The Sub-Epidermal Moisture Scanner: the principles of pressure injury prevention using novel early detection technology

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During the inflammatory process triggered by localised events of cell death at the onset of a pressure ulcer/injury, the volume of blood plasma fluids escaping from the vasculature will build up gradually, eventually forming oedema. However, this process begins microscopically and progresses over time, as the immune system is recruited to deliver a sufficient number of immune cells to the damaged tissue site. The gradual accumulation of fluids changes the biocapacitance physical property of the affected tissue, making it progressively less resistant to electrical fields, which in physics terms means that the relative permittivity (dielectric constant) of the tissue increases towards that of water. This initial fluid content change is, hence, a biomarker that can be employed for early detection of a pressure injury (PI). The SEM Scanner utilises the above biophysical process for diagnosing the onset of a PI, by detecting the small increase in extracellular fluid contents very soon after death of the first cells. This article describes the clinical incentive, physical principles and technological concepts of the SEM Scanner, which is now in clinical use in Europe, in view of the strong need to introduce high-technology to wound care, which has been, traditionally, a low-tech field of medicine. In this context, there is a necessity to gradually introduce technologies to support the traditional examination process known as visual skin assessment (VSA). The currently-used VSA essentially documents macroscopic damage that has already occurred, instead of identifying the damage early enough to allow the body to self-repair the injury while it is still microscopic and reversible. The SEM Scanner, which is based on solid physiological foundations, is the first to offer a modern technological adjunct to VSA and clinical judgment, which further adds ability to detect an evolving injury under intact skin and at a much earlier stage than when the injury already presents itself on the skin.

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A pressure ulcer, now also termed a 'pressure injury' (PI) in the United States (by the National Pressure Ulcer Advisory Panel [NPUAP], *www.npuap.org*) and Australia, is defined in international guidelines as a localised injury to the skin and/or underlying tissues, usually over a bony prominence, resulting from sustained pressure, including pressure associated with shear (NPUAP/European Pressure Ulcer Advisory Panel [EPUAP]/Pan Pacific Pressure Injury Alliance [PPPIA], 2014). Pressure injury prevention (PIP) has become a primary goal for many healthcare organisations that focus resources in effective PIP as a first priority, and treat those injuries that were impossible to prevent according to their PIP strategy. However, according to most recent US epidemiological data, between one-in-three and one-in-four patients within long-term acute care systems will develop a PI, so the malady

is still very widespread (VanGilder et al, 2017). In nursing homes, specifically, the annual estimated incidence of PIs ranges from 2–14% (Bates-Jensen et al, 2017). Without specific technological aids designed for PIP, it would be difficult to achieve substantial improvements in the above statistics. Various conditions have been identified as risk factors of PI development. Age, malnutrition, sensory deficits, multiple morbidities, circulatory abnormalities, spinal cord injury, stroke, surgery, anemia, diabetes mellitus, peripheral vascular disease and hip fracture in older people are some of the major risk factors. Hence, new technological aids for PIP need to fit a wide variety of patient populations, ages and medical conditions.

The financial burden of PIs to healthcare systems has been estimated at billions of US dollars annually being spent on the treatment of PIs. There are additional, vast indirect expenses, which are mostly related to the drop in quality of life when a PI forms, as well as to litigation. Many of the serious PIs are deep tissue injuries (DTIs). For example, the term 'purple heel' is often being used to describe the syndrome of bruising-like changes in skin colour, which darkens locally at the pressure spots to either purple or black marks — both are characteristic to the clinical presentation of a DTI in the heels. The internal shearing deformations at the weight-bearing sacrum and posterior heels, in particular, are caused as the soft tissue layers attempt to slide upon each other, but cannot, as they are physically constrained by connective tissue fibres at the interfaces, which is causing the tissues themselves and the cells within to severely distort and change shape. The above phenomenon occurs in both static postures (due to static frictional forces) and during movement (such as repositioning or spontaneous). As an example, the body of a supine patient whose trunk is elevated to assist in breathing efforts is subjected to gravitational forces and simultaneous, counteracting static shear forces at the body-bed interface, and this system of forces acts to distort and deform tissues and cells.

The extent of tissue and cell distortions would be maximal near bony prominences, such as the sacrum and calcanei (heel bones), due to the geometrically irregular, sharp bony surfaces that indent the overlying soft tissues. Dynamic shear forces which can be generated in patient tissues, e.g. as a result of sliding in bed or during handling for hygiene, are also a cause of tissue and cell deformation. Over time, sustained cell deformations, which may be accompanied by episodes of repetitive deformation exposures, cause tissue breakdown as cell structures, such as the cytoskeleton (a complex protein scaffold that supports the cell structure from within) and plasma membrane (exterior cell walls), lose integrity (Gefen and Weihs, 2016; Gefen, 2017; Moore et al, 2017).

At the early phase of PI damage, when the damage is still microscopic and limited to small numbers of cells, the damaged or dying cells release chemokines (signaling/messenger molecules, also called chemo-attractant molecules) that act as inflammatory signals, and which attract immune system cells (e.g. neutrophils, macrophages, T-cells) to the affected site (Turner et al, 2014; Gefen, 2018). The existence of this inflammatory process is essential for the repair of microscopic tissue damage, as the immune system cells act to clear the debris of the dead cells. Inflammation by itself is a contributor to progressive cell death and tissue damage. Inflammation as a response to the early PI formation includes the release of the aforementioned inflammatory mediators, which are responsible for microvessel permeability, vasodilation and leukocyte recruitment. These processes are accompanied by release of reactive oxygen and nitrogen species that degrade the extracellular matrix in an attempt to relieve the pressures resulting from the additional accumulated fluids (Moore et al., 2017; Kim et al, 2018). The overall result is a tissue degradation spiral where continuous inflammation results in additional cell death and tissue damage, causing further inflammation and so on.

Surgical patients, patients at acute and critical care settings, patients with neuromuscular impairments, orthopaedic patients who are bed-bound and patients with impaired peripheral sensation prescribed to undergo prolonged examinations or treatments at a given (static) body posture, such as dialysis are all at risk for PIs. The current standard of nursing care requires routine visual skin assessment (VSA) as the practical means for detection of the onset and development of PIs. Clearly, and by definition, VSAs, even if performed comprehensively head-to-toe, document already-existing damage. In particular, VSAs do not detect early damage subdermally, or spot microscopic signs of damage.

Moreover, VSAs are unreliable and involve a risk to fail in assessing correctly for patients with dark skin colors (Kim et al, 2018). The task becomes even more problematic given the current understanding that most of the severe

sacral and heel PIs onset as DTIs (Bates-Jensen et al, 2017; Gefen, 2017), which cannot be seen by the unaided eye of even the most skilled, experienced and well-trained nurses or other medical practitioner. In other words, due to major gaps in diagnostic medical technology in wound care, nowadays, a nurse is expected to detect an injury that evolves sub-dermally, on the skin surface. Unfortunately, a nurse would be successful in doing that only when the injury actually presents itself at the skin surface, which is at the stage where substantial deep tissue necrosis has already been caused, and damage is potentially irreversible.

Role of the SEM Scanner in minimising the existing technological gap

The SEM Scanner (Bruin Biometrics), which is currently CE marked in Europe and is pending a Food and Drug Administration decision in the United States (not available for sale in the US), is designed according to well-established physiological and biophysical principles, which are discussed here, and has been introduced to minimise the above-described technological gap in PIP. As explained above, the first event in the onset of a PI is microscopic injury, which manifests as damage in individual cells, leading to multiple necrotic and apoptotic cell death events.

As growing masses of cells are dying, the injury progresses from the microscopic scale to the macroscopic level, i.e. to the tissue-scale, and becomes detectable by either medical imaging examinations such as MRI or ultrasound, and, eventually, once damage is visible, through VSA. Current aetiological research has identified sustained tissue deformations as the primary cause of PIs, both at the skin and in deeper tissues (as reviewed from a mechanobiology perspective in Gefen and Weihs, 2016).

Briefly, the sustained exposure to tissue deformations has multi-dimensional influence on tissue health and cell viability, primarily: (i) deformation inflicts direct structural damage to the distorted cells, e.g. failure of the cytoskeleton and causes pore formation in the plasma membrane of the cells; (ii) deformation compromises perfusion and lymphatic function (Moore et al, 2016). Different model systems, including medical imaging of humans, animal models, experiments in tissue-engineered constructs and cell culture models have pointed to the role of direct deformation damage to cells. These model systems also revealed the short time-course at which damage to cells is inflicted, in the order of tens of minutes — much faster than the previously assumed ischaemic damage pathway that takes several hours to develop (Gefen and Weihs, 2016).

The chronic tissue distortion is causing disruption of the cytoskeleton in cells which, especially without adequate supply of metabolic energy, loses its capacity of structurally supporting the mechanically-loaded plasma membrane. The plasma membrane, hence, gradually fails as well and pores (nanometre-wide openings) start forming at the failure sites over its surface. The stressed cell is typically unable to repair these local mechanical damages and so, a flux of ions and other biomolecules penetrates the cell body or leaves the cell in an uncontrolled manner through these pores, eventually causing loss of homeostasis (biological equilibrium) in the cells and resulting in apoptotic cell death (Gefen and Weihs, 2016; Gefen, 2017). The cell death cascade triggers the inflammatory response described above (Bates-Jensen et al, 2017). Additional references where tissue damage pathophysiology in PI development has been studied are reviewed in Moore et al (2017).

From a bioengineering perspective, PIP efforts are inherently limited given the existing technological gap that does not allow clinicians an insight beyond the visible skin changes (which develop late, when the injury is of a macroscopic nature). While in nearly every field of modern medicine, clinicians are being routinely supported by basic and advanced technological aids to effectively screen and diagnose beyond what is seen on the surface of the body (e.g. electrocardiography and blood pressure measurements in cardiology), in wound prevention and care, clinicians depend merely on their human senses as they perform VSAs. All risk assessment tools that are currently being utilised clinically either include a built-in VSA or are combined with a VSA. Moreover, VSAs are conducted as part of the usual care if a patient has been determined to be at risk. Importantly, a VSA can identify an injury only after it has visibly manifested, which is obviously too late in the tissue damage spiral (Bates-Jensen et al, 2017; 2018).

Over the past two decades, PI research has made considerable progress in understanding the aetiology, and specifically revealed that PIs may develop internally, under intact skin. Clinical practice has evolved accordingly, redefining PI classifications and adding the DTI PI type to classification systems (NPUAP/EPUAP/PPPIA, 2014). This new understanding and the global

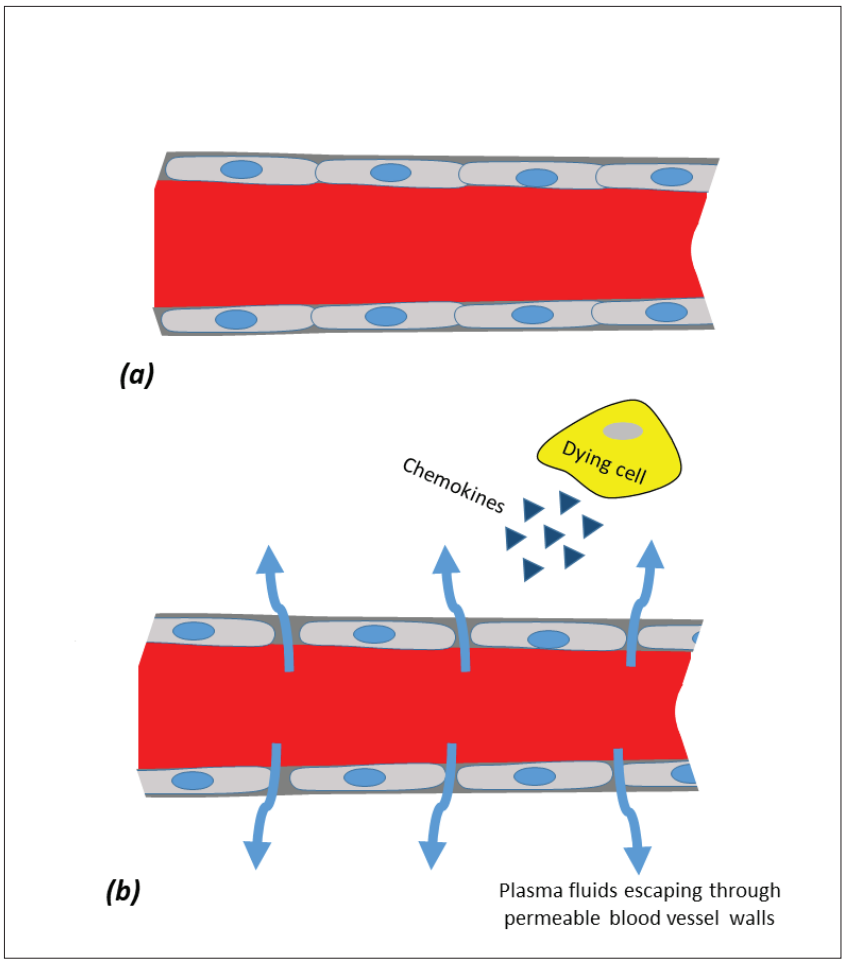

Figure 1. The pathophysiology of build-up of localised oedema (sub-epidermal moisture): (a) Normal blood vessel walls where endothelial cells are tightly attached. (b) Permeable vessel walls due to inflammatory chemokines.

consensus reflected in the up-to-date literature, that damage typically occurs in deep tissues first and progresses towards more superficial layers until eventually presenting itself on the skin, create an inherent fundamental problem. In the case of an existing or an evolving DTI, assuming that there are clinical signs, such as the typical red, maroon or purple local discolouration of the skin (as per the NPUAP definition of a DTI), a clinician performing a VSA as part of a risk assessment (e.g. using the Waterlow scale) or in conjunction with it, will be recording existing tissue death rather than actually assessing the PI risk (Bates-Jensen et al, 2017, 2018).

Likewise, even successful detection of these clinical signs in routine VSAs will, by definition (of a DTI), document existing (subdermal) tissue damage, rather than prevent it. In other words, though they do have a role in preventing further deterioration of tissue health, VSAs take the documentation approach, which is characteristic of forensic medicine, rather than an ultimate PIP approach. This striking unreasonableness essentially originates from the lack of biomedical technology — in both risk assessment and screening of forming PIs — to effectively and cost-beneficially detect cell and tissue damage under intact skin in clinical practice. Nurses and other healthcare professionals deserve and require novel, dedicated bioengineering technologies to support their VSAs and clinical judgement (including risk assessment based on experience) by looking at tissue health status and viability under the skin. The field, therefore, calls for technological breakthroughs, which will essentially provide information on pathophysiological phenomena that occur at subdermal/deep tissues and so cannot be detected visually and timely if one only observes the skin. The SEM Scanner addresses this specific need, being a technology-aid that is adjunct to clinical judgement.

The SEM Scanner is a handheld device that measures capacitance of tissues at a depth of several millimetres under the skin (depending upon the specific anatomical site, version of the device and examination protocol) (Tonar et al, 2017). Briefly, the (bio)capacitance of tissues rises when the extracellular water contents called the sub-epidermal moisture (SEM) increases, and water contents increases when the first cells in a tissue die.

The pathophysiological mechanism for the increase in extracellular water contents is activated by the death of these first cells, which release chemokines — signaling molecules that also cause blood vessel walls to be more permeable. That allows immune cells in the blood to cross the vascular walls (a process called extravasation) and reach the site of cell death (Turner et al, 2014).

Nevertheless, the aforementioned elevated vessel wall permeability also causes leakage of plasma fluids to the extracellular space, which eventually builds up to the clinically-evident edema (and swelling). Noteworthy is the gradual formation of oedema (Moore et al, 2017), and that it initiates as a localised, microscopic event (i.e. an increase in SEM). Accordingly, the SEM Scanner targets this early phase of cell death by detecting SEM changes, rather than exploring for macroscopic signs of tissue destruction as VSA does.

The SEM Scanner measures these SEM changes by employing electrodes to record a physical property called biocapacitance, which reflects the relative dielectric permittivity (dielectric constant) of the tissue, i.e. how much resistance to electrical fields is encountered in tissues. The greater the fluid contents is in a

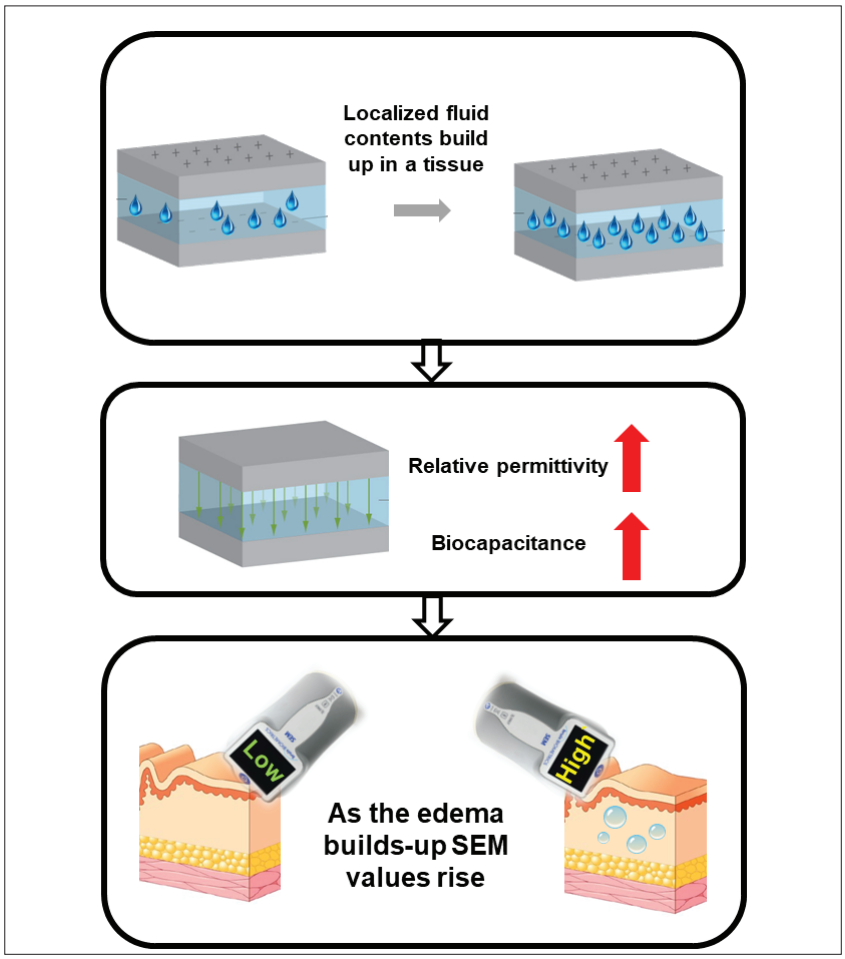

Figure 2. The physical biomarkers of the build-up of oedema: The greater the sub-epidermal moisture is in a tissue, the less resistant it becomes to electrical fields.

tissue, the less resistant it becomes to electrical fields (as water transmits electrical fields easily) and the higher the biocapacitance value becomes (Bates-Jensen et al, 2017) *[Figure 1]*. As the fluid contents (or SEM levels) rise, the dielectric constant and the biocapacitance increase; the biocapacitance is measured locally, recorded by the SEM Scanner and is displayed (after conversion to dimensionless units) to reflect the tissue health status at the examined site at the time of the examination.

Clinical effectiveness of the SEM Scanner versus alternative approaches

Published data clearly show that the theoretical basis explained above is well supported by clinical data, including large clinical trials. The SEM Scanner has been evaluated rigorously in large-scale clinical trials conducted primarily by the Bates-Jensen group in nursing home settings (Bates-Jensen et al, 2007; 2008; 2009; 2017; 2018) with one study that has been performed in spinal-cord injury care facility and a residential care facility (Guihan et al, 2012).

The SEM Scanner has been proved to be effective in detecting DTIs and in differentiating those which resolve, remain or deteriorate, and was also predictive of occurrence of visual skin damage approximately a week later. The Bates-Jensen published work concluded that abnormal SEM readings may precede positive VSA findings by 3–10 days (Bates-Jensen et al, 2017; Moore et al, 2017).

It is important to discuss the SEM Scanner technology in the context of other, perhaps alternative approaches for assessing the health status of tissues. Ultrasound, for example, has been identified as successful means for detecting PIs in multiple studies, as reviewed by Oliveira and colleagues (2017). Based on a systematic review, they suggested that ultrasound, together with SEM measurements, are in fact the best currently available methods for PI detection.

Nevertheless, there is a fundamental difference between ultrasound and SEM, which needs to be highlighted: Ultrasound detects macroscopic pockets of fluids (oedema), which are large enough to be visible to the expert radiologist, whereas the SEM Scanner has the sensitivity to detect the occurrence of oedema while it is still microscopic. There is no other currently feasible technology that obtains early PI detection comparable to that of the SEM Scanner, as reported by the Bates-Jensen group. Portable ultrasound, which has comparable costs, is not a suitable equivalent. Interpreting ultrasound images requires expertise and a substantial amount of training, and typically years of clinical experience. Additionally, there is the potential for inter-observer disagreements in interpreting ultrasound results (which are neither objective nor quantitative). In all these aspects, the SEM Scanner offers considerable advantages over ultrasound or any other imaging-modality-based approach to early detection.

The SEM Scanner, a revolutionary handheld medical device for PIP, offers an objective, standardised, quantitative and reliable method for the assessment of local tissue biocapacitance (which reflects tissue health status). The SEM Scanner, therefore, facilitates assessment of cell and tissue damage before signs become visible to the unaided eye (Moore et al, 2017; Kim et al, 2018). The SEM Scanner was designed for use by healthcare providers as part of PIP programmes, with the hope of leading to a medical culture of measurement-based, targeted interventional efforts in wound prevention and care, prior to tissue breakdown.

Summary

In an inflammatory process triggered by localised events of cell death as occurs in the onset of a PI, the volume of blood plasma fluids escaping from the vasculature will build-up gradually *[Figure 2]*. One should recall that this process begins microscopically and progresses over time, as the immune system is recruited to deliver a sufficient number of immune cells to the damaged site. The practical implication of this pathophysiological response — for diagnosis of the beginning of formation of a PI — is that there will be a small increase in extracellular fluid contents very soon post death of the first few cells. The SEM Scanner detects these changes in fluid contents, which are reflected in the biocapacitance property measured by the device *[Figure 2]* and, hence, it is able to alert the user to the onset of cell damage under intact skin of normal appearance. Accordingly, the device has an immense clinical utility in early detection of PIs.

Such a technology should support the traditional VSAs, which essentially document macroscopic damage that has already occurred, instead of identifying the damage early enough to allow the body to self-repair it while it is still microscopic and reversible. The SEM Scanner is based on solid physiological and biophysical scientific foundations and is mature to serve as an adjunct to VSAs and clinical judgement. Its ability to detect pathological processes that develop silently and microscopically under intact skin provides clinicians a critical capacity that they are currently lacking. WINT

Disclosure

Amit Gefen acts as a scientific advisor to multiple companies in the field of pressure ulcer/injury prevention, including to Bruin Biometrics LLC whose SEM Scanner technology is reviewed in this article. This had no influence on the conclusions from the analysis of literature, which is presented here.

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