Accuracy of ultrasound, thermography and subepidermal moisture in predicting pressure ulcers: a systematic review

Objective: Our aims were to: establish the clinical significance of ultrasound, thermography, photography and subepidermal moisture (SEM) measurement; determine the accuracy of ultrasound, thermography, photography and SEM measurement in detecting skin/tissue damage; determine the relative accuracy of one of these assessment methods over another; make recommendations for practice pertaining to assessment of early skin/tissue damage.
Method: The following databases, Cochrane Wounds Group Specialised Register, The Cochrane Central Register of Controlled Trials, Ovid MEDLINE, Ovid EMBASE, Elsevier version, EBSCO CINAHL, ClinicalTrials.gov, WHO International Clinical Trials Registry (ICTR) and The EU Clinical Trials Register were searched for terms including; thermography, ultrasound, subepidermal moisture, photograph and pressure ulcer.
Results: We identified four SEM, one thermography and five ultrasound studies for inclusion in this review. Data analysis indicated that photography was not a method which allowed for the early prediction of PU presence. SEM values increased with increasing tissue damage, with the sacrum and the heels being the most common anatomical locations for the development of erythema and stage I PUs. Thermography identified temperature changes in tissues and skin that may give an indication of early PU development; however the data were not sufficiently robust. Ultrasound detected pockets of fluid/oedema at different levels of the skin that were comparable with tissue damage. Thus, SEM and ultrasound were the best methods for allowing a more accurate assessment of early skin/tissue damage. Using the EBL Critical Appraisal Tool the overall validities of the studies varied between 33.3–55.6%, meaning that there is potential for bias within all the included studies. All of the studies were situated at level IV, V and VII of the evidence pyramid. Although the methodological quality of the studies warrants consideration, these studies showed the potential that SEM and ultrasound have in early PU detection.
Conclusion: SEM and ultrasound are promising in the detection and prediction of early tissue damage and PU presence. However, these methods should be further studied to clarify their potential for use more widely in PU prevention strategies.
Declaration of interest: The School of Nursing & Midwifery has a collaborative agreement with Bruin Biometrics, the manufacturers of the SEM scanner. Arising from this agreement, the School receives funding for independent research in the field of PU prevention.

pressure ulcer • photography • subepidermal moisture • ultrasound • thermography • systematic review

Pressure ulcers (PUs) are areas of skin damage that can include underlying tissue, and usually develop over bony prominences, because of pressure in tandem with shear.[1] For PUs to develop individuals need to be exposed to mechanical loading of the skin and underlying tissues, and those who suffer from restricted mobility or who are immobile, are particularly at risk.[2–5]

PUs are a major health-care problem, impacting the individual, health-care system and society as a whole.[6] Internationally, the prevalence and incidence of PUs varies between 2.2–42.7% and 1.4–49%, respectively.[7–15] From a financial perspective, PUs are expensive to treat. A study by Dealey et al. in 2012[16] identified that the mean cost per patient, per ulcer stage, varied from £1214 to £14 108. In an Irish retrospective cost analysis study[17] of 509 patients, 78 developed PUs, of which 13 had grade IV PUs. According to the authors the estimated equipment and treatment costs for these stage 4 PUs was around €1.5 million, with the cost per patient being €119,094.63. Furthermore, from a human perspective, quality of life studies[18–19] have shown that PUs impact negatively on all the activities of daily living.

Although pressure/shear are known to be the main causative factors for the development of PUs, how precisely they affect the underlying tissues and lead to tissue breakdown is not well understood. Thus, different theories have been developed to try and explain the onset. These include ischaemia, ischaemia-reperfusion injury, impaired lymphatic function and sustained cell deformation.[20–29] Ischaemia and ischaemia-reperfusion injury both contribute to tissue damage, the first by hindering the oxygen supply to the cells, which can lead to cell death and consequent tissue necrosis. The second mechanism causes cellular injury due to the reperfusion of oxygen rich blood to a previously ischaemic area,

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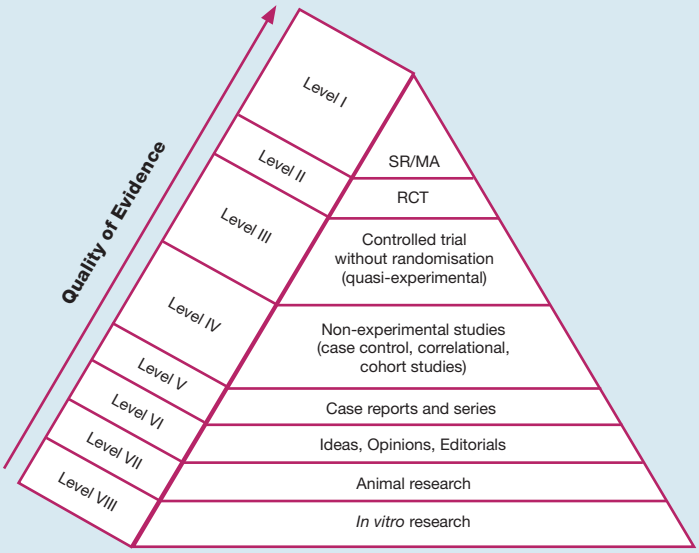
Fig 1. Evidence pyramid RCT–randomised controlled trial; SR–systematic review; MA–meta-analysis



leading to the production of oxygen derived free radicals which damage tissues.[20,23] Impaired lymphatic function occurs due to occlusion of lymphatic vessels, compromising the drainage of waste products resulting from cell and tissue activity.[24] Finally, cell-deformation arises from sustained exposure to external mechanical forces.[21–22,25,27–29] The changes that occur at the cellular level lead to inflammation and oedema, due to an abnormal increase of interstitial fluid at the area of injury, and these appear to be the first signs of PU development.[30–31]

PU development is usually determined through visual skin assessment (VAS). However, the reliability and validity of this assessment varies greatly, with overall figures suggesting only moderate agreement among assessors.[32–33] A further challenge is that visual skin assessment relies on evidence of changes at the skin surface and not what is happening beneath the skin surface. Of concern is that when damage becomes evident visually, it is already too late to prevent the PU, as often the damage has emerged from the deeper layers emerging outwards towards the surface of the skin.[1] Because visual assessment does not always show any evidence of early PU development, alternate methods of early prediction need to be put in place to accurately assess patients at risk. Therefore, we considered the role of sub-epidermal moisture (SEM) measurement, ultrasound, thermography and photography in predicting early PU presence.

Mechanisms of the techniques assessed

Inflammation and oedema, due to an abnormal increase of interstitial fluid at the area of injury are the first signs of PU development.[30,31] This increase in water/interstitial fluid content can be measured through the use of instruments that use electric and electromagnetic signals.

Skin tissue water varies according to anatomical site and tissue depth and this is an important biophysical measure, as a certain level of hydration is necessary for the skin to maintain its barrier function. Stratum corneum hydration can be used to assess skin water using capacitance, dermal water can be assessed using tissue dielectric constant and the transepidermal water loss (TEWL).[34,35] This dielectric constant will depend on the amount of free and bound water in the tissue volume through which the wave passes, and is a measure of the amount of skin and tissue water content (stratum corneum, dermis and epidermis).[35]

Sub-epidermal moisture (SEM) is related to the quantity of skin and tissue water.[31,36–38] Tissues have capacitive and conductive properties that are dependent on water content, with the uppermost layer being mainly capacitive and the deeper layers being mainly conductive.[34] Thus SEM can be measured through the use of surface electrical capacitance.[31,39] Surface electrical capacitance (which is related to the capacity of tissue to hold/store energy, in this case an electrical charge) of the skin is determined by the impedance (resistance/opposition) of the skin to electrical forces, and thus can reflect oedema and water content of the epidermal and sub-epidermal tissues.[31] Considering that SEM is related to skin and tissue water, this can be measured through the use of surface electrical capacitance.[31]

Ultrasound is a technique that, through use of a probe, emits sound waves to create images of soft tissues.[40–41] When the sound wave reaches the boundary of acoustically different tissues, such as fluid or soft tissue, part of the energy is reflected back which is dependent on the acoustic difference.[40–41] The ultrasound wave emitted will be absorbed if it encounters fluid, creating a dark area in the image, known as hypoechoic and non-echoic. Conversely, the ultrasound wave is reflected when it encounters dense tissue creating a bright reflection known as hyperechoic or echogenic.[41] If tissue damage is present there will be a less reflective pattern, and hypoechoic areas are expected at the subcutaneous, dermal and sub-epidermal tissues.[41]

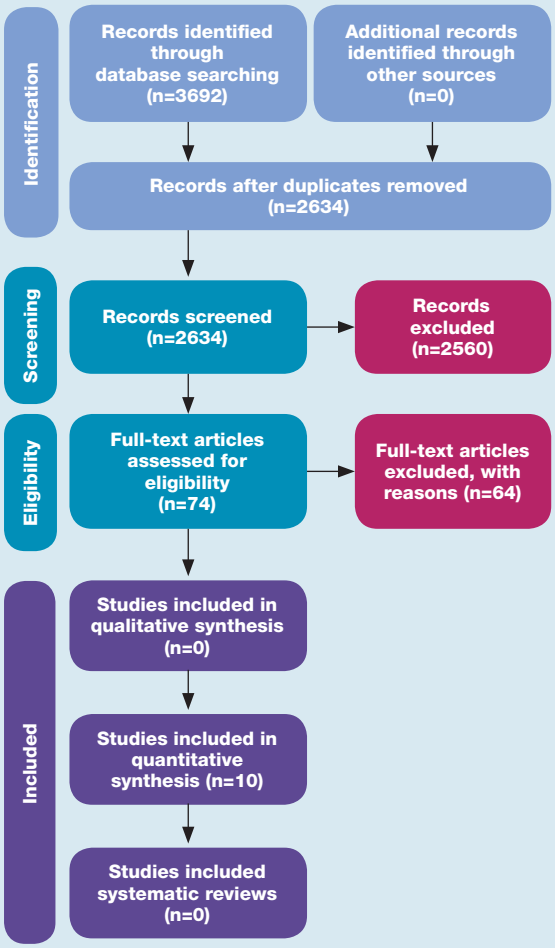
Thermography measures a proportion of the spectrum of the infrared energy released by the body skin and depicts it in an image where different colours are equivalent to skin temperature variation.[42] Photographs of the skin of patients have been used in research mainly to determine the validity and reliability of this method to detect the presence and categorise PUs.[43–45]

There is potential to use these methods of skin and tissue assessment to enable a more accurate prediction of early PU damage. However, to date, the evidence pertaining to the use of these methods has not been evaluated systematically. This systematic review set out to answer the following question: What is the accuracy of SEM measurement, ultrasound, thermography and photography in predicting early PU presence?

The objectives of this review were to:

- Establish the clinical significance of ultrasound, thermography, photography and SEM measurement

Fig 2. Search Strategy Flow Diagram.
Adapted from Prisma 2009 Flow Diagram[44]



- Determine the accuracy of ultrasound, thermography, photography and SEM measurement in detecting tissue damage and PU presence
- Determine the relative accuracy of one method of assessment over another
- Make recommendations for practice for the assessment of early PU damage.

Method

Design

A systematic review was undertaken following the guidance of PRISMA.[46] The primary outcome measure was an objective measure of the ability of SEM measurement, ultrasound, thermography and photography to predict early PU damage.

Inclusion and exclusion criteria

The inclusion criteria were: all quantitative original research studies including both animal and human studies. No limitations in terms of language or dates of publications were applied.

Databases and search strategy

The following databases, the Cochrane Wounds Group Specialised Register, The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library) (latest issue), Ovid MEDLINE (1946 to present), Ovid EMBASE, Elsevier version (1974 to present), EBSCO CINAHL (1982 to present) (see appendix 1), ClinicalTrials.gov, WHO International Clinical Trials Registry (ICTR), and The EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/) were search according to the following strategy:

- PU* (s), decubitus ulcer (s), bed sore (s), pressure sore (s); bed ulcer (s), pressure area* (s)
- Thermography, thermology, infrared imaging;
- Ultrasound, ultrasonic imaging, image (s), sonography; ultrasonography
- Photograph*, digital image (s)/ imaging; digital imaging (MH), photography MH
- Sub-epidermal moisture, subepidermal moisture.

The reference lists of all included studies and other relevant publications, such as systematic reviews and guidelines, were searched and any relevant research articles were retrieved. For studies that were identified as relevant and were not available, authors were contacted by email and where no contact details for the authors were available, the journal where the study was published was also contacted through email.

The article titles were assessed by two authors independently, as were the abstracts (where available) of the studies identified by the search strategy, for their eligibility for inclusion. Full versions of potentially relevant studies were obtained and two authors independently screened these against the inclusion criteria. Consensus between the two authors in relation to the studies and the data to be included was obtained.

Data extraction

Data from the retrieved articles were: author, date of study, title, source, impact factor of journal, geographical location, research question, aim and objectives, study type, study design, outcome measures, care setting, inclusion and exclusion criteria, sample size, participant characteristics, study procedure/details, device characteristics, data analysis, results and conclusions.

Data analysis

Initially, the data were narratively summarised giving an overview of study design, geographical location, study settings, populations, sample sizes, and a description of the study methods and devices characteristics. This was followed by quality analysis and a structured narrative synthesis of all the studies included, based on the outcome measures.

All included were quality appraised using the EBL Critical Appraisal check list.[47] This quality appraisal tool assesses the validity, the applicability and appropriateness of a study, based on four main steps of the research process:[47]

- Population

Table 1. Included Studies

Study	Title
Subepidermal moisture	
Bates-Jensen et al. (2007)[36]	Subepidermal moisture predicts erythema and stage 1 pressure ulcers in nursing home residents: a pilot study
Bates-Jensen et al. (2008)[37]	Subepidermal moisture differentiates erythema and stage 1 pressure ulcers in nursing home residents
Bates-Jensen et al. (2009)[31]	Subepidermal moisture is associated with early pressure ulcer damage in nursing home residents with dark skin tones
Guihan et al. (2012)[38]	Assessing the feasibility of subepidermal moisture to predict erythema and stage 1 pressure ulcers in persons with spinal cord injury: a pilot study
Thermography	
Judy *et al*. (2011)[50]	Improving the detection of pressure ulcers using TMI ImageMed System
Ultrasound	
Quintavalle et al. (2006)[40]	Use of high-resolution, high-frequency, diagnostic ultrasound to investigate the pathogenesis of pressure ulcer development
Kanno et al. (2009)[51]	Low-echoic lesions underneath the skin in subjects with spinal-cord injury
Deprez et al. (2011)[53]	On the potential of ultrasound for pressure ulcer early detection
Helvig & Nichols (2012)[52]	Use of high-frequency ultrasound to detect heel pressure injury in elders
Porter-Armstrong et al. (2013)[49]	Do high-frequency ultrasound images support clinical skin assessment?
Photography	
No included studies	

- Data collection
- Study design
- Results.

According to this checklist, if the overall validity of the study (Yes/Total) is ≥75% or ((No + Unclear)/Total) is ≤ 25% then the study is valid.[47]

The designs of the studies included were compared with the evidence pyramid[48] (Fig 1) which shows the different levels of research evidence according to the study design.

Results

Overview of all included studies

Arising from the search strategy (Fig 2),[46] 3692 records were identified in the databases. After removal of duplicates, the titles of the remaining articles, 2634, were screened, yielding a total of 74 articles for further screening. The abstracts of these records were read and the full-text of 10 records were retrieved.[31,36–38,40,49–53] These 10 articles (Table 1), met the inclusion criteria and formed the basis for this review. Of these, four were related to SEM, five to ultrasound, one to thermography. No studies related to photography met the inclusion criteria. Appendix 2 outlines the reasons for the exclusion of the 64 papers.[54–106]

Study design

Of the included studies four were cohort studies,[31,36–37,49] one was a prospective single-arm post-test observational study,[38] one a prospective repeated measures study,[50] one an observational prospective comparative study,[40] one a criterion standard and survey cases,[51] one a prospective, descriptive observational study[52] and the final study used numerical simulations, PU mimicking phantom and *in vivo* experiments[53]

Geographical location

The geographical location of the studies varied between the US,[31–38,40,50,52] Japan,[51] Canada[53] and UK.[49]

Study settings

The study settings varied between long-term care facilities,[31,36–37,40] rehabilitation service of a spinal-cord injury care facility and a residential care facility,[38] hospitals[49,51,52] and a medical centre.[50] One study did not mention the setting.[53]

Population

In eight of the studies, the participants were adult men or women with an age ≥18 years old, at risk of developing PUs.[31,36–38,49–52] One study did not present participants characteristics[40] and one study included animal subjects.[53]

Sample size

The mean sample size was 67 participants, varying between 31[37] and 134[40] participants.

Quality appraisal of included SEM studies

For the included SEM studies, the overall validities were 50%[31,36–37] and 55.56%[38] (Table 2). The study designs for SEM included three descriptive cohort studies[31,36–37] and a prospective single-arm post-test observational study.[38] Mapping them to the evidence pyramid (Fig 1),

Table 2. Analysis of EBL Appraisal Checklist Domains

Studies	Validity (%) not reported/unclear issues identified in each domain				Overall validity (%) of study
	Population domain	Data collection domain	Study design domain	Results domain	
Bates-Jensen *et al.* (2007)[36]	20% Inclusion/exclusion criteria, sample size, selection bias	66.66% Outcome measure time	80% Outcome measure report	40% External validity, confounding variables	50%
Bates-Jensen *et al.* (2008)[37]	20% Inclusion/exclusion, criteria, sample size, selection bias	66.66% Outcome measure time	80% Outcome measure report	40% External validity, confounding variables	50%
Bates-Jensen *et al.* (2009)[31]	20% Inclusion/exclusion criteria, sample size, selection bias	66.66% Outcome measure time	80% Outcome measure report	40% External validity, confounding variables	50%
Guihan *et al.* (2012)[38]	20% Inclusion/exclusion criteria sample size, selection bias	66.66% Outcome measure time	80% Outcome measure report	60% External validity, confounding variables	55.56%
Judy *et al.* (2011)[50]	60% Sample size, selection bias	66.66% Outcome measure time	80% Outcome measure report	40% External validity, confounding variables	55.56%
Quintavalle *et al.* (2006)[40]	0% Inclusion/exclusion criteria, sample size, selection bias informed consent, randomisation group's comparability	33.33% Outcome measure time	60% Outcome measure report ethical approval	60% External validity, confounding variables	33.33%
Kanno *et al.* (2009)[51]	20% Inclusion/exclusion criteria, sample size, selection bias	33.33% Outcome measure time, data extraction and service delivery by same person	80% Outcome measure report	60% External validity, confounding variables	50%
Helvig & Nichols (2012)[52]	40% Inclusion/exclusion criteria, sample size, selection bias	33.33% Outcome measure time, data extraction and service delivery by same person	80% Outcome measure report	60% External validity, confounding variables	55.56%
Porter-Armstrong *et al.* (2013)[49]	20% Inclusion/exclusion criteria, sample size, selection bias	33.33% Outcome measure time, data extraction and service delivery by same person	80% Outcome measure report	60% External validity, confounding variables	50%

these studies are in the middle of the pyramid corresponding to a level IV of evidence.

Results of outcome of interest for SEM

SEM measures were obtained using the NOVA Petite dermal phase meter (NOVA Technology Corporation, 75 Congress St., Portsmouth)[31,36–37] and the MoistureMeter D dermal phase meter (DPM), (Delfin Technologies, Ltd, Kuopio, Finland).[38]

The NOVA Petite dermal phase meter has a probe which is placed on the skin surface for 5 seconds. After the reading, the impedance value of the skin is displayed in dermal phase units (DPUs). The DPUs is an arbitrary relative value and readings range from 0 to 999, with higher readings indicating higher SEM.

The MoistureMeter D measures the dielectric constant in relation to stratum corneum thickness, with values that range from 1–80 dielectric constant with higher DPM readings indicating more water (e.g. oedema and inflammation). Readings are given immediately after 8 seconds of light skin touch and are stable with a coefficient of variation of only 2.8%.

SEM results are presented in Table 3, as can be seen, the mean sample size was 37.5. PU incidence rates varied between 24–46%,[31,36–37] and 80 stage 2+ PUs developed across the studies.[31,36–38] All studies showed that skin damage and higher PU stages were associated with high SEM measures. Moreover, once the SEM was elevated, this predicted PU development, one week later.

Table 3. Included SEM studies results

Study/ type of device	Pressure ulcer (PU) incidence rate	Sample Size	Anatomical sites	Main findings
Bates-Jensen *et al*. (2007)[36] NOVA Petite dermal phase meter	46%	n=28	Right/left trochanter Right/left ischium Right/left buttock Sacrum	28 stage 2+ PUs developed in 16 subjects; High SEM = greater skin damage; Increased skin damage=increased SEM values; Mean SEM (all sites): *Normal skin=96.7±122.3; erythema/stage 1=191.5±187.6; Stage 2+=568.9±319.5* SEM predicted the development of erythema/stage 1 PU one week later, OR=1.26 per 100 DPU; OR for predicting PU deteriorating to stage 2+ was not statistically significant.
Bates-Jensen *et al*. (2008)[37] NOVA Petite dermal phase meter	26%	n=28 completed the 20 weeks of the study	Right/left trochanter Right/left ischium Right/left buttock Sacrum	15 stage 2+ PUs developed in 8 participants; High SEM = greater skin damage; Mean SEM (all sites): *Normal skin=104±115 DPU; Erythema=185±138 DPU; Stage 1=264±208 DPU; Stage 2+=727±287 DPU* SEM changed as visual skin changes were observed from week to week; SEM predicted erythema, stage 1 and 2+ PUs, OR=1.99 per 100 DPU; SEM predicted erythema/stage 1 PU one week later OR=1.003 [99% CI]; OR for predicting PU deteriorating to stage 2+ was not statistically significant.
Bates-Jensen *et al*. (2009)[31] NOVA Petite dermal phase meter	Light skin tones (LST)=24% Dark skin tones (DST)=27%	n=66	Right/left trochanter Right/left ischium Right/left buttock Sacrum	13 participants with LST developed 21 stage 2+ PUs over 20 weeks; 3 participants with DST developed 9 stage 2+ PUs over 20 weeks; 16 PUs developed over sacrum; High SEM=greater skin damage; Mean SEM (pelvic sites): *Normal skin=83.45±100.62; erythema/stage 1=150.42±128.21; Stage 2+ = 564.42±368.53* SEM was lower for DST compared with LST, for all sites and skin damage level; SEM predicted erythema/stage 1 PU one week later [95% CI]: *LST–OR=1.14 per 100 DPU; DST–OR=188 per 100 DPU* SEM values predictors of stage 2+ PUs one week later (95% CI): *LST–OR=1.01 [1.001-1.01] per DPU; DST–OR=1.02 [1.007-1.024] per DPU* SEM threshold values (50 DPU, 150 DPU and 300 DPU) used to detect skin damage [95% CI]: *50 DPU—detected erythema/stage 1 in DST [OR=5.3]; 50 and 150 DPU—detected stage 2+ PUs one week later in DST [OR=8.5]; 300 DPU–detected stage 2+ PUs in LST [OR=4.3].*
Guihan *et al*. (2012)[38] MoistureMeter D dermal phase meter		n=28 completed the 52 weeks of the study	Sacrum Buttocks Ischium Trochanter Heels	11 participants developed 14 PUs: *7 were stage I; 3 stage II; 2 stage III; 2 stage IV* 22 participants developed 66 cases of erythema/stage I PUs: *Sacrum (n=7); buttocks (n=17); ischium (n=15); trochanter (n=6); heels (n=21)* SEM values (all sites): *Normal skin=40±10 DPU; erythema/stage I = 42±11 DPU* Sacrum and heels had more erythema/stage I PUs occurrence; Increased skin damage = to increased SEM values.

SEM—subepidermal moisture; PU—pressure ulcer; DPU—dermal phase units; OR–odds ratio; CI—confidence interval

Quality appraisal of the thermography study

In the study by Judy et al.[50] the overall validity was 55.56% (Table 2). This was a prospective repeated measures study.[50] Mapping this to the evidence pyramid (Fig 1), the study is at a level V.

Results of outcome of interest for thermography

In this study[50] measures were obtained using the TMI ImageMed System (Trillennium Medical Imaging, Inc [TMI], Holland, Ohio) which includes an infrared camera, software, and the server/database. The camera takes two separate images and captures 76.800 temperature readings, with 0.06°C accuracy, and then generates a thermal image by assigning coloured pixels to a specific temperature range. A visual light, or digital image, is captured by a visual light camera that is included in the device.[50] Results for this study are presented in Table 4. As can be seen, 100 participants were assessed based on three different methods, five of the participants developed a PU, data obtained from the infrared imaging was more likely to identify participants at high-risk of developing PUs then the Braden scale. From the three assessment techniques, the first identified 39% of the high-risk of observations

Table 4. Included thermography study results

Study/ type of device	Pressure ulcer (PU) incidence/ prevalence rate	Sample size	Anatomical sites	Main findings
Judy *et al.* (2011)[50] TMI ImageMed System	**Method 1** difference between the minimum and maximum temperature **Method 2** 75th percentile temperature minus the minimum temperature **Method 3** mean temperature minus the minimum temperature	n=100	Right/left heels Sacrum	5 subjects developed PUs: *3 at stage I and 2 at stage II* **Method 1**—identified 39% of high risk observations of PU development **Method 2**—identified 28% as being at high risk of PU development **Method 3**—identified 22% as being at high risk of PU development Data obtained from the infrared imaging was more likely to identify participants at high risk of developing PUs then the Braden scale There was no difference over time on Braden scores Braden Scale completion, had a statistically significant group effect (p=0.0006) No time effect or rater effect by time were noted Unit nurses attributed higher Braden scores to patients compared with research nurses Interrater reliability was poor with a κ=0.42 Infrared imaging was able to detect those at high risk of developing PUs Analysis of the OR of the infrared images using upper quartile: *Infrared imaging versus unit nurse OR=6.8; Infrared imaging versus research nurse OR=2.8* Analysis of the OR of the infrared images using mean temperature minus the minimum temperature; *Infrared imaging versus unit nurse OR=5.4;Infrared imaging versus research nurse OR=2.2*

PU–pressure ulcer; OR–odds ratio

of PU development, the second identified 28% and the third 22%.

Quality appraisal of included ultrasound studies

In the study by Quintavalle et al.[40] the overall validity was 33.33%, whereas in the studies of Kanno et al.[51] and Porter-Armstrong et al.[49] the overall validity was 50%, finally in the study by Helvig and Nicohls[52] the overall validity was 55.56%. For Deprez et al.[53] it was not possible to analyse it using the EBL critical appraisal checklist because this study involved a single experiment in an animal subject.

The study designs included a prospective comparative study,[40] a criterion standard and survey cases,[51] a prospective, descriptive observational study,[52] a cohort study[49] and an animal research study.[53] Mapping these to the evidence pyramid (Fig 1), three studies[40,49,52] are at a level IV of evidence and another study is at a level V.[51] The last study[53] is at a level VII.

Results of outcome of interest for ultrasound

Quintavalle et al.[40] used the Longport Digital Scanner (EPISCAN I-200; Glen Mills, PA). This is a portable 20MHz frequency system specifically developed to examine the skin and underlying soft tissue with 65µm resolution. It consists of four main elements: an ultrasound probe, a custom-designed proprietary ultrasound analogue-to-digital converter board, a portable computer, and operating software.

In the study by Kanno et al.[51] a high-frequency ultrasonography using a linear array, 10-MHz transducer of an ultrasound scanner LOGIQ 500 (GE, Tokyo, Japan) was used.

In the study by Deprez et al.[53] ultrasound data were acquired with a Visual Sonics Vevo 660 device (Visual Sonics Inc., Toronto, Canada), equipped with a 35MHz probe, dedicated for use in small animal studies.

Helvig and Nichols[52] used the Longport EPISCAN high-frequency ultrasound scanner to create ultrasonic images (EPISCAN; Longport, Inc, Glenn Mills, Pennsylvania). Furthermore, for improved sound conduction, a water-soluble gel was applied between the skin and transducer. Finally, in the study by Porter-Armstrong et al.[49] the EPISCAN I-200 high frequency ultrasound scanner (Longport Inc, US) was used to capture the images in this study.

All results for the included ultrasound studies are presented in Table 5. In these studies, the mean sample size was 81.5, and only one study[52] analysed prevalence rates, with a hospital acquired prevalence of 2% and a heel PU prevalence of 7.3%. All ultrasound images across studies identified areas of oedema within the tissues that were indicative of abnormal changes and skin damage.

Methodological issues within included studies

The EBL Appraisal checklist was used to assess the methodological issues of the included studies in this systematic review, by focusing on the four main domains of the checklist which are population, data collection, study designs and results.[47] These domains are summarised in Table 2, where validity figures can be found as well as any not reported or unclear issues identified in each domain.

All studies[31,36–38,49–53] presented with methodological issues. The main aspects related to the population domain that arose in all studies were inclusion and exclusion criteria, sample size, selection bias and

informed consent. For the inclusion and exclusion criteria these need to be clearly established, and reported, as they will influence the population and sample that will be selected. This is fundamental as they need to reflect and be relevant to the defined research question,[107] as well as to allow for study replicability.[107]

Sample size is another crucial aspect of research, and it is usual to undertake a power calculation to estimate the minimum sample size needed for a study.[108] If the sample size is too small, the risk of a type II error occurring exists and as such the detection of a difference between the groups, where one actually exists, could be missed because there are not enough subjects in the sample.[109]

Issues with selection bias relate to the fact that there could be systematic differences between the intervention and control group and is related to the allocation of participants to the intervention or control group.[110] This issue was evident in one of the studies[40] where subjects were not randomly allocated to the groups but were purposively chosen.

In the data collection domain the main area of concern was that it was unclear if the measurement of the outcomes was done at an appropriate time to capture data pertaining to the variable under exploration, which introduces detection bias in the study. Furthermore, it was not clear if those collecting the data were also involved in service delivery,[49,51–52] which can introduce performance bias. However, in one study[40] it was clearly stated that independent individuals assessed the scans. Any type of bias that is potentially introduced in the research will affect the believability and clinical significance of the results and the potential generalisability of outcomes.

In the study design domain, the main aspects of concern were unclear outcome measure reporting.[31,36–38,49–52] Study outcomes need to be clearly stated a priori, to assure that the relevant data collection methods were used, that the study researched what was originally set out in the proposal[47] and to avoid reporting bias. Furthermore, in one study[40] it is not clear if ethical approval was sought and/or obtained to conduct the study and if informed consent was obtained. Any issues related to ethical approval are fundamental, as this is a key aspect of the research process, without which the research should not be conducted, and if conducted its results may be questioned as there is no possibility to assure if subjects' confidentiality and autonomy were protected and that justice and non-maleficence were guaranteed.[109] Moreover, it is not possible to ensure that what was studied and that the methods employed were fair, limiting the validity, reliability and applicability of the results obtained.[108]

Finally, in the results domain, the main areas of concern related to external validity, chiefly related to non-reporting of inclusion and exclusion criteria and no sample size calculation. Another issue that arose from the included SEM studies was related to confounding factors. SEM is a measure of water tissue content and it is important to assure that increased water content is actually due to the damage that pressure/shear causes in the tissues, and not due to other factors presented by the subjects. For example, Björklund et al.[111] have suggested that skin membrane electrical impedance properties change depending on the skin water gradient. This is influenced by changes in skin hydration by occlusion, which can be achieved using certain creams or lotions. Skin moisture is also influenced by the cellular structure of the stratum corneum and lipid content of the skin and as such alterations in these will adversely affect moisture content.[112] If there are alternate influencing factors, other than pressure and shear, then researchers assessing skin moisture would need to explicitly account for these types of confounders.

Discussion

Heterogeneity of studies

Heterogeneity is related to the variability among studies that are chosen to be included in a systematic review.[110] This variability can be statistical and relates to differences in the effect estimates and methodologies and thus concerns the study design. Variability may also be a clinical issue and relates to differences among participants, interventions and outcomes.[107,110] Meta-analysis allows for the statistical combination of studies however, heterogeneity might hinder the appropriateness of undertaking this combination.[110]

In the studies included, heterogeneity was present, mainly arising due to issues surrounding the study populations and the methods under investigation. In relation to the population, although demographically similar, participants presented with differences that did not allow for comparability. These were mainly related to skin tone and mobility levels. In relation to the methods under research, these were also not comparable as they employed and measured different skin and tissue characteristics. Considering that the studies are not homogenous combining them would bring meaningless results and thus rendering any conclusions and recommendations lacking the potential for contribution to evidence based practice.

Thermography

Only one study was identified[50] that analysed the role of thermography in the early prediction of tissue damage and of PU presence. In this study[50] data were obtained with the infrared device using three different methods. All of these methods identified a percentage of images from subjects, which varied between 22% and 39%, and showed that these subjects were at high risk of developing subsequent visual PUs. Additionally, in determining the likelihood of infrared imaging identifying a subject at risk, when compared with the unit nurse and research nurse using the Braden Scale, infrared identified more subjects to be at high risk of developing PUs. The ability of thermography to detect temperature changes in the tissues and skin is related to the inflammatory processes caused by tissue damage pathways.[113]

Table 5. Included ultrasound studies results

Study/ type of device	Pressure ulcer (PU) incidence/ prevalence rate	Sample size	Anatomical sites	Main findings
Quintavalle *et al.* (2006)[40] Longport Digital Scanner	N/A	n=119 (study group) n=15 (control group)	Not all sites were identified, only coccyx is mentioned	All images obtained from the control group had homogenous patterns; Study group images were not always homogenous and some areas of low reflections could be identified; Images obtained from the study group: *55.3% demonstrated ultrasound patterns consistent with abnormal skin and soft tissue; 44.7% demonstrated ultrasound patterns consistent with normal skin and soft tissue* Ultrasound patterns identified: *Pattern 1 (47.5% of images) presented deep areas of weak reflection that seem to progress from the deep subdermal area to the superficial dermal area; Pattern 2 (7.8% of images) presented a superficial layer of weak reflection directly below intact epidermis. The weak reflective patterns areas corresponded to an increased fluid content or oedema in the tissues* Pre-ulcerative changes were induced through friction, in a healthy volunteer and a second area (skin covering the coccyx) was subject to prolonged pressure: *Images after friction showed oedema directly below the epidermis with no other changes; Images after pressure showed pockets of deep oedema with no superficial changes* Pattern 1 images were further analysed: *Subgroup 1: 16.8% of images, oedema present between the bone and dermal layer; Subgroup 2: 32.7% of images, oedema in the subdermal layer progressing to the dermal layer; Subgroup 3: 50.5% of images, oedema mainly under an intact epidermis, although the deep tissue also showed a weak reflective pattern* Abnormal scan images: *11.7% (n=74) of the individuals had documented visual clinical signs of erythema; Of these 74 images 23% were included in subgroup 1 and 2; 77% were included in subgroup 3; These images was evidence of PU formation before the emergence of visible skin changes* Pattern 2 images (subepidermal oedema) for the 60% of images that showed superficial changes, the individuals had erythema documented.
Kanno *et al.* (2009)[51] LOGIQ 500	N/A	n=43	Sacrum Bilateral ischial tuberosities	Inspection, palpation and ultrasound images were used for identifying ulcerative lesions; Ultrasound identified a higher number of lesions; 129 areas were assessed: *Inspection identified 2 lesions; palpation identified 8 lesions; ultrasound identified 17 lesions* Abnormal images showed heterogeneous patterns with echoic lesions; Low-echoic lesions identified through ultrasound were significantly deeper; Of 17 low-echoic lesions 64.7% also contained a high-echoic area.

The study[50] showed that thermography can identify temperature changes in tissues and skin, which may give an indication of early tissue damage and PU development. However, the study was not sufficiently robust to make strong conclusions that thermography is the most accurate method for the prediction of PU presence. More studies are needed that assess skin temperature of areas not exposed to pressure and compare these with areas exposed to pressure, to try and better understand the role of thermography in PU detection.

SEM measurement

The different PU causal pathways that lead to tissue damage and PUs all have their origin in pressure (and pressure in conjunction with shear) that causes tissue stress and cell deformation.[20–29] If damage occurs first at the deepest levels of the tissues and not at the outer layers, it is important to understand how this pressure damage might influence the skin structure. SEM measurement may offer potential for the detection of changes that indicate the presence of pressure damage.

Skin tissue water varies according to anatomical site and tissue depth and this is an important biophysical measure, as a certain level of hydration is necessary for the skin to maintain its barrier function. Interestingly, in a study by Mayrovitz et al.[35] the water content was measured by using an electromagnetic wave that is reflected according to the dielectric constant of the tissue. This dielectric constant depends on the amount of free and bound water in the tissue volume through which the wave passes, and is a measure of the amount of skin and tissue water content (stratum corneum, dermis and epidermis).[35] From the measures obtained,

Table 5. Included ultrasound studies results continued

Study/ type of device	Pressure ulcer (PU) incidence/ prevalence rate	Sample size	Anatomical sites	Main findings
Deprez *et al.* (2011)[53] Visual Sonics Vevo 660 device	N/A	18-week-old male rat Brown Norway breed	Thigh	Pressure was applied in the thigh of a rat for 60 minutes. Initial elastogram: *Tissues appeared to be homogenous although the area above the bone showed some strain* Second elastogram, post compression: *Small deformation, with the strain also developing in the deeper tissues* Superficial tissues, with higher strain, were identified when compared with those near the bone, showing that the tissue over the bone became stiffer, which according to the authors could indicate a developing PU.
Helvig & Nichols (2012)[52] Longport EPISCAN	Hospital acquired Prevalence rate = 2% Heel PU prevalence = 7.3%	n=99	Heels	2 participants developed PUs; Scans were normal for both heels for 10.1% of participants; 18% of patients had abnormal scans of both heels; 23.2% having abnormal and borderline scans; The authors could not answer if high frequency ultrasound predicts the development of clinically undetectable pressure ulcers.
Porter-Armstrong *et al.* (2013)[49] EPISCAN I-200		n=50	Heels Sacrum Coccyx	32 participants had both heels and sacral coccygeal areas scanned; 17 participants had only the heels scanned; 1 participant had only the sacral coccygeal area scanned Skin assessment identified: *3 participants as non-blanching erythema of coccyx (n=2) and sacrum (n=1); ultrasound scans were identified as normal for all participants* From all participants: *43 had at least one heel scan that identified oedema between the bone and dermal layer; 34 had at least one heel scan that presented oedema in the subdermal layer progressing to the dermal layer; 16 participants had at least one heel scan that presented oedema mainly under an intact epidermis*

PU–pressure ulcer

tissue dielectric constant decreased with tissue depth; however, none of the measures were undertaken at the sacrum, heel or ischium. Because these are common sites for PU development, it would be relevant to determine the water content of these, and other PU related, anatomical locations.

Through the use of SEM measurement in the studies included in this review, it was possible to predict erythema and the development of stage I PUs one week after the initial elevated SEM readings, with odds ratio values above 131.[36–37] This indicates that the water content in the skin and tissues are increasing, probably due to damage that is occurring at the deeper levels of the tissues, which will then only become visually visible after some time has elapsed. In the study by Harrow and Mayrovitz[39] SEM measurement also showed higher measures where visual skin damage was present, as compared with normal skin. The authors add that when compared with SEM measurement, VSA is limited as a tool to predict PU development, as VSA needs to have visible signs of damage to be effective, which are often developing in deeper levels of the skin. Thus, it is reasonable to conclude that SEM measures can be used to corroborate the fact that PU damage can start in deeper levels of the skin and tissue developing upwards, and not always at the skin surface and developing downwards. Furthermore, SEM measurement might be a reliable method for early prediction of tissue damage and of PU presence. Indeed, Clendenin et al.[114] in their study where the reliability of a SEM scanner was analysed, found that the device had a high reliability allowing for good reproducibility of outcomes. However, it is necessary that more studies are conducted for a stronger body of evidence to be developed and to demonstrate the benefits of this as a PU detection method.

Ultrasound

Studies focusing on the role of ultrasound for PU early detection are not abundant. However, from those included in this review, all the ultrasound images of suspected areas of PU damage showed regions with abnormal patterns.[40,49,51–52] In the study by Helvig and Nichols,[54] 41.2% of images had abnormal or borderline

Reflective questions

- Would you consider using ultrasound, thermography, photography or subepidermal moisture (SEM) measurement to detect tissue damage accurately? Explain why
- Think about how you usually determine pressure ulcer development, and reflect on the level of reliability of your assessment method
- Describe how ultrasound, thermography, photography and SEM measurement work, and identify at least three situations in which you could apply these techniques in your daily practice.

scans. Whereas, in Porter-Armstrong et al.[49] one heel scan showed oedema between the bone and dermal layer, while 34 scans showed oedema in the subdermal layer progressing to the dermal layer. Furthermore, 16 scans showed oedema under intact epidermis, but with deep tissue also showing abnormal patterns. The animal study by Deprez et al.[53] shows how pressure can create tissue strain, that with prolonged pressure exposure, can lead to the development of a PU. Although pressure causes tissue strain that can be assessed using ultrasound elastogram, this study differs from the others as it was not focusing on fluid content, but strain level.

Both SEM measurement and ultrasound predict tissue damage and PU presence based on tissue water content. Furthermore, the results of SEM measurement and ultrasound studies suggest that damage starts in the deeper tissues and progresses towards the surface of the skin. The only superficial skin damage that starts at the surface of the skin is related to friction, a parallel force[112] that, as revealed by Quintavalle et al.[40] shows oedema directly under the epidermis.

Both SEM measurement and ultrasound appear to be accurate methods in the early prediction of tissue damage and of PU presence and both methods support the fact that PUs start deep in the tissue, as the water content of these tissues increased as damage increased. Nonetheless, it is still necessary that more studies on the use of ultrasound and SEM measurement are conducted to consolidate the existent evidence.

Focusing on the outcomes and objectives of this review it is possible to conclude that the methods that show some clinical significance for the early prediction of tissue damage and of PU presence are SEM measurement, ultrasound and thermography. Furthermore, from what has been discussed, SEM measurement and ultrasound were the methods that showed best outcomes in early prediction of tissue damage and of PU presence. However, although results clearly identify that these methods detect early PU damage, more studies are necessary to consolidate this evidence.

Strengths and limitations

This systematic review followed and reported on all the steps necessary to conduct a systematic review, by using the PRISMA Checklist.[46] Moreover, it thoroughly reported on the search strategy implemented for the different databases and clinical registers, so that it can be replicated. However, one of the limitations of this systematic review is related to the small number of studies identified that analysed the role of SEM measurement, ultrasound, and thermography in the prediction of PU presence. This could be because the authors were looking only at studies where PUs had not developed yet, as these studies would give a real idea of the role that SEM measurement, ultrasound and thermography have in detecting what characteristics exist in the early development of PUs. Another limitation in this systematic review is the fact that it was not possible to conduct meta-analysis, due to the heterogeneity of the studies included.

Conclusion

SEM measurement and ultrasound are promising in the detection of early tissue damage and pressure ulceration; however, these methods should be further studied to clarify their potential for use more widely in PU prevention strategies. **JWC**

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