**Priority Statement Title:** Link biomechanical load to development of diabetic neuropathic plantar ulcerations

**Priority Statement Code:** CJ1D

**Domain:** Cell/Tissue, Lower Extremity

## Priority Statement

### Background and Relevance

Provide background information and supporting statements that indicate the relevance and potential impact of the recommendation.

Over 20 million Americans are afflicted with chronic hyperglycemia and are diagnosed with diabetes melitus. Approximately 15% of those individuals will develop distal, symmetrical, peripheral neuropathy. Lacking the ability to feel pain, a theorized hypoxia allows a spontaneous destruction of dermal and epidermal sof tissue in 15% of diabetic, neuropathic individuals. Although a history of ulceration is a strong indicator of a subsequent ulcer (75% recurrence over 5 years), there are no reliable risk factors for development of the initial insult. Ulceration increases morbidity and mortality and over 50,000 of these wounds lead to amputation in the USA annually.

Gordois estimated the health care cost of treating the neuropathic manifestations of diabetes at around $10 billion annually based largely on the treatment of lower extremity ulcers and amputations.(Gordois, Scuffham et al. 2003) It is estimated that over half of these LEAs could be prevented through education and regular foot care although this goal is unmet.(Aguiar ME 2003) Neither the Center for Disease Control (CDC) nor the American Diabetes Association have identified a mechanism for the diabetic neuropathic ulceration (DNU) although reducing the incidence of these lesions is expected to reduce the number of LEAs.(CDC 2004) The World Health Organization and International Diabetes Foundation have met similar disappointments after issuing the St. Vincent Declaration. Because off-loading body weight is necessary to heal the ulcer, it is suggested the diabetic ulcer is caused by plantar loading.

Contact with the ground during gait progresses from the heel toward the toes as the body passes over each foot and as each heel lifts from the ground. Courtemanche determined diabetic neuropathic individuals walk slower with a shorter single support period (suggesting a shorter swing phase) than healthy individuals.(Courtemanche, Teasdale et al. 1996) Zhu and Wertsch determined a shuffling gait led to longer contact time, more contact area with the ground and lower pressures.(Zhu, Wertsch et al. 1991)

Some authors suggested the etiology of DNU wounds be investigated from the perspective of the dynamic process of gait.(Hayes and Seitz 1997; Shaw, van Schie et al. 1998; Edsberg, Mates et al. 1999; Abouaesha, van Schie et al. 2001; Cobb and Claremont 2002) Edsburg, et al, suggested prolonged high frequency cycling might be indistinguishable from static loads.(Edsberg, Mates et al. 1999) Dynamic studies included gait, strain rate of endothelial tissue and finite element models but these failed to explain the genesis of DNU.

A pilot study using a unique device to simultaneously apply a controlled compressive load to the hallux while simultaneously monitoring microvascular flow determined temporal characteristics for a postocclusive hyperemic response test in groups of individuals distingiushed by relative risk of plantar ulceration. The high risk group demonstrated a longer time to begin a hyperemic response on an order similar in timing of the swing phase of gait. The investigators of this study expect to assay diabetic, neuropathic individuals with no history of plantar ulcer and determine relative risk of initial ulceration.

Exercising this activity as a priority addresses a complication of a metabolic disease well known to the public. The etiology of ulceration is not elucidated in medical or scientific literature. Establishing a link between biomechanical loading and ulcergenesis provides an opportunity for technical biomechanists and clinical biomechanists to work jointly on an important public health issue.

Describe the primary opportunities and outcomes associated with the priority area.
This priority area investigates a theorized **relationship between a biomechanical process (gait and posture) and the effects of a metabolic disorder** (diabetes mellitus). This investigation presents the opportunity as a common pathway for biomechanist and clinician allowing each to understand and see direct benefit from collaborating with the other: Whe biomechanist sees a physiological consequence of tissue loading and the clinician realizes a new tool for diagnosis and determining prognosis in a high-profile disease state.
Successful implementation of this effort provides new objective parameters for risk of ulceration and for determining new therapeutic directions engineered to reduce the morbidity and mortality of diabetes mellitus.

Describe the nature and magnitude of the barriers influencing the priority area.
The concept is new and not well-understood, even in the context of non-diabetic individuals. There is no established test protocol or test device for this phenomenon. A pilot study used a unique prototype, precluding multiple investigation sites for subsequent studies.

**Objectives**

List the objectives of the recommendation.
1. Explore the phenomenological effect of loads experienced in gait and in quiet standing on blood flow wthin the microcirculation of the plantar skin.
2. Challenge the plantar skin with compressive loads leading to measure the post occlusive hyperemic response and estimate a composite mechanical properities of dermal soft tissue..
3. Analyze plantar pressure data to suggest potential sites for ulcer development.

Indicate the domains to be bridged for each objective.
Implementing this recommendation bridges cell tissue and lower extremity domains.

Identify the translational nature and/or opportunity of the recommendation.
If the potential of these new, objective techniques are realized, medical attention can be focused on individuals of higher risk and may provide insight into the link between biomechanical loading and the ulceration process. In order to investigate this phenomenon, the results of any test may be provided by a biomechanist and a vascular specialist, but interpretation of the results and clinical follow up must be provided by a physician or a team of medical professionals committed to long term care of the diabetic foot.

**Recommended Actions**

List the specific actions or a series of actions to be taken. Describe how each action relates to achieving an objective and/or overcoming a barrier.

1. To improve understanding of microvascular response to biomechanical loading, a new area of investigation and additional data is needed before a clinical trial is started. Microvascular response to compressive loads must be better understood in the context of healthy individuals before it can be applied to the pathological situation.

2. A determination must be made as to whether the discrepancy in starting a response to occlusion seen in the pilot study is due to a pre-existing micrivascular variant in the general population or the due to changes in soft tissue mechanics due to hyperglycemia.
3. Characteristic microvascular responses must be simultanously established for male and female subjects to account for gender related differences in microcirculation.
4. A multi-site study evaluating the microvascular response to physiological loads should be performed diabetic individuals with and without neuropathy and without a history of prior ulceration to determine if biomechanical parameters can determine risk of developing plantar ulceration.
5. In order to evaluate subjects at multiple sites, a new test device must be developed, validated and produced in sufficient quantity.
6. Multiple sites participating in this effort must validate the reliability of microvascular flow monitors, plantar pressure measures and temporal sequencing of gait. Standards for this effort must be publicly available or made to be so in order for others to investigate this phenomenon.

**References**

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