



Review Article

Non-invasive Technologies of Tissue Viability Measurement for Pressure Ulcer Prevention in Spinal Cord Injury

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Abstract

Developing Pressure Ulcer (PU) is one of the most common devastating complications following Spinal Cord Injury (SCI). Following SCI, loss of sensation and mobility alongside changes in circulation leads to elevated risk of developing PU. Once a PU is formed, it significantly increases the burden on the individual with SCI individual and/or the caregivers and has substantial detrimental impact on the quality of life, independence, and dignity of a patient. Apart from personal consequences, PU also represents a significant cost burden for health and social care systems. Therefore, preventing PU formation is vitally important in SCI. Thus far, numerous prevention methods have been implemented, such as using various expensive specified cushions, patients regularly repositioning together with health professionals investigating significant time on monitoring patients using various subjective risk assessment tools. In spite of tremendous efforts, incidence of PU remains unacceptably high in people living with SCI. Without robust objective assessment tools to detect or monitor early sign of PU has been long considered as main challenges for clinicians and health professionals. This article reviews current non-invasive technologies for measuring risk of PU formation in SCI, and provides an insight in topics for further application and exploration.

Keywords: Non-invasive; Pressure ulcer; Spinal cord injury; Tissue integrity

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Introduction

Developing Pressure Ulcer (PU) is one of the most common secondary complications following Spinal Cord Injury (SCI). It is estimated that more than a half of people living with SCI develop a pressure ulcer during their life-time [1-4]. PU is commonly known as a pressure sore, bed sore or decubitus ulcer, and is described as an area of localised damage to the skin as a result of prolonged pressure alone, or pressure in combination with shearing forces (EPUAP/NAPUAP 2014) [5]. It is typically categorised into four key stages depending on the severity. Once PU is developed, it has substantially detrimental impact on the quality of life, independence, and dignity of a patient [5-7]. If PU is severe, it can lead to further disabilities, need for surgical interventions and even fatal infections [7]. Apart from personal consequences, PU also represents a significant cost burden for health and social care systems. According to National Institute of Health and Care Excellence (NICE) guideline 2014 [8], in addition to the costs of standard care, the daily costs of treating a pressure ulcer are estimated to range from £43 to £374 in the United Kingdom. Resources required for treating a pressure ulcer include nurse time, dressings, antibiotics, diagnostic tests and high specification pressure redistributing devices. Although exact cost of PU management in SCI is unknown, the total cost of treating PUs has been estimated to be between £1.4bn and £2.1bn per year, with the average cost to treat one Category IV PU being £14,108 per episode in general population [9]. Given the significant detrimental personal impact and health social cost burden, preventing PU development is vitally important.

Thus far, enormous efforts have been put to prevent PU development in SCI [8,10]. For instance, use of various specified mattress, cushions help relief pressure over bony prominences; patients are required to improve diet and reposition regularly. Health professionals have been constantly looking for the best clinical risk assessment tools to monitor these patients. Yet, despite the extreme expensive equipment together with tremendous staff time, the incidence of PU remains unacceptably high in SCI [1-4].

Indeed, effective PU prevention strategies are based on a thorough understanding of pathological changes following SCI that leads to PU formation. While PU development is undoubtedly multifactorial in individuals with different pathological conditions, the prolonged pressure loading sufficient to produce ischemia, cell deformation, lymphatic impairment and reperfusion injury has been identified as important process of PU formation [11]. Following SCI, loss of mobility results prolonged lying or sitting for their daily activities. The interruption of spinal vasomotor pathways results in the loss of vasomotor control over skeletal muscle and skin, which lowers the tone of the vascular bed below the level of the lesion. The impaired vascular patency causes the vessels to be less able to withstand normal loading conditions. Concurrent with the loss of capillary networks due to lost muscle bulk, the volume of blood in the tissues is reduced [11-13]. Considering microcirculation being crucial for tissue viability in terms of supply of oxygen and nutrients and removal of waste products, interrupted microcirculation leads to ischemia and local tissue starvation. Moreover, following SCI, lack of sensation below the level of injury leads to insensitivity to the ischemia which consequently leads to greater risk of PU formation. The ability of

quantitative assessment of tissue integrity plays a key role for PU prevention. Therefore, robust objective assessment tools to detect or monitor early sign of PU are needed.

As early as 1980s, Levine and associates measured blood flow of gluteal muscle in response to electrical stimulation in eight nondisabled subjects and six subjects with SCI [14]. They found that all subjects showed increased muscle blood flow during stimulation, but the increase was greatest for the nondisabled group. In their study, the blood flow was measured by injecting radioactive element and measuring Xenon133 clearance. Such an invasive technique has significant drawbacks for clinical and research applications. Since 1990s, a variety of non-invasive technologies have been explored on skin blood perfusion and/or tissue integrity assessment for research purpose on PU prevention in SCI. In comparison to subjective clinical risk assessment tools, non-invasive technologies monitoring risk of PU formation have enormous potentials in terms of accuracy, cost effectiveness for both staff and patients on PU prevention.

The purpose of this review is to provide basic explanations of some non-invasive technology concepts, a brief review of applications of these non-invasive modalities for measuring risk of PU formation in SCI, and provides an insight into topics for further application and exploration.

Search Method

Key words for electronic database (PubMed) search included SCI, tissue integrity and PU. Search terms for SCI included quadriplegi*, tetraplegi*, paraplegi*, spinal cord trauma*, and spinal cord injury*. Search terms for PUs were: pressure sore*, PU*, decubitus ulcer*, ischemic ulcer*, bed sore*, and skin sore*. Search terms for tissue integrity were: blood flow, blood perfusion, tissue integrity, tissue viability and tissue health, The National PU Advisory Panel (NPUAP), European PU Advisory Panel (EPUAP), National Institute for Health and Clinical Excellence (NICE) were searched for relevant published guidelines. In addition, the reference list of included studies and other relevant papers (eg: available reviews) were screened to identify relevant studies.

Literature Review

Laser Doppler Flowmetry (LDF)

Laser Doppler technique was first described by Stern in 1975 [15]. It utilises the frequency shift of laser light in response to the movement of red cells for measuring blood flux. Principally, LDF is based on the fact that when a coherent, low-powered laser illuminates tissue, light is scattered in static structures as well as in moving blood cells within the microcirculatory beds. Photons scattered by the moving blood cells, are spectrally broadened according to the Doppler Effect. In practice, when light is applied to the surface of skin via a fibre optic probe, the back-scattered light is picked up by detectors via a separate fibre in the probe. Laser light determines perfusion quantities in tissue. A Doppler shift is caused by the movement of erythrocytes. The magnitude and frequency of dermal distribution of the shifted laser light is related to the number and velocity of moving blood cells, regardless the direction of movement. The returned signal is analysed by the instrument giving a value of blood cell movement, which is called blood flux. The blood flux is defined by the product of the number of moving blood cells in the sample volume and their velocity. It is expressed in arbitrary units and considered a relative indicator of cutaneous blood flow. In general, LDF can monitor

microvascular perfusion up to 0.5-1 mm deep underneath the skin and record blood flux in a skin section of about 1 mm³. The sample volume comprises capillaries and more deeply localized shunt vessels. A concise review of the developments in laser Doppler methods has been described previously [16,17].

LDF has been extensively used by researchers to measure tissue perfusion across many medical realms [16,17]. It is also expended to certain clinical applications. For instance, in plastic surgery, LDF have been used to monitor perfusion in free skin flaps and has proved useful in providing early indications of reduced perfusion and flap vulnerability, before clinically observed signs [17]. LDF is widely used by researchers as well to assess microvascular function in SCI [18-26]. Back to 1990s, Schubert and Fagrell [18] used LDF to examine the response of skin blood cell flux to locally applied pressure over the sacrum and the gluteus maximus muscle in 20 patients with SCI (10 with tetraplegia, 10 with paraplegia) and 10 healthy subjects. They observed that people with SCI have an impaired hyperaemic response, and concluded that the impairment is related to the loss of sympathetic tone over the microvascular system. Most recently, Sonenblum and colleagues [19] investigated the effectiveness and interactions of two methods of pressure ulcer prevention, wheelchair cushions and pressure relief manoeuvres on blood perfusion of the buttocks of seventeen SCI. They found that regardless of the cushion being used, the conventional pressure relief manoeuvres with full and intermediate leans in both forward and sideward directions resulted in significant increases in buttock blood flow. But the small frontward lean was shown to be ineffective in increasing blood flow. Hence, they suggested that clinical instruction should cover those intermediate leans in both forward and sideward directions to impart sitting behaviours that may lead to better tissue health.

LDF is an accurate and reliable method for assessing microcirculatory function and offers advantages of non-invasive measurement. It provides real-time measurement of skin blood perfusion as well as microvascular dynamic function, such as blood flow oscillations reflecting vasomotor and microvascular control mechanisms. LDF causes no harm or disturbance of the normal physiological state of microcirculation. However, LDF has its own disadvantages. One major limitation of LDF is that it does not measure absolute perfusion values. LDF measures cutaneous blood flux rather than blood flow, a relative indicator of cutaneous blood flow. Although some researchers have tried to convert millivolts to conventional blood flow units using theoretical calculations, this is not widely accepted. Measurements in most studies are expressed as arbitrary perfusion units or millivolts (1 perfusion units = 10 mV) and are often referred to as flux rather than flow. Cracowski and colleagues recommended a more physiological approach by expressing LDF data as conductance (i.e., flux divided by arterial pressure (in mV/mmHg)) to take into account differences and variations in blood pressure [27]. Yet this does not enable the comparison of absolute flux or conductance values across studies using different probes and/or brand of device and/or sites of measurement. Furthermore, the depth of LDF measurement is about 0.5 mm-1 mm, which has significant limitation to measure tissue health below sub-epidermal level, in particular for detecting those deep tissue injuries that develop deep in the tissue and without exhibiting early skin signs. In addition, the rigid probe has to be attached to the tissue and movement of the optic fibre during measurements can result in artefacts and produce erroneously high

flux readings, which can make the results difficult to interpret, thus limiting its applications for continuous monitoring in bony areas where PU occurs.

Transcutaneous gas tension measurement

Transcutaneous gas tension measurement is a method of measuring the oxygen and carbon dioxide level in the blood by attaching electrodes to the skin. The technology was advocated by pioneering experimental physiologists who discovered over 150 years ago that human skin can 'breathe'. The skin takes up oxygen and gives off carbon dioxide to the surrounding air.

Non-invasive monitoring of oxygen and carbon dioxide has been used for about 40 years [28]. The covered polarographic blood gas electrode for oxygen was first modified for transcutaneous use by Evan and Naylor in 1967 [29]. The electrode was initially used to measure the oxygen level at normal skin surface temperature without heating the underlying skin. They found that the level of oxygen diffusing from the dermal capillaries to the skin surface is mainly controlled by skin blood flow and temperature. If the skin is covered by a flat, unheated oxygen tension (pO_2) electrode, the surface pO_2 falls to zero in a few minutes. However, if the skin blood flow is greatly increased by locally heating the skin to the highest tolerable temperature ($45^\circ C$) the surface pO_2 rises to approximate the arterial pO_2 [30]. As such, this result led to the development of transcutaneous electrodes which incorporated a thermostatically controlled heating element to maximise local blood flow. Transcutaneous measurements of oxygen and carbon dioxide are based on the principle that a heating element in the electrode elevates the temperature of the underlying tissues. This increases the capillary blood flow and the partial pressure of oxygen and carbon dioxide, and makes the skin permeable to gas diffusion. A good relationship between transcutaneous oxygen tension and arterial oxygen tension was demonstrated in neonates and this led to the use of continuous non-invasive transcutaneous oxygen tension monitoring in neonatal intensive care units [31]. Other subsequent studies have also shown that this technology works well for older children and adults [32,33]. The transcutaneous electrode for the assessment of carbon dioxide consists of a Stow-severinghaus glass electrochemical sensor that has been modified for transcutaneous use by the incorporation of a thermostatically controlled heater unit as in the transcutaneous oxygen tension electrode [34]. Close correlations between transcutaneous carbon dioxide tension and arterial carbon dioxide tension have again been demonstrated in adults as well as in neonates [35,36].

In order to aid interpreting transcutaneous data, normal values of transcutaneous PO_2 and transcutaneous PCO_2 in healthy population has been described previously [37,38]. An average of 70 mmHg (45-90 mmHg) for transcutaneous PO_2 [37] and an average of 38 mmHg (30-45 mmHg) for transcutaneous PCO_2 [38] were identified in the healthy population. When excessive pressure is applied over the skin and soft tissues, a decrease of transcutaneous PO_2 and, in some cases, an increase in transcutaneous PCO_2 occur due to the local ischemia [39]. Tissue viability thresholds for these changes have been defined for PU risk [39,40] and wound healing [41]. The transcutaneous gas tension measurement has been widely used for research and clinics across many medical fields including PU prevention [17]. In terms of research applications in SCI, transcutaneous gas tension measurement has been used to study microcirculatory changes in SCI since 1980s [42-46]. Mawson and co-investigators compared transcutaneous oxygen tension levels in

21 subjects with spinal cord injury and 11 able-bodied controls lying prone and supine on egg-crate mattresses. They found the transcutaneous oxygen tension level of the SCI group was lower than that in the able-bodied group in the prone position (65.3 +/- 16 mmHg vs 76.4 +/- 13 mmHg; $p = 0.053$), and markedly lower in the supine position (49.1 +/- 26 mmHg vs 74.2 +/- 10 mmHg; $p = 0.004$). People with SCI had a lower transcutaneous oxygen tension under a constant pressure while healthy controls show an adaptive recovery of oxygenation after 15 minute loading. By measuring both oxygen and carbon dioxide tension in response to regional interface pressures, bogie and colleagues studied 42 subjects who had spinal cord injury (23 above T6, 19 below T6) within 1 year and assessed the effectiveness of prescribed wheelchair cushions in terms of tissue response at the ischial tuberosities [43]. They evaluated oxygen and carbon dioxide tension distributions during sitting under the prevailing active pressure relief regime of the subjects. They reported that SCI individuals with lesions below T6 showed a progressive decrease in ability to maintain blood flow during sitting while SCI subjects with lesions above T6 show a progressive improvement in tissue viability status, therefore they concluded that paraplegics are actually at a potentially higher risk than tetraplegics subjects.

Although this technique offers advantages of providing the real value of oxygen and carbon dioxide level, heating effects of the sensor can potentially cause local erythema or skin burn. In fact, it was reported that more skin burn marks have been seen in clinic follow-ups 20 years ago when the transcutaneous temperature of $44^\circ C$ was used. Due to the heating side effect, $43.5^\circ C$ is now widely recommended [17]. Another disadvantage of this technique is that the rigid probe can potentially increase local pressure when it is applied over bony areas. Therefore, this measurement is limited for continuous application in high pressure loading areas where PU develops. Moreover, the transcutaneous monitoring is relatively expensive and more complicated to use than other techniques.

Tissue Reflectance Spectrometer (TRS)

TRS is an optical technique for providing detailed measurement of spectrum changes associated with haemoglobin content and oxygenation. The principle of TRS relies on the absorption by haemoglobin, a chromophore absorbing light in the visible range of the spectrum (500-600 nm). TRS uses the characteristic absorption of light by the constituents of skin to measure the amount of various constituents present. Light passes through the epidermis (melanin layer) and a plexus of blood vessels in the epidermis (haemoglobin layer) before being reflected off collagen in the dermis. Haemoglobin (Hb) absorbs light with a characteristic curve showing broad bands of absorption spectrum. Oxyhaemoglobin (oxyHb) has two maximums at approximately 542 nm and 574 nm wavelengths. Deoxyhaemoglobin (deoxyHb) shows a single maximum at approximately 545 nm. Thus, TRS can theoretically produce information about both the amount of haemoglobin present and its degree of oxygenation. Anatomically, the human skin is described in terms of 2 different scattering and absorbing layers. The stratum corneum, mainly includes diffuse forward scattering, and influences total skin reflectance by approximately 8% (Wan et al., [47]) which is negligible. The most dominant layer for scattering is the dermal collagen [48,49]. The light penetrating the stratum corneum is heavily absorbed by the epidermal melanin and then the haemoglobin-containing papillary dermis. The absorption spectrum of each of these compounds allows quantitative measurements of their relative concentration to be made.

By using TRS, Hagusawa and Ferguson-Pell [50] investigated the reactive hyperaemia response in the skin over the great trochanters of able bodied and SCI subjects, and found that the reflow rate after loading was slower in SCI than in able-bodied subjects. Liu and colleagues used TRS to measure skin blood perfusion incorporating a customised probe in spinal cord injury during functional electrical stimulation via a sacral nerve root implant. The customised probe was placed under the ischial tuberosity while individuals were sitting in a wheelchair. They reported an increase in skin blood perfusion over the ischial tuberosities during sacral nerve root stimulation [51].

TRS has its own major advantages of being non-invasive, a real-time and continuous measurement, of not altering the physiological nature by the measurement and being effective for pigmented skin if the effect of melanin can be corrected [52-55] furthermore, and the measurements are not affected by the movement artefact. However, TRS does not provide an absolute value of haemoglobin content or oxygenation. The depth and area of skin measured is relative small (theoretically 0.5 mm), which was limited by the light wavelength and the size of probes.

Near-infrared Spectroscopy (NIRS)

Near-infrared energy was discovered as early as the 19th century and was ascribed by William Herschel. The first industrial application of NIRS was not launched until the 1950s. Initially, NIRS was only used as an add-on unit to other optical devices that used other wavelengths such as ultraviolet, visible, or mid-infrared spectrometers. Up to the 1980s, a single-unit, stand-alone NIRS system was made available. With the introduction of light-fibre optics in the mid-1980s and the monochromator-detector developments in early 1990s, NIRS became a more powerful tool for scientific research. Using near infrared wavelengths (700-1100 nm), NIRS has capability to provide quantitative information on the structural and chemical components of cutaneous tissue, specifically oxygen saturation, haemoglobin content and water content. Technically, NIRS devices illuminate skin tissue at near infrared wavelengths and reflectance of light is collected via fibre optic probes (or by camera in near-infrared imaging). Light in the near-infrared range is absorbed by various skin chromophores specifically water, oxy-haemoglobin, and deoxy-haemoglobin. Deoxy-haemoglobin has a maximum absorption at 760 nm, whereas absorption of oxyhaemoglobin is greatest at 900 nm. Water, which may have implications for identifying oedema, has a peak of absorption at about 980 nm. While some of the penetrating light will be absorbed by these chromophores, some of the light is scattered and reflected by other skin components. NIR reflectance is collected by a detector and analysed to provide measurements of chromophore content. The subsequent analysis of this data can be applied to the assessment of local tissue integrity.

By using NIRS, Jan and co-investigators measured muscle perfusion over the ischial tuberosity by using NIRS during wheelchair tilt-in-space and recline in people with spinal cord injury [56]. Twenty participants were asked to perform pressure relief in wheelchair in six combinations of wheelchair tilt-in-space and recline angles in a random order. The muscle perfusion was significantly increased at 25° and 35° tilt-in-space when combined with 120° recline, while skin perfusion was significantly increased at 3 tilt-in-space angles (15°,25°,35°) when combined with 120° recline. They concluded that a larger angle of tilt-in-space and recline is needed to improve muscle perfusion compared with skin perfusion. A position of 25° tilt-in-space combined with 120° recline is effective

in enhancing muscle perfusion of weight-bearing soft tissues at the ischial tuberosities in spinal cord injuries.

Li and colleagues [57] assessed the blood oxygenation oscillations in the tissue over the sacrum using NIRS in ten spinal cord injury (3 women, 7 men, age = 34.5 ± 5.2 years) and the other ten were healthy subjects (3 women, 7 men, age = 36.5 ± 6.2 years). Their results showed that the amplitude of the oxygenated haemoglobin and haemoglobin component was significantly lower during the resting conditions in SCI than normal subjects ($p < 0.05$). During the post-loading period, the response of oxygenated haemoglobin and haemoglobin oscillatory activities were significantly lower in the tissue over the sacrum for persons with SCI than that for normal subjects ($p < 0.05$). Their results indicated that the low oscillatory activities might be related to early tissue injury in persons with SCI.

In comparison with other optical technologies, one advantage of NIRS is that it can typically penetrate much further into tissue, eg: muscle or bones; therefore it can provide more information of tissue integrity. Such technology has significant potential to aid in wound assessment, specifically the classification of wound depth and the quantification of oedema. The addition of water content measurement to the oxygen and haemoglobin data allows further differentiation, distinguishing between superficial, intermediate partial thickness, deep partial thickness and full thickness wounds [58]. However, such a device is not sensitive when lights near the infrared wavelength range are used to penetrate to deep tissue in a relevant large area. In addition, the dermal probes are relative large and suitability of application over the bony areas is questionable.

Combination modality

Recently, a device in combination of LDF and TRS techniques has been developed. The equipment called Oxygen-to-See (O2C) uses laser Doppler flowmetry and diffuses reflectance spectroscopy for non-invasive determination of oxygen supply in tissue perfused with blood. The measurement principle of the device relies on a combination of laser-Doppler-technique and tissue spectrometry. Diverse application at the skin, internal organs and in the intestinal tract is possible by flexible glass fibre probes. O2C transmits continuous wave laser light (830 nm and 30 mW) and white light (500-800 nm; 1-nm resolution; 20 W). The sample frequency of the O2C is 0.5 Hz. The reliability of this modality to measure oxygenation in muscle tissue has been reported by Reenalda et al., [59]. By using this technique, Smit and co-investigators [60] measured gluteal regional blood flow and oxygenation in 12 men with SCI. They compared effects of ES-induced gluteal and hamstring muscle activation with pressure relief movements (push-ups, bending forward and leaning sideward during sitting). Their results showed that all pressure relief movements significantly increased gluteal region blood flow and oxygenation, whereas ES-induced muscle activation only increased for peak blood flow.

This combined technique offers more advantages than single LDF or TRS. It can noninvasively measure the subcutaneous tissue oxygenation up to a depth of 8-10 mm, reaching the muscle tissue. Such technique is suitable for measuring the dynamic response in blood flow in reaction to the changing seating load. However, the equipment is very expensive; the commercial probe is a rigid glass fibre that has potential confounding effect on the measurements. Therefore application on the bony area is questionable. Again the value given is arbitrary rather than local real oxygen level.

Subepidermal Moisture (SEM) measurement

The SEM scanner/monitor has been designed to measure the water content of the extracellular space below the surface of the tissue. Using 300 MHz electromagnetic waves it measures subepidermal moisture/localized oedema, determined by dielectric and water content changes which has been investigated for association with erythema, Stage I, and Stage II PUs [61-64], as well as for its ability to differentiate between healthy skin and skin with pressure-induced tissue damage [65]. Subepidermal moisture has also been examined as a predictor of imminent ulceration in various populations [61,62,66].

The principles of measuring dielectric properties of tissue, including capacitance with a coaxial electrode, is a signal is generated by the device and transmitted to the tissue through the sensor. The signal response is affected by dielectric characteristics of the subepidermal tissue and the amount of free and bound water in the tissue, which is compared to internal reference values. The depth of the transmitted signal or the depth of measurement is dependent upon the size of the probe and the applied signal frequency. By using this device, Guihan and co-investigators [63] measured Subepidermal Moisture (SEM) in 34 SCI participants. Twelve participants received daily, 22 received weekly SEM measurement alongside visual skin assessment across nine anatomic locations for up to 6 weeks. They found that SEM was lowest for normal skin (39.3 dermal phase units, SD=12.6) and higher for erythema/stage 1 PUs (40.8 dermal phase units, SD=10.4) across all anatomic sites. Buttocks SEM were different between normal skin (40.5 dermal phase units, SD=10.3) and erythema/stage1 PUs (43.8 dermal phase units, SD=9.5). SEM taken at heels was lower across all skin conditions (normal skin 28.2 dermal phase units; erythema/stage I PUs 34.7 dermal phase units).

This newly developed modality is portable, hand-held with ease of application. The changes in SEM measured by the device could be utilized for both prevention and detection of PUs. However, the capability of remotely monitoring tissue integrity continuously over the bony area is questionable. The reliability and validity of the measurement still remains unclear so far.

Discussion

Non-invasive technologies measuring risk of PU formation objectively have enormous potential to aid research in development and implementation of various modalities for preventing PUs. Our review focussed on non-invasive technologies of tissue integrity assessment in SCI. Non-invasive technologies reviewed in this paper measure different tissue parameters including skin/muscle blood perfusion, skin microvascular function and tissue biomechanical properties. The diversity of techniques available indicates the complexity of measuring different aspects of tissue integrity. The four aspects of tissue integrity, which were measured in this review, were physical movement of blood cells, heat transport and the oxygen content of blood and dielectrics values. Undoubtedly, there are many more important aspects of PU prevention and management, such as spasticity, range of motion of the joints, positioning, interface pressure, shear force and the type of surfaces on the bed or wheelchair. However, these aspects are beyond the scope of this review.

Without a doubt, effectively preventing PU is challenging because the combination of pressure and duration that results in tissue damage varies largely among individuals. The underlying damage is often severe by the time a surface ulcer becomes visible, in particular for people with dark skin which is difficult to remark. Currently, no

modality exists to detect early tissue damage and enable intervention for preventing PU formation. Yet interestingly, Swisher and colleagues recently developed a flexible, electronic device that non-invasively maps pressure-induced tissue damage *in vivo* on a rat model. They found that impedance is robustly correlated with tissue health across multiple animals and wound types [67]. Such technology is worthy to further investigate in order to apply on human subjects.

Worth to note, this review is written as a topic scope review. Unlike a systematic review, we did not include quality assessment of articles reviewed, which has limited the depth of our review. And also only one electronic database (PubMed) and relevant guideline websites alongside the hand search was used to identify relevant studies. Nevertheless, the purpose of our review was to present basic information of non-invasive technologies for monitoring risk of PU formation in SCI, and provide an insight in such topic for further application and exploration.

Finally, our review focussed on non-invasive technologies for research purpose other than clinical practice. Certainly a robust objective assessment tool for detection of early sign of PU ultimately should be practical and realistic in clinical use. However, such aspect was beyond the scope of this topic review. Nevertheless, our current review provided basic information and explained the concept of those technologies that have been applied for research in SCI. These modalities included in our review have potentials for further development in terms of clinical application. To provide level I evidence for clinicians who deal with PU management, future rigorous reviews on such topic incorporating both research and clinical implementation are warranted.

Conclusion

All currently available techniques applied for risk assessment in SCI have limitations for continuous, real time monitoring of tissue integrities in high risk areas and require further investigation. Subepidermal moisture measurement and combination spectroscopy with LDF has potential for clinical monitoring risk of PU formation application. However, there is lack of evidence of reliability and validity of former technology and high cost for latter technology. A reliable low cost, wearable wireless devices incorporated with current available modalities is warranted for investigation for PU prevention in SCI.

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