Skin Microvascular and Metabolic Response to Sitting and Pressure Relief Maneuvers in People With Spinal Cord Injury

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Pressure ulcers (PUs) continue to be prevalent despite technologic advances in equipment development and repeated attempts to improve education and preventive efforts. Diligence and timeliness of adequate pressure relief are felt to be the cornerstone to PU prevention. The evidence supporting clinical recommendations for pressure relief is lacking, however, leading to inconsistencies in clinical guidelines. The purpose of this study is to contribute to the evidence base on PU pathophysiology and prevention in people with spinal cord injury (SCI) by delineating the microvascular mechanisms that occur during sitting and pressure relief maneuvers, including perfusion, oxygenation, and interface pressure. By understanding these key physiologic responses, health care professionals and consumers with SCI will be enabled to more effectively prevent the onset of PUs. The overriding goal of this project is to develop an algorithm that will assist clinicians in providing individualized recommendations specifying optimal pressure relief technique, duration, and frequency to reduce PU incidence in consumers with SCI. **Key words:** *pressure relief, pressure ulcer, pressure ulcer prevention, spinal cord injury*

The prevalence of pressure ulcers (PUs) in the United States is estimated at 14% to 17% and incidence ranges from 7% to 9% (2000-2004).[1,2] This is even higher abroad, with the European Pressure Ulcer Advisory Panel (EPUAP) reporting PU prevalence to be 18.1% in 5 participating countries.[3,4] With PU-related health care costs estimated in excess of $3 billion annually (2005) in the United States,[5] this serious health condition places a significant burden on the individual and society.

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During initial acute medical and rehabilitation hospitalization, a staggering 27% to 40% of individuals with spinal cord injury (SCI) will experience a PU.[6-8] Data from the National SCI Statistical Center's annual report in 1998 indicated that an additional 15% had a PU during their first year after inpatient rehabilitation and that, by year 20, 29% had at least one PU since their initial rehabilitation episode. Overall, 20% to 31% of individuals with SCI will experience a PU annually,[9,10] with the incidence of PUs increasing in the years following rehabilitation compared with earlier years. If left untreated, PUs can lead to immobility, surgery, and, in extreme cases, death.[1] Hence, people with SCI remain at high risk for PUs and continue to be responsible for a disproportionate amount of the overall cost associated with PUs.[11,12] Despite extensive research, this secondary medical complication has unsatisfactory prevention options and continues to pose a medical hazard for declining health, activity, function, quality of life, well-being, and longevity.[13-15]

Most individuals with SCI and health care professionals are keenly aware of the risks for PUs, their disruptive effects, and the resources needed to manage a new ulcer.[16] This awareness has led to the development of a large and impressive evidence base and to the production of an array of education and training materials for individuals with SCI, their family members, and health care providers. Given the impressive investment in scientific synthesis, education, and development of guidelines for clinical practice, one would expect a dramatic decline in the incidence of PUs.[11,17,18] However, this expectation has not been realized despite best efforts of consumers and professionals, and PUs remain exceptionally common among persons with SCI.

Another indication of the importance of this secondary condition is reflected in the sustained commitment to prevention by a variety of preeminent SCI organizations. Established under the auspices of the Paralyzed Veterans of America (PVA), the Consortium for Spinal Cord Medicine developed its clinical practice guideline (CPG) for PU prevention and treatment aimed at both consumers and health care professionals that remains, perhaps, the best and clearest synthesis of what is currently known about PU prevention and treatment for individuals with SCI.[19-21] In short, despite all the advances in knowledge about PU prevention, their stubborn persistence requires new information be generated from high-level research. The incidence rate of PUs for people with SCI must be considered inexcusable given what is presumably known about both PU prevention and SCI management.[22]

Pressure and Skin Metabolism

Data indicate that altered tissue perfusion and oxygenation occurring under pressure loads, such as during sitting, induce various pathophysiologic changes that may lead to PUs.[23-30] Pressure causes a cascade of responses, including tissue hypoxia, ischemia,[23,24] vascular leakage,[25] tissue acidification,[23,24] compensatory angiogenesis,[25] thrombosis,[23] and hyperemia.[26-29] In a rat model, Herrman et al found that 5 hours of pressure-induced ischemia caused a persistent hyperemic response in rat skin, and anoxia superimposed on an already ischemic environment may trigger capillary bed restructuring that results in a permanent increase in skin perfusion.[30] This persistent hyperemia manifests as clinically observable superficial hyperemia, or stage I breakdown,

according to the National Pressure Ulcer Advisory Panel (NPUAP).[31]

Preliminary evidence suggests that these physiologic responses to pressure are altered in people with SCI. Sae-Sia et al[32] examined skin blood flow (SBF) responses in people with acute SCI compared with matched groups of subjects with orthopedic trauma and healthy controls. Subjects with SCI had shorter time to reactive hyperemia and a more negative change in SBF during pressure loading compared with normal subjects and persons with orthopedic trauma. In a pilot study, Thorfinn et al[28,29] used a laser Doppler (LD) flowmeter to demonstrate that, when exposed to pressure loads for varying durations, skin buttock perfusion differs in subjects with SCI when compared with healthy controls. Hence, microvascular dysfunction occurs in people with SCI (even in the first days after injury), indicating that clinical recommendations need to be based on data obtained from people with SCI as opposed to data extrapolated from other populations.

Evidence on Pressure Reliefs

Although successful PU prevention requires diligence with multiple strategies, the mainstay of PU prevention is position changes performed correctly and regularly. This includes turning while in bed and pressure reliefs while seated.[19] The current standard of care for repositioning patients during bedrest or at night is to turn every 2 hours to relieve pressure loading on sensitive tissues, yet this recommendation is not supported by data and recent evidence indicates that this may be too infrequent.[33,34] Breuls et al[35] demonstrated tissue damage occurring within 1 to 2 hours of pressures typical in the clinical setting. Further, pressures lasting 2 hours subsequently increased release of interleukin-1α (IL-1α), an inflammatory mediator associated with tissue damage.

Similarly, there is no consensus as to the frequency, duration, or type of pressure relief prescription. The CPG for PU prevention states that "…a weight shift every 15-30 minutes is recommended to allow the skin to be replenished with oxygen" and to "do a weight shift every 15 minutes for 15 seconds if [the] SCI is at T1 or lower." For people who cannot shift their weight, the recommendation is "…for independent pressure relief every 30 minutes for 30 seconds."[19,20] Although this resource is highly relied upon by clinicians, these recommendations are based on a 20-year-old study[36] and a 25-year-old book chapter.[37] These sources combined for a level of evidence of V (lowest level of evidence, which is a case series with no controls) and grade of recommendation of C, yet the importance was reflected in a "strong" opinion of the expert panel. Recent evidence from small trials suggests that these recommendations may be too infrequent, of inadequate quality, and of too short duration.

Coggrave and Rose[38] retrospectively analyzed data from their seating assessment clinic and found that brief (15-30 seconds) pressure lifts or pushups were ineffective in raising transcutaneous oxygen tension over the ischial tuberosities. In fact, a mean duration of 1 minute 51 seconds was required to raise the tissue oxygen to unloaded levels. It was concluded that other means of pressure relief such as forward lean or side-to-side tilt were preferred by patients and were superior in improving tissue oxygen tension. These findings were supported by Makhsous et al[39] in a 2007 study in which 2 pressure relief protocols were compared in people

with paraplegia, tetraplegia, and healthy controls. Similar to Coggrave and Rose's 2003 study,[38] when performing wheelchair pushups to relieve pressure, mean perfusion recovery time (200-250 seconds) was in excess of that typically done for a wheelchair pushup. A more dynamic pressure-relieving protocol was recommended for improved tissue oxygenation. Critical findings from both studies indicate that (1) our current recommendations for pressure relief using wheelchair pushups are inadequate and not substantiated by high-level evidence; (2) wide variation exists between patients and their response to pressure relief; and (3) even though pressure mapping may show complete relief of pressure, recovery of tissue perfusion is incomplete, indicating a need to examine perfusion.

Method

Clinicians do not have enough detailed data upon which to base their recommendations for wheelchair pressure reliefs in the context of the high prevalence of PUs that occur in people with SCI. The profoundly deleterious impact of PUs on health, wellness, participation, and employment demands more attention. The overriding goal of this project is to develop the evidence base for recommendations on pressure reliefs. We anticipate accomplishing this goal through a multistep process, including the following:

1. Completing a systematic review to analyze the existing evidence on skin response to pressure and position changes.
2. Developing a streamlined sensor that can measure blood flow and tissue oxygenation during sitting.
3. Analyzing skin metabolic responses to sitting, pressure, and pressure reliefs using the skin sensor.
4. Providing feedback to individuals with SCI so they can modify their pressure relief practices to improve skin metabolism as much as possible.
5. If appropriate, making the skin sensor available for use by either clinicians or patients.

Our progress in steps 1 and 2 is summarized in this report.

Step 1: Systematic review

According to the definition advanced by the Model Systems Knowledge Translation Center (MSKTC), a systematic review "is a formal, organized method for compiling, evaluating and summarizing all of the published research evidence related to a specific medical or health topic."[40] The findings of a systematic review represent the best available information on the topic studied and provide guidance for best practice in treatment decision making. The evidence-based knowledge produced by the Rehabilitation Research and Training Center (RRTCs) pressure relief systematic review (PRSR) will provide content for learning materials to be used in this project's behavioral intervention and also serve as the point of departure for teaching persons with SCI optimal positioning to prevent skin breakdown. The PRSR is being conducted in collaboration with the MSKTC at the University of Washington, a National Institute on Disability and Rehabilitation Research (NIDRR)–funded center that provides knowledge translation services in support of Model Systems in the area of traumatic brain injury and burns, as well as SCI.

The MSKTC systematic review method

is process-driven, implements a project management plan, and leverages on-line data collection and extraction tools. In developing the PRSR, a 10-step process was followed. Subject matter experts in the area of PU management including physicians, nurses, therapists, engineers, and consumers (both internal and external to the RRTC) were recruited to collaborate with MSKTC staff in the systematic review development process.

Because conducting a systematic review can be a lengthy and complex process, adopting a project management plan and framework is essential. Further, proceeding according to a project development/management plan is an a priori requirement for a systematic review to be considered a quality review in such rating systems as AMSTAR.[41] For this systematic review, the team organized its activities in an on-line wiki platform, PBWorks.com. This tool is one of many available on-line as both licensed and free services. The key functionality of a wiki is its ability to keep track of versions of documents and allow selective rollback. A wiki creates a "safe" collaborative space where teams can pool resources and read and annotate each other's additions in real time without fear of losing data. PBWiki also allows reference document repositories, messaging and creation, and assigning and tracking of tasks.

With the project management plan and team in place, the first step of the systematic review is to develop a clinical question. The clinical question drives the planning and execution of the systematic review. It must be specific to the purpose of the review and the intended audience for the information to be produced. Once a clinical question is developed, a quick scan of the literature is necessary to validate the question as formed. A serious consideration is whether the literature contains enough relevant information to make the systematic review productive. This process is repeated for each question to be answered in the review. The initial set of questions are revisited and finalized based on this initial scan of the literature. After these steps, the final questions for the PRSR were as follows:

- What is the optimal frequency of pressure release?
- What is the optimal type of pressure release?
- What are the optimal positions in bed and out of bed for skin protection?
- What is the optimal frequency of turning/repositioning in bed and pressure relief when out of bed for skin protection?
- When in bed, what is the optimal elevation of the head of the bed?

Based on these questions, we specified key words for searches, guiding article inclusion and exclusion criteria (see **Tables 1-3**). Trained research assistants carried out the final search of the literature, applying team-defined criteria. These activities and details of their execution were captured in PBWiki tasks.

Using the key words agreed upon in the development plan, we conducted a final literature search using the MEDLINE, CINAHL and PubMed databases. Based on information in the development plan such as outcomes of interest, research design types, interventions of interest, the target population, and publication dates, an inclusion categorization system was created. The purpose of this categorization system was to fully document the process and also to promote a high degree of uniformity in analysis of

Table 1. Key words used in literature searches

Key text words and index words for spinal cord injury or closely related conditions linked by the word "OR" as appropriate	Pressure sore; pressure ulcer; assessment; guidelines; recommendations; position; barriers; turn; pressure release; mattress; pressure relief; bed; wheelchair; car planning; patient compliance; discharge

articles despite inevitable unevenness in the domain expertise of reviewers called upon to categorize the articles across a variety of disciplines (eg, medicine, nursing, physical and occupational therapy).

The inclusion categorization system is made up of 5 hierarchical categories (see **Table 2**) where the first 2 categories meet all the inclusion criteria but are divided by research articles that appear experimental

Table 2. Article inclusion criteria

Level (in order of preference)	Description
1	The primary outcome or one of the primary outcomes of the experimental study is related to positioning for pressure releases to prevent PUs; this can include positioning in a wheelchair or outside of a wheelchair such as bed, furniture, etc. This is for all persons who may be affected by PUs (wheelchair users, bed ridden, limited movement, etc). This is not SCI only.
2	The primary outcome or one of the primary outcomes of the observational study is related to positioning for pressure releases to prevent PUs; this can include positioning in a wheelchair or outside of a wheelchair such as bed, furniture, etc. This is for all persons who may be affected by PUs (wheelchair users, bed ridden, limited movement, etc). This is not SCI only.
3	A secondary outcome of the experimental study is related to positioning for pressure releases to prevent PUs; this can include positioning in a wheelchair or outside of a wheelchair such as bed, furniture, etc. This is for all persons who may be affected by PUs (wheelchair users, bed ridden, limited movement, etc). This is not SCI only.
4	A secondary outcome of the observational study is related to positioning for pressure releases to prevent PUs; this can include positioning in a wheelchair or outside of a wheelchair such as bed, furniture, etc. This is for all persons who may be affected by PUs (wheelchair users, bed ridden, limited movement, etc). This is not SCI only.
5	A prevalence/incidence study, not fitting in the first 4 categories, where the main focus of the study is to learn about overall positioning and PU prevalence.

Note: PU = pressure ulcer.

Table 3. Article exclusion criteria

Exclusion category/code	Description
a	Review/editorial/letters/expert opinion that does not fit into design categories from the research design decision tree
b	Not related to seating position, pressure release, or prevention of pressure ulcer
c	Used animals
d	Not printed in English
e	Not wheelchair users, not bed ridden, etc.
f	A mixed sample; those who need pressure releases are not reported on separately
g	Prevalence/incidence study where main focus is on general outcomes pressure ulcers
h	All others

versus observational. The next 2 categories include articles where the outcomes of interest are secondary and are also divided by experimental or observational articles. The last category captures prevalence studies in the area of interest that may report some findings of interest for the review. The reason an article does not meet any of these categories (exclusion categories) is captured. This process does not grade articles based on research design but categorizes them by possible overall design (experimental vs observational) and by how closely the article meets the inclusion criteria established in the project development plan.

Once articles of interest were aggregated into an Endnote library, they were categorized based on the inclusion categories developed in the systematic review plan. This process was organized using a *research design decision tree*, which is a flowsheet that applies specific criteria to individual studies to classify their research design. The research design decision tree (see **Table 3**), along with an approach to grading of articles agreed upon by the team, were incorporated into the on-line, database-driven process used to extract data.

Once a final list of articles was compiled, trained project staff read, reviewed, and extracted data into a Web-based data entry system using a structured query language (SQL) database. Research design data, including the design itself, allocation data, masking/blinding data, and method by which the analysis was conducted, were collected using the research design decision tree. Detailed group data (treatment, control, survey group) were collected separately. Outcome measures used, including validation data on the measures used, were also collected. Last, data on all the outcomes of interest from the project development plan were also collected and included effect sizes, if reported. Data from each article were extracted by one reviewer and validated by a second reviewer. The second reviewer made corrections for errors and suggestions for further extraction, and then the first reviewer implemented the changes based on the second reviewer's comments. If the first and second reviewers disagreed at this point, they met and came to a consensus.

Upon completion of data extraction, tables of evidence were automatically generated from the article database for review. These

tables of evidence are evaluated by author team members, who also perform the final grading of evidence using a grading system, such as GRADE (Grading of Recommendations Assessment, Development and Evaluation),[42] across studies and synthesize knowledge for the written review. Authors can also nominate external reviewers who can suggest additional articles to review based on the inclusion/exclusion criteria. The RRTC team expects to submit the PRSR for review and publication at the end of the 2010 calendar year.

Step 2: Development of the streamlined skin sensor

Essential to the generation of new research-based information on pressure and the effects of pressure reliefs is the development of a more advanced skin sensor with greater capability to measure blood flow and oxygenation changes. To do this, we utilized bio-photonics techniques that rely on hemoglobin absorbance (for the assessment of skin oxygen saturation) and scattering from red blood cells in the superficial vasculature (for LD perfusion measurements). Oxygenated and deoxygenated hemoglobin play an important role in the visible region of the spectrum used in these measurements. Epidermis pigmentation due to melanin is also relevant in this wavelength range because it decreases light penetration and the retro-reflected signal. Nevertheless, its impact on the total retro-reflected light can be quantified, allowing for consistent assessment of oxygen saturation regardless of skin tone. The absorption coefficients (ie, the ability of a skin component to absorb light at different wavelengths) of the main skin chromospheres are shown in **Figure 1**.

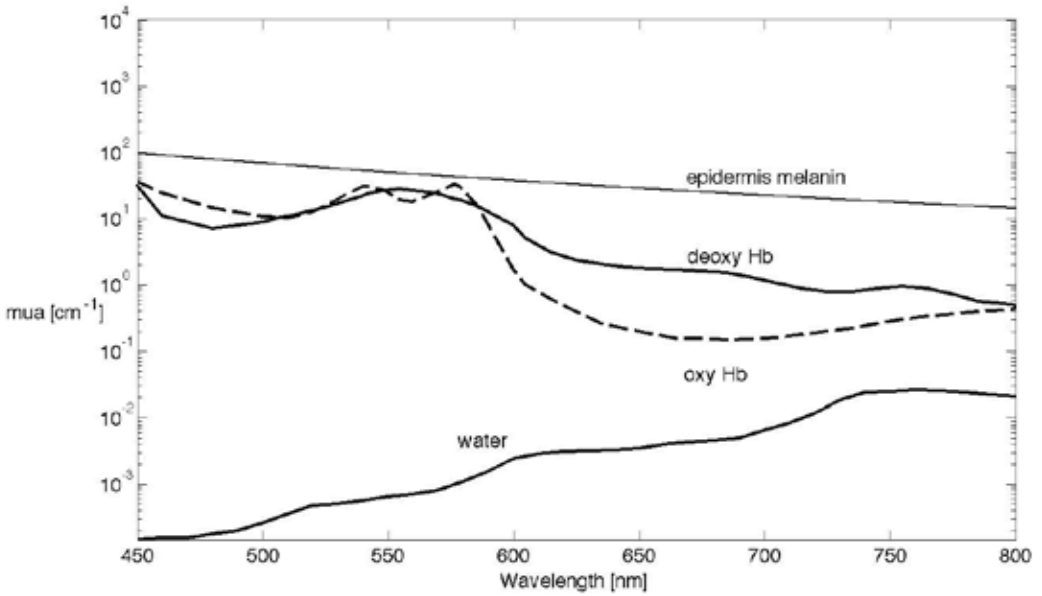

Figure 1. Main skin absorbers.

There have been significant developments in fiber-based measurements of tissue optical properties in the last 10 years.[34-40] By controlling source and detector separations, different depths in the skin can be probed and the diffusion approximation, or models derived from it, can be used to calculate the optical properties of the probed portion of tissue (valid when source–detector separations are of the much larger of the tissue scattering length, which is 50 to 100 μm for human skin).[34,35]

What is ultimately obtained is an average value of the tissue optical properties at different depths. In the deep dermis, absorption from hemoglobin tends to dominate (especially at shorter wavelengths), and the sum of arteriole and venule flow equals values of oxygen saturation between 60% and 70%. We point this out to differentiate this technique from pulse oximetry, in which only the arterial flow is probed. In our setup, the spectroscopic measurements of tissue absorption include both arterial and venous and are combined with measurements of perfusion through LD.

LD is a well-established fiber-based technique, and its instrumentation is commercially available. The Doppler effect is a change of frequency in an impinging waveform induced by a moving object. If the object moves in the direction of the waveform source, the frequency increases compared to the original value; the opposite occurs if the object moves farther away from the waveform source. The same principle is true if the source moves relative to the object.

In preliminary studies, we developed a fiber sensor that could contemporaneously measure perfusion and oxygenation of the skin. The sensor has been used successfully to monitor changes in oxygenation of the skin during induced autonomic dysreflexia (AD)[43] as described by Ramella-Roman in an article in this issue.[44] However, at 1.2-cm thick, this system could not be used over the seated surfaces with pressure applied.

Over the past year, reduction of fiber thickness has been necessary to comfortably and safely locate the sensors over the ischial tuberosities under the conditions of sustained weight bearing and repetitive pressure releases. The new sensor was designed using a fiber bundle as shown in **Figure 2**. Tissue oxygenation is measured via a spectrophotometer, hence the bundle was chosen to maximize light delivery and collection while simultaneously allowing for probe flexibility and robustness. One side of the bundle was connected to a 3-mm mirrorized prism, which diverged incoming and remitted light to a 90° angle similar to previously implemented probes. Thirty percent of the fibers constituting the probes were connected to a SubMiniature version A (SMA) connector and were used for light delivery, while the remaining fibers were also connected to an SMA connector and directed to a spectrophotometer. The fiber and prism assembly were housed in a 1 x 3 x 0.3 cm aluminum housing with an LD probe (Moor Instruments, Millwey Axminster Devon, United Kingdom) at a distance of 1 cm from the fiber-prism assembly and connected to a DRT4 Laser Doppler System. The sensor is indirectly attached to the skin, sandwiched between 2 layers of readily available, waterproof, transparent dressing, such as Hydrofilm. Finally, an imaging pressure pad (Xsensor Inc, Calgary, Canada) was used to evaluate patient and probe pressure onto the skin.

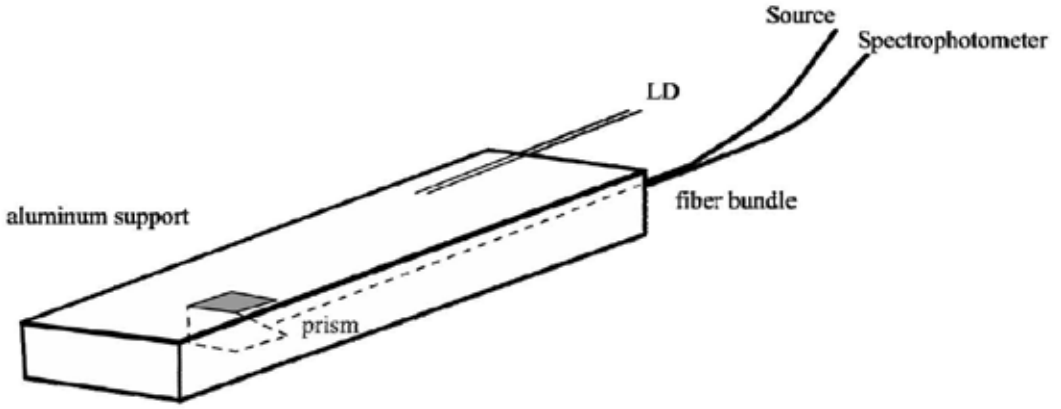

Figure 2. Schematic representation of the coupled laser Doppler (LD) and spectrometer probe. The low profile was designed to deliver and collect the maximum amount of light while maintaining shallow penetration depth to minimize risk of skin breakdown.

Step 3: Analyze skin metabolic response to sitting, pressure, and pressure reliefs

After safety and validation testing of the sensor with healthy human subjects, 46 subjects with SCI will be asked to participate in initial use and testing of the sensor. Subjects must

1. Have sustained an SCI;
2. Be discharged from the acute care facility and have obtained a permanent wheelchair or be at least 6 months after the injury, whichever comes first;
3. Use a permanent manual wheelchair as their primary means of mobility;
4. Be able to perform wheelchair pushups for pressure relief;
5. Not have an existing PU at select anatomic sites (ischium, sacrum, or trochanters) but may have previous PUs;
6. Be admitted for any reason other than a PU; and
7. Be 18 years or older.

With the skin sensors attached bilaterally over the ischial tuberosities and sacrum, skin microvascular data will be collected over a 3-hour period, every 2 seconds. Assessments will include baseline (unloaded), loaded, and recovery (unloaded) based on Doughty's[30] study of post hip arthroplasty patients in which 15 minutes of recovery time was not sufficient for heel oxygen tension to return to baseline after 15 minutes of pressure loading.[45] Thirty minutes is the interval for defining persistent erythema by previous PU staging guidelines.[46] The entire session will be monitored by a physical therapist.

Step 4: Provide feedback to consumers with SCI

Both behavioral objective measures and individually tailored PU self-management techniques must be incorporated to improve PU prevention in persons with SCI. This approach provides the clinician with immediately usable information that can be

incorporated into practice and provides the consumer with greater knowledge on self-management techniques for skin protection. Participants will be randomized into equal control or intervention groups using a block randomization technique.[47] The control group will receive feedback from the microvascular baseline assessment (step 3) including their pressure and microvascular responses, their pressure relief frequency, and their pressure relief technique, as measured via the Pressure Relief Behavior Mapping Instrument (PRMap). Intervention participants will receive a self-management program, which will include 3 interactive modules:

1. An interactive PU prevention educational module incorporating knowledge synthesized from the PRSR and made available via both DVD and 24/7 online access,
2. PU self-management skill-building via phone-based motivational interviewing, and
3. Weekly monitoring of participants' adherence to PU management guidelines.

After the intervention trial is completed, participants from both control and intervention groups will be required to return at 3 months for postintervention assessment. Measures of skin care–specific knowledge and skills will be administered, including the Pressure Ulcer Knowledge Scale (PRES) (a 10-item measure to assess perceived skin care self-efficacy along the domains of skin hygiene, PU monitoring, and pressure relief techniques) and the PRMap, which is a behavior-mapping instrument. The purpose of these observations is to get an objective baseline and postintervention measurement of the level and degree of individual skills related to pressure relief techniques and to confirm that various pressure relief techniques are more effective for persons with various levels of injury and SCI experiences.

Step 5: Market skin sensor

As we develop knowledge about the interplay of sensor readings, pressure relief, and variations across individuals with different levels of SCI, we will work with key collaborators to develop a plan to transfer our sensor technology to markets where it can be broadly used. We envision use in seating evaluation and as a component of automatic PU risk alerting systems of the future

Conclusions

PUs remain a prevalent and costly secondary medical condition for people with SCI that has the potential to affect health, quality of life, function, and longevity. Preventive efforts have met with limited success as prevalence rates persist. Further, preventive efforts are hampered by a lack of high-quality evidence. In this 5-year project, we aim to add to the evidence base on effective measures of prevention, develop a skin sensor that will provide much needed information on skin perfusion and oxygenation, and, utilizing these core elements, develop and translate new information on the effects of pressure and pressure relief to people with SCI and the health care professionals caring for them.

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