces on cells and tissues, cells in the soft tissues under or near a skin-contacting medical device typically undergo extreme shape changes and deformations that result from the forces applied by the device, which ultimately leads to the loss of biological function of the deformed cells. Cells are essentially physical structures that contain structural elements — made of proteins – with specific mechanical roles, of resisting mechanical forces, supporting loads (at the microscale) and also, allowing shape adaptations and cell movement. As with any other physical structure, the cells depend on these structural elements and once damaged, the cells are likely to die.

A practical analogy is to think of a cell as a larger structure that is loadbearing, such as a submarine (Gefen, 2021a). When a submarine dives too deep, it is subjected to extreme pressures that would cause its hull to lose the reinforcing structural elements, which yield or break under the water pressure. When these reinforcing elements of the hull are damaged, the walls of the vessel may crack and water will penetrate and flood the interior spaces of the submarine. Like submarines, living cells contain reinforcing elements that structurally support their walls, the cytoskeleton that supports the plasma membrane (the physical envelope of cells). The plasma membrane functions not only as the wall of the cell body, but also as the gate keeper, facilitating and controlling the traffic of all the molecules and ions into and out of the cell body, through specialised mechanisms (much like underwater airlocks function to allow safe passage into or out of a submarine). When the plasma membrane does not receive sufficient structural support (from a dysfunctional cytoskeleton), after several protein structures have failed under the sustained loading, and the cell is therefore unable to maintain its plasma membrane intact, pores appear along the plasma membrane, through which molecules and ions may cross freely. Under such conditions, the main control mechanisms that cells have on their plasma membrane to regulate molecular and ionic traffic, such as ion channels or endocytosis, become ineffective, and hence, the affected cells cannot actively regulate that traffic anymore. The homeostasis of the affected cells, which is the delicate state of steady internal, physical, and chemical balances maintained by living cells, cannot be conserved under such conditions and apoptotic cell death rapidly follows, typically within several minutes (Slomka & Gefen, 2012; Leopold & Gefen, 2013; Gefen & Weihs, 2016; Lustig et al, 2021).

The deformation-inflicted cell damage leading to loss of cell homeostasis, which is triggered by the sustained cell deformation exposure, initiates and perpetuates the vicious cycle of MDRPUs (*Figure 1*). The primary activating factor and the driving vigour for the formation and progression of the cell and tissue damage is the sustained mechanical loading, which causes the cell deformation and leads to the first mass cell death events. This results in localised inflammatory oedema, which, particularly in cases where tissue expansion due to the accumulated fluids (i.e. tissue swelling) is restricted or limited, elevates the interstitial tissue pressures. The build-up of high interstitial pressures due to the inflammatory oedema further deforms the cells, causing additional loss of cytoskeletal integrity and more poration of the plasma membranes of the affected cells. As the process escalates, and without relief or repositioning of the medical device, the localised rise in interstitial pressures may eventually cause the obstruction or even partial occlusion of the vasculature, or the lymphatics. If that occurs, the cells under or near the device are not only affected by mechanical stresses, but also by chemical stress, which relates to the hypoxia and low pH (acidosis), as cells are using their glucose reserves and produce lactic acid in the forming anaerobic environment. A MDRPU caused by a continuous positive airway pressure (CPAP) mask is a classic example of an injury cascade that follows the above aetiology, and where the tissue conditions are synergistically amplifying the damage (*Figure 1*).

A CPAP-based ventilation therapy is indicated in patients with acute or chronic respiratory failure. Facial MDRPUs caused by CPAP masks appear among 10% to 33% of CPAP users within several hours of application of the mask; these injuries are associated with the sustained soft tissue deformations caused by mounting and tightening the mask to the head, and the extreme microclimate conditions that expose the facial skin under and near the mask to almost 100% humidity (Yamaguchi et al, 2014; Schallom et al, 2015; Rathore et al, 2016; Otero et al, 2017; Alqahtani & AlAhmari, 2018; Alqahtani et al, 2018; Brill et al, 2018; Peko Cohen et al, 2019). As the mask directly compresses and shears the heated facial skin and underlying soft tissues against the rigid skull surface (and more so when the straps are overtightened), extreme mechanical stress concentrations develop in the affected tissues. It is noteworthy that if strong tightening of the straps of a CPAP mask is required often to prevent air leakage, this is an indication that the mask does not fit the patient properly. Moreover, the facial tissues under a CPAP mask have very little space for swelling when the oedema progresses, and therefore, if oedema develops, the interstitial pressures will rise sharply and rapidly, further accelerating the MDRPU vicious cycle that is depicted in *Figure 1* (Lustig et al, 2021).

While sustained tissue loading is the primary causative and triggering factor across all pressure ulcers (i.e. either those caused by the bodyweight forces of a patient or those inflicted by external objects), there are some additional conditions that are unique to the aetiology of MDRPUs, as follows (Gefen et al, 2020a; Gefen, 2021a). First, skin-contacting materials in medical devices are often substantially stiffer than native skin and the underlying soft tissues (Bader et al, 2019; Gefen et al, 2020a; Gefen, 2021a). Second, some medical devices require securement onto the body by applying external forces, such as the tension in the straps of a CPAP mask, which are tightened to prevent air from leaking out. Third, the vast majority of externally applied medical devices are produced in uniform shapes and sizes (for which there are limited choices), hence, ideal fitting to the contours of the body of an individual is unlikely and, therefore, sites or spots of indentation of device parts into the skin will nearly always be present. Fourth, ventilation equipment (CPAP masks again being an example) is applied in a hot and moist environment (that is induced by the exhaled air), which compromises the tolerance of the skin to the mechanical loads applied by the device, increases the frictional contact forces and thereby the shearing of skin (Kottner et al, 2018; Schwartz et al, 2018). Fifth, it is challenging to conduct regular visual skin assessments under medical devices without detaching or moving the device (which may affect its function). Finally, there appears to be less overall awareness of MDRPUs among health professionals with respect to the awareness to bodyweight-induced pressure ulcers (PU) and the need to prevent them. Accordingly, devices are not always repositioned in a timely way and routine skin care under applied devices is sometimes not delivered adequately.

The influence of the COVID-19 virus on the vicious cycle of device-related injuries

Recent reports of the effect of the COVID-19 virus on the epidemiology of PUs in general and MDRPUs in particular demonstrate a (non-surprising) sharp rise in incidence and prevalence. For example, in the UK, the overall PU rate per 1000 beds in acute care increased from a pre-pandemic level of around 1 to over 2.7 in the first month of the pandemic (Vowden & Hill, 2021). This rise is specifically associated with the increase in MDRPUs and prone positioning in the expanded critical care patient population (Martel & Orgill, 2020; Vowden & Hill, 2021). These findings agree with data collected in the US, where hospital-acquired PU numbers have increased steadily from March to May 2020 (Polancich et al, 2021).

The scenario of MDRPUs caused by CPAP masks is likely the most relevant device-related injury in the context of the COVID-19 pandemic, as CPAP treatment became the first-line intervention for patients with breathing problems due to the virus. The pathophysiology of COVID-19 infection strongly interacts with the vicious cycle of MDRPUs in several aspects (Gefen & Ousey, 2020a; Lustig et al, 2021; *Figure 1*). First, the systemic cytokine storm in patients with a serious COVID-19 illness compromises the sensitivity of their inflammatory system to detect the molecular signalling from a local source of a forming MDRPU, which allows cell deformation-inflicted damage to progress unnoticed by the inflammatory system until massive cell death has already occurred (Gefen & Ousey, 2020b; *Figure 1*). Second, once the inflammatory system initiates its response to the localised cytokine signalling from the MDRPU site, the inflammatory oedema that results would likely be more extensive and would spread more widely, due to the endothelial dysfunction in such seriously ill patients. This will escalate the associated inflammatory damage caused by the rise in the interstitial pressures, which would result in additional sustained high distortions of cells under and near the CPAP mask and, simultaneously, metabolically starve these cells, since nearby vasculature and lymphatic vessels would also collapse under the rising pressures of the fluids that escape from the leaky vessels (Lustig et al, 2021; *Figure 1*). Third, any localised clotting and thrombotic showers that are caused by the hyper-coagulation observed in COVID-19 patients (Abou-Ismail et al, 2020) would further exacerbate the already decreased tissue perfusion and oxygenation and thereby worsen the metabolic status of the affected tissues.

Hence, all the above COVID-related factors combine to fuel the vicious cycle of MDRPUs, namely:

- The primary deformation-inflicted cell and tissue damage, directly through the application of the device and the sustained tissue loading state
- The secondary inflammatory damage, due to the cytokine storm
- The tertiary ischaemic damage, due to the hyper-coagulation and tendency to micro-thrombotic events, or due to heart dysfunction associated with myocarditis or cardiomyopathy from the COVID-19 infection, or any combination of these conditions (*Figure 1*) (Gefen & Ousey, 2020a; Lustig et al, 2021; Gefen et al, 2021).

Indeed, Martel & Orgill (2020) reported a series of photographic evidence of facial MDRPUs in COVID-19-positive patients, demonstrating massive tissue destruction at the nose and cheeks (see Figure 3 in their publication), which appears to be overall more severe than the facial MDRPUs caused by CPAP masks that were reported in the pre-pandemic medical literature.

CPAP masks as a COVID-19-relevant case study

A focused discussion of MDRPUs caused by CPAP masks is warranted, since CPAP masks were long known to be a device that often and quickly lead to a facial injury, with incidence rates that are as high as 50%, and now, these specific medical devices are the first intervention offered to patients presenting with COVID-19-related acute respiratory distress syndrome (Alqahtani et al, 2018; Barakat-Johnson et al, 2017; Dang et al, 2021; Kofod et al, 2021). Relatively early during the pandemic, it was recognised that ventilation by means of CPAP masks is an easier and more cost-effective option compared with intubation, for managing the massive influx of COVID-19-positive patients with acute respiratory failure (Alviset et al, 2020). Later clinical findings indicated that the use of oral-nasal CPAP masks eliminates the need for intubation in almost half of COVID-19 patients who required respiratory support (Menzella et al, 2021). With the dramatic increase in using CPAP masks as the pandemic continued, it is not unexpected that there was a reported rise in MDRPUs (Martel & Orgill, 2020; Vowden & Hill, 2021). Moreover, before the pandemic, the CPAP treatment method was typically used for short periods of time, but unfortunately for patients with COVID-19 who are seriously ill, the ventilation support is required for substantially longer periods (Percy, 2020). All of this is added to the well-established knowledge that prolonged use of CPAP masks endangers the viability of facial soft tissues, due to the combined sustained mechanical deformations caused by the tightening of the mask onto the skin, and the altered microclimate conditions at and near the mask-skin contact sites (Alqahtani et al, 2018; Gefen et al, 2019; Peko Cohen et al, 2019; Lustig et al, 2021).

The facial locations that are most susceptible to CPAP-related injuries are the nasal bridge and the cheeks (Schallom et al, 2015; Otero et al, 2017). This is explained by anatomical and physiological factors, including a lower soft tissue mass over the nasal and cheek bony prominences, as well as the lower blood perfusion at these specific facial sites, compared, for example, with the soft tissue thickness and perfusion levels at the chin (Brill et al, 2018; Peko Cohen et al, 2019). The compressive and shear forces applied by a CPAP mask to facial skin along narrow contact regions and especially at the above locations cause indentation of the mask contours into the skin. This device indentation into the skin is associated with compound tissue loads (i.e. concurrent compression, tension and shear stresses), which concentrate at and below the mask-skin contact regions and that rapidly trigger the vicious

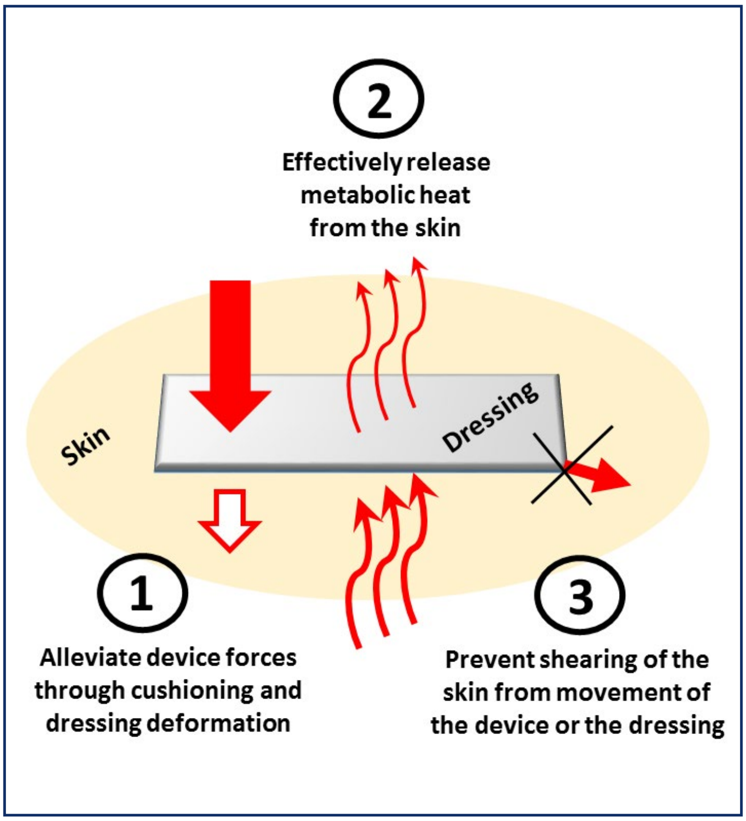

Figure 2. The three primary functions of a prophylactic dressing, which are critical for protecting from a medical device-related pressure ulcer

cycle of MDRPUs (Peko Cohen et al, 2019; *Figure 1*), typically already within the first few hours of use. Specifically, according to Carron and colleagues (2013), the incidence of CPAP-related MDRPUs is between 5% and 50% after a few hours, and increases further, and dramatically, to nearly 100% after two days of continuous use, which is more typical to the respiratory needs of seriously ill COVID-19-positive patients. Added to that is the lack of biomechanical knowledge-driven guidance for health professionals regarding how to safely apply CPAP masks during the pandemic, sometimes leading to over-tightening of the masks (Gefen & Ousey, 2020a; Percy, 2020) and that the generic mask designs, using relatively stiff polymeric materials, often do not fit the contours of the individual face (Shikama et al, 2018). The unavoidable result is extreme, localised facial tissue stress concentrations, which are sustained from hours to days, and that may lead to serious injuries (Lustig et al, 2021). For patients with acute respiratory distress syndrome who are COVID-19-positive and are treated by means of CPAP masks for long periods to avoid intubation, without effective protective means, a facial MDRPU caused by the CPAP will be almost inevitable.

The preventative potential of hydrogel-based prophylactic dressings

In the seminal biomechanical work *Transferring Load to Flesh*, Murphy (1971) discussed the two imperative factors that intensify stress concentrations in skin and underlying soft tissues when in contact with an external object, and which may lead to tissue breakdown: (i) sharp transition from high (i.e. medical device material) to low (i.e. soft tissue) stiffnesses and; (ii) geometrical irregularities of either the device surfaces or the body contours. Indeed, a CPAP mask meets both of these conditions: its materials are substantially stiffer with respect to those of facial soft tissues and its curved narrow contours, together with the irregular topography of the face (particularly at the nasal bridge), are conducive to tissue stress concentrations (Brill et al, 2018; Peko Cohen et al, 2019). In addition, over-tightening the mask would further intensify these tissue stress concentrations. Accordingly, the most important biomechanical intervention in order to reduce the risk of a CPAP-related MDRPU is to alleviate the localised, intensified facial tissue deformations and stress concentrations induced by the mask, which is achievable through application of additional soft and flexible cushioning materials at the susceptible mask-face contact areas. This local cushioning directly addresses the two aforementioned biomechanical principles identified by Murphy (1971). Specifically, the cushioning smoothens the sharp material stiffness gradient between the relatively stiff CPAP mask materials and the substantially more compliant facial tissues and, further, increases the contact area for transfer of the mechanical loads delivered by the mask, which redistributes and alleviates the tissue stress concentrations (*Figure 2*; Peko Cohen et al, 2019).

Health professionals are aware of the clinically positive outcomes based on the above biomechanical principles and have therefore commonly used cuts they prepare from wound dressing materials as cushioning elements under

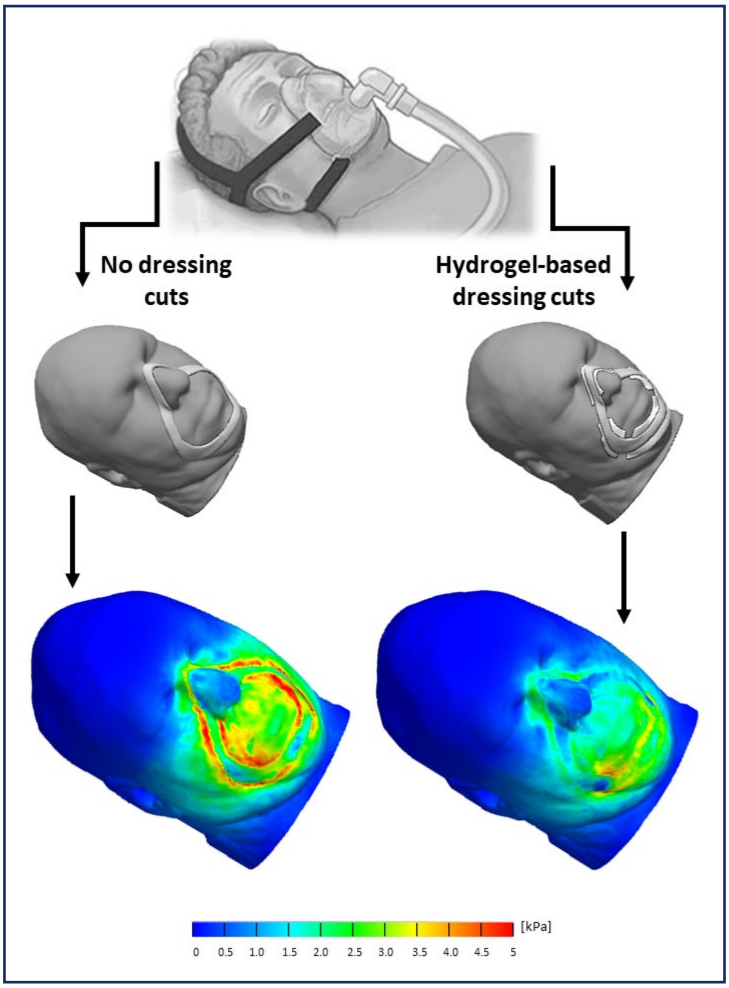

Figure 3. Computer modelling demonstrates the protective effect of hydrogel-based dressing cuts in alleviating facial skin tissue stresses under a continuous positive airway pressure (CPAP) mask, with respect to a case where dressings were not applied to protect the facial tissues

CPAP masks for prophylaxis (Peko Cohen et al, 2019). Nevertheless, the quality of the biomechanical protection that a dressing material provides in preventing the CPAP-related MDRPUs clearly depends on its stiffness properties, which determine its ability to smoothen the mask-skin stiffness gradient and, in addition, to effectively increase the contact area for load transfer through self-deformations (Grigatti and Gefen, 2021).

Another important aspect in the function of dressing materials under a CPAP mask is their ability to influence the microclimate of facial skin. This aspect of the function of dressings is primarily quantified through the thermal conductivity of the materials and structure in each given dressing, which is, like the mechanical stiffness, a fundamental physical property of high clinical relevance (Gefen et al, 2019; Gefen et al, 2020a; Gefen, 2021b). Specifically, the thermal conductivity measurement of a dressing expresses the extent of metabolic heat transfer from the tissues under the dressing, outward through the dressing structure (Gefen, 2021b). This value can provide a means to evaluate the expected heating of the skin under the dressing, whereas excessive heating of the skin under the dressing leads to perspiration, which compromises the ability of skin to resist the external forces applied by the CPAP mask, and also positively correlates with a state of tissue inflammation (*Figure 2*; Gefen, 2021b). Hence, the synergistic influences of geometrical, mechanical and thermal mismatches between a CPAP mask and the facial skin may cause tissue stress concentrations and sharp temperature gradients, both of which contribute to the risk for MDRPUs (Gefen et al, 2019; Peko Cohen et al, 2019; Gefen, 2021a; Grigatti and Gefen, 2021).

To address the above complexity in material selection for dressings in prophylactic use under medical devices and CPAP masks in particular, the author and his research team recently developed an innovative, integrated experimental bioengineering approach, encompassing mechanical stiffness, friction and thermal property studies for testing the biomechanical suitability of dressing materials (Grigatti and Gefen, 2021). The focus of this work has been on a hydrogel-based dressing (HydroTac Transparent, manufactured by Paul Hartmann AG, Heidenheim, Germany) as a test case for this new integrated bioengineering methodology (Grigatti and Gefen, 2021). The work characterised the viscoelastic stress relaxation of this hydrogel-based dressing material, and determined its long-term stiffness (i.e. elastic modulus), which is relevant to the sustained loading state associated with CPAP usage. The coefficient of friction of this hydrogel-based dressing was further measured at dressing-device and skin-dressing interfaces, using a tilting-table tribometer, to assess whether movement of the dressing on the skin, and thereby additional skin shearing under the CPAP, are a likely scenario (Grigatti and Gefen, 2021). Lastly, the thermal conductivity of the hydrogel-based dressing was determined, using a heat-flow meter and infrared thermography-based methods. All these measurements considered dry and moist dressing conditions, the latter simulating skin perspiration effects (Grigatti and Gefen, 2021). The results revealed that the long-term stiffness and the thermal conductivity of the hydrogel-based dressing matched the corresponding properties of human skin for both the dry and moist dressing conditions. The studied hydrogel-based dressing further demonstrated a relatively high coefficient of friction at its skin-facing and device-facing aspects, indicating that minimal frictional sliding on the skin can be expected. All these properties make the above hydrogel-based dressing advantageous for prevention of MDRPUs (*Figure 2*; Grigatti and Gefen, 2021).

In follow-up work that is currently underway, the author's research group had used an anatomically-realistic computer model of an adult head wearing the CPAP mask without the protective dressings, versus with the hydrogel-based dressing cuts applied at the nasal bridge, the cheeks and the chin, to quantitatively analyse the facial tissue exposure to the sustained forces induced by the CPAP mask (*Figure 3*). Because the nasal bridge and the cheeks are the less tolerable sites to sustained tissue deformations (Otero et al, 2017; Peko Cohen et al, 2019), they require the highest level of tissue load alleviation. The findings from the computer modelling work demonstrated that the hydrogel-based dressings provided adequate protection at the nasal bridge and the cheeks, which is evident by the tissue stress dispersion at these facial sites (Figure 3). This biomechanical efficacy of the hydrogel-based dressings in protecting facial tissues should be mostly attributed to their stiffness-matching (modulus-matching) with skin (Grigatti and Gefen, 2021), as well as to their conformability to fit the curved facial contours at the at-risk (nasal bridge and cheek) sites.

CONCLUSION

This article reviewed the complex aetiology of MDRPUs and its interlinks with COVID-19 patients using the CPAP mask as a relevant and timely example under the circumstances of the pandemic. Bioengineering studies, such as the laboratory testing of mechanical and thermal properties of dressings used in the prophylaxis of MDRPUs (*Figure 2*), and likewise, the computer modelling work demonstrated in *Figure 3*, are vital for further understanding the aetiology of MDRPUs and, in particular, for targeting and focusing effective preventative interventions, before their confirmation through clinical research. In previously published work, the author demonstrated that hydrogel-based dressings are advantageous for the prevention of MDRPUs from a bioengineering standpoint, by following the biomechanical principles and using the bespoke laboratory methods that stem from the contemporary aetiological knowledge on the formation of MDRPUs (*Figure 2*). The computer modelling results reported here (*Figure 3*) demonstrate the power and effectiveness of this scientific approach through the substantial alleviation of skin tissue loads following the application of the studied hydrogel-based dressings, the effect of which was particularly influential in protecting the nasal bridge and the cheeks (*Figure 3*). This performance can be specifically attributed to the laboratory findings reported by Grigatti and Gefen (2021), indicating that hydrogel-based dressings had optimal stiffness-matching (also known as modulus-matching) with skin.

Finally, laboratory bioengineering evaluations and clinical research go hand-in-hand in the context of preventing MDRPUs. This pertains not only to understanding the fundamental causes of the MDRPU problem (i.e. the detailed aetiology), but also to directing bioengineers to find effective and clinically relevant technological solutions to this problem. Since the fundamental essence of MDRPUs is the sustained soft tissue exposure to the device-induced localised and intense mechanical loads (*Figure 1*), applying the principles reviewed here (*Figure 2*) leads to considerable alleviation of the tissue stress exposures under and near the (CPAP) medical device (*Figure 3*). The latter eventually translates to better patient safety, an improved quality of life for patients and a substantial reduction in direct and indirect healthcare costs. Over many years, the author's work consistently points to the need for investing in bioengineering and material engineering research to identify and optimise dressing materials that are best suitable for the prophylaxis of MDRPUs (Gefen et al, 2019; Peko Cohen et al, 2019; Gefen et al, 2020a; Gefen, 2021a, 2021b; Grigatti and Gefen, 2021). The non-evidence-based choices often made by health professionals in their efforts to prevent MDRPUs, such as application of stiff hydrocolloid materials (Gefen, 2021c), are rarely based on laboratory science and may therefore lead to poor preventative outcomes. Adequate selection of a prophylactic dressing type must be based upon peer-reviewed, laboratory science that is clinically verified.

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