bruin BIOMETRICS

Realizing Prevention: Evidence Report of the Provizio® SEM Scanner

July 2022

FOREWORD

"Implementing scanning technology into routine clinical practice achieves consistent reductions in pressure injury/ulcer incidence." (Nightingale and Musa, 2021)[i]

Few disease states ever present themselves to an attainable and near-term preventative solution as pressure injuries. Pressure injury incidence can and should be reduced.

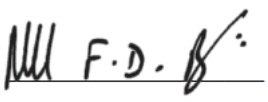
Realizing the goal of preventing preventable pressure injuries (PI/PUs) benefits the millions of patients who are affected and the tens of thousands who die from complications from pressure injuries on an annual basis. Economic savings through prevention, accruing to providers, payors and patients extend to many tens of billions of dollars annually. The emotional benefits of prevention are equally worthy.

These results have been the lifelong work of legions of healthcare practitioners and academics globally, potentially including readers of this document.

No matter how diligent and committed caregivers have been to the highest quality of care, pressure injuries remain stubbornly persistent. In the face of calls to "prevent" and "do more", the temptation of provider managers and policy makers is to make a policy adjustment here and another there: hire quality nurses, add new reporting metrics, launch awareness campaigns, intensify visual and tactile skin assessments, or provide additional training. These initiatives risk adding burden rather than addressing the root causes of pressure injuries. "Do more" alienates caregivers, adds stress to lean care organizations, and typically fail to inculcate long-term changes. The return on investment is low. We now know these strategies fail to recognize our contemporary understanding of PU etiology and pathophysiology. The condition of "persistent focal edema" has been well recognized in the North American International Classification of Diseases (L89), yet focal edema management has waited until skin redness manifests. Red skin is not right.

A singular goal of keeping patients' skin intact – preventing preventable pressure injuries – when addressed with early, objective skin and tissue data is a modern, percipient clinical strategy grounded in contemporary science and practice.

By focusing on the etiology of PIs and providing easy-to-use and easy-to-interpret technology which statistically-significantly advances clinical assessments of skin and tissue susceptible to PIs, clinical practitioners using Bruin Biometrics' Provizio® SEM Scanner have achieved significant incidence reductions of reportable, broken skin PI/PUs – many at 100% reductions - at scale and in year, without the need for new interventions or new staff.



Martin. F. Burns

NOTES TO READERS OF THIS DOCUMENT

Readers are requested to be aware of important contextual notes in reading this document.

1. The authors have deliberately heavily edited Bruin Biometrics' 100+ page Data Dossier into this shorter document for ease of reading. Details of the burden of illness, epidemiology, incidence and prevalence by care setting, risk factors, and the description of the unmet need have been substantially shortened for this document. Each of these areas are widely studied in the literature and are briefly summarized herein.
2. The authors have compiled this document under the assumption that readers will be expert and/or highly qualified in the area of PI prevention and management.
3. The National Pressure Injury Advisory Panel (NPIAP. Formerly, NPUAP) made changes to their PI classification in April 2016 and suggested using the terminology *pressure injury* instead of *pressure ulcer* to describe these wounds in order to recognize lesser degrees of skin damage and the deep tissue injuries that occur which may not be associated with a skin ulcer (Stage I)[ii]. The term Pressure Injury is used herein.
4. The volume of literature about sub-epidermal moisture, PI etiology, the inflammatory phases of PI development, the SEM Scanner technology, PI prevention using the SEM Scanner technology, and other economic and econometric analysis of PI prevention using the SEM Scanner technology has expanded considerably in the recent years. The authors of this document have selected a limited number of the most relevant publications for inclusion in this submission.
5. References are used judiciously, again for brevity.
6. Patent and Trademark information has not been included.
7. Portions of the following text have been excerpted from Bruin Biometrics peer-reviewed publications. Permission has been sought and obtained to do so.
8. In February 2020 Bruin Biometrics launched the second-generation device called Provizio® SEM Scanner – for ease of reading the first and second-generation devices are collectively described as SEM Scanner technology.

Should assumptions underpinning either or both of the first two notes be incorrect, the authors stand ready to provide additional information or address questions as needed.

1. Contents

Table of Figures and Tables

List of Abbreviations

AHRQ	Agency for Healthcare Research and Quality
CMS	Centers for Medicare and Medicaid Services
DTI	Suspected Deep Tissue Injury
FA	Facility Acquired
HAC	Hospital Acquired Condition
HAPI	Hospital Acquired Pressure Injury
HAPU	Hospital Acquired Pressure Ulcer
ICER	Incremental Cost Effectiveness Ratio
IPUP	International Pressure Ulcer Prevention
IRF	Inpatient Rehabilitation Facility
MPSMS	Medicare Patient Safety Monitoring System
NICE	National Institute for Care Excellence
NPIAP	National Pressure Injury Advisory Panel
NPWT	Negative Pressure Wound Therapy
POA	Present on Admission
PSI	Patient Safety Indicator
PURP	Pressure Ulcer Reduction Program
QALY	Quality Adjusted Life Years
RAT	Risk Assessment Tool
sDTI	Suspected Deep Tissue Injury
SEM	Sub-Epidermal Moisture
SNF	Skilled Nursing Facility
STA	Skin and Tissue Assessment
VSA	Visual Skin Assessment

1. Introduction

Pressure injuries (PI) are a widespread and serious complication of reduced patient mobility. Annually, PIs occur in more than 2.5 million US patients, of whom approximately 60,000 die due to infection and other sequelae (Berlowitz et al., 2014). Due to the substantial impacts of PIs on patient quality of life, recovery, and lengths of stay, PI prevention is prioritized by providers and policy makers[iii,iv]. The United States' Agency for Healthcare Research and Quality' (AHRQ) statistics, however, show PIs being the only Hospital Acquired Condition whose incidence worsened during 2014-17[v]. The overall costs of PIs in the USA are estimated to exceed $26.8 billion[vi] with per-patient costs ranging from $500 to $70,000[vii].

Currently, patients are initially screened on admission into two PI groups: 1.) patients admitted with an existing PI or, 2.) patients without a PI at admission. A patient presenting with a PI formed prior to admission will immediately undergo a variety of treatments, each dependent on the condition of the patient's skin and tissue, the clinical goals being, healing, pain management, avoidance of the chronic wound cascade, or infection, and ultimately recovery.

Those without an existing PU are further assessed (in some care settings all patients, regardless of PU state on admission will be periodically risk assessed), typically using validated risk-assessment tools (RATs) (e.g., Braden scale). RATs seek to answer the question, "to what extent is my patient at risk of developing a pressure injury?" Depending on assessed risk, patients will receive a bundle of "universal preventions" designed to reduce PI risk for the whole patient. Universal prevention activities are those clinical interventions intended to facilitate whole-body offloading and care planning such as patient repositioning and the use of pressure redistributing mattresses and medical devices. They are applied when patients are deemed to be at risk of a PI, but where no PI is diagnosed at any particular anatomy. **Figure 1,** excerpted from Padula's 2019 British Medical Journal paper, presents a Markov state transition view of patient flow from admission, through risk assessment to a number of transitory and end-states including surgery, death, acute or chronic care, and discharge. This model reflects the clinical course of PIs, absent the current understanding of PI etiology.

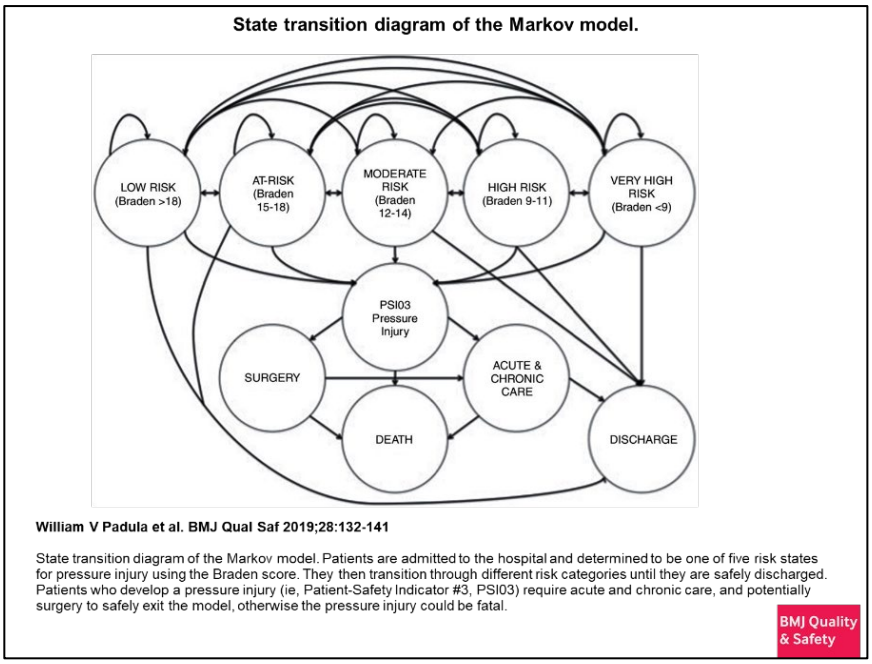


FIGURE 1: STAGING OF PRESSURE-INDUCED SKIN AND SOFT TISSUE INJURIES (PADULA ET AL, 2019)

Risk assessments are supplemented by a skin and tissue assessment—visible and palpation tests— (STA) intended to diagnose a developed PI. If the STA diagnoses a PI, then anatomy-specific interventions (e.g., a heel boot at a patient's left heel together with a bundle of other interventions) are initiated[viii]. STAs appraise skin color, blanchability, temperature, hardness, and other visible or palpable indicators of injury. Clinical judgment of nurses, informed by risk tools and skin and tissue assessment, however, "achieved inadequate capacity to assess PU risk[ix]" and suffered from "high inter-examiner variability[x]. Clinical Judgement has a sensitivity of 50.6% and specificity of 60.1%. Because of the skill dependency of skin and tissue assessment, correct identification of a Stage I pressure ulcer has been observed as low as 60% in a diverse group of 1,452 nurses[xi].

A combination of PI risk assessments, supplemented by skin and tissue assessments and mechanical offloading (such as patient repositioning and the use of pressure redistributing mattresses and medical devices) comprises most PI prevention programs[viii]. Bruin Biometrics' safety systems analytical assessment of risk assessment tools provided a different perspective on risk assessment tools and their combination with treatments and STAs, namely the diagnostic standard currently in use suffers from "latency".

1. *Diagnostic latency*: This is the gap between the time when the damage actually begins and the time, under the current standard of care, at which it is detected and confirmed.
2. *Anatomical interventional latency*: Prevention (which we define as 'keeping the patient's skin intact', followed by rescuing and reversing the damage) requires knowing where on the body to intervene, when and how intensively, not only that the patient is at risk. STAs achieve the diagnostic threshold required to trigger anatomy-specific interventions *only* once the wound has developed and can be diagnosed by STA. The sensitivity and specificity of clinical judgement of ward level nurses aided by STA is too low and too late to reliably assure timely and accurate interventions at specific anatomies.

The mechanobiology of hospital acquired pressure injuries (HAPI) is such that soft tissue damage initiates near bony prominences – typically the sacrum and heels - where the force of concentrated bodyweight causes intensified and sustained cell and tissue deformations which compromise cell integrity, transport function, leading to tissue death[xii]. Since these HAPIs may not form initially on skin, even the best nursing skills and diligence relating to tissue care will be ineffective in achieving timely detection of sub-epidermal injuries. In other words, without an insight into deep

tissue viability, there is no feasible way for a nurse relying on current risk assessment scales and STAs to detect the developing injury in a timely way[xiii] nor take the timely, appropriate, anatomy-specific interventions necessary. The resulting insight therefore is that PI prevention – keeping the skin intact – is improbable under the current standard of care[xiv]. Figure 2 presents a modification of Padula's 2019 clinical state Markov model (Figure 1) updated to reflect all PU stages, plus the preceding "Non-visible Tissue Damage".

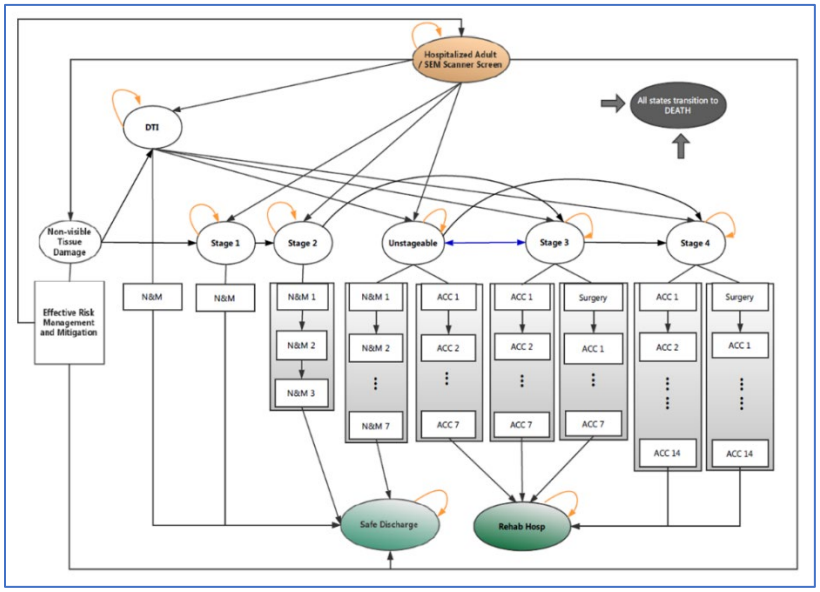


FIGURE 2:11-STATE MARKOV MODEL CAPTURES THE PREVENTION AND TREATMENT PATHWAY OF PRESSURE INJURIES, WITH RECURRING PATTERNS AND TUNNELING STATES INCLUDING THE "NON-VISIBLE TISSUE DAMAGE" STATE (PADULA 2020). [KEY: DTI: DEEP TISSUE PRESSURE INJURIES (DTPI), N&M: NURSING AND MONITORING, ACC: ACUTE AND CHRONIC CARE]

Due to the subjective, latent nature of STAs and subsequent anatomy-specific interventions, there is a clear clinical need for an objective, point-of-care tool for diagnosing or assessing developing PIs on at-risk patients before the invisible, sub-clinical, damage manifests at the skin's surface as visible damage.

The ICD-10[xv] (L-89), US codes defines stage I as *"Pre-ulcer skin changes limited to persistent focal edema"* (Figure 3). Localized edema also known as persistent focal edema (or Sub-epidermal Moisture (SEM)) is an important precursor to the onset of PI/PU progression, which, left untreated, can progress into visible erythema (stage 1) and progressive pressure-induced tissue damage. Evidently SEM, is a biophysical marker in pressure injury/ulcer (PI/PU) and deep tissue injury (DTI) pathophysiology; validated in current literature and in International Clinical Guidelines (Section 4.5). Therefore, the treatment and management of SEM (or persistent focal edema) is critical to effective PI prevention.

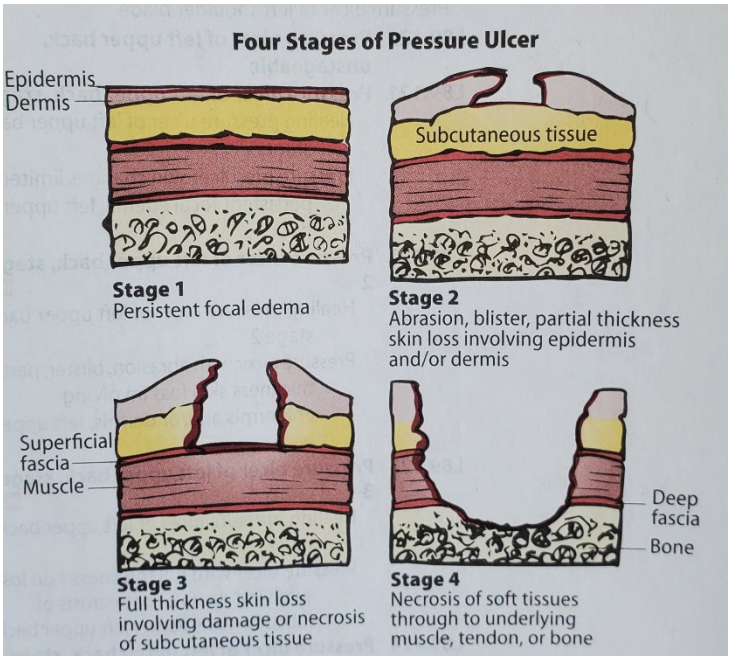


FIGURE 3: PERSISTENT FOCAL OEDEMA – STAGE PI (ICD-10 GUIDELINES) [xv]

The SEM Scanner technology, a hand-held device, offers an objective, early and reliable method to identify risk for pressure injury at specific anatomies. Where the current standard of care is subjective and misses too many patients in their early diagnosis of PIs, SEM Scanner Technology can realize consistent reductions in PI/PU incidence when implemented into PI/PU care pathways. The Scanner has already been shown to readily fit into PI prevention and management care pathways in acute, post-acute and home health settings. Aggregate, real-world evidence suggests that implementing the technology enables universal prevention across multiple care settings, regardless of skin tone; PI incidence risk is reduced to one-third when implemented into daily PI care practice.[xvi]

The beneficial outcomes arising from inclusion of the SEM Scanner technology in the care pathway are described herein.

2. Bruin Biometrics, LLC

Bruin Biometrics, LLC was founded on the insight that sensing technology could be developed to detect and monitor diseases earlier and with greater diagnostic certainty than prevailing methods.

Formed in 2009, Bruin Biometrics identifies, develops and commercializes biometric-sensor-based diagnostic medical devices to support practitioners' goal of prevention. Bruin Biometrics develops potential solutions to each condition by relying on three approaches:

1. *A full (re)assessment of the etiology of the disease state* – Equipped with etiological insights, potentially measurable biomarkers were chosen for further research and development. In the case of PIs, the developing etiological insight that PIs emerge from the inside outwards and are aggravated by skin-surface sheer and friction lead the company to focus on the early, invisible indicators of the wound. Since PIs are wounds and the preponderance of wounds pass through the inflammatory phase, Bruin Biometrics focused on Sub-Epidermal Moisture (SEM) as an indicator of incipient damage.
2. *The application of biometric sensors to measure the early indicators of damage* - Bruin Biometrics' devices noninvasively measure bodily changes that are indicative of the early stages and progression of disease states.

Measurement of biomarkers offer new, immediate, inexpensive and clinically valuable medical data at the point of care. Biocapacitance is the measurement method used in the SEM Scanner technology.

3. *A safety-systems view of disease prevalence* – The work of Levison 2011 "Engineering a Safer World"[xvii] has informed Bruin Biometrics' systemic root cause analysis of "why PIs occur", well beyond the understanding of proximate etiology to a hierarchy of causality of PIs, including Clinical Care, Provider, and External (policy) factors. In the PI case, this safety-systems view of clinical workflows, the standard of care and prevailing protocols has led to the insights that full prevention is a clinical and mathematical improbability without a different (earlier, anatomy-specific, more sensitive and specific) clinical approach.

Equipped with clinical data from Bruin Biometrics' information, clinicians' effect earlier and more certain interventions in pursuit of significantly better patient health outcomes. Bruin Biometrics Provizio SEM Scanner, its resultant clinical insights and the modestly modified clinical workflow are summarized in this document.

Bruin Biometrics' platform was built on technologies exclusively licensed from the University of California, Los Angeles (UCLA).

2.1 Bruin Biometrics Scientific Advisory Board

Recognizing the complexity of new-to-the-world clinical data, devices and workflow, Bruin Biometrics collaborates with a board of globally recognized experts (Table 1). This diverse group have expertise in PI etiology, wound biomechanics, clinical workflow development, policy development and health economics.

FIGURE 4: BRUIN BIOMETRICS INTERNATIONAL SCIENTIFIC ADVISORY BOARD

Many of the Board and Advisory group have published their own SEM Scanner technology research over recent years or have ongoing research programs.

3. The SEM Scanner Technology

The SEM Scanner technology has been designed to integrate – be adjunctive – to the current standard of care such that, if a patient is assessed as being at risk then SEM readings are obtained from heels and sacral areas (accounting for the majority of all PIs).

The device is used at admission, during the episode of care and at discharge. SEM values are recorded as an integral component of patients' records and are passed with patients between care settings between discharge and admission. The SEM Scanner technology introduces a shift to PI prevention and management by moving from reactive treatments to proactive preventative pathways.

The SEM Scanner technology is an FDA authorized[xviii] (CE class IIa) portable, wireless, non-invasive, hand-held device for the detection of changes in Biocapacitance of skin and tissue. It compares multiple local measurements to determine the difference in SEM values between potentially damaged and nearby healthy tissue.

3.1 Biocapacitance defined

A biomarker is a substance that is measured in a living system as an indicator of exposure, effect, susceptibility or clinical disease. Biocapacitance is one such marker.

An increase in tissue Biocapacitance is associated with localized inflammation and edema in the early stages of pressure induced tissue injury. In early-stage PIs changes to microscopic tissue structures, increase tissue water contents (micro-edema or sub-epidermal moisture (SEM)) when the first cells die **(Figure 5)**, and this can be evaluated by means of the (bio)capacitance of the tissue. This (bio)capacitance value rises when the extracellular water content increases[xix]. The greater the fluid contents in a tissue, the less resistant it becomes to electrical fields (water transmits electrical fields easily), and, therefore, the higher the Biocapacitance value becomes[xiii] (**Figure 6**).

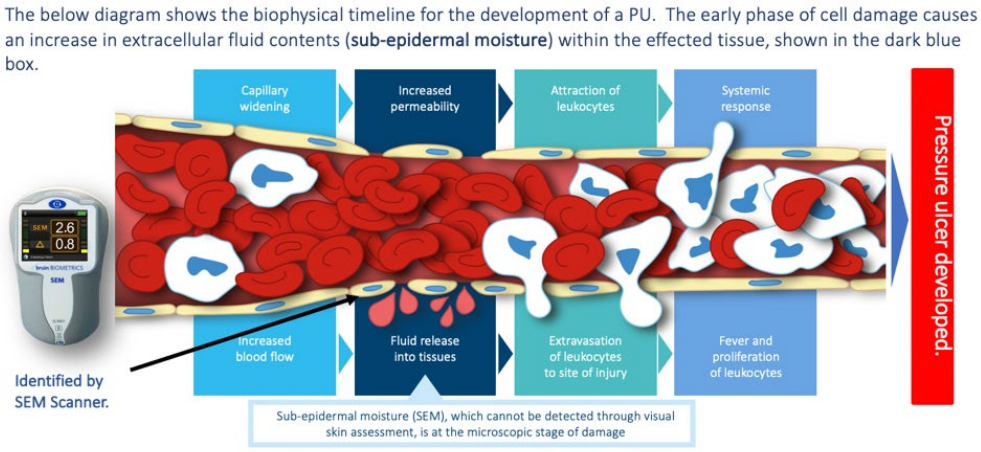


FIGURE 5: BIOPHYSICAL TIMELINE FOR THE DEVELOPMENT OF A PI. GEFEN 2018

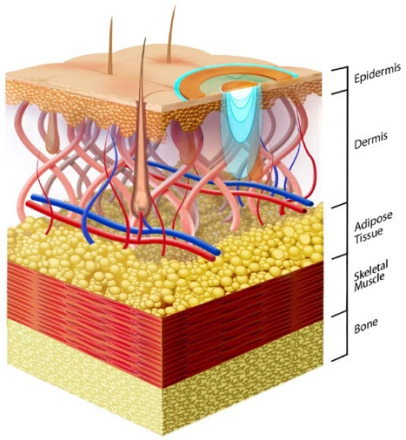


FIGURE 6: ILLUSTRATION OF THE ELECTRIC FIELD USED IN THE PROCESS OF MEASUREMENT OF THE LOCAL BIOCAPACITANCE PROPERTY OF TISSUES, SHOWING THE SHAPE AND DEPTH OF PENETRATION OF THE ELECTRIC FIELD OF THE SEM SCANNER INTO THE EPIDERMIS AND DERMAL LAYERS

3.2 The SEM Scanner Technology

The SEM Scanner (Bruin Biometrics, LLC, Los Angeles, CA) technology assesses the fluid contents of epidermis and subdermal tissues. The device makes a direct steady-state measurement of the capacitance of its sensor, which is affected by the equivalent dielectric constant of the material (i.e. the layered tissue structures) that is within the electric field between the sensor electrodes to a depth of 0.15 inches (4 millimeters), and converts the Biocapacitance from SI units to an SEM value. Two values are displayed on the device's screen, an individual value for each single scan, and after three readings are taken, the SEM Delta (ΔSEM), calculated as the difference of the minimum and maximum SEM values obtained at and immediately contiguous to an anatomical site. Calculation of a "delta" value compares measurements from several sites, some of which will be healthy tissue, compensates for systemic changes, overcomes the limitation of inter- and intra-patient variability and provides a measure of tissue health condition[xii].

The range of device values is 1.0 to 4.5, with known tolerance of ± 0.2. Two values are displayed on the device's screen, an individual value for each single scan, and after three readings are taken, the SEM Delta (ΔSEM), calculated as the difference of the minimum and maximum SEM values obtained at and immediately contiguous to an anatomical site. Calculation of a "delta" value compares measurements from several sites, some of which will be healthy tissue, compensates for systemic changes, overcomes the limitation of inter- and intra-patient variability and provides a measure of tissue health condition. Clinical studies determined a threshold delta value:

- Δ<0.6 indicating lower risk for a pressure injury at the anatomy; and,
- $\Delta \geq$0.6 indicative of increased risk for pressure ulcers at the anatomy being measured.

The delta value is a measure of the difference in the SEM values between potentially damaged tissue and nearby healthy tissue. This computation eliminates common-mode effects in the local tissue, such as a change in the overall hydration level of a patient, as well as differences between patients and differences between body locations. The delta value is compared by the healthcare practitioner to a threshold to identify tissue that is likely to develop into a PI if an intervention is not implemented. Using delta values for PI evaluation eliminates sensitivity to variation between patients and PI localization, as well as compensating for differences in user technique.

When patients have a delta value of ≥0.6 at an anatomical site, this indicates increased risk for PI. This objective data facilitates earlier, and anatomically specific interventions designed to reverse the damaging effects of pressure ulceration. Delta values provide practitioners with days of advanced notice compared to visual skin assessment that a patient's skin and tissue is compromised over a given anatomy[xx]. This is a clinically significant time advantage with considerable clinical utility for potential reversal of damage to skin and tissue prior to the breakage of the skin's

surface. In comparison with visual skin assessment, the SEM Scanner technology supports clinicians to identify specific anatomical areas at increased risk of PI development 5 days (median) earlier[xx].

3.3 The Device – Technology, Warranty, Safety

The device consists of a pair of concentric coplanar electrodes, an integrated pressure sensor, software that computes a delta value from a set of SEM measurements and a user interface screen that displays the most recent SEM reading, the calculated delta value and the device and battery status.

The device itself has a warranted three-year lifespan and is returned to the manufacturer for disposal (where component parts are recycled as appropriate). The SEM Scanner is covered by a three-year warranty, which covers essentially all failure scenarios with the exceptions of theft and customer mishandling.

The device is intended to be used by healthcare professionals as an adjunct to standard of care when assessing the heels and sacrum of patients who are at increased risk for pressure ulcers.

No Adverse or Serious Adverse Safety Events have been reported since the device was first marketed in 2014.

4. The Provizio® SEM Scanner

The Provizio SEM Scanner is the next evolution of the original SEM Scanner. Like the original SEM Scanner 200 series, Provizio SEM Scanner:

1. is a hand-held, portable, wireless device that consists of a single electrode sensor, an integrated pressure sensor, and hardware and software to run a user interface device screen that displays the device status, battery status, SEM Value, and SEM Delta (SEMΔ);
2. uses the same mechanism of operation as the SEM 200;
3. uses the same sensor array as the SEM 200;
4. is pre-calibrated;
5. is provided with a Charging Hub and power supply for recharging the scanner; and,
6. is approved for use on the heels and the sacrum of adults and is designed to be used on intact skin.

Provizio differs from the original SEM device in that it:

1. has an updated form-factor;
2. is provided with a separately supplied, non-sterile, single-use sensor;
3. includes bar code scanning capabilities
4. stores individual encrypted patient SEM data on the handset's internal flash memory, obviating the need for paper records;
5. ports those data to the Provizio Gateway residing on the provider's local servers, within the firewall and then erases all patient data from the handset to maintain HIPPA compliance; and,
6. facilitates either, a.) stand-alone reporting of PI incidence by care setting and site of service, and/or, b.) including electronic patient record integration on a "pull" basis by the EMR software from the Gateway)
7. allows encrypted/decrypted data export for detailed analyses

4.1 Recognition and Awards

The SEM Scanner has been awarded seven international prizes since 2015 ranging from "2017 Best Product or Innovation for Patient Safety - Private Sector – winner" (Health Services Journal), to "2018 Best Innovation in Medical Technology" (HSJ Partnership Award), to the UK NHS's Bionow, "2019 Product of the Year". Most recently the Provizio SEM Scanner was named in TIME'S list of 100 Best Inventions of 2020.

4.2 Competition

In some sense the SEM Scanner technology's main competition is against the current standard of care, namely, STA. There are three additional categories of potential competitors: skin and tissue measurement devices; patient movement sensors; and prophylactic treatments.

Skin and Tissue Measurement

To the best of our knowledge there are no direct competitors to our dielectric constant Biocapacitance measurement technology with the intended use of detecting early stage pressure ulcers (viz, pre-stage 1). No other device has the legal claim required by the US Food and Drug Administration to legally market their devices as a competitor to Bruin Biometrics' SEM Scanner without making "off-label" claims.

We are aware of other impedance devices (e.g., Delfin) but to our knowledge, none have regulatory authority to market their devices for PI detection and are unaware of validation studies of any such devices.

We are further aware of the use of thermography and potentially ultrasound in PI detection. Each have their own challenges, for example, Gefen et al in looking at infrared thermography states, "IRT does not appear to be effective, specific and sensitive enough or early detection of [pressure ulcers] or for monitoring [pressure ulcer treatment] interventions, specifically since it cannot distinguish between opposite trends of effects on tissue temperature that originate from inflammation versus ischaemia."[xxi] We are aware of significant concerns raised in published literature regarding IRT's ability diagnose the early stages of PIs.

Patient Movement Sensors

Several companies are marketing devices which monitor patient movement, e.g., mobility detection devices such as mattress patient movement monitoring devices. The idea is to monitor patient movement; immobility being a contributing factor to non-medical device related PI development. An additional positive of these technologies is their passive monitoring intended use. Bruin Biometrics has not conducted an evaluation of any of these technologies, so can only comment at the theoretical level of their efficacy. In any formal evaluation we would look at which movements are detected by the device, their costs, clinical and cost outcomes, and applicability to all PIs (e.g., heel PIs), including medical device related ulcers (i.e., from face masks and other disposables). Patient movement is irrelevant in those later circumstances; early knowledge of skin and tissue damage matters most.

Boldly stated, we maintain our assertion that only through transforming the evaluation of patient's skin and tissue at the PI-proximate level to detect cellular-level damage with technology; reassessing care to include episodes of care which give rise to PIs; and, taking a care continuum rather than institution level view, will PIs be prevented at scale.

Prophylactic Treatments

Finally, some device manufacturers are making claims about the preventative efficacy of prophylactic application of their treatments on PI prevention in Intensive Trauma/Critical Care units. Published data show efficacy for an intensive-care cohort of patients. We are unclear on the clinical efficacy and cost-effectiveness of these types of interventions beyond the critical care units. These publications also show considerable overtreatment and waste.

In our assessment, the right solution for PI preventative care is a combination of early detection (e.g., SEM Scanner technology) with targeted interventions to rescue the tissue and reverse the damage (e.g., a dressing, turning protocol or mattress).

In the final analysis, it is inconceivable that modern wound care practice should be so absent of diagnostic technology capable of directing care to the right anatomical site prior to manifestation of damage. No detection

solution other than the SEM Scanner technology has shown to have such high clinical utility (as measured by incidence reduction) and positive cost consequences.

4.3 Policy, Coverage and Reimbursement

The Deficit Reduction Act (DRA) of 2005, section 5001(c) requires that Medicare and Medicaid no longer pay for the costs of treating 8 conditions which should "never" occur in a care setting, Stage III and IV pressures being high on that list. The legislation has been implemented. The Patient Protection & Affordable Care Act (PPACA, 2010), commonly known as "Obama Care" imposes reimbursement penalties on non-reporting and high-incident care settings, mostly effective starting October 2014.

Additional legislative interventions, updated on the Federal Register, are imposed on an annual basis. All policy interventions point to a shift to the ***outcome of PI prevention***.

In the acute care setting, PI assessment is included in the global payment (MS-DRG) as defined by the Inpatient Prospective Payment System (IPPS). Payment reductions of up to two percentage points may occur for hospitals not meeting quality measures as defined by the Hospital Inpatient Quality Reporting Program.[xxii] Inpatient outcome measures include 30-day risk-standardized mortality measures (acute myocardial infarction, heart failure, pneumonia); 30-day risk-standardized readmission measures and AHRQ Patient Safety Indicators (PSIs). PSI 90 Composite refers to complication/patient safety for selected indicators. The Hospital Value-Based Purchasing (VBP) rewards quality performance of hospitals by adjusting payments based on the quality of care provided.

The Medicare Physician Fee Schedule permits reimbursement for pressure ulcer assessment of patients within a facility provided by physicians and other qualified health providers under Part B in accordance with the consolidated billing provisions of the Balanced Budget Act of 1997. CPT procedure codes for Evaluation & Management are designated to encompass various types of assessments including skin integrity and risk of pressure injury development.

Padula, Bryant, et al. (2021) discuss the reimbursement landscape's financial burden to providers.[xxiii] In their letter to the editor, Padula et al. note that, to avoid penalties levied by the CMS and to improve overall facility quality ratings, hospitals tend to "prioritize preventing outcomes that are least labor-intensive" and more cost-efficient than PI/PU prevention. They propose three alternate models to incentivize prevention:

- A two-sided risk model that rewards hospitals that achieve pre-determined incidence rate reductions, including PIs
- A deferred payment model where the CMS shares the cost of prevention for on-time discharge
- A capitated payment model that provides upfront payment to hospitals to invest in prevention technologies.

The SEM Scanner technology is positioned as an adjunct to current assessment tools and represents an advancement in the standard-of-care in the early identification of risk and PREVENTION of PIs. The SEM Scanner technology can (and increasingly is) an integral part of an evidenced-based, *best practice* care bundle. In USA facilities, it is a pillar in the *Center of Excellence* programs for skin integrity assessment and prevention.

According to AHRQ, a best practice for preventing PIs in the hospital setting include application of a care bundle[xxiv] including:

- Comprehensive skin assessment
- Standardized pressure risk assessment
- Care planning and implementation to address areas of risk

Included in the implementation of a best practices plan is utilization of a clinical pathway or structured multidisciplinary plan of care supporting clinical guidelines. An important aspect of the clinical pathway is to ***reduce variation*** and standardize care in order to provide efficient, evidence-based care for improved outcomes.

The SEM Scanner technology significantly reduces the variation in the process of PI risk assessment and provides objective documentation supporting the care plan. Care plans, therefore, become more standardized based on the objective SEM Scanner technology scores and serve to improve clinical outcomes. Evaluation & Management codes may be used for physician and other health practitioners (physician assistants, nurse practitioners, clinical nurse specialists) when performing evaluations, including skin integrity in a variety of settings. Representative coding options for E&M (99218-99238), which may include a PI risk assessment such as those performed with standardized risk assessment tools or use of the SEM Scanner technology.

4.4 Patient record, Root Cause Analyses, Litigation

SEM delta values are recorded for each scanned anatomy. These data form part of the patient record and are evidence of compliance to government, payor and local policies. These can and are being used to support root cause analyses of PI cases.

4.5 Pressure Injury Guidelines

As of July 2022, there are fifty-one (51) peer-reviewed articles published in twenty-three (23) international journals. The increasing body of evidence describing the clinical utility of the technology has resulted in evidence based clinical practice recommendations in multiple national and international guidelines.

4.5.1 Clinical Practice Guidelines

The new 2019 Clinical Practice Guidelines[xxv] were launched in 2019. Three relevant sections of these CPGs are:

1. *Understanding the pathophysiology of how and why PU/PIs develop has advanced*
    a. "Damage Cascade" (Figure 2.4, page 23) was introduced and explained as sequential damage associated with; direct deformation, inflammatory response, and ischemia.
    b. The work of researchers exploring processes occurring before the manifestation of a Category 1 PU/PI has advanced in the last 5 years. We are delighted that the role of localized inflammatory edema/sub-epidermal moisture (SEM) was recognized as "one of the earliest signs of cell death in pressure injuries" (page 22). Further, this is detectable via measurement of the biophysical marker; Biocapacitance of tissues.
    c. SEM is a biomarker which notifies practitioners of incipient damage[2], even if the skin and tissue are not exhibiting other signs of PU/PI damage, such as erythema. This is early, actionable information.
2. *The days of <u>only</u> using visual and palpation skin assessment for early-stage PU/PI diagnosis are past*
    a. The primacy of clinical judgment pervaded the CPG text, rightly in our view. Recommendation 2.6 states that healthcare practitioners using their own qualified clinical judgement, "Consider using a sub-epidermal moisture/edema measurement device as an adjunct to routine clinical skin assessment." Practitioners, patients, and providers will all benefit from the clinical insights derived from SEM/edema measurements.
3. *Patients with darkly pigmented skin have a higher risk of under-detection of Category/Stage 1 pressure injuries*
    a. In and of itself, the health-disparity for patients with darkly pigmented skin is well known and is not new. For the first time, these CPGs state (Recommendation 2.7) that healthcare practitioners using their own qualified clinical judgement when assessing darkly pigmented skin, "….consider assessment of skin temperature and sub-epidermal moisture as important adjunct assessment strategies."

4.5.2 AORN Guidelines

In Operating Room care settings, patients are at increased risk due to multiple comorbidities and increased periods of immobility and by the time PI presents at the skin surface, the damage is often irreversible resulting in increased incidence rates post operatively. The 2022 Guidelines for Prevention of Perioperative Pressure Injury by the Association of periOperative Registered Nurses (AORN) recognize the need technology-based examinations of skin and tissue status. Two recommendations relevant to SEM assessment technology are:

a. Recommendation 7.2.1 "Technology-based skin assessments that focus on the biophysical changes (i.e., biocapacitance…….may be used"
b. Recommendations 7.4.1: "Darkly pigmented skin should be assessed by checking the patients's skin temperature and the presence of edema, induration and pain."

4.5.3 Other Guidelines

The spinal cord injury consensus statement in New Zealand recommends "use a sub-epidermal moisture (SEM) scanner" as part of comprehensive skin and tissue assessments for managing PIs for those with spinal cord injuries. This statement (September 2021) is part of the Accident Compensation Corporation's (ACC's) work in collaboration with the Ministry of Health and Health Quality & Safety Commission New Zealand to prevent pressure injuries in people at highest risk.[xxvi]

Additionally, as of June 2022, SEM assessment is included in standard pressure injury prevention protocols as part of the official Pressure Ulcer Prevention recommendations of the Polish Wound Management Society.[xxvii]

5. Evidence

Bruin Biometrics' Claims-Data-Value (CDV) framework (**Figure 7**) comprises: 1) a progressive sequence of claims regarding the performance, efficacy and safety of the SEM Scanner technology; 2) a "Pyramid of Evidence" laying out the primary and secondary data supporting those claims; and 3) the value proposition of the claims.

Data is represented in a Pyramid of Evidence format suitably modified for new-to-the-world medical devices and is used to show the evolution of the SEM Scanner technology through the requisite levels of proof, from concept, through marketable device, to finally, becoming the gold standard for its respective field of use; prevention of PIs. Bench and in-human clinical studies were sequenced in a logical order to build evidence progressively. Clinical value and utility of the device increases and strengthens as the evidence builds about each in individual claims agreed with regulators.

Bruin Biometrics' CDV framework was applied to the SEM Scanner technology to build evidence incrementally which showed that the device : 1) works as claimed; 2) has clinical utility, such that the device is equal to or better than the current standard of care and, ultimately, 3) that should be the standard of care device supporting nurses in their prevention of preventable PIs without any new, additional interventions or staff members.

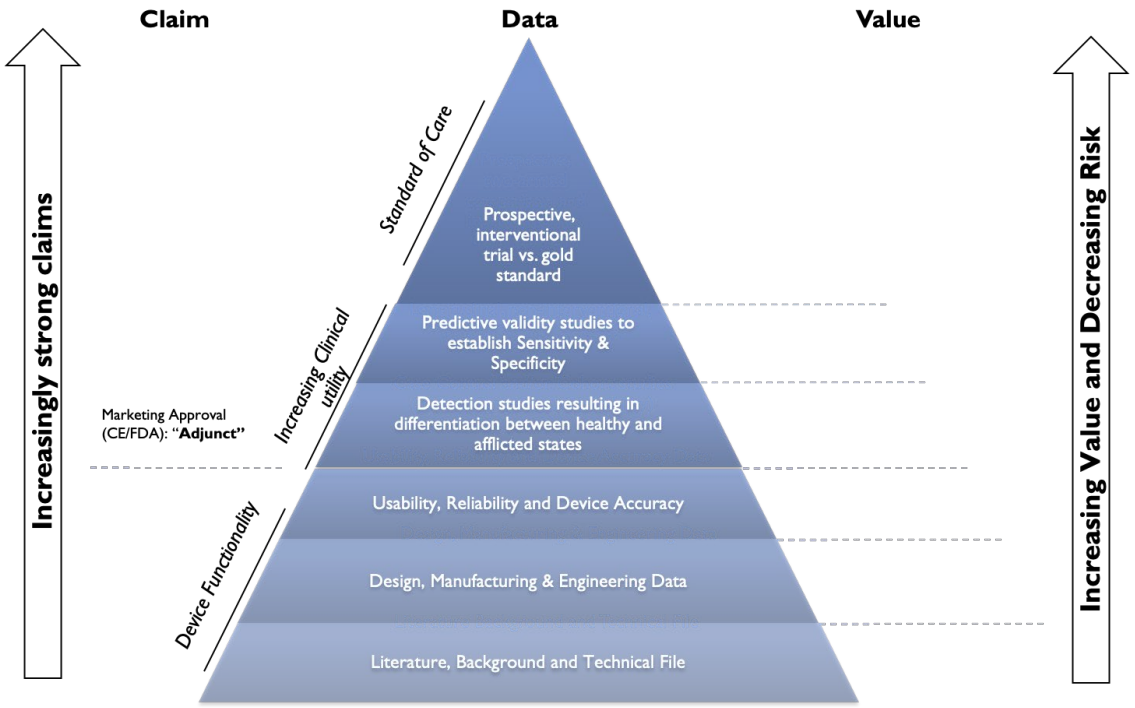


FIGURE 7: BRUIN BIOMETRICS' CLAIMS DATA VALUE FRAMEWORK FOR DEVELOPMENT OF BENCH AND CLINICAL EVIDENCE

The appended bibliography provides details of one hundred and twelve (111 relevant publications, conference oral presentations, or conference posters, all of which fit into one or more layers of the pyramid. Of these, Fifty-one (51) peer-reviewed publications extensively support the clinical utility of the technology or the concept of SEM.

5.1 Device Functionality Layer

Publications relating to SEM and inflammation are shown in the bibliography, these map to the bottom layer of the pyramid.

The initial steps were to complete a comprehensive review of sub-epidermal moisture and its associated biomarkers (inflammation, localized edema). Results have been extensively reported in the literature. A large number of papers from different research groups indicated the clinical efficacy of sub-epidermal moisture in early-detection of HAPIs, including in large clinical trials (particularly the ongoing work published by the Bates-Jensen group at the University of California in Los Angeles).

Collectively, these studies show that when the inflammatory response to (micro-scale) cell death events is triggered, blood vessels adjacent to the micro-damage site become more permeable, which allows immune cells to escape the vasculature and migrate towards these cell death sites, as a first step in the process of tissue repair. As a result, plasma which also leaves the (leaky) vasculature accumulates gradually in the interstitial space over time, increasing from a microscopic to a macroscopic volume, and eventually forming edema. This buildup of plasma fluids progressively increases the *Biocapacitance* physical biomarker of the affected tissues, as their dielectric constant approaches that of water[xii]. This Biocapacitance property is the inflammatory marker measured by the SEM Scanner.

These studies contributed to sub-epidermal moisture being included in the etiology chapter of the 2019 NPIAP Clinical Guidelines.

5.2 Device Design; Device Usability, Reliability, Accuracy Layers

A series of bench-tests, validation and verification studies were performed to support the SEM Scanner technology. Ross and Geffen (2019)[xii], in their 2019 publication, comprehensively describe the underlying principles and measurement procedures of the SEM Scanner technology.[xxviii] Additional foundational studies showed the device to have high inter-operator and inter-device agreement, exceeding 0.8 for all assessed anatomies[xxix].

The emphasis was to assess and report the general bench and clinical reliability of the SEM Scanner Biocapacitance technology to reliably evaluate tissue health. The SEM Scanner technology's CE Mark and FDA authorization relied on these and other unpublished studies.

5.3 Increasing Clinical Utility Layer

The SEM Scanner technology has been formally evaluated in three key clinical studies in the United States and United Kingdom, totaling 357 subjects. To overcome the conundrum of an agreement study where there are no objective references (traceability) for early stage PI identification, it was necessary to perform a series of evaluations that in total would provide the necessary evidence.

- First was to *characterize* and *discriminate* differences in confirmed pressure-damaged tissue ("003) and no pressure-damaged tissue ("004") with the SEM Scanner 200[xxx],[xxxi].
- Second, in in a prospective, longitudinal multi-site study within the clinical setting demonstrate that measured changes in the SEM biomarker by the SEM Scanner technology are associated with the later manifestation of a PI (Stage 1, Stage 2, Deep Tissue Injury) compared to the reference standard of clinical skin and tissue assessment. Secondly, that the SEM biomarker gives notification of such changes prior to an expert skin assessed PI manifesting at the skin's surface[xx].

  In the first two -003 and 004 - initial clinical studies conducted by the company in the United States, the SEM Scanner 200 was used to assess sacral and heel regions in persons affected and unaffected by pressure ulcers. These studies enrolled 125 subjects with pressure ulcers, involving 129 wounds (e.g., Stage I/II and deep tissue injury), as well as 50 unaffected study subjects.

  An algorithm (the SEM Delta) was developed with a range of cutoff thresholds from the results indicating a sensitivity of 82% and a specificity of 51% at the conservative cutoff of SEM delta of equal to or greater than 0.6. These results indicate that SEM Scanner technology readings have considerable clinical utility in aiding clinicians' determination of healthy versus damaged tissue and that Scanner readings are more accurate than STA alone. A receiver operating characteristic curve with a computed area-under-the-curve of 0.7809 (95% CI 0.7221, 0.8397, <0.0001) **(Figure 8).**

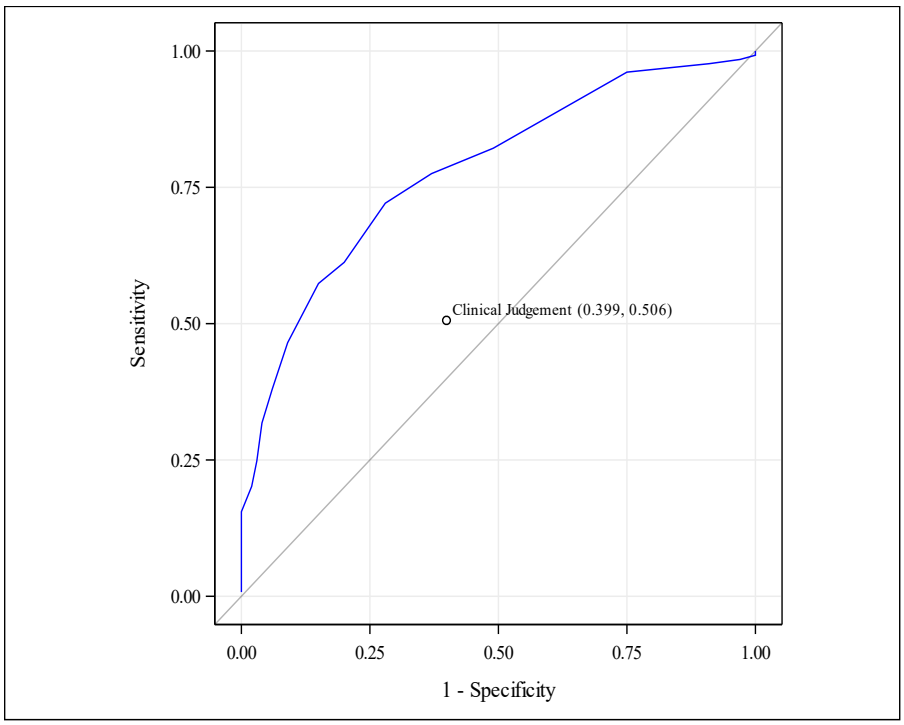


FIGURE 8: RECEIVER OPERATING CHARACTERISTIC CURVE FOR SEM 003/04 (GERSHON 2020 & 2021)

The second study, 008-study, enrolled 189 subjects, 182 of which were included in the intent-to-treat population, accounting for 437 evaluable anatomical locations. The 008 study showed a very high sensitivity of 87.5%. multi-site clinical study[xx] designed to demonstrate that the SEM Scanner 200 could detect PIs in patients before they are diagnosed through clinical judgment alone ("diagnose PI before clinical judgment") and the average number of days of early detection ("time to detection"). Study assessments included (i) daily Risk Assessment and (ii) daily Skin Assessment performed by the Specialist blinded to the SEM readings; and (iii) daily SEM Scanner technology readings collected by the Generalist blinded to the Risk and Skin assessments. The presence or absence of a PI was ultimately diagnosed by the Specialist based upon clinical judgment via skin assessment.

Sensitivity was 87.5% (95% CI: 74.8%-95.3%) and, specificity 32.9% (95% CI: 28.3%-37.8%). Area Under the Receiver Operating Characteristic Curve (AUC) was 0.6713 (95% CI 0.5969-0.7457, p <0.001)**(Figure 8).** SEM changes were observed 4.7 (± 2.4 days) earlier than diagnosis of a PI via STA alone. Latency between the SEM biomarker and later onset of a PI, in combination with Standard of Care interventions administered to at-risk patients, may have confounded specificity. Aggregate SEM sensitivity and specificity and 67.13% AUC exceeded that of clinical judgement alone. While acknowledging specificity limitations, these data suggest that SEM Biocapacitance measures complement STAs, facilitate earlier identification of the risk of specific anatomies developing PIs, and inform earlier anatomy-specific intervention decisions than STAs alone. This early signal is clinically meaningful for patients and healthcare providers in that it allows them to reduce pressure on a specific anatomical site thereby allowing patients' skin to be rescued.

Specificity results of this study were confounded through the unusually high level of interventions (even though the study staff was blinded to SEM Scanner technology results), such as more frequent turning, that likely reversed tissue damage before physical manifestation with visible signs of damage that would be detected by VSA.

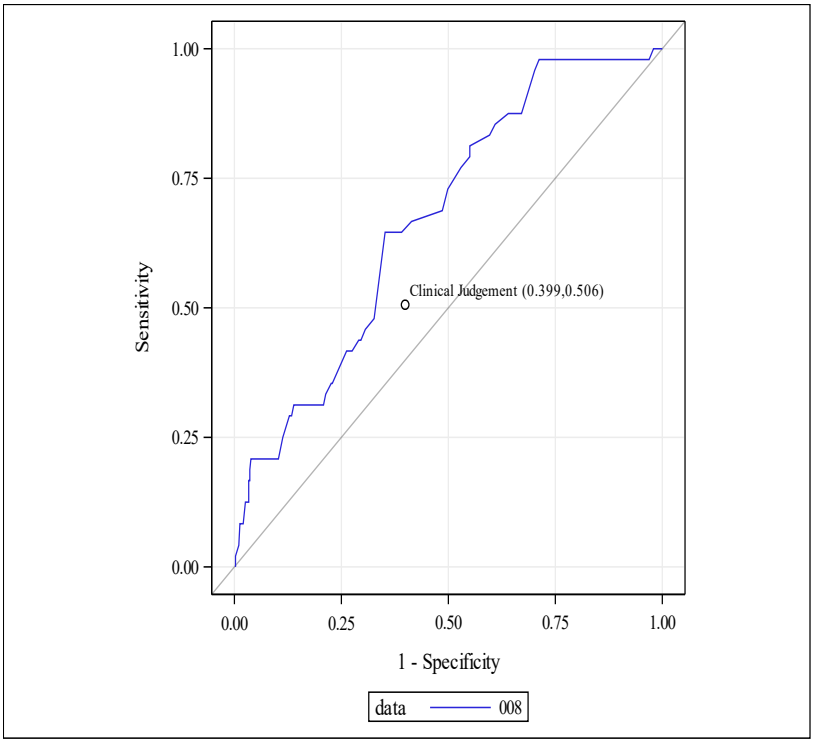


FIGURE 9: RECEIVER OPERATING CHARACTERISTIC CURVE FOR SEM 008 (OKONKWO ET AL 2020)

The 67.13% area under the curve significantly exceeds that of clinical judgement alone. Recall, *this* ROC curve is for patients without visible or tactile signs of a PI, but who will develop a PI if not intervened on at the specific anatomy. The earlier ROC curve **(Figure 8)** is for discrimination of healthy vs visibly or palpably damaged tissue.

Even acknowledging specificity limitations, these data suggest that SEM Biocapacitance measures can complement visual skin and tissue assessments, facilitate earlier identification of the risk of specific anatomies developing PIs, and inform earlier anatomy-specific intervention decisions than visual skin and tissue assessments alone.

5.4 Detection Effect, Intervention Effect

The National Institute for Health and Care Excellence (NICE), UK recognized in its review of the SEM scanner technology that two effects were present through the Scanner's use: "prevention from the diagnostic effect" - - detecting more of the right at-risk patients, at a specific anatomy, and then the "prevention from the early intervention effect"- early, anatomy-specific interventions being provided at a time when they are more effective in reversing pressure-induced damage [manufacturer's notation].

Enhanced prevention from the diagnostic effect was not disputed by NICE, rather was accepted in their models and written comments. Prevention from the diagnostic effect is the prevention that occurs from an increased Area Under the Curve statistic.

This means the Scanner aids clinicians in their abilities to detect more of the right patients who will go on to develop a PU unless they are intervened on. The current standard of care misses too many patients (see the "clinical judgement" plot on the AUC figure, below) who ultimately develop a PU since they did not receive the current standard of care interventions because their PU diagnosis was initially missed. Okonkwo 2020 and Gershon 2021 extensively compute and discuss these Area Under the Curve Statistics.

It is this accepted detection effect we are recommending be included in the community. Additional data published since the NICE review also show the prevention-from-intervention effect. We direct you specifically to Nightingale and Musa (2021)[i], and Roper (2021)[xxxvi].

5.5 Towards the Standard of Care; Health Economy Layers

Conference oral presentations or posters relate to the next layers of the pyramid showing the logical, sequential build of evidence.

- Those[xxxii, i] that relate to the top of the pyramid, the use of the SEM Scanner technology to achieve PI prevention at scale and in year without any new, additional interventions or staff members.
- External regulatory review papers such as the UK's NICE Medical Innovation Briefing MIB182[xxxiii], 2019 are included in the Bibliography.
- Health economic papers specifically about the cost-consequences of the SEM Scanner technology in clinical practice are also included in the bibliography[xiv, xxxiv]. The data and models supporting these papers show the SEM Scanner technology in a preventative pathway as the dominant quality intervention, which subordinates all others. Details are provided in the Health Economic section of this submission.

When the SEM Scanner technology was launched in the European Union (2014) and Canada (2015), Bruin Biometrics introduced the Pressure Ulcer Reduction Program (PURP) to provide an opportunity for potential customers to conduct evaluations of the product. PURPs were conducted at multiple acute care, post-acute, home-health, and palliative end-of-life settings in the United Kingdom, Belgium, Spain, and Canada between 2015-present, and in the USA (2019+). PURPs were structured to evaluate the impact on the rate of hospital-acquired pressure injuries (HAPIs) and the ability to incorporate use of the SEM Scanner technology into the clinical workflow over a period of one to twelve months.

Raizman et al (2018)[xxxii] conducted a consecutive series study of 284 patients with the objective to evaluate the clinical utility of the SEM Scanner technology. The authors concluded that use of the SEM Scanner technology to influence clinical interventions resulted in a 93% decrease in HAPI and Hawthorne effect did not influence the improvements in PI incidence.

A real-world case series of 35 patients on a single medical-surgical unit over a two-month period was conducted to evaluate the impact of the SEM Scanner technology use for early PI detection on clinical outcomes. When compared to risk assessment tools, several patients were assessed to be "at-risk" by the tools, but their SEM readings indicated no damage was present. The authors concluded that daily scanned proved to be a more effective method of assessing damage objectively as opposed to using visual assessment alone.[xxxv]

A formal, repeatable, pragmatic framework (a study framework designed to mimic routine clinical care and practices in the real-world care settings) was conducted at Chelsea and Westminster hospitals in the UK[i] to evaluate the impact on reportable PI incidence and the HCP experience-changes in decision making and the interventions prompted by SEM results. Six hundred and ninety-seven (697) patients were enrolled during a 6-month period in 4 different wards. Zero pressure injuries/ulcers were recorded in three wards resulting in an 81% incidence (p=0.011, 95%CI: 0.38-1.77) reduction across all four wards. Improved clinical decisions from clinical judgement based on Sub-Epidermal Moisture (SEM) Scanner data were reported in 83% patients (n=578/697).

Roper R (2021)[xxxvi] undertook a 6 week Improvement project comparing the impact on PI incidence and use of Dynamic Therapy Systems. Two pathways were implemented in 7 wards– the first included SEM Scanner technology into the SoC and the second utilized a newly developed equipment pathway. The SEM Scanner technology wards (n=2) achieved zero HAPI and a 100% reduction in PI relative to prior year with 75%/79% of patients changed the clinical decision making of the staff introducing additional interventions with 33%/11% reduction in dynamic therapy usage sustained for 6 weeks post project. Whilst the equipment pathway wards (n=5) achieved zero HAPI and an 86% reduction in PI relative to prior year with 64% reduction in dynamic therapy usage for 2 wards, however this was not sustained post project and a 40% increase in 3 wards sustained post project. Roper also estimated potential cost

savings of £1,204,708 (offset against device purchase related to reduction in spend for dynamic therapy systems, reduction in staff time, cost of dressings, medication and occupied bed days.

Scafide et al (2020) published a full systematic review of bed side accessible technologies including: ultrasound (n=5), thermography (n=7), SEM (n=5), reflectance spectrometry and Laser Doppler (n=1). There is significant detail in the publication with regard to the outcomes of the 5 SEM publications included in this evaluation, these publications include 581 patients. The authors state that "evidence from our review supports the use of SEM measurement as a potential tool for the early identification of PI" they go onto comment that "a body of research regarding SEM measures, which includes multiple, high-quality studies increases the reliability of our findings identified in our review". They also point out the value in darker skin toned patients.[xxxvii]

Chaboyer et al (2022) published an independent systematic review to analyze studies that reported the association between oedema measurement and PIs. The rapid systematic review design, quality assessment methodology, GRADE assessment and reporting of meta-analyses uses globally peer reviewed and accepted frameworks. The systematic review showed a strong association between oedema, as a prognostic indicator, and PI incidence (sacrum and heels) using the SEM assessment technology. Evidence suggested that an abnormal SEM delta (≥0.6) results in a large increase in the risk of developing PIs and that an abnormal SEM delta (≥0.6) is a strong indicator of a PI occurring 4 to 5 days later.[xxxviii]

Mersey Care Foundation Trust (MCFT), UK successfully integrated the technology into every day clinical practice as part of patient's individual holistic assessment. During their pilot study period, improved clinical decision-making, early implementation of SoC interventions as a direct result of SEM delta readings, resulted in a reduction in community acquired PI incidence of 26.7%. The impact of this pilot analysis enabled MCFT to directly correlate implementing SEM technology to their PI incidence reduction objectives.[xxxix]

Raine (2021) implemented the technology in palliative care (Marie Cure Hospices, UK). The 6-month study period resulted in a 47% reduction incidence rates. Post-study conclusion, patient safety incident reports indicated a consistently decreasing PI incidence rate after fully implementing the device into routine clinical practice. Facility nurses reported a 69% PI/PU incidence reduction in year one of implementing SEM assessments in routine clinical care: 15 months post-study completion. During a period of 6 months in 2020 (year two, pre-COVID-19), a 100% PI/PU incidence reduction was demonstrated for several months.[xl]

Lustig et al (2021) 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 using the SEM scanner.[xli]

Oliveira et al (2022) evaluated the predictive ability of SEM assessment as a means of detecting early PI damage development among adults undergoing surgery and confirmed early pressure-induced tissue damage in surgical patients in the operating room. Regression analysis of SEM data from 231 patients indicated, a.) the odds of developing an abnormal SEM Δ was likely to increase by 45% with an increase in surgery time ($p<0.05$), b.) patients undergoing orthopaedic surgery were 53% more likely to have an abnormal SEM Δ than non-orthopaedic surgery patients ($p<0.05$), c.) patients having spinal anesthesia were twice as likely to develop abnormal SEM Δ (pv0.05), and, d.) the Braden and Waterlow mobility scores were associated with high SEM results ($p<0.05$). [xlii]

Real world evidence (RWE)[xliii] from Bruin Biometrics' Pressure Ulcer Reduction Program (PURP) shows that the device is providing increasing clinical utility and impact by reducing PI incidence rates in different care settings including Acute Care, Post-Acute Care, Community Care and Palliative Care. The program aims at measuring the impact of the SEM Scanner technology across all care settings, driving significant outcomes towards eliminating avoidable PI incidence rate in individual departments or care units. The objectives of the PURP programme were to provide real-world evidence of use of SEM Scanner technology as an adjunct in a prevention focused protocol as follows.

- From visually manifested to *earlier*: Identify increased risk of PI earlier than visual skin assessment.
- From subjective to *objective*: Act on objective, anatomically specific data.
- From total body, to *anatomy specific*: Allows shift from whole body preventions to anatomically specific interventions.
- No increase in staff numbers. No new staff needed (Note, Chelsea & Westminster NHS Trust added a PURP project manager for the duration of their PURP. He has now moved to an unrelated project in a different hospital).
- No additional interventional equipment required.
- Limitations – varying length of PURP programmes, small number for short time period – analysis shows impact remains.

As of May 2020, a total of 34 care facilities across multiple clinical settings have participated in the PI reduction program with 2,439 patients scanned with the SEM Scanner:

- In the Acute Care cohort, a 90.5% (weighted) reduction in PI incidence was achieved;
- A 47% reduction in PI incidence in Palliative Care; and,
- A 27% & 100% reduction in 2 Community Care sites.

74% of sites in the Acute Care cohort experienced zero (0%) PI during the PURP.

Further, 69% of healthcare practitioners stated that SEM data influenced their decision making with 72% patients receiving additional, targeted preventative interventions.

This real-world data was further independently analyzed under the leadership of Prof K Ousey – a leading global KOL in the PI segment. The primary aim was to assess the effectiveness of sub-epidermal moisture (SEM) assessment technology as an adjunct to visual assessment to reduce PI incidence alongside standard PI care pathways. Implementing SEM technology resulted in universal reductions across all care settings. Facilities achieved a statistically significant 3-fold reduction ($p<0.01$) in PI incidence post-implementation of the scanner device into existing SoC. In many individual settings, post- PURP incidences drop to zero (100% reduction). Six (6) sites achieved statistically significant reductions in PI incidence post SEM technology implementation ($p<0.05$). These results indicated strong evidence that the use of SEM assessment technology is significantly associated with a reduction in PI incidence (Category 2 or above) across a wide range of clinical settings. When implemented daily, at the bedside, as an adjunct, SEM assessments enable objective and improved nurse practitioner clinical judgement with timely, targeted interventions. Ousey et al (2022) recommend that healthcare professionals should consider a translational approach, with a focus on clinical decision-making science to implementing this technology into everyday PI care pathways.[xliv]

To further strengthen the evidence for the SEM assessment technology, and to translate the clinical effects of the scanner into the real world and enable widespread adoption of the scanner into daily clinical practice, a translational strategy is being applied to update Bruin Biometrics' CDV framework (Figure 10).

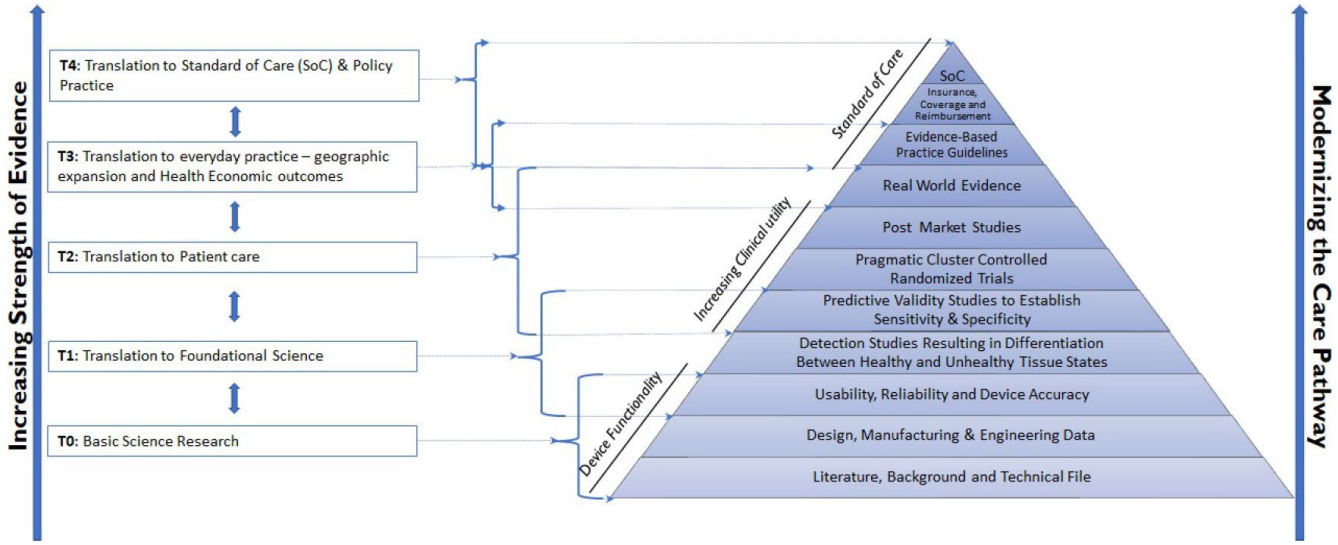


FIGURE 10: A TRANSLATIONAL APPROACH TO "MODERNIZE THE STANDARD PI CARE PATHWAY"

5.6 Clinical Workflow of PI Prevention Using the SEM Scanner Technology

The SEM Scanner technology is used in care settings where there is an incidence rate of PIs where the intention is to eliminate all avoidable cases and also where patients are identified as being at risk of developing a PI.

In terms of the use within the current pathway, Bruin Biometrics recommends that the SEM Scanner technology be used (in addition to standard of care):

1. Upon admission – identifying increased risk or PI through raised deltas on admission;
2. During the patient's stay; and,
3. At discharge.

To assess risk, patients are scanned on admission and throughout their care as an adjunct to risk assessment protocols. The SEM Scanner technology is integrated as part of the patient risk assessment and is introduced into clinical workflow (Figure 11) **(**King T. et al 2018)[xlv].

Anatomy specific SEM values form part of the patient record and are passed from site of service to site of service.

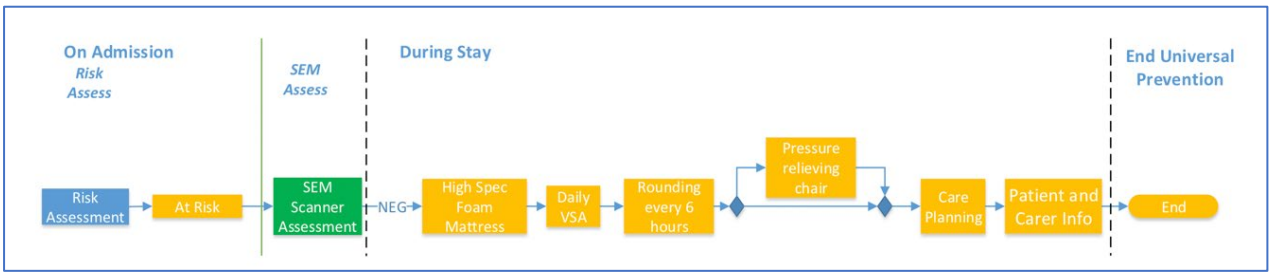


FIGURE 11: INCLUSION OF SCANNER IN CARE PATHWAY. SEM SCANNER ASSESSMENT OF AT-RISK PATIENTS' ANATOMIES (KING T. ET AL 2018)

5.7 SEM Scanner Technology as an adjunct to the Universal Prevention Pathway

If the initial risk assessment outcome is the patient is at At-Risk for a PI, then the technology is used to assess heals and sacral areas.

1. If SEM assessment indicates risk of developing PI on, for example, the left heel (≥0.6 SEM Delta), then,
2. Use SEM Assessments to inform patient centered care
    a. Implement anatomically targeted interventions
    b. Perform daily SEM assessment of damaged area(s)

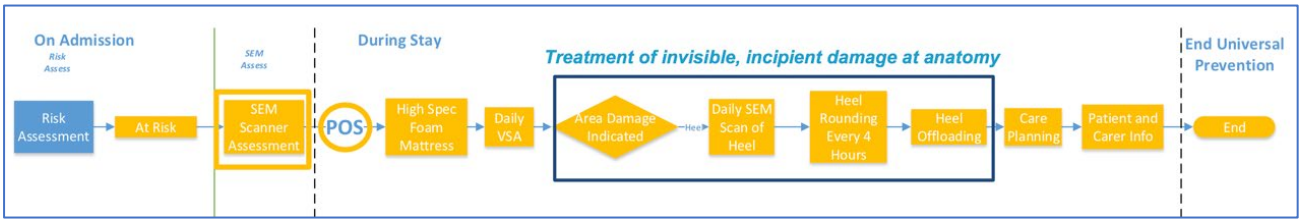


FIGURE 12: INCLUSION OF SCANNER IN CARE PATHWAY. SEM SCANNER "POSITIVE" RESULT (KING T. ET AL 2018).

The following graphics (gratefully accepted from Acute and Post-Acute sites using the technology) give an overview of how the SEM Scanner technology is being effectively used to enhance the holistic assessment of patients. Early identification of increased risk of PI and the relevant interventions aligned to the patient's care plan is resulting in the reduction of PI incidence.

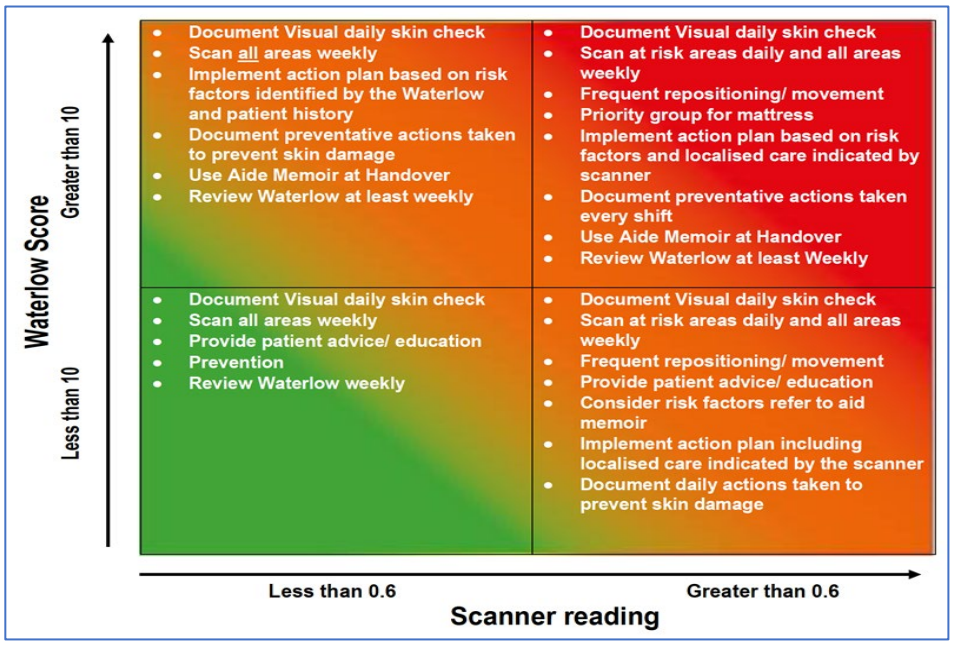


FIGURE 13: PI PREVENTION PROTOCOLS USING RISK ASSESSMENT SCORES AND SEM SCANNER VALUES[xlvi]

6. Clinical Resource impact

Using the technology enables earlier identification of increased risk of PI and anatomically targeted interventions intended to keep skin intact. Importantly the implementation of the SEM Scanner technology requires:

- No new staff
- No additional equipment
- Interventional equipment remains the same (within the facility)

PI Prevention protocols are updated to advise nurses (and nurse assistants) to use their SEM Scanner technology informed clinical judgement to start anatomically specific interventions at a given anatomy. These protocol changes are very modest in their substance and their word count. They support the current standard of care. Bruin Biometrics' Health Economic models highlight the time required to assess one patient with the device is approximately 5 minutes. Bruin Biometrics work closely (Figures 14, 15) with healthcare practitioners to ensure easy and efficient implementation of the technology.

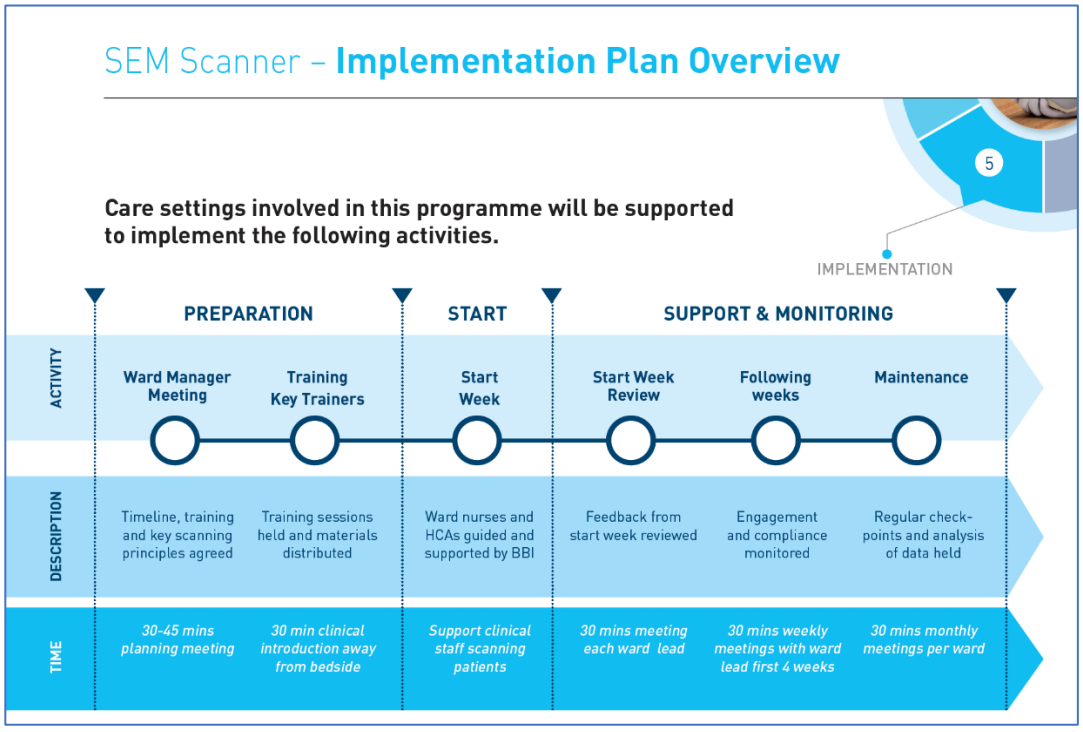


FIGURE 3: BRUIN BIOMETRICS SUGGESTED SEM SCANNER PLANNING AND IMPLEMENTATION PROGRAM

Ward/Unit implementation plan

Activity	Content	Responsibility
Planning process	• Outline Implementation process • Identify key trainers • Set pre-implementation training dates and scanning start date • Confirm documentation to be used and PU pathway guidance	Project Lead Clinical Manager
Training	• Clinical Introduction – programme outline, ensure understanding of SEM • 'Hands on' practical session, how to scan correctly • SEM Implementation folder – outline content • Ensure understand PU pathway documentation	Clinical Manager Key Trainers
Week 1	• Work with Key Trainers only – observing, supporting good scanning technique • Complete Verification document and sign off • Observe key trainers teaching other staff, ensuring good practice upheld • Ensure compliance with pathway documentation and recording	Clinical Manager Key Trainers
Week 2	• Key Trainers – feedback, discuss experience, make any necessary updates • Clinical Manager – discuss the weeks findings, feedback from staff • Data Collection – reaffirm importance of good data, staff compliance	Clinical Manager Key Trainers
Week 3/4	• Assess adoption – plan time to overcome any training/compliance issues • Reduce support twice weekly dependent on confidence levels • Maintain weekly contact to review adoption progress	Clinical Manager Key Trainers
Maintenance	• Monthly meetings with Clinical Manager to review progress • Quarterly reviews with Project Lead, Clinical Manager, TVN – track progress on PU reduction	Project Lead Clinical Manager Matron/TVN

FIGURE 4 BRUIN BIOMETRICS SUGGESTED SEM SCANNER WARD LEVEL IMPLEMENTATION PLAN AND RASCI

7. Health Economics and Policy

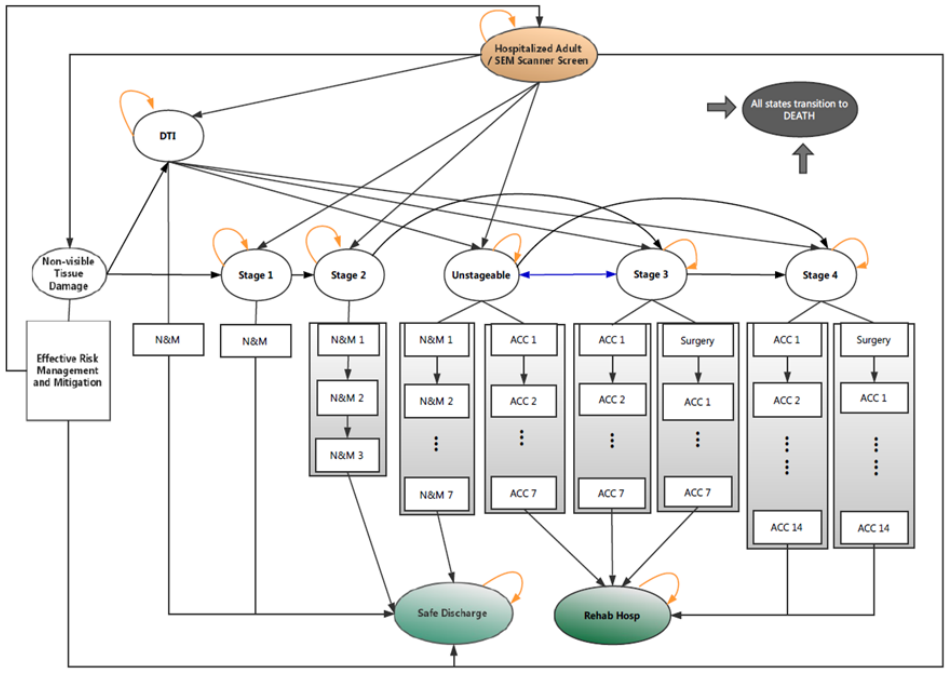
A Cost-Impact and Markov model[xxxiv] was developed with Monument Analytics led by Prof W Padula to evaluate the cost-effectiveness of using the SEM Scanner technology compared with the current standard of care using a cohort of simulated patients. The model focused on the prevention of HAPIs in three clinical settings: acute care, rehabilitation and skilled nursing (only the acute care model's results are shown here). The Markov model is a dynamic framework which models the progression of PIs through days and repeated observations or interventions throughout a hospital stay.

7.1 Health Economics Decision Making Model Methodology

A health state-transition model was developed using a Markov structure to dynamically assess the cost-effectiveness and financial benefits of using the SEM Scanner technology in the United States. The focus was on the prevention of HAPUs in three clinical settings: acute care hospitals (ACH), skilled nursing facilities (SNF) and inpatient rehabilitation facilities (IRF) (Please note, only acute care models are shown). The model was capable of being further customized to specific facility characteristics in the US through a user-friendly model interface. Results are examined from the perspective of the healthcare sector and all analyses were performed using Microsoft Excel® 2016.

The main structure of the model is the same for each setting, consisting of 11 mutually exclusive health states. For the SEM Scanner technology prevention protocol, there is an additional health state for "Non-visible tissue damage" in which the SEM Scanner technology identified patients with potential HAPI development receive in-time mitigation efforts to decrease the likelihood of further disease progression. Patients start from the hospitalized adult / SEM Scanner health state, with either standard prevention protocol provided, or SEM Scanner screening provided; either prevention protocol is provided daily or weekly depending on the setting. From there, when the SEM Scanner is used, patients may move to a non-visible tissue damage state if the SEM Δ is ≥ 0.6, indicating PI risk mitigation should be provided to prevent further advancement to any stage of PIs.

The Markov model for the ACH setting (**Figure 16**) captures the prevention and treatment pathway of PIs, with recurring patterns and tunneling states over a one-year time horizon with 365 one-day cycles.



Abbreviations: DTI = deep tissue pressure injuries; N&M = nursing and monitoring; ACC = acute and chronic care

FIGURE 16: COST-IMPACT MODEL AND MARKOV MODEL FOR ACUTE CARE SETTINGS

In projecting the outcome benefits of using the SEM Scanner technology compared with SoC, the model calculates the additional length of stay (LOS) needed to treat HAPI compared with the typical LOS of a hospitalization without HAPI by using weighted average durations of all health states.

Model Parameters

Model parameters related to the SEM Scanner technology were obtained from the SEM200-008 clinical study (Okonkwo et al 2020). For parameters related to SoC or where data was not otherwise available, we used data from the peer-reviewed literature to build the model structure.

Model Inputs

Table 1 summarizes key model inputs for resource use and costs for the three settings.

Variables	ACH Input	SNF Input	IRF Input	Reference
Total Beds	150	4400	50	AHA, 2019; Assumption based on Windsor; MedPac, 2015
% of Patients that are 'At Risk'	30%	50%	50%	Padula BMJ QS, 2018; Assumption based on Windsor; Assumption
Bed Utilization	62%	86%	65%	MedPac, 2015 for hospitals; MedPac, 2015 for SNFs; MedPac, 2015 for IRFs
Average Length of Stay	4.6 Days	28 Days	13.3 Days	HCUP, 2014; HHS, 2010 for SNFs; HHS, 2010 for IRFs
Annual # of At-Risk Admissions	2,214	24,664	446	Calculated as Number of Beds At-Risk x Bed Utilization x (365 days / Avg. LOS)
Annual incidence based on admissions	2.5%	2.2%	20.2%	NPUAP reports incidence range of 0.4%-38% for hospitals; 2.2%-23.9% for SNFs. (Lynder and Ayello, 2008); Based on Ayello, 2014 rehabilitation facility PU prevalence rate
HAPIs distribution (Stage I / II / III, IV and Unstageable / DTI)	38% / 38% / 24% DTI – 64%	20% / 20% / 60% DTI – 1%	20% / 20% / 60% DTI – 1%	Padula et al., 2011; Pham et al., 2011; Pham et al., 2011
Number of Scanners Needed	6	275	3	Based on # of at-risk beds and assumption input of 8 beds covered per scanner
First Year Scanner Costs for Facility	$7,414	$333,929	$3,643	Calculated as per scanner cost ($8,650) / Pay-off period (7 years) x # of scanners required for facility
Current Annual HAPIs Prevention Costs at Facility	$0.71 Million	$38.88 Million	$0.22 Million	Model simulation results
Current Annual HAPIs Treatment Costs at Facility	$5.24 Million	$2.29 Million	$0.23 Million	Model simulation results

TABLE 1: TABLE OF MODEL INPUTS THE UTILITIES USED IN THE MODEL WERE OBTAINED BASED ON PADULA ET AL (2019) AND ARE BASED ON EQ-5D.

7.2 SEM Scanner Technology HE Decision Making Model Results (US)

Cost-effectiveness analysis

For all clinical settings, using the SEM Scanner technology is a dominant strategy compared with using SoC, thus producing cost savings while prolonging QALY, Padula W. et al (2020) presents the results of the cost-effectiveness analysis based on current input parameters for the three clinical settings.

The cost-effectiveness effect is largest in the ACH setting; HAPI cost per admission is estimated to be $4,996 using SoC whereas cost is estimated to decline to $912 per admission using the SEM Scanner technology prevention protocol, which yielded an average cost saving of $4,054 per admission and a 0.35 gain in QALY. This result is a net monetary benefit of £39,335 at the $100,000/QALY willingness-to-pay threshold level (ACH setting). Using the SEM Scanner technology also produced comparably high return on investment under all three setting (e.g. for every dollar invested, return is $142 for ACH, $57 for SNF and $34 for IRF) with time to achieve investment breakeven within 2 weeks based on current specified scenarios.

Per Admission Basis				
Setting	Cost Savings	QALY Gained	ICER (per QALY)	NMB at $100k
ACH	$4,054	0.35	$11,491	$39,335
SNF	$3,661	0.11	$36,634	$14,232
IRF	$2,391	0.41	$5,841	$43,334
In Aggregate Basis				
Setting	Cost Savings	QALY Gained	ICER (per QALY)	NMB at $100k
ACH	$4.86 Million	423	$11,491	$39,335
SNF	$40.44 Million	1,168	$36,634	$14,232
IRF	$0.41 Million	70	$5,841	$43,334

TABLE 2: RESULTS OF COST MODEL. COSTS SHOWN ARE IN 2018 US DOLLARS. ABBREVIATIONS: ICER = INCREMENTAL COST-EFFECTIVENESS RATIO; NMB AT 100K = NET MONETARY BENEFIT AT $100,000/QALY

7.3 Financial benefits outcomes matrix

In addition to the cost-effectiveness analysis, the model also provides six other dimensions by which to assess the financial benefits of using the SEM Scanner technology in HAPI prevention compared with using SoC. The six dimensions are:

1. HAPI incidence reduction achieved with number of HAPI related deaths averted
2. Total cost savings achieved with percentage of savings specified for treatment costs or prevention costs
3. Reduced labor hours related to HAPI prevention and treatment with number of full-time nurse equivalents freed from attending HAPI patients
4. Lost revenue captured for freeing facility room and board resources related to HAPI
5. Released bed days from reduced HAPI cases and additional admission equivalents produced, and
6. Litigation savings related to HAPI cases.

For every 1,000 admissions in high-risk acute care, SEM Scanning could avert around 7 HAPI-related deaths and decrease HAPI-related re-hospitalization by approximately 206 bed-days. Similar cost-effectiveness results were also found in SNF and IRF settings (not shown). Detailed results for the matrix for each setting are shown in Figure 17.

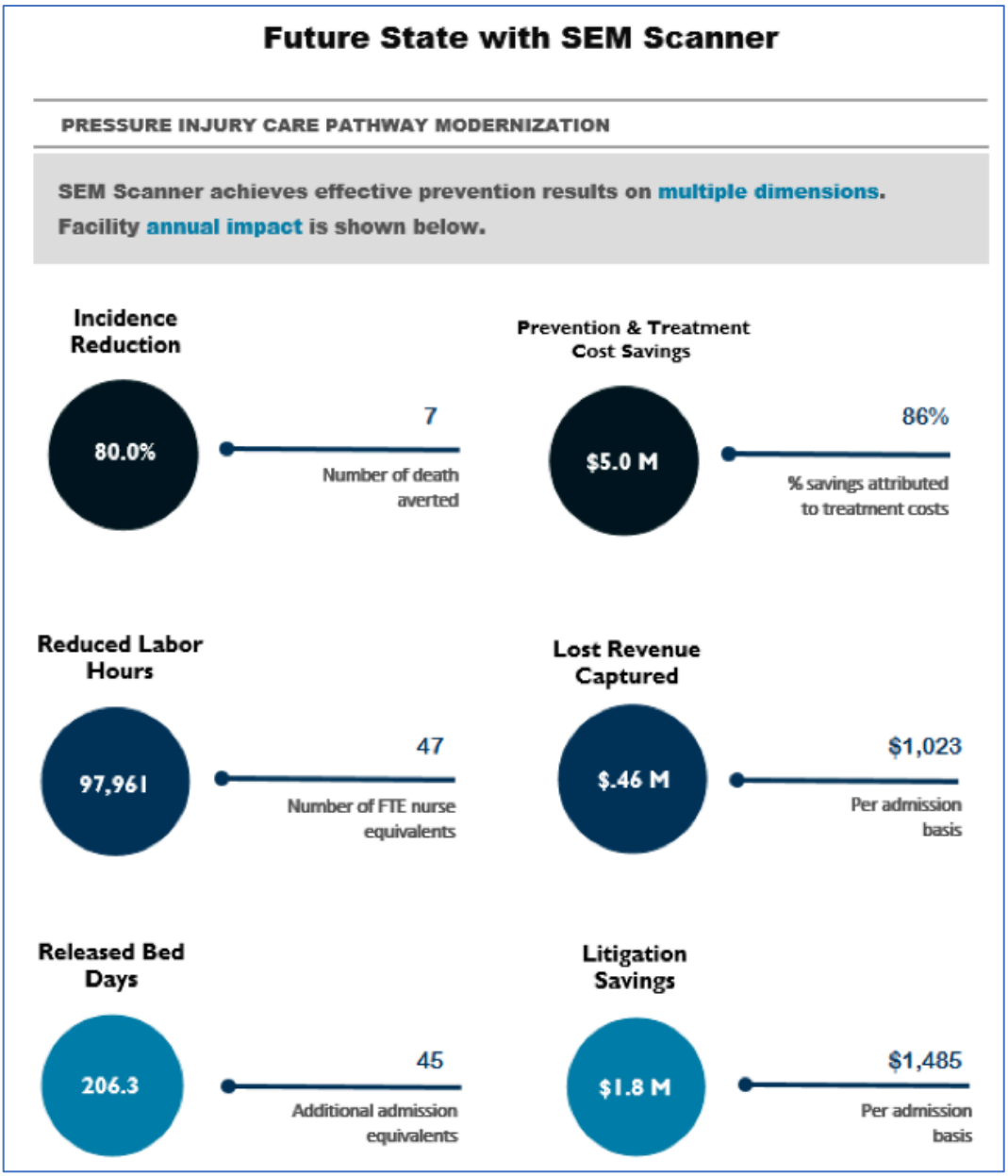


FIGURE 17 MULTIPLE DIMENSION OUTCOMES FOR ACH

7.4 Conclusions drawn from the US HE Decision Making Model

The US HE Decision Making Model suggests cost-effectiveness associated with SEM Scanner technology application in Acute, SNF and IRF care settings. With the SEM Scanner technology impacting HAPI prevention and treatment cost savings, facilities can adopt the US HE Decision Making Model in using the SEM Scanner technology as a dominant strategy compared to the standard of care.

The SEM Scanner technology provides clinical quality, economic outcomes, and aids the transition towards preventative and early intervention pathways.

8. Value Proposition – the Value of PI Prevention

8.1 Clinical

- Use of the SEM Scanner technology can result in up to a 100% decrease in HAPIs
- The SEM Scanner technology allows clinicians to perform anatomy-specific risk assessments before visible damage manifests at the skin surface
- The technology's performance augments clinical decision making and is statistically significantly better than clinical judgement alone in assessing PI risk at patients' anatomies
- Is the world's first and only FDA authorized device to objectively alert clinicians to specific anatomical areas of a patient's body at increased risk for developing pressure damage
- Award winning, globally recognized technology
- Aids adherence to the 2019 Clinical Practice Guidelines recommendations for skin and tissue assessment
- Provides objective measure of PI risk with inter-operator and inter-device reliability of 80%
- Supports clinicians' ability to identify specific anatomical areas at increased risk of PI development 5 days (median) earlier than visual skin assessment
- Supports the treatment and management of SEM (localized persistent focal oedema) for effective PI prevention

8.2 Economic

- The handset of Provizio SEM Scanner can be provided on consignment free of charge or for a small rental charge
- Single use sensors are paid for out of the operating budget. No capital budget allocation is required.
- Prevention using the SEM Scanner technology in a PI prevention pathway is the dominant quality intervention which subordinates all other
- Prevention results in materials (e.g., dressings) costs savings
- Prevention frees up nursing time to care
- Prevention releases bed days
- Prevention allows facilities to be paid for the treatment costs they incur for properly treating a PI detected on admission

8.3 Operational efficiency and Compliance

- Supports present on admission testing and documentation
- Provides objective, numerical evidence of assessment and compliance to facility protocols
- Addressing health-disparity challenges for darkly pigmented patients
- Provides supporting documentation for root cause anlayses and litigation

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