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A machine learning algorithm for early detection of heel deep tissue injuries based on a daily history of sub-epidermal moisture measurements

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Abstract

Sub-epidermal moisture is an established biophysical marker of pressure ulcer formation based on biocapacitance changes in affected soft tissues, which has been shown to facilitate early detection of these injuries. Artificial intelligence shows great promise in wound prevention and care, including in automated analyses of quantitative measures of tissue health such as sub-epidermal moisture readings acquired over time for effective, patient-specific, and anatomical-site-specific pressure ulcer prophylaxis. Here, we developed a novel machine learning algorithm for early detection of heel deep tissue injuries, which was trained using a database comprising six consecutive daily sub-epidermal moisture measurements recorded from 173 patients in acute and post-acute care settings. This algorithm was able to achieve strong predictive power in forecasting heel deep tissue injury events the next day, with sensitivity and specificity of 77% and 80%, respectively, revealing the clinical potential of artificial intelligence-powered technology for hospital-acquired pressure ulcer prevention. The current work forms the scientific basis for clinical implementation of machine learning algorithms that provide effective, early, and anatomy-specific preventive interventions to minimise the occurrence of hospital-acquired pressure ulcers based on routine tissue health status measurements.

KEYWORDS
artificial intelligence, predictive bioengineering modelling, pressure ulcer/injury prophylaxis, preventive interventions, SEM scanner

Key Messages
- sub-epidermal moisture is a biophysical marker of pressure ulcer formation
- we used sub-epidermal moisture in a predictive machine learning algorithm

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Abbreviations: AI, Artificial intelligence; DTI, Deep tissue injury; EHR, Electronic health record; FPR, False positive rate; ML, Machine learning; PI, Pressure injury; PU, Pressure ulcer; SEM, Sub-epidermal moisture; STA, Skin and tissue assessment; TPR, True positive rate.

- the algorithm was trained using clinical data of heel deep tissue injury cases
- the algorithm sensitivity and specificity were 80% and 77%, respectively
- machine learning of sub-epidermal moisture can guide preventive interventions

1 | INTRODUCTION

Pressure ulcers (PUs), also known as pressure injuries (PIs), continue to cause death and compromise the quality of life of millions of patients and even more so during the current COVID pandemic.[1] The average cost of treating a single hospital-acquired PU/PI in the United States is as high as $21 767, but Category-4 wounds cost more than triple ($67 198), and Category-3 PU/PIs cost more than double that amount ($54 151).[2] It is not surprising, therefore, that these treatment costs add up to a worrying annual expenditure of $26.8 billion in the United States alone and only in direct costs, not including, for example, litigation and insurance premiums.[3] Etiological research indicate that the more severe, category-3/4 open-cavity wounds often develop when the skin breaks down above a deep tissue injury (DTI); a DTI is a mass of subdermal necrotic soft tissue forming under intact skin, primarily due to cell and tissue exposure to sustained deformations.[4,5] Prevention of DTIs or at least their early detection at a time point where they are mild and reversible can therefore not only prevent the mortality and suffering associated with serious, open-cavity wounds but also substantially reduce the above financial burden on health care.[4,6]

In the early stages of development of DTIs, before the injury presents itself on the skin, the fluid content within the interstitial tissue spaces increases as blood vessels dilate and become leaky, as part of the localised inflammatory response to the onset of cell death.[6,7] This change in sub-epidermal moisture (SEM), which leads to a detectable elevation of the biocapacitance property value of the affected soft tissues, is the underlying biophysical phenomenon monitored by the SEM Scanner technology (Bruin Biometrics LLC, Los Angeles, CA, USA) to early-detect a forming PU/PI.[8-10] Many published clinical studies have confirmed that consistently elevated or an increasing trend of SEM readings may be linked to the risk of developing a PU/PI, including DTIs, in the following days.[11-20] The literature overall indicates that the SEM Scanner technology is able to indicate early development of PUs/PIs 5 days (median) prior to the clinical presentation of a wound, which aids health care practitioner's clinical judgement in traditional clinical risk assessments, skin tissue assessments (STAs), and routine PU/PI management protocols.[20-25] The aforementioned timeframe appears to be the predictive window for the SEM Scanner technology, but if further powered by artificial intelligence (AI), the performances of the SEM Scanner technology may be maximised.

Over the past few years, AI-based methods have been incorporated in a growing number of clinical studies and research techniques designed for binary classification of whether a patient is positive or negative to a specific disease condition or pathology. The main advantage of using AI, particularly employing the branch of machine learning (ML) to improve a classification algorithm automatically (through experience and by the use of a growing set of data), is that it may ultimately reduce human diagnostic errors when sufficiently trained.[26,27] Dermatology is a natural medical discipline for adopting AI-based methods given, for example, the need to differentiate between benign vs malignant skin lesions, but allergies and psoriasis were also identified as candidate conditions for AI-supported diagnosis.[28-37] More recently, applications of AI have expanded to the classification of chronic wounds, including leg ulcers, diabetic foot ulcers, and PUs/PIs.[38-43]

To date, no methods or studies have integrated AI/ML with the diagnostic abilities of the SEM Scanner technology, to detect the formation of DTIs before they are diagnosed visually through STAs. In the present study, we aim to retrospectively analyse an extensive clinical database of SEM measurements acquired using the SEM Scanner technology, to develop a novel AI-powered decision-algorithm for effective differential diagnosis and prediction of heel DTIs (before they appear visually), based on the daily history of collected SEM assessments.

2 | METHODS

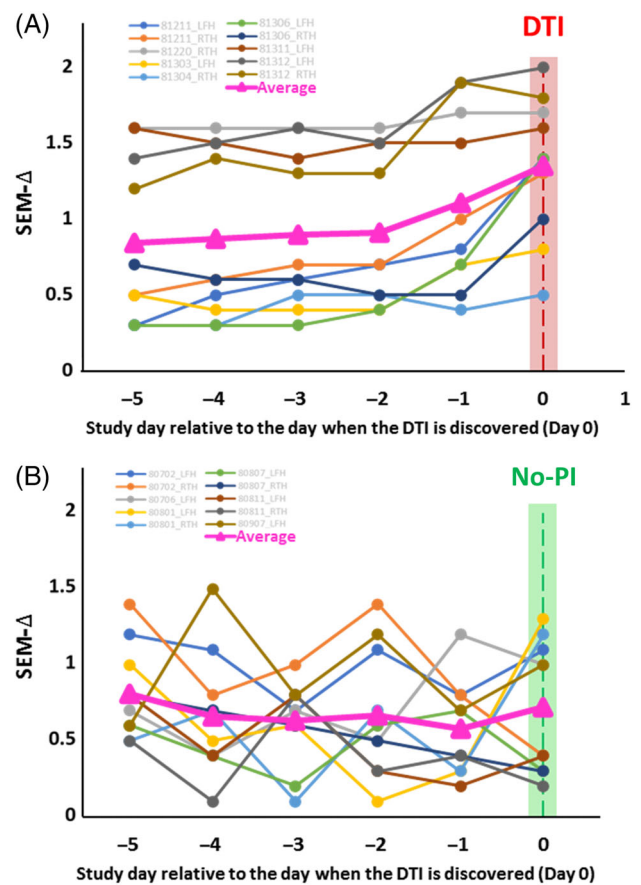## 2.1 | The dataset of sub-epidermal moisture measurements

We used an existing database of SEM measurements from a published clinical study designed to evaluate the contribution of SEM measurements relative to the current standard of care, that is, STAs, in identifying patients at increased risk of developing DTIs.[18] This blinded clinical study enrolled 189 patients at multiple acute and post-acute sites in the United Kingdom and the United States, all of whom consented to participate in writing (further information on the ethical approval is

detailed in the original study[18]). Using a commercial SEM Scanner (Bruin Biometrics LLC, Los Angeles, CA, USA), each participating subject was evaluated for their heel SEM-Δ values, which compares spatial SEM measurements acquired at and around the bony prominence of the anatomy. The calculation of SEM-Δs from spatial SEM measurements, as opposed to single point measurements, eliminates potential effects of systemic changes in tissue fluid contents and provides a consistent, robust quantitative measure of the tissue health conditions at the anatomy.[7-10,23,44,45]

Daily SEM-Δ measurements were collected from the heels of the enrolled patients beginning at admission and continuing until one of the following events: (a) a monitored patient developed a DTI confirmed by STA; (b) a patient was discharged from the hospital or had died; (c) a total of 21 days of SEM-Δ measurements have elapsed. Our aim in the present work was to develop a novel ML algorithm to predict the formation of heel DTIs based on the aforementioned dataset of SEM-Δ measurements. Accordingly, as a first pre-processing step, the SEM-Δ database was filtered to include only subjects with valid SEM-Δ data defined as SEM-Δ ≥ 0.6 in two out of three assessments). Furthermore, a complete patient dataset eligible for further processing included at least 6 consecutive days of numerical SEM-Δ readings for the heels and in addition, that the outcome of the STA in the last day was either 'no-PI' or 'suspected DTI'. This reduced the number of (eligible) patient entries in the database to n = 173, of which 163 participants had no PIs and were therefore considered control subjects, while 10 patients had a suspected heel DTI diagnosis.

2.2 | The acceleration effect

Visual examination of the database entries against time to DTI diagnosis indicated a recurring trend (Figure 1). In patients who eventually developed a heel DTI, SEM-Δ values generally increased over time before a DTI was confirmed through an STA, demonstrating a so-called 'acceleration effect' where the SEM-Δ value in the day preceding the discovery of the DTI on the skin surface was typically greater than the average of the SEM-Δ readings in the prior measurement days. In the control group, however, the SEM-Δ measurements typically fluctuated over time in an apparently random pattern and therefore, the average SEM-Δ values of these patients (who did not develop a heel DTI during the study period) were similar across all the study days. Following this observed behaviour, we designed our ML algorithm to first detect (Figure 2A) and then predict (Figure 2B) the development of heel DTIs, based on a daily history of SEM-Δ

FIGURE 1 Sub-epidermal moisture delta (SEM-Δ) readings from the heels of the participating subjects, acquired over 6 consecutive days: (A) The SEM-Δ measurements of the 10 patients who developed a heel deep tissue injury (DTI). These SEM-Δ measurements typically increased prior to the clinical presentation of the DTI in a visual skin assessment, demonstrating an acceleration effect, that is, the SEM-Δ value in the day preceding the DTI was typically greater than the average of the SEM-Δ readings in the prior days. (B) The SEM-Δ measurements of 10 randomly selected control subjects, which typically fluctuated over time and therefore, the average SEM-Δ values of those patients who did not develop a heel DTI were similar across all the study days. PI, pressure injury

readings, for the purpose of developing an AI-supported early diagnosis aid, as described further below.

2.3 | The detection algorithm

In ML algorithmics, *detection* generally refers to mining information from an existing database that is being investigated. In contrast, *prediction* is the process of estimating future events based on the detected trends (ie, the data patterns) in the studied database. *Supervised* ML enables the *detection algorithm* to learn from an existing dataset where the labels are known, which in this study are the clinical
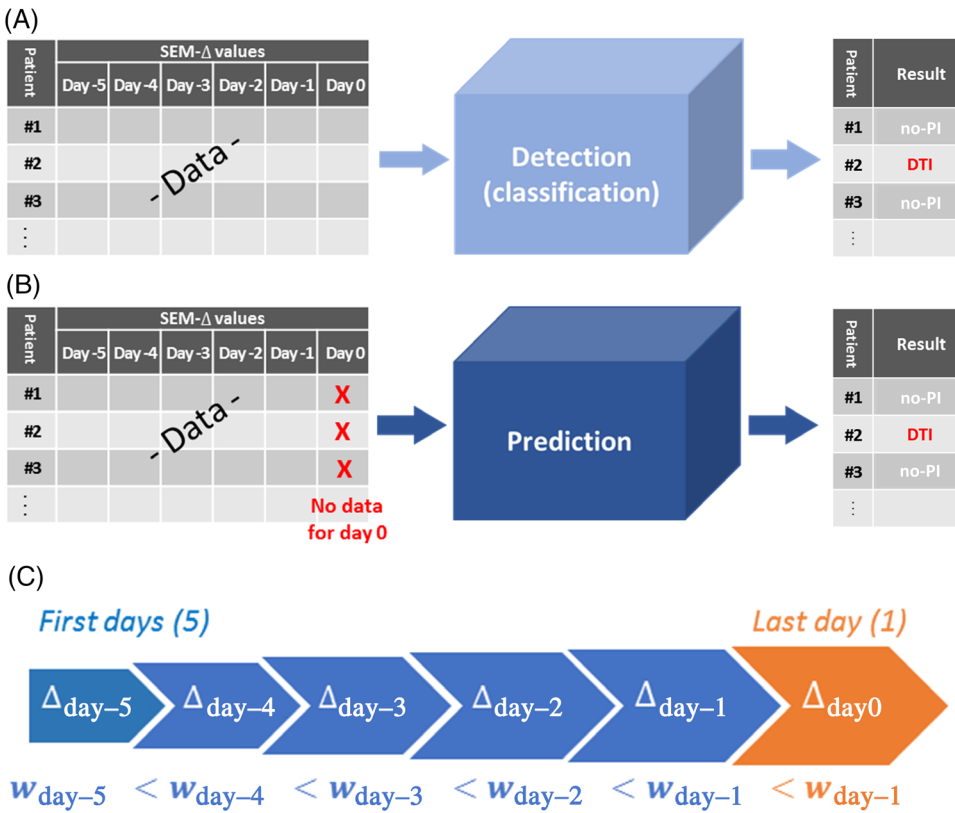
FIGURE 2 Schematic representation of the (A) machine learning (ML) detector, based on readings from all the 6 consecutive days, (B) ML predictor, for forecasting whether a heel deep tissue injury (DTI) will appear in the next day based on the previous sub-epidermal moisture delta (SEM-Δ) readings from the last 5 days; and (C) the concept of incorporation of weights ($w_{\text{day}(i)}$) to predict the development of a heel DTI based on a daily history of SEM-Δ readings. PI, pressure injury

outcomes defined as 'no-PI' and 'suspected DTI'. Once a detection algorithm is established, it serves as the basis for forecasting the outcomes of unlabeled cases using a *prediction algorithm*. Accordingly, we first describe the detection algorithm used to learn the present SEM-Δ database.

The goal of the detection algorithm in the present work is to accurately classify patients into two buckets or labels: (a) at-risk patients who developed a heel DTI, (b) at-risk patients who did not present a clinical injury on the sixth (and last) day of SEM-Δ measurements. Therefore, the inputs of this algorithm are the SEM-Δ readings of the six consecutive measurement days, where the first measurement day is termed 'day -5' and the last day is termed 'day 0'. Based on the observed acceleration effect described above (where the SEM-Δ value in the day preceding the DTI was typically higher than the average of the SEM-Δ readings in the prior days), the following inequation was formulated to classify the clinical cases to 'DTI' vs 'no-PI' labels (or groups):

$$w_{\text{day }0} \cdot \Delta_{\text{day }0} - Average\left(w_{\text{day}(i)} \cdot \Delta_{\text{day}(i)}\right) > threshold \quad (1)$$

where $\Delta_{\text{day}(i)}$ is the SEM-Δ reading at day i ($i = -5$ to 0) and $w_{\text{day}(i)}$ is a set of dimensionless weight values, each of which can range between 0 and 2 and is assigned to amplify or de-amplify the contribution of the SEM-Δ reading acquired at a specific measurement day i to the

result of the above calculation. The average on the left side of the inequation is calculated over the multiplication of the SEM-Δ values acquired in each day $\Delta_{\text{day}(i)}$ by the respective weights $w_{\text{day}(i)}$.

If, for a given set of consecutive $\Delta_{\text{day}(i)}$ measurements that were acquired from a specific patient and for a pre-set weight $w_{\text{day}(i)}$ and threshold values, Inequation (1) holds true, then an acceleration effect is said to be present, and that patient is highly likely to develop a heel DTI. The specific pre-set of weight and threshold values determines the classification accuracy and the true/false positive rates (TPR/FPR) of the ML algorithm and should therefore be optimised, based on the information in the existing SEM-Δ database, as will be described next. Moreover, because the SEM-Δ measurements acquired in the days nearer to the latest SEM-Δ reading are physiologically and clinically more significant than older SEM-Δ data (ie, the newer SEM-Δ measurements are more representative of the current health status of the monitored tissues relatively to prior days), we constrained the $w_{\text{day}(i)}$ values to be monotonically increasing with i (Figure 2C).

2.3.1 | Extracting the optimal weight and threshold values

We applied an optimization process programmed in Python (the Python Software Foundation, Fredericksburg

VA, USA; python.org) to determine the optimal weight $w_{day(i)}$ and threshold values that result in the best classification performances of the detection algorithm (Figure 3). This code first reads the SEM-Δ values of the six consecutive measurement days from the registries of all the study participants, with the known label (clinical outcome) for each participant (ie, if a heel DTI appeared on day 0, or not). In addition, a threshold in the range of 0 to 1 is inserted as input datum [Inequation (1)]. Starting with a threshold value of zero, a 'For' loop is initiated and set to run for 2000 iterations. The specific loop steps are as follows: (a) random values are chosen for each weight $w_{day(i)}$ (in the range of 0 to 2) so that the $w_{day(i)}$ are assigned ascending values (to fulfil the aforementioned constraint that the more recent SEM-Δ readings are physiologically and clinically more important). (b) A true or false result of Inequation (1) is calculated for each patient, using their specific $\Delta_{day(i)}$ set. If the result of this calculation is 'true' then the relevant patient is classified into the 'DTI' group; otherwise, the patient is classified into the 'no-PI' group. (c) The aforementioned classification result is then evaluated based on the STA of the respective patient (that serves as the ground truth), which facilitates determination of the 'true positive' and 'false positive' occurrences and, ultimately, calculations of the respective TPR and FPR. For adequate performances of the above ML algorithm, we require the minimization of

$(1 - TPR + FPR)$ and in addition, that $TPR >> FPR$. After completion of the 2000 iterations of the above 'For' loop, the threshold value is progressed by a 0.1 interval, and the calculation process described here repeats until the threshold equals unity [Inequation (1)]. The specific weight and threshold values that performed best, that is, had the highest TPR and lowest FPR, were extracted as the outputs of the detection algorithm. We further calculated the sensitivity and specificity for these best outcome measures, as per their definitions by the US Food and Drug Administration (FDA)[46]:

$$Sensitivity = TPR/(TPR + FNR) \qquad (2)$$

$$Specificity = TNR/(FPR + TNR) \qquad (3)$$
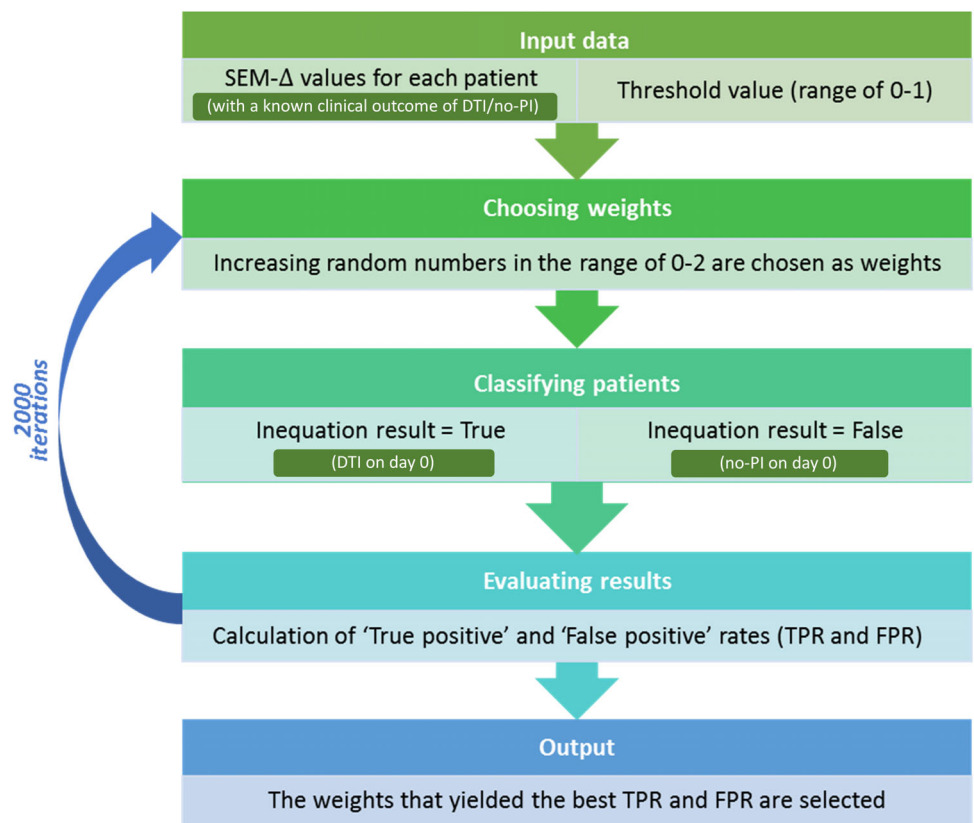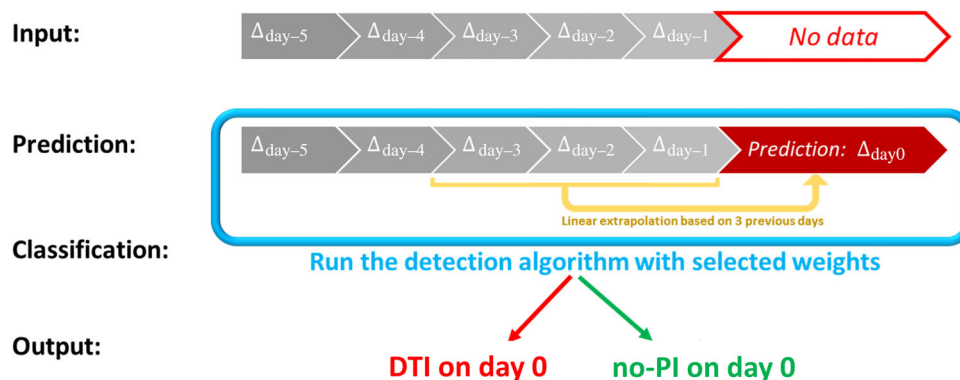
where $FNR = 1 - TPR$ is the false negative rate and $TNR = 1 - FPR$ is the true negative rate. The calculated TPR and TNR reflect the conditional probabilities $P(Diagnosis = PI \mid DTI = false)$ and $P(Diagnosis = no\ PI \mid DTI = true)$, respectively.[47]

2.4 | The prediction algorithm

Unlike the detection algorithm, the prediction algorithm is designed to forecast whether a heel DTI will occur at

FIGURE 3 The flow chart of the machine learning (ML) optimization algorithm (programmed in Python), applied to determine the optimal set of weights ($w_{day(i)}$, Figure 2C) that provided the best classification performance of the ML detector (Figure 2B). Based on the input data, which were the sub-epidermal moisture delta (SEM-Δ) values for each patient with a known clinical outcome at the end of the 6-day study period, that is, of either a heel deep tissue injury (DTI) diagnosed through skin tissue assessment (STA) vs a no-pressure injury result, the ML algorithm is trained to extract the optimal set of weights ($w_{day(i)}$) as an output. PI, pressure injury

Input:

Δ_{day-5} > Δ_{day-4} > Δ_{day-3} > Δ_{day-2} > Δ_{day-1} > *No data*

Prediction:

Δ_{day-5} > Δ_{day-4} > Δ_{day-3} > Δ_{day-2} > Δ_{day-1} > *Prediction: Δ_{day0}*

Linear extrapolation based on 3 previous days

Classification:

Run the detection algorithm with selected weights

Output:

DTI on day 0   **no-PI on day 0**

FIGURE 4 The input data for the machine learning (ML) predictor are the sub-epidermal moisture delta (SEM-Δ) values for each participating subject, for days −5 to −1 (ie, unlike the function of the ML detector, there are no 'day zero' data in the case of the ML predictor). The value representing 'day zero' is predicted by the ML predictor through linear extrapolation, based on the SEM-Δ values from the three previous days, to have a complete SEM-Δ set of six consecutive days. The ML detector algorithm is then applied using the optimised set of weights ($w_{day(i)}$, Figure 2C) and threshold value of 0.7, to predict whether a heel deep tissue injury will appear on the next day. PI, pressure injury

Days −5 to −1					Day 0	
w_{day-5}	w_{day-4}	w_{day-3}	w_{day-2}	w_{day-1}	$w_{day\,0}$	**Threshold**
0.945	1.050	1.167	1.297	1.441	1.601	0.7

TABLE 1 The specific weight and threshold values of Inequation (1) that were associated with the highest true positive and lowest false positive rates

'day 0' based on the SEM-Δ readings of a scanned patient from days −5 to −1 only. That is, for ML-based predictions, there are no available 'day 0' data, and the forecast must be made for the next day, that is, into the future (Figure 2). Accordingly, the first step in the prediction algorithm is to artificially extend and complete the set of SEM-Δ readings for each patient by adding a theoretical value for the sixth (ie, 'the next') day, through linear extrapolation of the SEM-Δ readings from the three previous days (Figure 4). We used the *numpy.polyfit* function in the Python programming language, which returns the first-degree polynomial (ie, a linear function) based on a least-squares fit to the SEM-Δ values of three previous days (ie, days: −3, −2, and −1). We then employed this linear function to extrapolate the SEM-Δ of day 0. This complete set of SEM-Δ values (five empirical plus one theoretical) for each patient is then fed as input to the detection algorithm, together with the optimal set of weights and thresholds that were calculated beforehand (as detailed in the previous section). The detection algorithm is then able to ultimately classify each monitored patient into the 'DTI' or 'no-PI' groups, thereby identifying those patients who are at an immediate risk for a heel DTI, earlier, before the injury manifests on the skin surface, while the extent of tissue damage is likely reversible.[45] This classification and detection is much earlier than diagnosis via STAs and clinical judgement in the current PU/PU prevention pathway.

3 | RESULTS

The specific weight and threshold values that performed best as calculated by the detection algorithm, that is, provided the highest TPR (90%) and lowest FPR (21%), were extracted as outputs of the detection algorithm and are listed in Table 1. The general classification accuracy (ie, the rate of correct classifications to both the 'DTI' and 'no-PI' groups) associated with the aforementioned weight and threshold values was 79% (sensitivity = 90%, specificity = 79%). Next, for realising the prediction algorithm, theoretical SEM-Δ values were calculated for the (supposedly unknown) sixth day per each patient registry (through linear extrapolation of the SEM-Δ readings from the 3 previous days), to result in a complete set of SEM-Δ values for each patient that could be fed back to the prediction algorithm. For the optimal set of weights and threshold (Table 1), the ultimate classification performance metrics achieved by the prediction algorithm were TPR = 80%, FPR = 23%, and general classification accuracy of 77% (sensitivity = 80%, specificity = 77%).

4 | DISCUSSION

In this work, we developed a novel ML-based algorithm for early detection of heel DTIs. The algorithm was trained using a database comprising six consecutive daily SEM-Δ measurements acquired from 173 patients in a previous, multi-centre (acute and post-acute) clinical study.[18] A relatively strong predictive power of this new algorithm that demonstrated, already at this stage, sensitivity of 80% and specificity of 77% in forecasting heel DTI events the next day, points to the potential clinical utility of our present approach. In a broader scope, these performance metrics show the promise, effectiveness, and expected impact of ML in supporting clinical decision-making in wound care in the near future.

In the past few years, AI has gained popularity in dermatological research, with a relatively large number of publications addressing the problem of automated identification of skin malignancies.[28-30] Other dermatological work involving AI pertains to inflammatory skin diseases,[31-33] response to exposure to allergens,[34] dermatopathology,[35] and gene expression profiling for atopic dermatitis.[36] Some AI work also considered chronic wounds including leg ulcers, diabetic foot ulcers, and PUs/PIs.[38-43] The above wound-related AI studies typically employed image recognition, segmentation, and classification of skin and wound tissues,[37] but this is just a small fraction of the wide spectrum of potential applications of AI in skin and wound care.

Focusing the discussion on employing AI-based methods for risk assessment and predictive modelling of the occurrence of PUs/PIs, the work of Kaewprag et al[42] is noteworthy for their use of a Bayesian network to predict the formation of PUs/PIs in intensive care patients through analysis of electronic health records (EHRs). However, their analyses were severely limited by the processing of Braden Scale scores completed by the care teams; that is, while they have used an advanced AI algorithm, they fed it with risk assessment scores that were still acquired through subjective clinical judgement and were not anatomy specific. Later on, Alderden et al[43] developed an AI algorithm that is less impacted by such subjective clinical assessments, by extracting traditional, yet numerical clinical data from EHRs such as the age and body mass index, the haemoglobin and creatinine levels, and the operative time. Alderden et al[43] reported TPR of 65% and FPR of 22%, that is, sensitivity of 65% and specificity of 78% [Equations (2) and (3)] for predicting category-1 PUs/PIs and a substantially lower, clinically unacceptable TPR of 54% and FPR of 13% (sensitivity of 54%, specificity of 87%) for predicting category-2 PUs/PIs. Of note, a random classifier could have achieved similar performances to their algorithm in

terms of sensitivity. One can argue that while they had used quantitative values as inputs to their AI algorithm, they did not select the relevant physiological parameters that predict the development of PUs/PIs at a clinically acceptable accuracy. For a predictive AI tool to be able to exhibit adequate clinical precision, the measured physiological parameters must be (a) objective, (b) standardised, (c) clinically relevant, and (d) anatomically specific to the pathophysiology of PUs/PIs. It is essential that both of these conditions are met. This has not been achieved so far in the literature. Our present work is the first to accomplish both of the aforementioned aims, as manifested in the superior performance metrics of our AI algorithm that is reported here.

Specifically, the present AI algorithm builds upon the inherent advantage of the SEM Scanner technology over STAs and clinical judgement as a technological aid in the detection of PUs/PIs, as reported by Okonkwo et al.[18] Without using AI/ML, Okonkwo's group demonstrated sensitivity of 87.5% and specificity of 37.8% for the SEM Scanner in PU/PI detection, approximately 5 days (median) prior to the presentation of a PU/PI as diagnosed via STAs and expert health care practitioners' clinical judgement. Most recently, Gershon and Okonkwo[20] evaluated SEM-Δ thresholds and reported a range of sensitivities (82%-87%) and specificities (51%-88%) for a SEM-Δ threshold equal to or greater than 0.6, exceeding the clinical utility of clinical judgement alone, which is the current gold standard.[48] Based on the present findings, it appears that the use of AI/ML algorithms provides an excellent balance of both high sensitivity and high specificity (80% and 77%, respectively). Importantly, even with a limited data set of true positives (ie, the n = 10 patients diagnosed with heel DTIs), the AI/ML algorithm shows promise in early detection of DTIs and increasing the clinical utility of the SEM Scanner technology in the early detection of deep and early PUs/PIs.

Moreover, our present approach is unique to the pathophysiology of DTIs, which are hidden from the unaided eye and are impossible to discover timely through STAs alone.[23] An exemplary form of implementation of the present ML algorithm in a clinical setting is depicted in Figure 5. First, a SEM-Δ measurement is taken by a health care professional as part of the clinical daily routine. Based on this reading and the readings collected (and automatically stored) in the previous days, a prediction of the theoretical SEM-Δ value for the next day is calculated by the ML predictor. Next, the SEM-Δ value of each day is multiplied by its corresponding weight, and the result of Inequation (1) is calculated, following which the patient is classified into either the 'DTI' or 'no-PI' groups. If the classification is to the 'DTI' group, there is a high likelihood that a DTI will
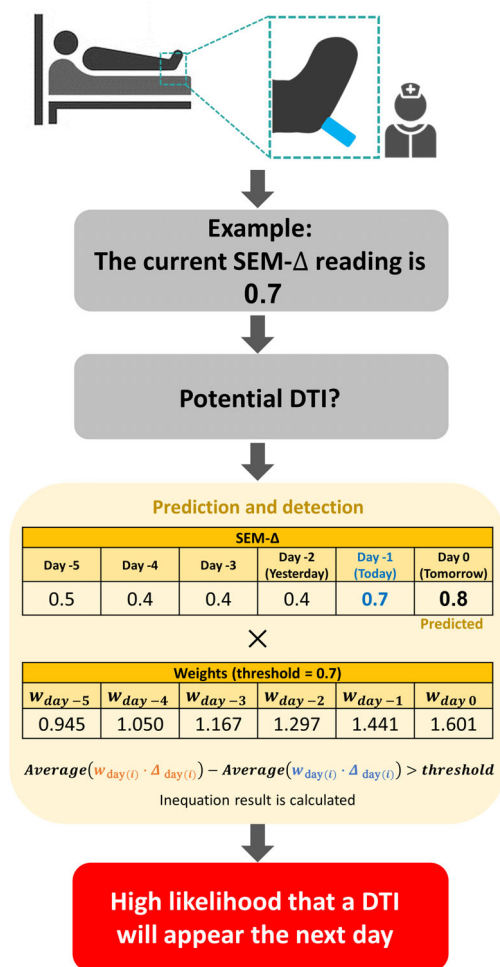
FIGURE 5 An example of practical use of the present machine learning (ML) algorithm in a clinical setting. First, a sub-epidermal moisture delta (SEM-Δ) measurement is taken by a health care professional. Based on this reading and the SEM-Δ readings that were similarly acquired in the previous days, the SEM-Δ value of the next day is being calculated by the ML predictor. Next, all the daily SEM-Δ values are multiplied by their corresponding weights ($w_{day(i)}$) and the relevant inequation result is calculated. In this specific example (for which real subject data were taken from the present study database), the result of the inequation calculation is 'True' and therefore, the ML algorithm has determined that there is a high likelihood that a heel deep tissue injury will appear on the next day

appear the next day and the health care professional is alerted accordingly. Of note, our AI/ML classification algorithm, which considers SEM-Δ data from six consecutive days, reduces the potential influence of localised alterations in tissue fluid contents that do not relate to a forming PU/PI.[6-10,23,44,45] In addition, a 6-day SEM-Δ dataset is consistent with the timeframe of 5 days (median) that has been reported in previous research as the predictive window for the SEM Scanner technology.[21-24]

As with any clinical research, this work has limitations that should be discussed. While our study population of eligible patients was relatively large for a wound care trial (n = 182 intention to treat population), the standard of care and subsequent intervention protocols were rigorous in all the participating medical centres. As a result, only 10 patients (~6%) developed a suspected heel DTI during the study period. We expect that the diagnostic accuracy of this ML algorithm can be improved even further with training using larger databases. Another limitation of the current study is that the training dataset used to develop the algorithm was from adult at-risk patients who developed a heel DTI in acute and post-acute care settings. The performance metrics reported in this work cannot be generalised to other anatomical locations or patient populations. For example, the physiology and pathophysiology of the skin are different in neonates and paediatric patients.[49,50] To be able to translate the present ML algorithm into care settings for other at-risk anatomical locations or sub-populations, the algorithm needs to train on corresponding SEM-Δ databases to obtain optimal weights and thresholds for the anatomical region and/or setting of interest [Inequation (1)]. The 6-day follow-up parameter may need an adjustment as well. As this is the first attempt to marry ML with SEM measurements, we decided to use the simplest, linear prediction method for the current research work (based on three previous days). Future investigations, potentially analysing larger datasets, may include a quadratic interpolation or a spline function to extrapolate the SEM-Δ of day 0.

Similarly to all predictive models, extrapolation of the current ML algorithm beyond the dataset, which was used to train it, such as for additional future days (beyond day zero), may be prone to errors (this may also apply to larger data cohorts). With that said, using greater datasets, it may be possible to improve the current ML algorithm so that it will be able to predict the SEM-Δ development over a time course beyond the 'next day', and, therefore, facilitate an even earlier detection of a potential DTI.

Until ML is integrated in the software of devices for automated early-detection analyses, bedside carers should be aware of the need to manually monitor trends observed in the daily history of the SEM-Δ data acquired from individual patients and use their clinical judgement to evaluate whether there is suspected worsening or escalation of the risk of a particular patient as manifested by their daily SEM-Δ measurements combined with the holistic clinical assessment.

In conclusion, we developed a first-of-its-kind ML-powered, automated clinical decision-support algorithm for predicting heel DTIs based on a daily history of

SEM-Δ measurements. The current standard of PU/PI prevention and care still relies on subjective risk assessment scores and is sensitive to nurse practitioner experience and clinical judgement. We envision that such AI algorithmics, processing sensitive physiological markers of PUs/PIs that flag the specific risk of PUs/PIs, at a stage where the cell and tissue damage is reversible, will provide health care practitioners with objective data, enable early interventions and transform the clinical practice of PU/PI prevention. With the increase in database sizes and the development of big data of SEM-Δ measurements for different medical settings, the clinicians of the near future will no longer remain blind to the early subclinical changes under the skin and will be able to leverage the predictive capabilities of ML-based algorithms to provide effective, early, and anatomy-specific preventive PU/PI interventions.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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