

**THE EARLY DETECTION OF DIABETIC PERIPHERAL NEUROPATHY:  
THE DEVELOPMENT AND VALIDATION OF A NOVEL  
SMARTPHONE APPLICATION**

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## ABSTRACT

The dissertation project developed and validated a novel smartphone application capable of measuring postural instability in individuals with Type 2 Diabetes (T2D) and Diabetic Peripheral Neuropathy (DPN). DPN is a common complication of T2D and is associated with impaired balance and increased risk of falls. Conventional diagnostic methods often rely on subjective reports or expensive equipment, limiting accessibility in many clinical and at-home settings. Given the widespread use of smartphones, this project explored whether a novel smartphone application using built-in sensors could detect subtle postural changes associated with DPN.

By leveraging smartphone accelerometers, Aim 1 demonstrated both construct and criterion-related validity of a custom application in relation to force plate center of pressure (COP) and motion capture system center of mass (COM) postural data. Participants completed quiet stance tasks under varying visual (eyes open/closed) and surface (firm/foam) conditions. The application demonstrated strong test-retest reliability within and across devices as well as high criterion-related validity. It was sensitive to changes in postural control across sensory conditions; however, no differences were found between each device when synchronously collecting postural data, supporting its use as a reliable, accessible measurement tool.

Aim 2 examined whether the application could detect differences in postural control between healthy individuals, individuals with T2D, and those with DPN. The smartphone successfully demonstrated the feasibility of using a validated application capable of detecting subtle postural changes across different diagnostic groups, specifically differentiating individuals with and without DPN using postural outcome measures.

Measures such as sway area and sway velocity were especially sensitive, highlighting the progressive impact of diabetic symptoms on balance and the critical role of multisensory integration.

Building on these findings, Aim 3 evaluated the application's diagnostic performance relative to the Utah Early Neuropathy Scale (UENS). By comparing the postural outcome measures for diagnostic performance against the established UENS in a "known groups" analysis, this investigation provides evidence supporting postural instability, particularly under sensory-challenging conditions, as a viable biomarker for early neuropathic dysfunction. Sway velocity emerged as a robust metric, capable of distinguishing between groups even in the early stages of neuropathy.

The findings suggest that postural sway metrics collected through a widely available and low-cost device could offer a practical solution for early screening and remote monitoring. This work laid the foundation for broader implementation of balance assessments in diabetic care, especially in underserved or resource-limited settings, with the goal of enabling earlier intervention, enhancing clinical judgment, and improving patient outcomes.

To Nasreen and Riaz Hussain,

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This is for you. Every accomplishment, every opportunity, every step forward is because of you. And it is my deepest honor to live the life you dreamed for me to have.

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## CHAPTER 1: INTRODUCTION

Diabetic Peripheral Neuropathy (DPN) remains one of the most prevalent complications associated with diabetes mellitus, often progressing insidiously until irreversible neural and functional deficits have occurred. Despite advancements in diagnostic technologies and interventions, the early detection of DPN remains a substantial clinical challenge. The research of this dissertation examined the use of postural instability as a straightforward yet quantifiable early indicator of DPN. To evaluate this concept, a novel smartphone-based application was developed and validated against gold-standard posturography tools, including motion capture and force plate systems, as well as a clinically validated assessment for peripheral sensory loss, the Utah Early Neuropathy Scale (UENS).

By shifting focus to balance impairments that may precede detectable sensory deficits, this research proposes a novel approach to early screening and clinical decision-making. The integration of smartphone-based technology into routine assessments could facilitate the timely identification of at-risk individuals and support more targeted interventions, thereby improving patient outcomes.

The following sections will provide important background on diabetes and DPN, current diagnostic and treatment approaches, the gaps that remain in care, and the potential for novel technological solutions, such as smartphone-based assessments, to address these challenges. Through this work, the dissertation aimed to make a meaningful contribution to diabetic care and management, specifically using postural instability as a component in early neuropathy detection.

## Diabetes

Diabetes has become a global public health crisis, affecting approximately 415 million individuals worldwide.<sup>1</sup> In the United States alone, diabetes affects more than 37.3 million people, of which 90-95 percent of cases in adults are classified as Type 2 Diabetes (T2D).<sup>2</sup> Diabetes has been defined as a chronic metabolic disorder characterized by persistent hyperglycemia.<sup>3</sup> It can be diagnosed using common clinical tests such as the A1C test, which provides the average blood glucose levels for the last 2-3 months, or a Fasting Plasma Glucose test, which measures blood glucose for a singular point in time. In either test, elevated levels provide an indication of pre-diabetes or diabetes.

By 2045, diabetes is projected to affect more than 700 million individuals globally.<sup>4</sup> Racial and ethnic minorities have a higher prevalence of T2D than non-minority individuals, with the highest prevalence among American Indians/Alaska Natives (14.7%), Hispanics (12.5%), and non-Hispanic blacks (11.7%) in comparison to White Americans (7.5%).<sup>2</sup> The onset and complications of diabetes are influenced by biological, clinical, health system, and social factors,<sup>2,5</sup> and result in a myriad of poor outcomes.<sup>6</sup> It is estimated that 25% of total health care costs are spent on individuals with diabetes.<sup>7</sup>

Without proper care and management, diabetes increases the risk of developing additional complications such as neurological, peripheral, cardiovascular, renal, endocrine/metabolic, and ophthalmic dysfunction. This places both direct and indirect burdens on the health system.<sup>6,7</sup> Significant disparities in diabetes-related lower extremity amputations have been identified based on factors such as race, ethnicity, sex, age, residential area characteristics, income levels, and hospital characteristics. These disparities highlight the complexities of addressing this issue.<sup>8</sup> These poor outcomes

contribute to diabetes being the eighth leading cause of death in the United States.<sup>9</sup> Hence, education, accessible treatment options, and management in high-risk populations are essential for reducing the rates of diabetes and the complications associated with this chronic disease.<sup>10–13</sup>

### Diabetic Peripheral Neuropathy (DPN)

Diabetes is associated with many systemic health issues, several of which are peripheral nervous system disorders. The most common complication is DPN,<sup>2,5,12</sup> a microvascular complication experienced by more than 50% of all individuals with diabetes, which develops within 25 years of their initial diagnosis.<sup>14</sup> Diabetic peripheral neuropathy primarily causes neurodegeneration of the small and large nerve fibers in the extremities,<sup>12,15–19</sup> and traditionally presents itself in a “glove and stocking” distribution.<sup>15,20–22</sup> If left undiagnosed or unmanaged, large fiber degeneration associated with DPN can increase negative outcomes,<sup>1,2,5,10,12,23</sup> and is a critical risk factor in developing foot infections, ulcerations, and amputations.<sup>24–29</sup> Among those who develop DPN, 25% of those individuals will also develop a foot ulceration.<sup>30</sup> Approximately 50% of all diabetic foot ulcers become infected,<sup>25–28,31</sup> and among those, nearly 20% result in non-traumatic lower-limb amputations.<sup>8,25,28,31</sup>

Poor outcomes attributed to DPN can be prevented with early diagnosis and treatment.<sup>32–34</sup> However, due to its insidious nature, DPN is often unnoticed by both the patient and physician until the physical signs are apparent and irreversible nerve damage has already occurred.<sup>16,17,35,36</sup> The American Diabetes Association (ADA) recommends annual foot examinations and neuropathy screenings starting after the diagnosis of T2D.<sup>37</sup> However, at a national level, the CDC found only a 52% compliance rate among general

care clinics in 2019 in the United States.<sup>38</sup> Failure to comply with the ADA's preventive measure recommendations is believed to be the result of a lack of awareness of DPN symptoms, a lack of training to utilize instrumentation, lack of appropriate equipment, and a lack of time during appointments to perform the examination.<sup>39-41</sup> **With the proper intervention and preventative measures for addressing large fiber degeneration in DPN, poor outcomes such as ulcerations can be reduced by 50%, which could ultimately reduce the number of non-traumatic lower leg amputations.**<sup>30,42</sup>

### Functional Balance and Postural Control

Many injuries and diseases, including diabetes, can alter postural control and increase the risk of falls in adults. Diabetes arises from the dysregulation of metabolic pathways, which can then lead to segmental demyelination and axonal degeneration of the distal nerve fibers of the extremities.<sup>43,44</sup> This process ultimately contributes to DPN and presents itself with an array of signs and symptoms ranging from loss of protective sensation in the limbs,<sup>45</sup> muscular weakness,<sup>46-49</sup> decreased nerve conduction velocity and amplitude,<sup>45,50-52</sup> and insensate feet.<sup>12</sup> These symptoms have a detrimental effect on one's functional ability, as large afferent (1A/B) fibers are critical inputs involved in producing complex patterns to control and counteract external forces during postural control.<sup>53</sup>

Human balance involves maintaining and restoring balance to a state of equilibrium and upright orientation.<sup>54</sup> Spinal and supraspinal neural circuitry involved in this process,<sup>55</sup> receive constant sensory feedback from the visual, somatosensory, and vestibular systems, which help guide the motor responses for postural stabilization. Even during unperturbed quiet stance, small postural fluctuations reflect motor activity that is needed to maintain the body's center of mass safely within its base of support.<sup>56</sup> There are many reasons for

postural instability, including age, metabolic, and neuromuscular dysfunction. Changes in postural stability may be subtle and are often compensated in routine activities of daily living (ADL), as our bodies are constantly adapting and reweighting sensory inputs to maintain balance. As fall-risk factors increase, the likelihood of postural instability also rises. Therefore, postural deficits are often only noticeable after a fall has occurred. This reactive approach to falls leads to considerable medical costs. In the US alone, the costs related to falls are expected to exceed \$100 billion annually by 2030.<sup>57</sup>

Falls in the general aging population are internationally recognized as a significant public health issue, with one in every three older adults experiencing a fall each year.<sup>58</sup> In diabetic communities, falls are a greater clinical risk. Adults with DPN have been shown to have up to a 20-fold increase in instability when compared to age-matched healthy controls,<sup>59,60</sup> due to peripheral sensory loss in the feet and motor system deterioration. Previous research has established DPN as a strong predictor of postural instability and fall risk.<sup>61-65</sup> Among neurological populations, those with peripheral neuropathy report to be categorized as the third highest rate of falls.<sup>66</sup>

Traditionally, balance and postural control have been assessed through subjective clinical tests, such as the Romberg test and the Timed-Up and Go (TUG) test, or instrumented/computerized tests, such as the Sensory Organization Test.<sup>67-69</sup> Such instruments may include kinetic (e.g., center-of-pressure: COP) and kinematic (center-of-mass: COM) metrics to derive variables such as postural sway area and sway velocity.<sup>70,71</sup> In research settings, criterion measures for COM and COP include motion capture systems and force plates; however, each has its own limitations. Most notably, the qualitative tests can be subjective and or have low inter-/intra-rater reliability, while the professional-grade

instrumented methods require expensive equipment, a trained clinician, and dedicated space. Together, these factors limit the accessibility of objective fall risk detection and, as a result, the state of the disease progression may not be recognized until it's too late.<sup>72</sup>

Due to the etiology, postural instability and fall risk in adults with diabetes is beginning to gain broader recognition in clinical and research settings.<sup>64,73-75</sup> Corriveau et al. used a force plate to demonstrate clinically significant postural instability in T2D individuals with DPN compared with a group of age-matched healthy elderly controls.<sup>76</sup> However, **individuals with diabetes do not always report their unsteadiness as a clinical problem because they do not recognize it to be potentially caused by DPN; rather, they may simply excuse it as a byproduct of age.** Vileikyte et al. found 23% of 484 patients with DPN perceived themselves as being unsteady only when asked specifically about it.<sup>77</sup> **As such, clinicians must often rely on subjective recollections concerning falls and instability.** This is a detrimental gap between patients with diabetes and clinical providers in the prevention of falls and potentially the early detection of large fiber degeneration associated with DPN.

#### Diagnostic Tools for Diabetic Peripheral Neuropathy

Depending on the severity and progression of DPN, small fiber (temperature and pain)<sup>15,34</sup> and large fiber (fine touch, vibration) sensory nerve loss traditionally will present itself in a glove and stocking distribution starting distally and progressing proximally in the affected limbs. **Two main factors are essential for diagnosing DPN: a careful medical history and a detailed physical examination.**<sup>78</sup> Unfortunately, the symptomology associated with DPN is highly variable from patient to patient, making standardized assessments difficult.<sup>78</sup> Commonly used clinical tools to assess nerve function

include the gold standard Nerve Conduction Velocity (NCV) test, which measures the affected nerves' ability to conduct an electrical impulse from a starting point to an endpoint.<sup>79</sup> The other assessments commonly used in clinical spaces are the Semmes-Weinstein monofilament examination, the vibration perception threshold test using a 128-Hz tuning fork, the Achilles tendon reflex assessment, and physical examination of the foot. These assessments are often combined to determine the severity of sensory deficits that may exist in the foot or limb, and the combination of more than one assessment with another has demonstrated an 87% sensitivity in detecting DPN.<sup>80,81</sup>

The Utah Early Neuropathy Scale (UENS) is a physical examination scale developed specifically to quantify the early stages of DPN and detects modest changes in the severity and distribution of sensory loss.<sup>33</sup> Additionally, the UENS is unique because it contains a combination of validated clinical measures for both large and small fiber neurodegeneration. Among individuals with existing neuropathy, the UENS closely correlates with that of the established scales, including the Michigan Neuropathy Screening Instrument (MNSI)<sup>40</sup> and the Neuropathy Impairment Score–Lower Leg (NIS-LL),<sup>82</sup> providing further support for its validity. In a study conducted by Singleton et al., the UENS demonstrated a high level of interrater reliability, with an interclass correlation of 94% and showed a significant correlation with both MDNS and NIS-LL ( $p < 0.01$ ).<sup>33</sup> Additionally, confirmatory tests were used to diagnose neuropathy, including nerve conduction studies (NCS) of the sural and peroneal nerves, skin biopsy for determination of intraepidermal nerve fiber density (IENFD), quantitative sudomotor axon reflex testing (QSART), and quantitative sensory testing (QST). Results demonstrated that the UENS was more strongly correlated with confirmatory tests than either MDNS or NIS-LL.

Furthermore, within this cohort, the UENS outperformed both MDNS and NIS-LL in receiver operating characteristic (ROC) analysis across various scores, achieving a sensitivity of 92%, which was higher than MDNS (67%) and NIS-LL (81%), without compromising specificity.<sup>33</sup>

That said, many pitfalls currently exist in the diagnosis of DPN. Some of the biggest factors to consider are that these diagnostic tools and techniques require a clinical setting with a trained specialist to perform the examination and specialized equipment that is not always available in general care facilities.<sup>40,83,84</sup> In general care facilities, both the patients and providers often lack awareness of DPN symptoms and/or lack the time during appointments to perform the examination.<sup>39-41</sup> This makes it increasingly challenging to detect DPN in its early stages. **As it currently stands, DPN is underdiagnosed and undertreated in US primary care settings,<sup>85-87</sup> missing potential opportunities for early intervention and prevention of poor outcomes associated with DPN.<sup>87</sup>** In many of the commonly used diagnostic measures and tools, there is a big emphasis on subjective clinical expertise. In one study investigating general physicians' perceptions of the diagnosis of DPN, results indicate that there was only a 14% concordance with the monofilament testing and visual examination of the foot. Furthermore, there was minimal success in diagnosing mild/moderate neuropathy compared to severe neuropathy.<sup>87</sup>

If postural instability caused by large fiber degeneration can be caught during the early stages, as might be indicated by incremental postural changes over time that might not be obvious in day-to-day activity, there is potential to catch DPN before late-stage degeneration has occurred and poor outcomes become inevitable. While there is a myriad of tools and measures that have been validated for the diagnosis of DPN, they all share the

same pitfalls that ultimately contribute to DPN being underdiagnosed and untreated in US primary care settings. The first step in alleviating this is the creation of an objective, time-efficient, patient-driven assessment that has the possibility to be used both at home by a patient or in a clinic by a provider to enhance clinical judgment.

### Leveraging Smartphone Sensors to Measure Postural Instability

Current DPN diagnostic tools investigate mechanisms revolving around sensory detection. Balance assessments are not considered components of DPN diagnosis and management despite the consensus that DPN affects sensation in the lower limbs and the somatosensory system.<sup>76,88-90</sup> With the growing advancements in technology, smartphone devices are becoming a promising tool to assess postural control<sup>91-95</sup> as they are embedded with electronic accelerometers and gyroscopes to measure motion in six degrees of freedom.<sup>91,92</sup> This has led to novel approaches to measure balance with minimal expertise objectively.<sup>95-102</sup> As of 2023, it is estimated that 92% of the US population owns a smartphone device, making them a convenient and accessible tool.<sup>103</sup> However, to make smartphone IMUs effective for clinical applications, it is crucial to evaluate their validity, reliability, and sensitivity in comparison to gold-standard laboratory and clinical assessments.

To date, many studies have demonstrated the validity of smartphone inertial measurement units (IMUs) for posturography against gold-standard instrumentation (e.g., force plates, motion capture systems, and accelerometers).<sup>92,93,97,100,104-106</sup> Nonetheless, these studies differ considerably in their approaches (e.g., postural tasks, device placement, and orientation), equipment used, and populations tested.<sup>92,93,104-107</sup> Given the increasing consensus that smartphone-based IMUs can serve as effective tools for measuring human

movement, a considerable body of research has emerged over the past decade to assess their functionality.<sup>92,104,108–112</sup>

Preliminary results and previous research suggest that postural measures collected through IMUs in smartphone devices may provide a sensitive means of measuring subtle balance deficits in clinical settings. To accomplish the current aims, pilot research by Hussain and Wright (2025) was conducted and published utilizing various methodologies to investigate the integrity of an iPhone 14's IMUs when using a custom application as a tool to measure postural stability in adults ( $N = 22$ ).<sup>112</sup> Results of the study demonstrated validity, inter- and intra-reliability, and sensitivity of a novel smartphone application by testing various postural conditions and comparing data to validated research-grade posturography instruments. This is essential for the smartphone application to be accepted and trusted by clinicians and researchers.

Specifically, within T2D and DPN communities, a body of research has emerged regarding postural instability and IMUs. Najafi et al. demonstrated that DPN patients exhibit significantly greater COM sway than healthy individuals for both eyes open (EO) and eyes closed (EC) conditions ( $p < 0.005$ ) when accelerometers were worn on the lower back and shins. The difference became highly pronounced while eyes were closed.<sup>90</sup> Fernandes et al. conducted a study investigating smartphone IMU-based measurements of static balance control and mobility (TUG) in T2D participants and an age-matched control group with no occurrence of DPN.<sup>113</sup> Results demonstrated motor impairments worsened in the T2D group when compared to the control cohort, and postural instability caused by T2D could be identified using the IMUs from smartphone devices.

The apparent disconnect between the time of diagnosis of diabetes and the detection of the first signs of large fiber degeneration associated with DPN represents a critical gap in the healthcare continuum for this population. **Using an affordable, portable, easy-to-use device, such as a smartphone, that measures balance and fall risk could meet an essential need for high-risk diabetes patients who have limited access to clinical resources.** These factors led to the specific aims of this project, which focused on developing and validating a smartphone application for the early detection of postural instability in individuals with DPN.

### Specific Aims

The following dissertation explores postural instability as an indicator for the early detection of large fiber degeneration associated with DPN. To achieve this, Aim 1 focuses solely on the development and validation of the smartphone application relative to validated lab-based motion capture and force plate systems. Aim 2 investigates the normalized postural control values among individuals with T2D (with and without DPN) using the novel smartphone application. Lastly, Aim 3 explores the validation of the smartphone application relative to the Utah Early Neuropathy Scale, a validated measure for the early detection of DPN, guided by the findings of Aim 2.

**Aim 1: Develop and validate a novel smartphone application relative to the validated research-grade posturography techniques.**

*H1.1: There will be test-retest reliability of the smartphone application within and across devices and criterion-related validity when compared to the gold-standard force plate and motion capture systems.*

*H1.2: The smartphone application will be sensitive to differences in postural stability known to occur when comparing eyes closed to eyes open quiet stance.*

In preparation for the aim, and as noted above, we developed and validated a novel smartphone application, testing it on a small cohort ( $N = 22$ ) of adults between the ages of 20-60 years.<sup>112</sup> By using a wide age range, kinematic data across balance tasks were used to test both the upper and lower sensitivities and limitations of the iPhone IMUs when measuring postural sway during quiet stance. Results highlighted that the novel smartphone application demonstrated strong validity and agreement with gold-standard instruments, reliability across and within trials and conditions, and was sensitive to postural stability for both visual and surface conditions. In this aim, criterion and construct validity will be explored to further establish the smartphone IMUs and custom smartphone application as a valid, reliable, and sensitive instrument when compared to lab-grade gold standards (motion capture and force plate systems). Participants ( $N = 42$ ) will be instructed to perform quiet stance during varying visual (eyes open and eyes closed) and surface (firm and foam) conditions while three types of instrumentation synchronously collect postural data. Postural outcome measures (sway area and sway velocity) in varying visual and surface conditions will be compared between and within each of the three devices.

**Aim 2: Determine normalized postural control values for individuals with and without type 2 diabetes (T2D) using the novel smartphone application.**

*H2.1: Individuals with diabetes will have statistically more postural instability across conditions when compared to age-matched healthy controls.*

Building upon data collected in Aim 1, participants ( $N = 42$ ) will be categorized based on diagnosis group: (1) healthy age-matched controls, (2) individuals with T2D with, (3) and without DPN. For the proposed study, postural outcome measures (sway area and sway velocity) in varying visual and surface conditions will be compared between each cohort. Additional analysis will be conducted to determine if covariates, such as years since diabetes diagnosis and BMI, have a statistically significant moderating effect on the main postural outcome measures.

**Aim 3: Validate the smartphone application for early detection of DPN when compared to a validated early diagnostic functional assessment.**

*H3.1: There will be a strong correlation between the sensitivity of the lower extremities, as measured by the Utah Early Neuropathy Scale (UENS), and postural outcome measures, as measured by the smartphone application.*

DPN is a progressive condition that affects the body over time. One of the hallmark symptoms of DPN is the inability to feel one's feet and, in more chronic cases, one's lower extremities. Previous research has established DPN's effect on functional balance.<sup>76,88-90</sup> As such, Aim 3 will explore the validity of the novel smartphone application when data obtained from it (Aim 2) is compared with the UENS score. A Sensitivity and Specificity Analysis using a Receiver Operating Characteristic (ROC) Curve<sup>114,115</sup> will be applied in a series of "known group" analyses, including those with and without neuropathy and subgroup analyses (healthy vs. T2D, healthy vs. DPN, and T2D with vs. without DPN). The accuracy of the smartphone and UENS will be compared using a modified version of DeLong's test based on the difference in paired AUC curves estimated by the non-

parametric method,<sup>116</sup> with a “non-inferiority” expectation when comparing the smartphone application to the UENS.<sup>117</sup>

## CHAPTER 2: THE DEVELOPMENT AND VALIDATION OF A NOVEL SMARTPHONE APPLICATION TO DETECT POSTURAL INSTABILITY

Parts of this chapter have been previously published in the *Sensors MDPI Journal* <sup>112</sup>

### Introduction

Human balance involves maintaining and restoring balance to a state of equilibrium and upright orientation.<sup>54</sup> Spinal and supraspinal neural circuitry involved in this process<sup>55</sup> receive constant sensory feedback from the visual, somatosensory, and vestibular systems, which help guide the motor responses for postural stabilization. Even during unperturbed quiet stance, small postural fluctuations reflect motor activity that is needed to maintain the body's center of mass safely within its base of support.<sup>56</sup> There are many reasons for postural instability, including age, metabolic, and neuromuscular dysfunction.<sup>118</sup> Changes in postural stability may be subtle and can often be compensated in routine activities of daily living (ADL), because our bodies are constantly adapting and reweighting sensory inputs to maintain balance. However, as fall-risk factors increase, the likelihood of postural instability increases, so it is often only after a fall has occurred that postural deficits are noticeable. This reactive approach to falls leads to considerable medical costs. In the US alone, the costs related to falls are expected to exceed \$100 billion USD annually by 2030.<sup>57</sup>

Traditionally, balance and postural control have been assessed using clinical tests such as the Romberg test (subjective) and Timed-Up and Go (TUG), or instrumented or computerized tests such as the Sensory Organization Test.<sup>67-69</sup> These objective measures include kinetic (e.g, center-of-pressure: COP) and kinematic (center-of-mass: COM) metrics to derive variables such as postural Sway Area and Sway Velocity.<sup>56,71</sup> In research settings, criterion measures for COM and COP include motion capture systems and force

plates. However, each has its own limitations. Most notably, the qualitative tests can be subjective and or have low inter-/intra-rater reliability, while the quantitative methods require expensive equipment, a trained clinician, and/or dedicated space. Together, these factors limit the accessibility of objective fall risk detection and, as a result, may not be recognized until it's too late.<sup>72</sup>

In the last decade, advances in smartphone technology have created the potential for balance screening tools because of their built-in inertial measurement units (IMUs) with the capacity to measure movements in six degrees of freedom with great accuracy. This has led to novel approaches to objectively measure balance, which may require minimal training or expertise to perform.<sup>95–102</sup> As of 2023, it is estimated that 90% of the US population owns a smartphone device, making it a convenient and accessible tool.<sup>103</sup> However, to make smartphone IMUs effective for clinical applications, it is crucial to evaluate their validity, reliability, and sensitivity in comparison to gold-standard laboratory and clinical assessments. To date, few studies have validated smartphone IMUs for posturography against gold-standard instrumentation (e.g., force plates, motion capture systems, and accelerometers)<sup>92,93,97,100,104–106</sup> and those that have, vary considerably in approach (e.g., postural tasks, device placement and orientation), equipment used, and populations tested.<sup>92,93,104–107</sup>

Given the increasing consensus that smartphone-based inertial measurement units (IMUs) can serve as effective tools for collecting human movement, a considerable body of research has emerged over the past decade to assess their functionality. Ozinga et al., used an iPad application and found it was significantly correlated ( $r = 0.89–0.99$ ) with their 3D motion capture measurements during quiet stance.<sup>108</sup> When both gait and standing

posture was evaluated with an iPod Touch against standalone accelerometers, results demonstrated strong correlations ( $r = 0.85-0.99$ ) and a good to excellent degree of reliability ( $ICC = 0.78-0.99$ ).<sup>109</sup> Cerrito et al. additionally evaluated their Android application against force plate measurements on a sit-to-stand test, in which strong correlations ( $r = 0.86-0.93$ ) and reliability ( $ICC = 0.42-0.96$ ) were observed.<sup>110</sup>

More recently, Grouios et al. assessed the validity and reliability of acceleration data from across three smartphones of different makes and models against a motion capture system during various gait trials. The study demonstrated no statistically significant differences in mean acceleration values between the devices. Additionally, for the smartphones evaluated, the study demonstrated that devices were both valid and reliable for estimating acceleration when compared to an established gold standard.<sup>111</sup> These findings align with other studies that have compared the performance of IMU sensors in smartphones to gold-standard instrumentation. Frechette et al. compared their Android application with research-grade accelerometers and found strong correlations between the outputs from both devices across various balance tasks ( $\rho = -0.75$  to  $1.00$ ;  $p \leq 0.01$ ).<sup>104</sup> Hsieh et al. reported moderate to high correlations ( $\rho = 0.42-0.81$ ;  $p < 0.01-0.05$ ) when comparing a force plate system to an Android application during quiet stance.<sup>92</sup> These results are promising, as the outcome of a smartphone application that accurately measures balance could meet an essential need for high fall risk populations who have limited access to clinical resources.

Using an affordable, portable, easy-to-use device, such as a smartphone, opens the potential for at-home or clinical assessments without the initial need for a clinician. The purpose of this study was to develop a novel smartphone application and validate it relative

to research-grade posturography instrumentation (i.e., motion capture and force plate systems). Demonstrating construct and criterion-related validity of a smartphone application relative to gold-standard posturography devices will help substantiate its potential for clinical applications.

## Methodology

Forty-two participants (demographic data, see Table 2.1) who were free from any pre-existing condition that may have altered their ability to balance normally were tested in a single session, repeated-measures design study.

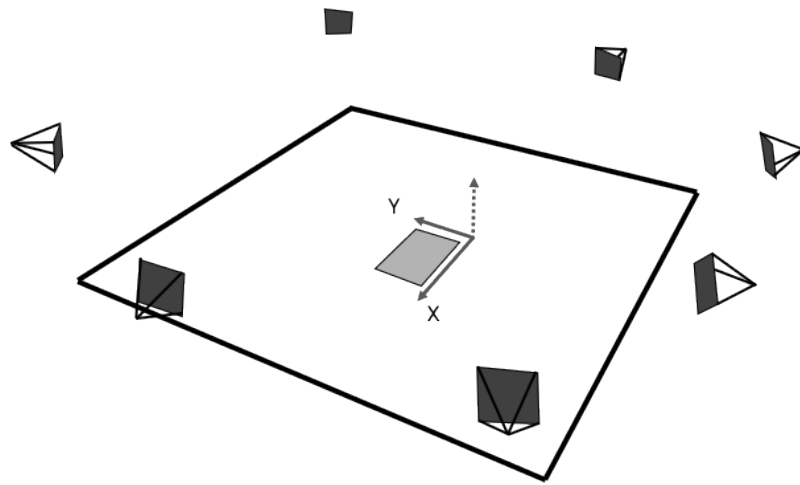
To be eligible, participants had to be: 1) between 30-60 years of age, and 2) able to give informed consent. Exclusion Criteria was as followed: 1) lower limb or musculoskeletal injury or amputation which affects balance, 2) clinically significant orthopedic, muscular, or neurological (excluding peripheral neuropathy) disability that affect their ability to perform the postural task protocol, 3) inability to stand independently for at least 10 minutes, 4) individuals who suffer from substance abuse, 5) currently pregnant, 6) vitamin B deficiency.

The Temple University Institutional Review Board approved the procedures, and all participants provided informed consent prior to participation.

### *Instrumentation and Data Processing*

Quiet stance was measured using (1) a smartphone device (Apple iPhone 14, Apple Computer Inc., Cupertino, CA, USA), (2) a 7-camera motion capture system (Motion Analysis System, Inc., Santa Rosa, CA, USA), and (3) a force plate (Bertec corporation, Columbus, OH, USA). In each test trial, postural data was collected simultaneously from the three electronically synchronized devices (see Figure 2.4). To synchronize each of the

three devices during data collections, the smartphone was linked to a local desktop over WIFI (IP address) using a TCP/IP protocol and a custom Python script (Version 3.12). A Macro Recording application (Macro Recorder, Bartels Media Inc., Version 2.0.79) was used to send a signal to the motion capture system, force plate system, and smartphone device's user interface to begin each data collection trial. Previous research has typically achieved synchronization through a post-processing methodology.



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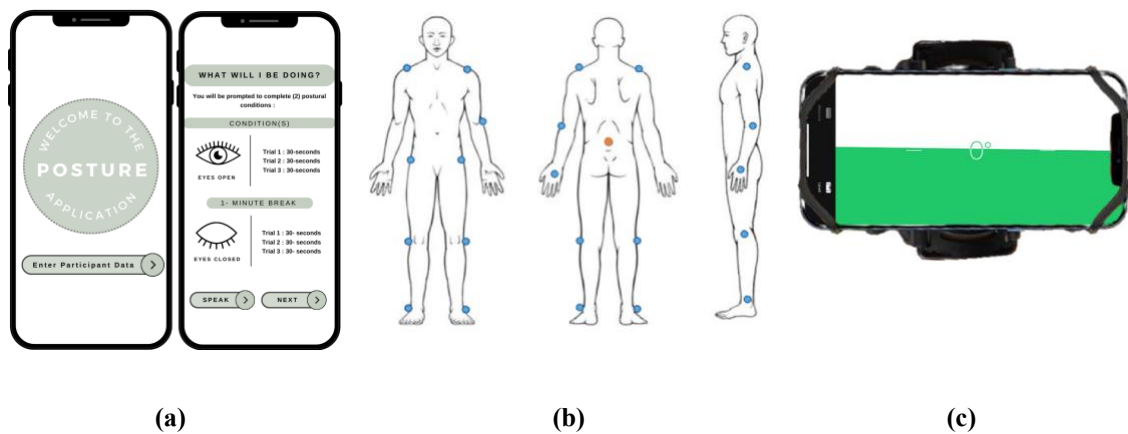
**Figure 2.1.** Illustrates the research equipment set-up as data was collected synchronously via the force plate and motion capture systems, and the novel smartphone application.

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### *Smartphone Application*

A smartphone application was developed for an iPhone 14 using XCODE (Apple Computer Inc., Cupertino, CA, USA), Apple's integrated development environment for Mac iOS. A single iPhone 14 was used to collect kinematic postural sway metrics.<sup>119</sup> The built-in IMUs in the smartphone are capable of detecting movement in 6-degrees-of-freedom, with the primary axes of measure for this study being linear displacement along the intrinsic axes of the smartphone, defined as  $x$  (width),  $y$  (length), and  $z$  (thickness)<sup>94</sup>

Pilot testing revealed that the iPhone’s  $z$ -axis maintained the same accuracy regardless of the orientation, and thus was used to collect anterior–posterior (AP) displacements. However, there were significant differences in the IMU sensitivity for the other two axes. When measuring medial–lateral (ML) postural motion, the smartphone’s correlation with the research-grade motion capture measurements were significantly lower for  $x$  ( $r = 0.12–0.71$ ;  $p < 0.05$ ) than  $y$  ( $r = 0.64–0.89$ ;  $p < 0.05$ ). Therefore, the smartphone was oriented horizontally (Figure 2.2c), such that the  $z$ - and  $y$ -axes were the primary axes used to estimate the COM movement.



**Figure 2.2.** (a) The smartphone application user interface (b) Motion capture markers placed on the participant’s body, where the orange dot illustrates the marker located on top of the smartphone device at the L5 region. (c) The smartphone orientation secured using a belted phone holder.

Prior studies using IMU’s have attached the sensor to the lower back to estimate the motions of the center of gravity.<sup>120–123</sup> As such, the smartphone was positioned at the participant’s L5 to approximate COM position,<sup>107,124</sup> and securely fastened to the waist via a modified running belt (VUP Phone Holder) (Figure 2.2c). The phone belt served two purposes: (1) standardizing the location of the smartphone; and (2) mitigating the horizontal component of the gravity vector due to any tilt of the device that would affect

the accelerometers in the horizontal measurement axis. The smartphone level was determined using the Measure application (a preloaded application in iOS) to ensure the absence of tilt prior to data collection (Figure 2.2c). In addition, any constant bias in the signal due to the gravity component was subtracted out during post-processing by normalizing the dataset (i.e., subtracting the average of the samples in a trial from each individual sample in the trial). Ghislieri et al.<sup>125</sup> points out that very little to no information is provided in the literature about how misalignment of sensor axes might affect the measurements, particularly for gravity's influence on the ML and AP axes. However, because even small misalignments could lead to measurement errors, we followed their guidance of using a more rigorous approach to orienting the sensor axes in relation to the global reference frame.

The smartphone's accelerometers were sampled at an average of 100 Hz. The raw acceleration data from the device was collected using the Application Programming Interface (API) and the CoreMotion Library provided by Apple.<sup>119</sup> During post-processing, high-frequency noise was filtered from the data with a 4<sup>th</sup> order low-pass Butterworth filter using a custom MATLAB R2022a script. Positional data was derived using a double-integration method during the post-processing step following filtering.

#### *Motion Capture (MC)*

A seven-camera motion capture system (Motion Analysis System, Inc., Santa Rosa, CA, USA) was used to collect body kinematics. Eleven reflective passive markers were placed on each participant in the following locations: left and right acromion processes, left elbow, left hand, the left and right anterior superior iliac spine (ASIS), left and right lateral patella, left and right lateral malleoli, and the L5 (placed on top of the smartphone

see Figure 2.2b). This model assumes the body is a single-link inverted pendulum<sup>126</sup> and the lumbar marker was used to approximate COM position<sup>107,120–123</sup> to derive the postural metrics for analysis. The position from the motion capture system was sampled at an average of 100 Hz and processed with a 4<sup>th</sup> order low-pass Butterworth filter using a custom MATLAB script.

#### *Force Plate (FP)*

A force plate with Digital Acquire 4.1.20 software (Bertec corporation, Columbus, OH, USA) was used to collect kinetic center of pressure (COP) data in the ML and AP directions. The COP time series data from the force plate was sampled at an average of 1000 Hz. It was exported and processed with a 4<sup>th</sup> order, low-pass Butterworth filter at a cutoff frequency of 10 Hz using a custom MATLAB script.<sup>127</sup> COP was transformed into a COM estimate using an established single-link inverted pendulum model, which applies a zero-phase low-pass filter to the time series data.<sup>127,128</sup>

#### *Postural Formulae*

Using normalized and filtered data, Sway Area was derived using a Principal Component Analysis (PCA) and the following equation:

$$\text{Sway Area} = \pi * a * b \quad (1)$$

where  $a$  = the maximum and minimum of the major axis and  $b$  = the maximum and minimum of the minor axes.<sup>129,130</sup> The major and minor axes were determined based on the AP and ML displacements of the L5.

Sway Velocity was derived using the following equation:

$$\text{Sway Velocity} = \frac{\sum_{i=1}^n \sqrt{\frac{(z_{(i+1)} - z_i)^2 + (y_{(i+1)} - y_i)^2}{t_{(i+1)} - t_i}}}{n} \quad (2)$$

where  $z_i$  and  $z_{(i+1)}$  are the AP coordinates of two consecutive samples, and  $y_i$  and  $y_{(i+1)}$  are the ML coordinates of the two consecutive samples. The Pythagorean distance between two consecutive samples was calculated and then divided by the time ( $t$ ) between the samples ( $t_{(i+1)} - t_i$ ) to obtain the instantaneous velocity between the consecutive samples. The Sway Velocity was then calculated from an average of these instantaneous velocities. The force plate data was downsampled from 1000 Hz to 100 Hz after filtering to synchronize data with the smartphone and motion capture systems. This ensured the consistent timing across all data sources, thus avoiding any discrepancies in the sampling rates.

The Somatosensory Ratio was derived using the following equation based on the visual conditions for each postural outcome measure (Sway Area and Sway Velocity):

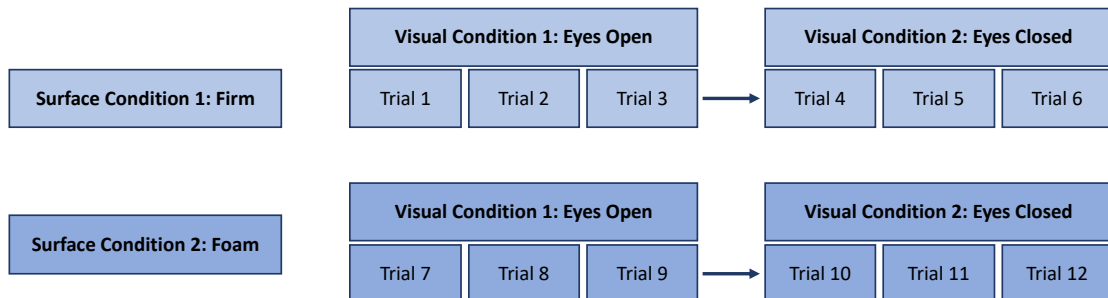
$$\text{Somatosensory Ratio} = \frac{(\text{eyes closed})}{(\text{eyes open})} \quad (3)$$

#### *Postural Task and Protocol*

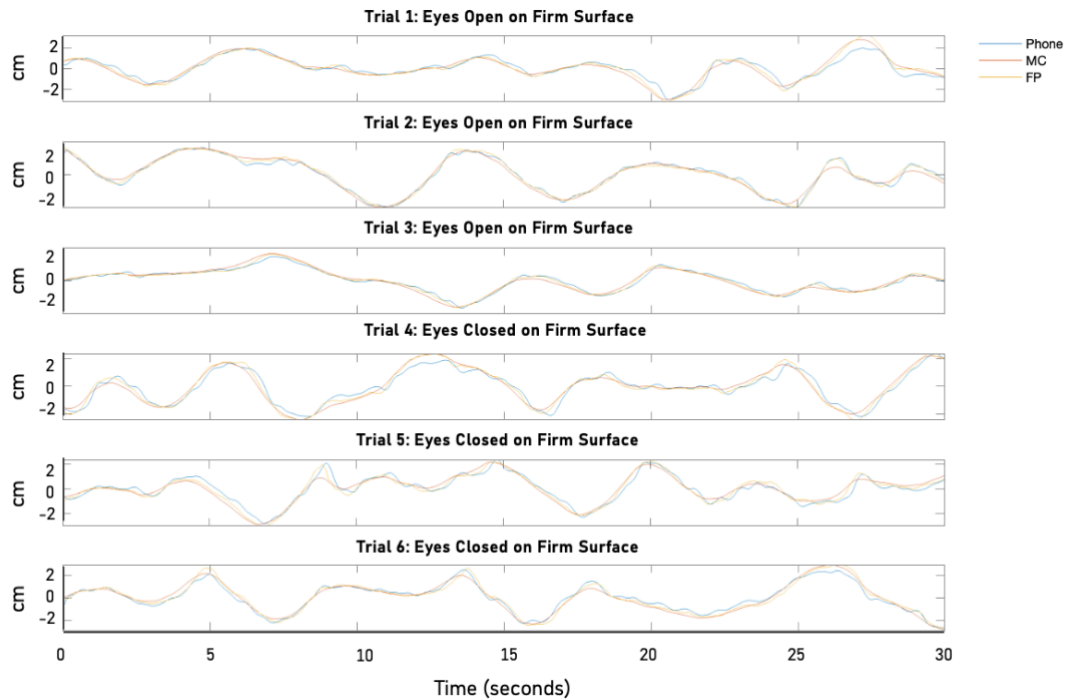
Participants were instructed to stand still and upright with their feet hip-width apart and their hands crossed over their chest, wearing a modified running belt around the waist

to securely hold the iPhone in place. The postural task focused on the instrumented version of the Modified Clinical Test of Sensory Interaction in Balance (mCTSIB), measuring each participant’s COP using the force plate system and the COM using the motion capture system. These instruments served as our criterion measure against which the custom smartphone application was compared.

Postural data was collected during a single 60-minute session, with each participant performing 12 postural trials in the same prescribed order (Figure 2.3). During the session, all participants were instructed to stand barefoot on a firm and then a foam surface. The trials were collected while the participants were standing on a force plate (or with foam placed on top of the force plate), while collecting the COP, 3D translation of the L5 marker, and 3D translation of the smartphone attached to the waist. Three 30-s trials for each visual condition were collected, with a 1-min break between eyes open (EO) and eyes closed (EC), for a total of 6 trials per surface condition (Figure 2.3). Testing both visual (EO and EC) and surface (Firm and Foam) conditions in the research design provided a gauge of the sensitivity and accuracy of the smartphone sensors during highly stable conditions (e.g., EO–Firm) and potentially unstable conditions (e.g., EO–Foam) for validation purposes.



**Figure 2.3.** The order of testing for each participant. Firm surface and Eyes Open visual conditions were performed first during each data collection session, then repeated on the foam surface condition. A total of twelve 30-second trials were administered in a set order to each participant.



**Figure 2.4.** Time-series plots illustrating the postural movement data (AP sway) collected using three synchronized instruments from one representative participant tested in trials 1–6.

Surface conditions were implemented to test whether the participant's vestibular and visual systems were intact and if poor balance was primarily a result of somatosensory loss. Surface condition was not included in the primary aims, as it was an exploratory measure to understand if there are possible confounding variables (visual or vestibular dysfunction) when measuring postural stability.

### *Statistical Analysis*

The primary aim of the study was to validate the novel smartphone application relative to multiple validated research-grade posturography instruments (i.e., motion capture and force plate systems) to establish both construct and criterion-related validity. The independent variables included the instrumentation systems (force plate, motion capture, smartphone application), visual (EO and EC) conditions, and surface (Firm and

Foam) conditions. The dependent variables were sway outcome measures (Primary: Center of Pressure (COP) and Center of Mass (COM) Sway Area; Secondary: COP and COM Sway Velocity, and AP and ML standard deviation).

To address criterion validity, Pearson Correlation Coefficients were calculated by comparing postural variables (Sway Area or Sway Velocity) between the gold-standard instruments and the novel smartphone application. Additionally, time series correlations were calculated to assess moment-to-moment variations in positional data of the smartphone and motion capture system across visual and surface conditions for both the AP and ML axes. Correlation coefficients of 0.1 were considered weak, 0.3 were considered moderate, and 0.5 to 1.0 were considered strong.<sup>131</sup>

To gain further insight into the individual spread of the measurement error between the smartphone application and each of the gold-standard instruments, the postural outcome measures, Sway Area and Velocity, were analyzed using Bland–Altman plots. In each plot, the average value for each pair of measurements was plotted against the mean difference between the two values of the two measurement devices for individual data. In addition, the upper and lower limit of agreement, as  $1.96 \times$  standard deviation, was calculated for the two devices.<sup>132</sup>

A repeated-measures (rm) ANOVA was conducted to examine the effects of surface (Firm vs. Foam), device (MC, Phone, and FP), and visual condition (EO vs. EC) on the dependent variables Sway Area and Sway Velocity. Mauchly's test was used to evaluate sphericity. If sphericity was violated, then degrees of freedom were adjusted using a Greenhouse-Geisser correction. Paired T-tests were applied to compare EC and EO visual conditions of the smartphone device and research-grade instrumentation (motion capture

and force plate systems) to determine if the smartphone was sensitive to decreases in postural stability during EC conditions of the postural task. A  $p$ -value less than or equal to 0.05 denotes the presence of a statistically significant difference.

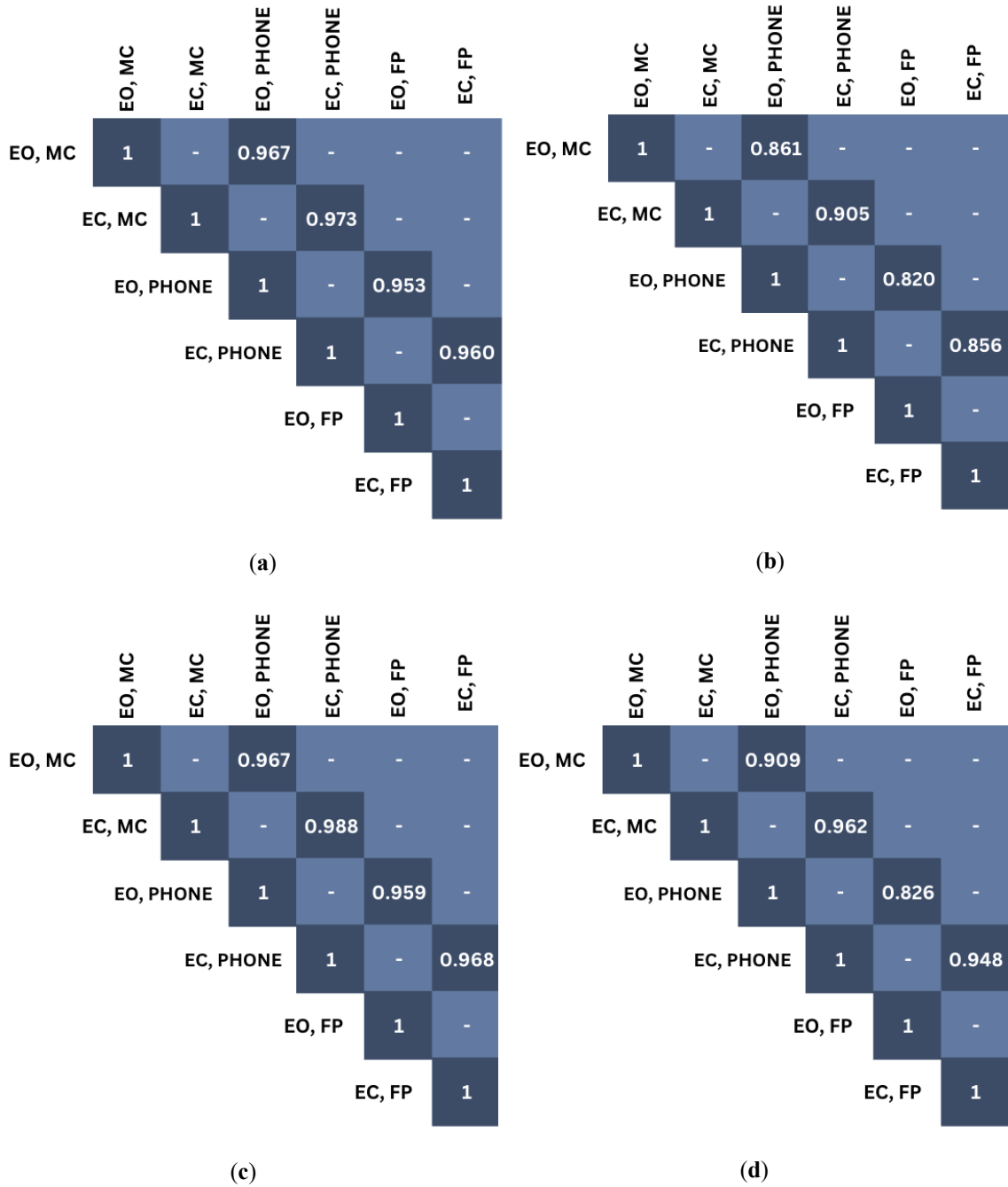
A series of Intraclass Correlation Coefficients (ICC) were calculated to examine the validity and reliability of the smartphone device. To assess test-retest reliability, ICC (3,1) estimates and their 95% confidence intervals were calculated. This was based on a mean-rating ( $k = 3$ ), absolute-agreement, and a 2-way mixed-effects model that was applied to measurement outcomes (Sway Area or Sway Velocity) for each of the three trials collected per device (MC, Phone, FP). An ICC (3, $k$ ) estimates and their 95% confidence intervals were calculated based on a mean-rating ( $k = 3$ ), absolute-agreement, and a 2-way mixed-effects model for measurement outcomes (Sway Area or Sway Velocity) somatosensory ratio of the novel device when compared to the motion capture or force plate system. An ICC (3, $k$ ) was calculated based on a mean-rating ( $k = 3$ ), absolute-agreement, and a 2-way mixed-effects model to examine the averages of measurement outcomes (Sway Area or Sway Velocity) across the three devices. ICC values below 0.5 were interpreted as demonstrating poor reliability, values ranging from 0.5 to 0.75 reflected moderate reliability, values between 0.75 and 0.9 indicated good reliability, and values above 0.90 signified excellent or a high degree of reliability.<sup>131</sup> Data post-processing and statistical analysis were performed using MATLAB R2022a (Mathworks Inc., Natick, MA, USA) and SPSS, Version 29 (IBM Corp, Armonk, NY, USA).

## Results

The demographic information of all participants is presented in Table 2.1.

Age (mean $\pm$ sd; range)	52.1 $\pm$ 6.4 yrs.; 35–60 yrs.
Gender	M: 18; F: 24
Height	65.9 $\pm$ 4.7 inches
Weight	181.9 $\pm$ 39.4 pounds

The novel device demonstrated strong correlations with the motion capture and force plate systems in all of the visual and surface conditions for both the Sway Area and Sway Velocity postural outcome measures, as shown in Figure 2.5. Under foam surface conditions, the  $r$ -values appear to increase with both the Sway Area ( $r = 0.96$ – $0.99$   $p < 0.001$ ) (see Figure 2.5c) and Sway Velocity ( $r = 0.83$ – $0.96$ ;  $p < 0.001$ ) (see Figure 2.5d) when compared to firm surface conditions ( $r = 0.95$ – $0.97$ ;  $p < 0.001$ ;  $r = 0.82$ – $0.91$ ;  $p < 0.001$ ) (see Figure 2.5a,b). As the conditions increased in difficulty (i.e., EO–foam and EC–foam), the correlations strengthened.



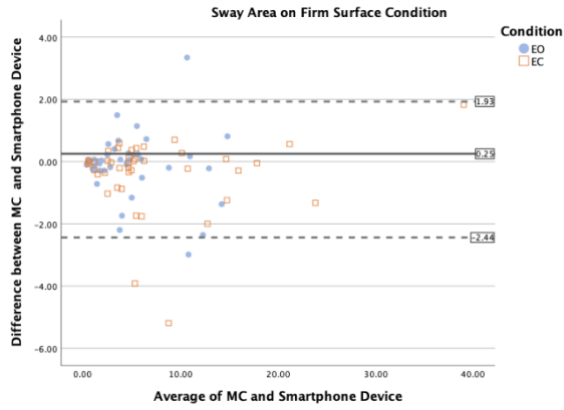
**Figure 2.5.** Pearson correlations were applied across the group mean postural variables: (a) Firm Sway Area; (b) Firm Sway Velocity; (c) Foam Sway Area; (d) Foam Sway Velocity.

The AP linear displacements of both systems demonstrated strong correlations across both the visual and surface conditions ( $r = 0.84\text{--}0.93$ ;  $p < 0.001$ ). The ML linear displacements of both systems showed moderate-to-strong correlations across the visual and surface conditions ( $r = 0.35\text{--}0.73$ ;  $p < 0.05$ ) (Table 2.2). While the ML positional correlations were statistically significant, they were comparatively weaker than the AP positional correlations, suggesting a more variable relationship between the motion capture system and the smartphone’s ML positional time-series data across the visual and surface conditions. As the conditions increased in postural difficulty (i.e., EO–Foam and EC–Foam) and the sway increased, the ML time-series positional correlations increased in strength (see Table 2.2).

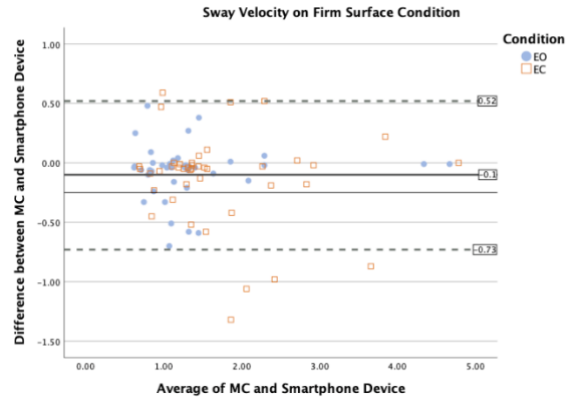
**Table 2.2.** Average Pearson correlations across the participants comparing positional time series data from the smartphone position to the motion capture system for the AP and ML axes.

Condition (Vision, Surface)		MC vs. Phone	
		AP Position	ML Position
EO, Firm	r	0.844	0.345
	p	≤ 0.001	0.002
EC, Firm	r	0.845	0.385
	p	≤ 0.001	0.008
EO, Foam	r	0.881	0.674
	p	≤ 0.001	≤ 0.001
EC, Foam	r	0.932	0.734
	p	≤ 0.001	≤ 0.001

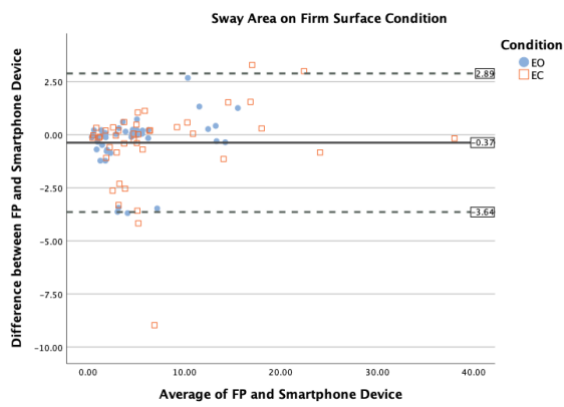
*Note:* 42 participants per condition and 3 trials per participant; N = 3000 per trial.



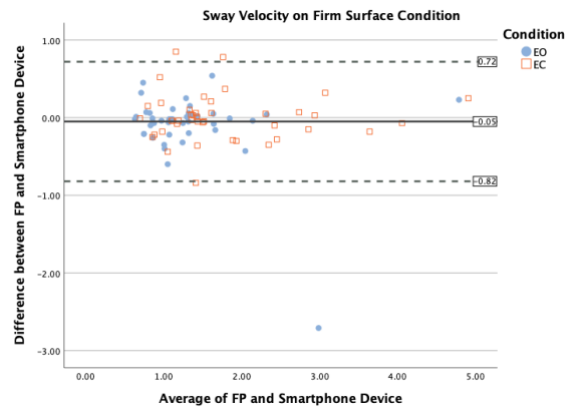
(a)



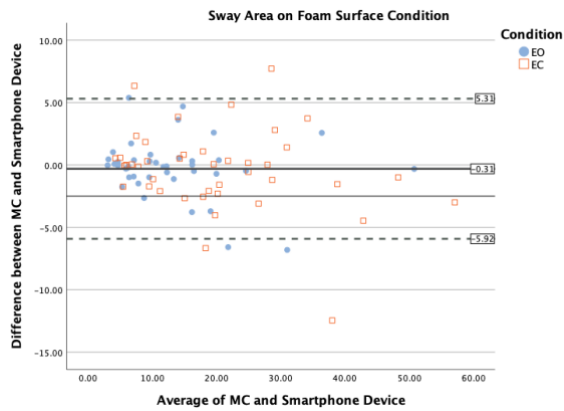
(b)



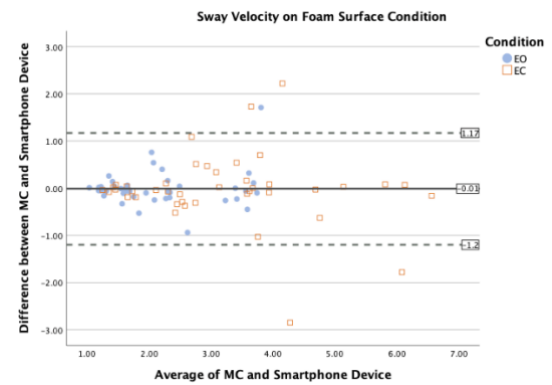
(c)



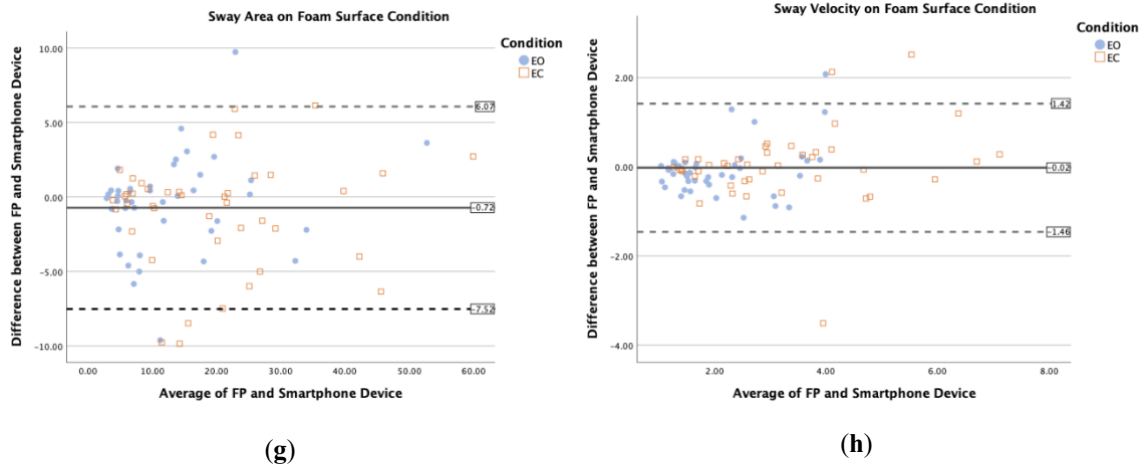
(d)



(e)



(f)



**Figure 2.6.** Bland–Altman plots of the mean of the measurements of the smartphone and each gold-standard instrument (motion capture and force plate) were compared against the difference in the measurement of individual participants for the Sway Area (left: 2-7a,c,e,g) and Sway Velocity (right: 2-7b,d,f,h) for each visual and surface condition.

Bland–Altman plots for the Sway Area and Sway Velocity illustrated minimal measurement errors between the smartphone and each of the gold-standard methods (see Figure 2.6). The plots revealed that the mean differences between the smartphone and the reference devices were close to zero, indicating that the smartphone provided measurements that were largely in agreement with the gold-standard instruments. Furthermore, the limits of agreement (LOAs) were narrow, with only five outliers, suggesting that the variation between the two measurement methods was consistently small. Finally, no consistent trend was observed across the x-axis in any of the plots, indicating an absence of systematic bias or proportional differences between the devices.

**Table 2.3.** Mean  $\pm$  standard deviation of the dependent variables, Sway Area (cm<sup>2</sup>) and Sway Velocity (cm/s) ( $N = 42$ ), for each test condition per device.

	Device	Mean $\pm$ Standard Deviation
Sway Area (EO), Firm	MC	4.76 $\pm$ 3.9
	Phone	4.87 $\pm$ 4.0
	FP	4.57 $\pm$ 4.4

**Table 2.3.** (Continued)

Sway Area (EC), Firm	MC	7.19 ± 7.6
	Phone	7.58 ± 7.5
	FP	7.14 ± 7.9
Sway Velocity (EO), Firm	MC	1.30 ± 0.8
	Phone	1.37 ± 0.8
	FP	1.27 ± 0.7
Sway Velocity (EC), Firm	MC	1.63 ± 0.9
	Phone	1.77 ± 0.9
	FP	1.76 ± 0.9
Sway Area (EO), Foam	MC	12.81 ± 9.5
	Phone	13.03 ± 9.8
	FP	12.59 ± 10.6
Sway Area (EC), Foam	MC	19.81 ± 12.3
	Phone	20.21 ± 13.1
	FP	19.19 ± 13.3
Sway Velocity (EO), Foam	MC	2.13 ± 0.9
	Phone	2.13 ± 0.8
	FP	2.05 ± 1.0
Sway Velocity (EC), Foam	MC	3.19 ± 1.4
	Phone	3.22 ± 1.5
	FP	3.25 ± 1.7

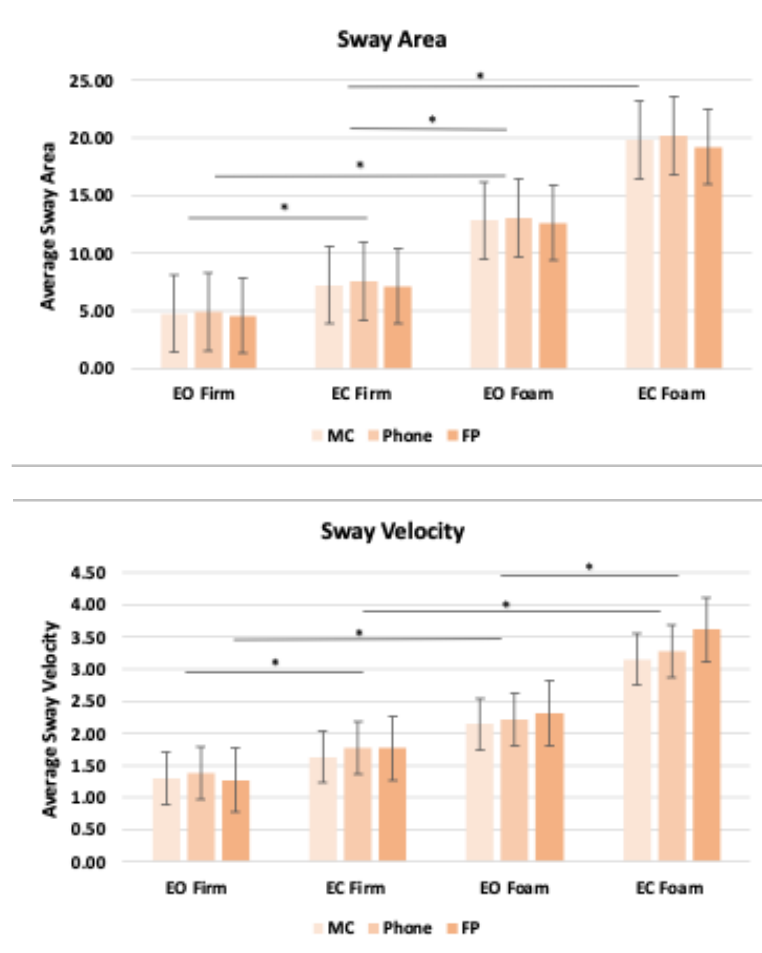
When the postural data from the smartphone, motion capture, and force plate systems were collected synchronously (see Table 2.3), no significant differences ( $p > 0.05$ ) were found between the devices for either Sway Area and Sway Velocity, irrespective of the visual and surface conditions (see Table 2.4 and Figure 2.7). The small effect sizes and non-significant results suggest that postural sway measurements were consistent across the different devices tested, indicating reliability and comparability of the data regardless of the equipment used.

**Table 2.4.** Summary table of the repeated-measures analysis of variance (rmANOVA) for the dependent variables ( $N = 42$ ).

		df		F	Sig.	Partial Eta Squared ( $\eta^2$ )
Variable		Between Groups	Within Groups			
Sway Area	Surface Condition	1	41	84.78	<0.001	0.67
	Device	1.53	62.90	1.65	0.204	0.04
	Visual Condition	1	41	56.85	<0.001	0.58
Sway Velocity	Surface Condition	1	41	69.79	<0.001	0.63
	Device	2	82	0.59	0.557	0.01
	Visual Condition	1	41	75.81	<0.001	0.65

*Note:* Device degrees of freedom were adjusted using a Greenhouse–Geisser correction for Sway Area

The results for the postural outcome of the Sway Area indicate a main effect of the visual condition (EO vs. EC) and a main effect of the surface condition (Firm vs. Foam). Similar findings were observed in the Sway Velocity. These results demonstrate that both reduced visual input and decreased surface stability significantly impaired postural control, and with respect to the device used to measure this, all three devices were sensitive enough to detect these differences.



**Figure 2.7.** Comparison of synchronously collected data from the smartphone, motion capture, and force plate systems in each visual and surface condition for the postural outcome measures. *Note: the asterisk (\*) denotes statistically significant differences between visual and surface conditions, whereas no statistically significant differences were found between devices.*

**Table 2.5.** Paired Samples *t*-Test comparing visual conditions (EO and EC) averages per device.

Condition	Device	$t_{(41)}$	Sig.	Cohen's <i>d</i>
Sway Area, Firm	MC	-3.46	<0.001	4.57
	Phone	-4.05	<0.001	4.35
	FP	-3.89	<0.001	4.28
Sway Area, Foam	MC	-8.13	<0.001	5.88
	Phone	-7.07	<0.001	6.20
	FP	-6.26	<0.001	4.54
Sway Velocity, Firm	MC	-6.07	<0.001	0.36
	Phone	-5.69	<0.001	0.45
	FP	-6.99	<0.001	0.46
Sway Velocity, Foam	MC	-7.72	<0.001	0.85
	Phone	-7.50	<0.001	0.99
	FP	9.42	<0.001	1.23

Paired samples *t*-tests revealed significant differences ( $p \leq 0.001$ ) between the EO and EC visual conditions for all devices (Phone, MC, FP) across both postural outcome measures, Sway Area and Sway Velocity (see Figure 2.7, Table 2.5). These findings indicate that each device was sensitive even to subtle postural changes associated with visual input.

**Table 2.6.** Test–retest reliability within each device for all visual and surface conditions.

Device	Visual, Surface Condition	ICC (3,1) (95% Confidence Interval)	
		Sway Area	Sway Velocity
MC	EO, Firm	0.908 (0.848–0.947)	0.974 (0.957–0.985)
	EC, Firm	0.944 (0.907–0.967)	0.960 (0.934–0.977)
	EO, Foam	0.904 (0.840–0.945)	0.949 (0.914–0.971)
	EC, Foam	0.862 (0.771–0.921)	0.923 (0.867–0.957)
Phone	EO, Firm	0.917 (0.862–0.952)	0.972 (0.951–0.984)
	EC, Firm	0.940 (0.901–0.966)	0.968 (0.947–0.982)
	EO, Foam	0.901 (0.836–0.943)	0.929 (0.879–0.960)
	EC, Foam	0.869 (0.783–0.925)	0.938 (0.890–0.965)
FP	EO, Firm	0.903 (0.840–0.944)	0.974 (0.956–0.985)
	EC, Firm	0.918 (0.863–0.953)	0.972 (0.953–0.984)
	EO, Foam	0.927 (0.878–0.958)	0.990 (0.983–0.994)
	EC, Foam	0.931 (0.884–0.960)	0.947 (0.909–0.970)

*Note:* Test–retest reliability was evaluated using an ICC (3,1) 2-way mixed-effects model, absolute agreement and their 95% confidence intervals were calculated to evaluate repeated trials ( $n = 3$ ) within each device.

The test–retest reliability across repeated trials ( $n = 3$ ) for each device showed good-to-high reliability (ICC (3,1) = 0.86-0.99;  $p < 0.001$ ) for each of the visual/surface conditions (Table 2.6).

**Table 2.7.** Intraclass correlations comparing somatosensory ratios between devices for each surface condition.

Postural Outcome Measure	Surface Condition	ICC (3, $k$ ) (95% Confidence Interval)	
		MC vs. Phone	FP vs. Phone
Sway Area	Firm	0.940 (0.890–0.968)	0.782 (0.594–0.833)
	Foam	0.939 (0.886–0.967)	0.881 (0.779–0.936)
Sway Velocity	Firm	0.896 (0.806–0.944)	0.674 (0.400–0.824)
	Foam	0.961 (0.927–0.979)	0.827 (0.674–0.907)

*Note:* ICC (3, $k$ ) estimates and their 95% confidence intervals were calculated based on a mean-rating ( $k = 3$ ), absolute-agreement, 2-way mixed-effects model for the somatosensory ratio calculated using the Sway Area or Sway Velocity for the novel device when compared to the motion capture or force plate systems.

Moderate-to-high reliability was found (ICC (3,  $k$ ) = 0.67–0.96;  $p < 0.001$ ) when comparing the somatosensory ratios from the smartphone application to the MC or the FP (Table 2.7).

**Table 2.8.** Intraclass correlations comparing the averages between each of the three devices for each visual and surface condition of each postural outcome measure.

Postural Outcome Measure	Visual, Surface Condition	ICC (3, $k$ ) (95% Confidence Interval)
Sway Area	EO, Firm	0.985 (0.976–0.992)
	EC, Firm	0.992 (0.987–0.995)
	EO, Foam	0.984 (0.973–0.991)
	EC, Foam	0.985 (0.974–0.991)
Sway Velocity	EO, Firm	0.951 (0.919–0.972)
	EC, Firm	0.972 (0.952–0.984)
	EO, Foam	0.946 (0.910–0.969)
	EC, Foam	0.946 (0.910–0.969)

*Note:* ICC (3, $k$ ) estimates and their 95% confidence intervals were calculated based on a mean-rating ( $k = 3$ ), absolute-agreement, 2-way mixed-effects model for measurement outcome (Sway Area and Sway Velocity) averages for the novel device, and motion capture and force plate systems.

Primarily high reliability was observed for each device when analyzing the average Sway Area ( $ICC(3, k) = 0.98-0.99; p < 0.001$ ) or average Sway Velocity ( $ICC(3, k) = 0.95-0.97; p < 0.001$ ) in all of the visual and surface conditions (Table 2.8).

## Discussion

This study cross-validated a custom postural smartphone application to both force plate COP and motion capture system COM postural data synchronously. Current findings provide both criterion and construct validation for our novel smartphone application.

To address the validity, postural outcome measures, Sway Area, and Sway Velocity were compared during a range of visual and surface conditions administered to each participant to gain knowledge of the limitations of the smartphone when compared to research-grade gold standards. When compared, the smartphone application demonstrated strong, positive correlations under conditions with small (EO on a firm surface) and larger (EC on a foam surface) postural movements (Figure 2.5). As the postural conditions became more challenging and the Sway Area and Sway Velocity increased, the r-values also increased. Additionally, time-series correlations (Table 2.2) were employed to assess the relationship between the motion capture system and smartphone, analyzing both the AP and ML axes. Moderate-to-strong correlations were observed in both axes, indicating a relationship not only in terms of the average across an entire trial, but also changes in the spatiotemporal data. Interestingly, when analyzing the ML axis, while statistically significant, it proved to be less sensitive when collecting more stable (smaller postural movements) versus more challenging conditions (i.e., EO-Firm vs. EC-Foam). The findings align with the correlations between the postural outcome measures. This suggests

that the threshold sensitivity was exceeded, and the smartphone was better able to detect the postural adjustments accurately.

A plausible reason for this may be due to the design functionality of smartphone IMUs, which are primarily marketed towards day-to-day usability to capture larger movements during walking, fitness, gaming, and general user experience. However, these types of movements are not meant to test the lower limits of the smartphone IMUs. By altering the level of difficulty of the various standing tasks and eliciting a range of postural responses, the current study gained insight into whether the smartphone is capable of being a stand-alone balance-measurement device. Our findings suggest that it is, as no matter the surface or visual condition (Figure 2.7), there was no statistically significant difference in the postural measurements among the devices.

The novel application indicated a high degree of inter-rater reliability compared to each gold-standard device when analyzing the Sway Area and Sway Velocity averages for each visual and surface condition, as well as a moderate-to-high degree of reliability between the custom smartphone application and each gold-standard device's somatosensory ratio. This affirms the smartphone's ability to measure data consistently when compared to two widely used gold-standard devices in posturography. Additionally, there was a good to high degree of intra-rater reliability among the trials ( $n = 3$ ) within each device (in this analysis, rater = device). Demonstrating both inter-rater reliability against gold-standard measures and intra-rater for test-retest reliability is essential for the smartphone application to be accepted and trusted by clinicians and researchers. This reliability ensures consistent results, which are vital for accurate diagnoses and treatment

plans. Furthermore, it promotes standardized practices in healthcare settings and home use, ultimately enhancing patient care and quality.

To examine the sensitivity of the device for detecting changes in balance as the task difficulty changes, we compared the output of the novel smartphone application between several conditions, in which one or both of the visual and somatosensory feedback systems were altered. The results demonstrated that our novel application was sensitive to detecting multisensory balance conditions. As the application is sensitive to a large range of postural movements, it allows for the potential for individuals to track postural decline over time.

This is especially important in clinical settings, where many conditions include the progressive deterioration of the postural control systems (i.e., neuropathy), decreasing balance, and increasing fall risk. Clinicians often must rely on their patients' subjective recollection concerning past falls and balance instability. By using objective and trackable assessments, clinicians will be better informed with the critical information necessary to shape proper treatment plans to reduce falls and prevent chronic complications associated with poor balance. Our proposed application provides a convenient, portable, and easy-to-use instrument that has the potential to be used at home or in any clinical setting without the initial need for a specialist. While it is not meant to be a diagnostic tool, it can serve as a screening tool that can be coupled with other assessments to enhance clinical judgment.

Several factors differentiate our custom application from other studies on smartphone IMU use for postural measurements. Previous studies have used smartphone devices to investigate various postural, functional, and gait movements that traditionally elicit larger postural movement (i.e., single-leg stance and gait) when reporting the validity of a smartphone device.<sup>92,99,100,111,133</sup> However, few studies have validated smartphone

technology against gold-standard devices for smaller movements (i.e., quiet stance), and among those that have, we were able to replicate and add to their findings. From a methodological standpoint, the use of the waist belt in conjunction with using an electronic level to verify the phone orientation offers advantages, particularly during the validation process. The standardization of a rigorous set-up process enhances the quality of the data of the smartphone's IMUs, contributing to increased correlations and the reliability of the smartphone across different trials and devices. Interestingly, the majority of studies investigating smartphone IMUs, and balance do not note misalignments between the phone and the gravity vector due to any tilt of the device,<sup>125</sup> particularly in multiple trials involving devices held by a human or in larger movements where the phone is not securely attached to the individual, which may cause extraneous movements of the device. This handheld methodology makes it difficult to standardize the orientation and tilt of the phone.<sup>97</sup> This variability may introduce additional noise into the signal, potentially compromising the data. By changing the orientation of the phone, the current study was able to increase the signal-to-noise ratio, enhancing the reliability and sensitivity of the data. More research will need to be performed to understand the design of the IMUs with respect to the sensitivity of each axis in capturing smaller postural movements.

The current study's methodology creates a minimal-risk task that can be administered both in a clinical setting and also in the comfort of one's home, which is a primary long-term goal of the present application. Challenging tasks used to validate smartphones in previous studies that elicit postural responses were not suitable for an at-home setting, as they require a spotter and can cause an increased fall risk, especially in populations with compromised postural control. The current study was able to utilize a

minimal-risk postural task when using the smartphone application without sacrificing the potential safety of the person in an at-home setting.

While this study provides valuable evidence for the use of this proposed application in clinical and at-home settings, it is important to acknowledge its limitations. A belt was used to secure the smartphone in a specific orientation during data collection to increase the sensitivity of the IMUs. Additionally, for the duration of the study, a single iPhone 14 was used for all 42 instances of data collection. Future studies should explore the intra-device reliability to generalize the application across smartphone models. Additionally, the current application was designed solely for Apple's iOS. Further development will be required to determine whether a solution that is platform-agnostic is possible, thus enabling the application to work independently of a smartphone operating system.

### Conclusion

The purpose of this study was to develop a novel smartphone application and validate it relative to research-grade posturography instrumentation (i.e., motion capture and force plate systems). By assessing the validity, sensitivity, and accuracy of a custom-designed smartphone application for measuring balance in adults regardless of cohort, we aimed to bridge the gap between at-home and clinical care. The results show strong agreement with established gold standards in posturography, supporting the application's criterion validity. Additionally, the application demonstrated construct validity by being sensitive to changes in postural stability as the visual and/or surface condition was altered, indicating good intra-rater reliability.

By leveraging smartphone sensors, the application offers the potential for remote balance monitoring and improved patient engagement, which is both critical for the early detection and management of fall risk, especially in populations with limited access to preventive care.

## **CHAPTER 3: IDENTIFYING POSTURAL INSTABILITY IN INDIVIDUALS WITH AND WITHOUT DIABETES USING A NOVEL SMARTPHONE APPLICATION**

### Introduction

Diabetes mellitus has become a major global public health crisis, characterized by its rapidly increasing prevalence, significant morbidity and mortality, and substantial economic burden.<sup>1</sup> In the United States alone, diabetes affects more than 37.3 million Americans, of which 90-95 percent of cases in adults are classified as Type 2 Diabetes (T2D).<sup>2</sup> The etiology of T2D is primarily a combination of genetic predisposition and lifestyle factors, leading to a condition where the body either doesn't produce enough insulin or becomes resistant to the insulin it does produce, which is detrimental to glucose utilization within the body.<sup>134</sup>

Unfortunately, T2D can be undiagnosed for many years if someone lacks regular access to preventive care. This is because hyperglycemia develops gradually and, at its earlier stages, may not be severe enough for individuals to notice symptoms.<sup>135</sup> The onset and complications of diabetes are influenced by a variety of factors, including biological, clinical, health system, and social factors,<sup>2,5</sup> resulting in disabling and life-threatening outcomes.<sup>6</sup> T2D can be diagnosed using an A1C test (an A1C level  $\geq 6.5\%$ ), which provides the average blood glucose levels for the last 2-3 months, or a Fasting Plasma Glucose test, which measures current blood glucose for a singular point in time (a blood glucose level  $\geq 126$  mg/dL).<sup>135</sup> In either test, elevated levels provide an indication of pre-diabetes or diabetes itself.

Without proper care and management, diabetes increases the risk of developing additional complications such as Diabetic Peripheral Neuropathy (DPN).<sup>1,2,5,12</sup> Regarded as the most common microvascular complication, DPN is experienced by more than 50% of all individuals within 25 years of the initial diagnosis of T2D.<sup>14</sup> As diabetes arises from the dysregulation of metabolic pathways, it leads to segmental demyelination and axonal degeneration of the distal nerve fibers of the extremities,<sup>43,44</sup> presenting itself in a “glove and stocking” distribution. Signs and symptoms of DPN range from loss of protective sensation in the limbs,<sup>45</sup> muscular weakness,<sup>46-49</sup> decreased nerve conduction velocity and amplitude,<sup>45,50-52</sup> and insensate feet.<sup>12</sup> These symptoms have a detrimental effect on one's functional ability, as large afferent (1A/B) fibers are critical inputs involved in producing complex patterns to control and counteract external forces during postural control.<sup>53</sup> If left undiagnosed or unmanaged, large fiber degeneration associated with DPN can increase negative outcomes,<sup>1,2,5,10,12,23</sup> and is a critical risk factor in developing foot infections, ulcerations, and non-traumatic lower limb amputations.<sup>24-29</sup>

The ability to stay balanced and upright relies on the body's ability to process and respond to sensory information from the world around us. Signals from the vestibular system, visual system, and somatosensory system are constantly integrated and processed in the brain and spinal cord. The somatosensory system provides information about the position and motion of the body's segments in relation to each other and the supporting surface by using proprioceptive (joint position/kinesthesia) and cutaneous mechanoreceptors (touch and vibration sensitivity), which provide information about the contact pressures and are pivotal for sensing changes in posture.<sup>136</sup> This processing helps to control the movements needed to guide the motor responses for postural stabilization.

Due to peripheral somatosensory loss in the feet and motor system deterioration, DPN has been associated with up to a 20-fold increase in instability when compared to age-matched healthy controls.<sup>59,60</sup> Among neurological populations, those with peripheral neuropathy report being categorized as having the third highest rate of falls, behind Parkinson's disease and syncope.<sup>66</sup> As such, DPN is considered a strong predictor of postural instability and fall risk.<sup>61–65</sup>

DPN is highly preventable with proper care and management. However, it is often underdiagnosed and undertreated in primary care settings due to the reliance on costly, clinic-based tools and expertise that isn't always accessible to those who suffer from the disease.<sup>40,83,84</sup> In general care facilities, both patients and providers often lack awareness of DPN symptoms and lack the equipment or time during appointments to perform the examination.<sup>39,40,83,137</sup> This makes it challenging to detect DPN in its earliest stages. Interestingly, current DPN diagnostic tools investigate mechanisms revolving around sensory detection. Balance assessments are not considered components of DPN diagnosis and management, despite the consensus that DPN affects sensation in the lower limbs and the somatosensory system.<sup>76,88–90</sup>

Smartphone-based inertial measurement units (IMUs) have been shown to be effective tools for collecting human movement.<sup>92,104,108–112</sup> A considerable body of research has emerged over the past decade to assess this functionality.<sup>97,100,104–106,112,138</sup> Fernandes et al. evaluated both static balance (varying visual condition – EO and EC) using a smartphone located on the L5 vertebrae in individuals with and without T2D.<sup>113</sup> Both visual conditions demonstrated significant differences found in the total acceleration and area of the ellipse, in which the T2D group had larger values than controls ( $p < 0.05$ ). However,

the authors did not state whether they controlled for potential confounders such as visual and/or vestibular dysfunction.

The primary goal of Aim 2 was to measure and compare postural sway using the validated smartphone application among our healthy cohort and T2D and DPN cohorts for each visual (EO and EC) and surface (Firm and Foam) conditions. To do this, normalized postural control values for individuals with and without diabetes were collected using the novel smartphone application. During a range of postural tasks, individuals with diabetes characteristically exhibit poorer balance than healthy controls when measured using force plates, motion capture systems, and accelerometers.<sup>61,139–143</sup> Specifically, during the EC versus EO visual condition, individuals with T2D, either with or without DPN, demonstrated greater postural instability during quiet stance compared to the control group.<sup>65,143–146</sup> Therefore, we predict that postural performance, measured by the novel smartphone device across various quiet standing tasks, will be worse in individuals with a clinical diagnosis of diabetes, when compared to age-matched healthy controls. If balance dysfunction and postural decline can be detected during various stages (mild to severe cases) of T2D and DPN, this affordable and accessible approach may provide a means to identify DPN outside of traditional healthcare settings.

### Methodology

Forty-two participants (see Table 3.1 for demographic data) were classified into three groups ( $n = 14$  per group): Control (healthy), Type 2 Diabetes (T2D), and Diabetic Peripheral Neuropathy (DPN), to participate in a single-session repeated-measures design study. Group assignments were determined at the beginning of the study based on clinical

diagnosis by a trained physician using medical standards for the diagnosis of T2D and DPN.

To be eligible, participants had to be: 1) Between 30-60 years of age, 2) Able to give informed consent, 3) Have a clinical diagnosis of Type 2 Diabetes or no history of diabetes (clinical diagnosis is based on HbA1C levels exceeding 6.5), 4) Able to ambulate without an assistive device. Exclusion Criteria was as followed: 1) lower limb or musculoskeletal injury or amputation which affects balance, 2) clinically significant orthopedic, muscular, or neurological (excluding peripheral neuropathy) disability that affected their ability to perform the postural task protocol, 3) inability to stand independently for at least 10 minutes, 4) individuals who suffer from substance abuse, 5) currently pregnant, 6) vitamin B deficiency.

Two factors were considered in selecting age parameters: 1) postural decline due to age, and 2) the onset of diabetes and DPN. Age-related physiological changes have been shown to increase the processing time of proprioceptive inputs.<sup>147</sup> Declines in sensory processing begins between 40-49 years of age.<sup>148-150</sup> This ultimately leads to a decline in postural control and balance, as well as a high risk of falling, especially in individuals 60 years and older. In most populations, the incidence of T2D is low before age 30 years but increases rapidly and continuously with older age.<sup>151</sup> Considering postural decline, the onset of both T2D and DPN, and recruitment limitations, we limited our recruitment age range between 30 and 60 years.

The Temple University Institutional Review Board approved the procedures, and all participants gave informed consent before engaging in the study. Participants were recruited from the Philadelphia community and compensated for time and travel.

Individuals with a clinical diagnosis of Diabetes and/or Diabetic Peripheral Neuropathy received a one-time \$50.00 gift card as compensation. Individuals who served as healthy controls for the study received a one-time \$25.00 gift card as compensation.

The sample size estimate for the proposed project was based on Aim 3 (see Chapter 4), which assessed the discrimination of a smartphone application for the early detection of DPN when compared to the Utah Early Neuropathy Scale (UENS). The prevalence of DPN has been reported as approximately 50% of all individuals diagnosed with T2D.<sup>14</sup> The predictive accuracy of the novel smartphone application for the presence of DPN was assessed using a Receiver Operating Characteristic (ROC) analysis. Currently, the UENS has provided 88% diagnostic accuracy in detection,<sup>33</sup> so we estimated a necessary sample size to achieve no less than 10% of this diagnostic accuracy (AUC = 0.79). Sample size estimations were performed with a two-sided z-test using PASS software, resulting in a recruitment target of 28 participants.<sup>116,117,152</sup> Of the total sample population, 14 diabetic individuals with DPN and 14 diabetic individuals without DPN (assuming an allocation ratio DPN/no DPN of 1:1) would suffice with 80% power to detect a difference of 0.29 between the area under the curve (AUC), under the null hypothesis of AUC = 0.5 (no diagnostic accuracy) and the alternative hypothesis of AUC = 0.79 (moderate diagnostic accuracy), at a significance level of 0.05.

#### *Postural Task and Protocol*

Participants were instructed to stand still and upright with their feet hip-width apart and their hands crossed over their chest, wearing a modified running belt around the waist to hold the iPhone in place securely (see Figure 2.2). During a single session data collection, participants were instructed to perform quiet stance, barefoot, under varying

visual and surface conditions: eyes open (EO) firm surface, eyes closed (EC) firm surface, EO foam surface, and EC foam surface. Each condition included three 30-second trials for a total of 12 trials (see Figure 2.1).

Data was collected by a novel smartphone application. In our prior work, and as detailed above, the validity, reliability, and sensitivity of an iPhone 14 novel smartphone application was evaluated to measure postural instability when compared to synchronized data from gold standard lab-based instrumentation (motion capture and force plate systems).<sup>112</sup> This study utilized the same post-processing methodologies for the iPhone accelerometers.

Balance control relies on input from the visual, somatosensory, and vestibular systems. The study methodology aimed to assess whether the vestibular and visual systems are intact and whether poor balance is mainly due to somatosensory loss. To explore this, the study used the Modified Clinical Test of Sensory Interaction in Balance (mCTSIB), which includes both firm and foam surfaces. On a firm surface, postural control involves small corrective movements coordinated by sensory and motor systems, but this condition may lack sensitivity to detect balance impairments due to a ceiling effect. Foam surfaces reduce the reliability of somatosensory input, and the EC foam condition removes visual cues as well, increasing the importance of the vestibular function to help maintain balance. The methodology also investigated whether there are limitations in the accuracy of very small postural fluctuations (firm surface condition) versus larger postural fluctuations associated with the foam surface condition.

### *Statistical Analysis*

The primary aim of this study was to examine the differences in normalized postural control values between individuals with and without diabetes, using a validated smartphone application. The between-group independent variables included cohort (healthy controls, individuals with T2D, and those with DPN). The within-group independent variable measured the visual condition (EO and EC) and surface condition (firm and foam). The dependent variables included Sway Area (primary analysis) and Sway Velocity (secondary analysis). Additionally, the Somatosensory Ratio (see Equation 2.3) was investigated for both Sway Area and Sway Velocity.

A 2 (Vision: EO and EC)  $\times$  2 (Surface: firm, foam)  $\times$  3 (Diagnosis Group: control, T2D, DPN) omnibus repeated measures (rm) ANOVA mixed-design was conducted on both Sway Area and Sway Velocity, with vision and surface as within-subjects factors and diagnosis group as a between-subjects factor. Planned comparisons (contrasts) were conducted to investigate specific hypotheses regarding group differences and interaction patterns. A  $p$ -value of less than 0.05 denoted the presence of a statistically significant difference.

Sub-analyses were also conducted using an rmANOVA with a mixed interaction effect within and between groups to compare means within each visual condition (EO and EC) and cohort, as well as the interaction between the two. A secondary analysis was conducted using an rmANOVA with a mixed interaction effect design to compare means within each surface condition (firm and foam) and cohort, as well as the interaction between the two. Planned comparisons were implemented to understand the significance of all rmANOVA analyses.

To account for potential confounding variables, Omnibus rmANCOVA's were applied to Sway Area and Sway Velocity across various visual and surface conditions while controlling for relevant covariates (e.g., BMI, Years Since Clinical Diagnosis of T2D, and age). Dependent variables (BMI and Age) were log-transformed (log base 10) to improve normality and address ANCOVA assumptions. This approach enabled a more accurate assessment of the effects of experimental conditions on postural control by accounting for individual differences that could impact performance. If rmANCOVA revealed significance, Least Significant Difference (LSD) comparisons were used as post-hoc.

Descriptive statistics were computed for all variables to ensure data quality and to evaluate the assumptions of the statistical tests. All statistical analyses were conducted using SPSS, version 29 (IBM Corp, Armonk, NY).

## Results

Key demographics and clinical metrics for each group of participants are summarized in Table 3.1. Age, gender, and height were statistically similar across the healthy, T2D, and DPN groups ( $p > 0.05$ ). However, weight and BMI differed significantly among all three groups ( $p < 0.05$ ), with both progressively increasing from healthy individuals ( $157.4 \pm 30.2$  lbs;  $\text{BMI} = 24.8 \pm 3.8$   $\text{kg/m}^2$ ) to T2D participants ( $177.9 \pm 38.0$  lbs;  $\text{BMI} = 29.6 \pm 7.0$   $\text{kg/m}^2$ ) and reaching the highest values in the DPN group ( $210.4 \pm 31.7$  lbs;  $\text{BMI} = 34.9 \pm 7.2$   $\text{kg/m}^2$ ). Each group consisted of 14 participants, with an identical gender distribution (6 males and 8 females). The duration of T2D significantly differed ( $9.4 \pm 5.0$  years) from the DPN ( $19.2 \pm 8.4$  years) group ( $p < 0.01$ ). Glycemic control, measured by A1C, was higher in the DPN group ( $8.0 \pm 2.0$  %) than in the T2D

group ( $7.1 \pm 1.1$  %). Neuropathy severity, as indicated by UENS scores, also differed significantly between groups ( $p < 0.001$ ).

**Table 3.1.** Participant Characteristics ( $N = 42$ )

	Healthy	T2D	DPN
Number of Subjects	14	14	14
Gender	M: 6; F: 8	M: 6; F: 8	M: 6; F: 8
Age (years)	$51.0 \pm 6.7$	$51.9 \pm 6.3$	$53.5 \pm 6.7$
Weight (lbs.)	$157.4 \pm 30.2$	$177.9 \pm 38.0$	$210.4 \pm 31.7$
Height (In.)	$66.8 \pm 4.4$	$65.1 \pm 4.1$	$65.6 \pm 5.7$
BMI ( $\text{kg}/\text{m}^2$ )	$24.8 \pm 3.8$	$29.6 \pm 7.0$	$34.9 \pm 7.2$
Duration of T2D (years)	N/A	$9.4 \pm 5.0$	$19.2 \pm 8.4$
Duration of DPN (years)	N/A	N/A	$5.1 \pm 2.9$
A1C Level (%)	N/A	$7.1 \pm 1.1$	$8.0 \pm 2.0$
UENS Score	$1.4 \pm 2.2$	$9.4 \pm 4.3$	$30.9 \pm 5.7$

**Note:** BMI was derived using equation ((weight (lbs.) / height (in)) x 703)); UENS = Utah Early Neuropathy Scale.

**Table 3.2.** Mean  $\pm$  standard deviation of dependent variables: Sway Area ( $\text{cm}^2$ ) and Sway Velocity ( $\text{cm}/\text{s}$ ) ( $N = 42$ ) for each test condition per cohort.

	Cohort	Sway Area	Sway Velocity
EO Firm	Healthy	$2.37 \pm 1.9$	$1.04 \pm 0.3$
	T2D	$5.10 \pm 3.8$	$1.64 \pm 1.2$
	DPN	$7.13 \pm 4.6$	$1.44 \pm 0.5$
EC Firm	Healthy	$2.87 \pm 1.9$	$1.31 \pm 0.5$
	T2D	$6.78 \pm 4.6$	$1.87 \pm 1.1$
	DPN	$13.10 \pm 9.6$	$2.12 \pm 0.9$
EO Foam	Healthy	$7.57 \pm 5.0$	$1.46 \pm 0.3$
	T2D	$12.57 \pm 7.8$	$2.20 \pm 0.6$
	DPN	$18.93 \pm 12.3$	$2.27 \pm 0.9$
EC Foam	Healthy	$10.50 \pm 6.7$	$1.94 \pm 1.2$
	T2D	$19.11 \pm 7.9$	$3.17 \pm 1.2$
	DPN	$31.01 \pm 14.3$	$4.55 \pm 1.2$

A  $2$  (Vision)  $\times$   $2$  (Surface)  $\times$   $3$  (Diagnosis Group) mixed-design repeated-measures Omnibus ANOVA was conducted for both Sway Area and Sway Velocity, with Vision and

Surface as the within-subject factors and Diagnosis Group as the between-subjects factor, to assess overall main effects and interaction effects.

### *Sway Area*

There were significant main effects of Vision ( $F_{1, 39} = 85.58, p \leq 0.001, \eta^2 = 0.69$ ) and Surface ( $F_{1, 39} = 108.28, p \leq 0.001, \eta^2 = 0.74$ ), indicating that postural Sway Area increased under eyes-closed and foam surface conditions. Significant two-way interactions were found between Vision  $\times$  Diagnosis Group ( $F_{2, 39} = 16.13, p \leq 0.001, \eta^2 = 0.45$ ) and between Surface  $\times$  Diagnosis Group ( $F_{2, 39} = 6.00, p = 0.005, \eta^2 = 0.24$ ). However, the three-way interaction among Vision  $\times$  Surface  $\times$  Diagnosis Groups was not significant ( $F_{2, 39} = 1.62, p = 0.210, \eta^2 = 0.08$ ). A significant between-group effect was observed, indicating group differences in Sway Area ( $F_{2, 39} = 11.12, p \leq 0.001, \eta^2 = 0.36$ ). Planned contrasts revealed significant differences between healthy controls and participants with DPN ( $p \leq 0.001$ ), between DPN and T2D ( $p = 0.01$ ), and between T2D and healthy controls ( $p = 0.05$ ). Additional sub-analyses were performed by conducting mixed-model rmANOVAs with interaction effects of Sway Area for each test condition and between each cohort (see Table 3.3).

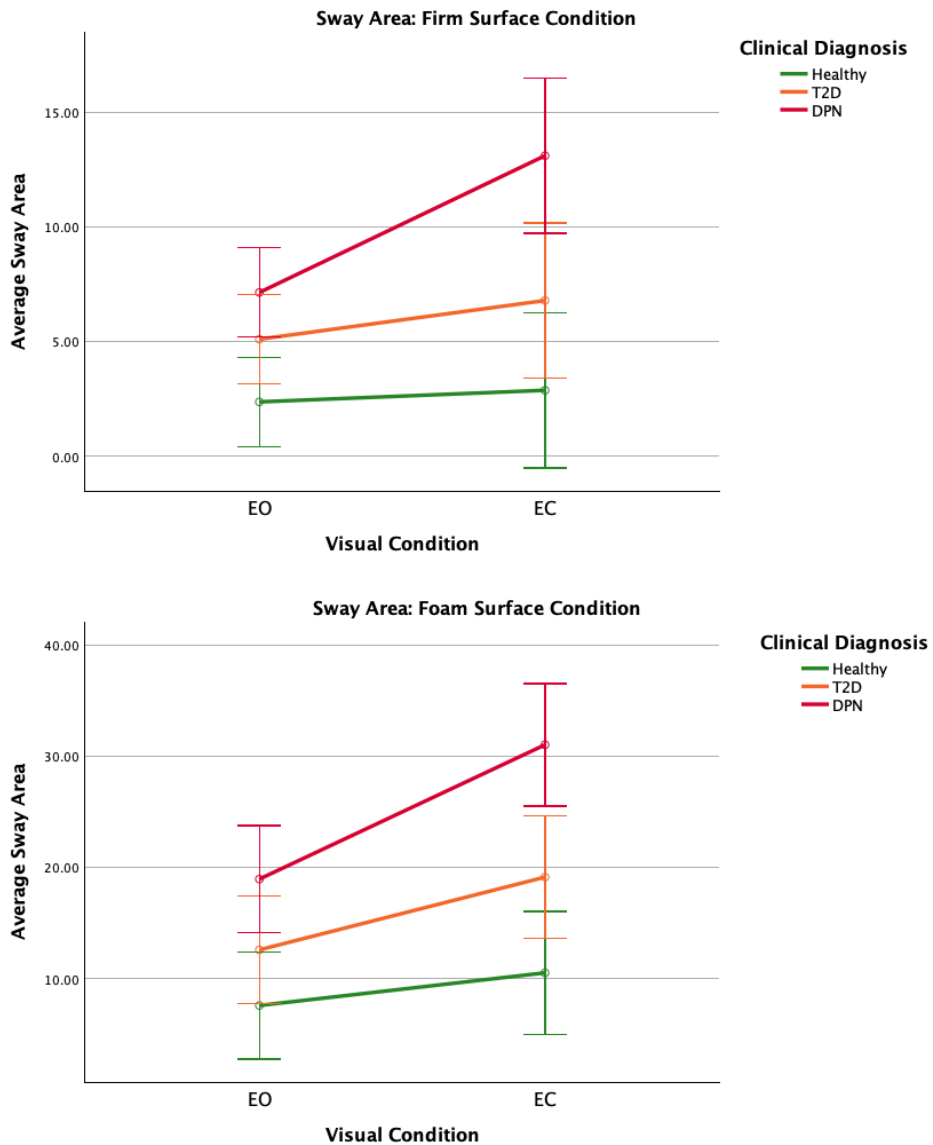
**Table 3.3.** Summary of rmANOVA results for Sway Area (cm<sup>2</sup>) and Sway Velocity (cm/s) per each test condition per cohort ( $N = 42$ ).

Measure	Condition	Main Effect	$p$ -value	$\eta p^2$	Interaction $F_{2,39}$
		$F_{1,39}$			
Sway Area	Visual $\times$ Cohort (Firm)	22.17	$\leq 0.001$	0.36	8.24 ( $p = 0.001$ , $\eta p^2 = 0.30$ )
Sway Area	Visual $\times$ Cohort (Foam)	85.92	$\leq 0.001$	0.69	11.78 ( $p \leq 0.001$ , $\eta p^2 = 0.38$ )
Sway Velocity	Visual $\times$ Cohort (Firm)	38.27	$\leq 0.001$	0.50	4.79 ( $p = 0.014$ , $\eta p^2 = 0.20$ )
Sway Velocity	Visual $\times$ Cohort (Foam)	69.01	$\leq 0.001$	0.64	8.80 ( $p \leq 0.001$ , $\eta p^2 = 0.31$ )
Sway Area	Surface $\times$ Cohort (EO)	60.86	$\leq 0.001$	0.61	3.42 ( $p \leq 0.001$ , $\eta p^2 = 0.15$ )
Sway Area	Surface $\times$ Cohort (EC)	126.31	$\leq 0.001$	0.76	6.70 ( $p = 0.003$ , $\eta p^2 = 0.26$ )
Sway Velocity	Surface $\times$ Cohort (EO)	49.71	$\leq 0.001$	0.56	6.27 ( $p = 0.004$ , $\eta p^2 = 0.24$ )
Sway Velocity	Surface $\times$ Cohort (EC)	49.35	$\leq 0.001$	0.56	6.48 ( $p = 0.004$ , $\eta p^2 = 0.25$ )

*i. Visual Condition  $\times$  Cohort*

When investigating Sway Area across visual conditions and between cohorts, results demonstrated a significant main effect measured on both firm ( $F_{1, 39} = 22.17$ ,  $p \leq 0.001$ ,  $\eta p^2 = 0.36$ ) and foam ( $F_{1, 39} = 85.92$ ,  $p \leq 0.001$ ,  $\eta p^2 = 0.69$ ) surface conditions. This indicates that Sway Area statistically differed between the eyes open and eyes closed conditions while participants stood on both the firm and foam surfaces (see Table 3.3 and Figure 3.1). Interaction effects were also observed between visual condition and cohort for each postural outcome measure ( $F_{2, 39} = 8.24$ ,  $p = 0.001$ ,  $\eta p^2 = 0.30$ ;  $F_{2, 39} = 11.78$ ,  $p \leq 0.001$ ,  $\eta p^2 = 0.38$ ). Under the firm surface condition, planned comparisons revealed that participants in the DPN cohort demonstrated a significantly greater Sway Area (see Table 3.2) than those in both the T2D cohort ( $p = 0.026$ ) and the healthy control group ( $p \leq 0.001$ ). However, the difference between the T2D cohort and healthy controls was not statistically

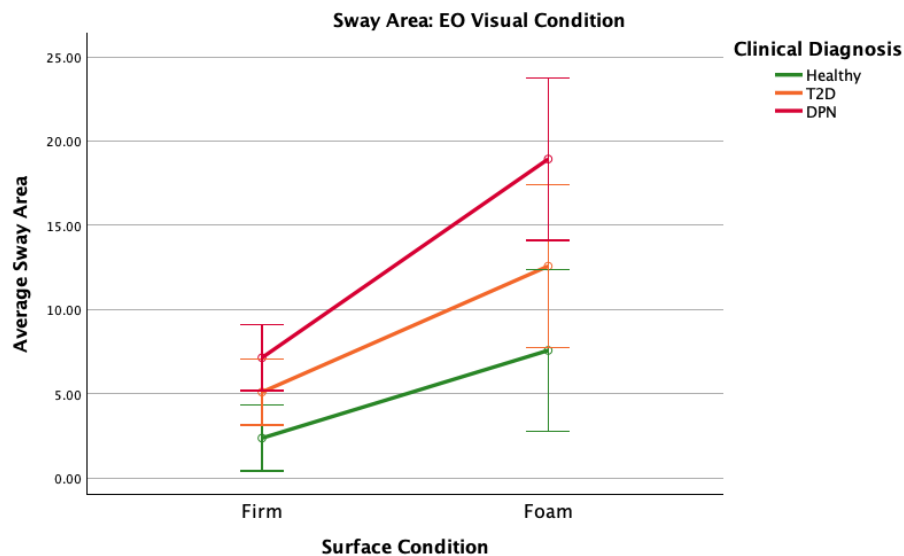
significant ( $p = 0.072$ ). A similar pattern was observed under the foam surface condition. The DPN group again exhibited significantly greater sway compared to both the T2D cohort ( $p = 0.013$ ) and the healthy controls ( $p \leq 0.001$ ). As with the firm surface, no significant difference was found between the T2D and healthy cohorts ( $p = 0.059$ ), though it trended towards significance.

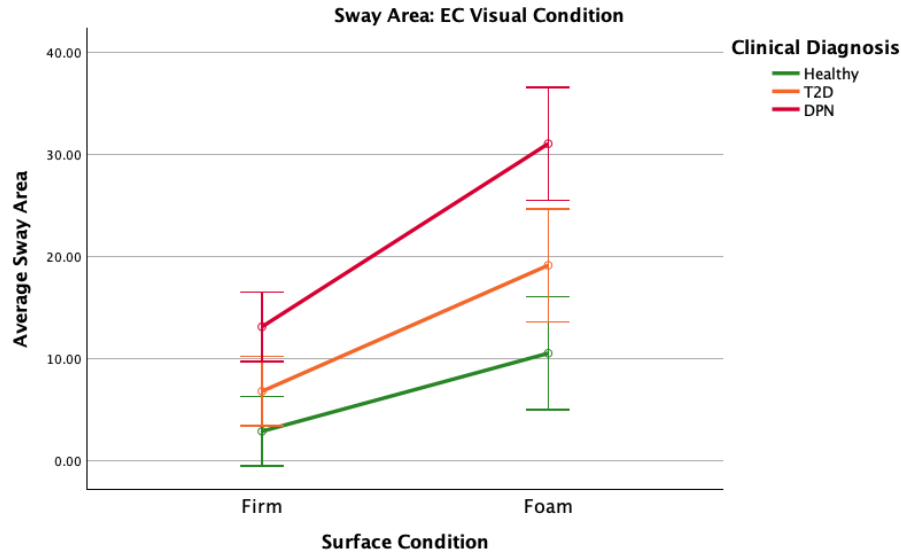


**Figure 3.1.** A mixed-model repeated-measures ANOVA was conducted to examine Sway Area (cm<sup>2</sup>) within visual conditions and between cohorts on (upper) firm and (lower) foam surface conditions.

ii. *Surface Condition* × *Cohort*

When investigating Sway Area across surface conditions and between cohorts, a significant main effect for both EO ( $F_{1, 39} = 60.86, p \leq 0.001, \eta^2 = 0.61$ ) and EC ( $F_{1, 39} = 126.31, p \leq 0.001, \eta^2 = 0.76$ ) surface conditions was observed. Sway Area significantly differed between the firm and foam surfaces (see Figure 3.2). Significant interaction effects were also observed between visual condition and cohort for each postural outcome measure ( $F_{2, 39} = 3.42, p \leq 0.001, \eta^2 = 0.15$ ;  $F_{2, 39} = 6.70, p = 0.003, \eta^2 = 0.26$ ). Planned comparisons revealed a significant difference between the healthy and DPN cohorts ( $p \leq 0.001$ ) in the EO visual condition Sway Area. However, no significance was found between the T2D and DPN cohort ( $p = 0.067$ ) or the T2D and Healthy cohort ( $p = 0.091$ ). Interestingly, when participants closed their eyes, planned comparisons revealed significant differences between DPN vs. T2D ( $p = 0.003$ ), the healthy vs. DPN ( $p \leq 0.001$ ), and the Healthy vs. T2D ( $p = 0.036$ ) cohorts.





**Figure 3.2.** The results of a mixed-model repeated-measures ANOVA for comparing Sway Area (cm<sup>2</sup>) revealed significant differences due to surface condition and between cohorts in the EO (upper) and EC (lower) visual conditions.

### *Sway Velocity*

There were significant main effects of Vision, ( $F_{1, 39} = 106.04, p \leq 0.001, \eta^2 = 0.73$ ) and Surface ( $F_{1, 39} = 56.24, p \leq 0.001, \eta^2 = 0.59$ ). Significant two-way interactions were found between Vision  $\times$  Diagnosis Group ( $F_{2, 39} = 12.95, p \leq 0.001, \eta^2 = 0.40$ ) and between Surface  $\times$  Diagnosis Group ( $F_{2, 39} = 7.21, p = 0.002, \eta^2 = 0.70$ ). A significant three-way interaction among Vision  $\times$  Surface  $\times$  Diagnosis Groups was also observed ( $F_{2, 39} = 22.32, p \leq 0.001, \eta^2 = 0.36$ ). In addition, a significant between-group effect was found for Diagnosis Group ( $F_{2,39} = 13.98, p \leq 0.001, \eta^2 = 0.42$ ), indicating overall group differences in Sway Velocity. Planned contrasts further revealed significant differences between healthy controls vs. DPN ( $p \leq 0.001$ ), between DPN vs. T2D ( $p = 0.05$ ), and between T2D vs healthy controls ( $p = 0.003$ ).

Additional sub-analyses were performed by conducting mixed-model rmANOVA with interaction effects of Sway Velocity for each test condition and between each cohort (see Table 3.3).

*i. Visual Condition × Cohort*

When investigating Sway Velocity across visual conditions and between cohorts, a significant main effect for both firm ( $F_{1, 39} = 38.27, p \leq 0.001, \eta^2 = 0.50$ ) and foam ( $F_{1, 39} = 69.01, p \leq 0.001, \eta^2 = 0.64$ ) surface conditions was seen. Sway Velocity was significantly greater during eyes-closed compared to eyes-open trials, irrespective of the surface condition (see Table 3.2). Furthermore, a significant interaction effect between visual condition and cohort was observed for each postural outcome measure on both surfaces: firm ( $F_{2, 39} = 4.79, p = 0.014, \eta^2 = 0.20$ ) and foam ( $F_{2, 39} = 8.80, p \leq 0.001, \eta^2 = 0.31$ ). Planned comparisons revealed no statistically significant differences between cohorts under the firm surface condition ( $p > 0.05$ ), indicating similar Sway Velocity responses across all groups in a less challenging condition. However, although the DPN and healthy cohorts were not significantly different at this time, the p-value is trending towards statistical significance between the two groups ( $p = 0.059$ ).

Under the foam surface condition, where somatosensory input is reduced and balance demands increase, the DPN cohort demonstrated significantly greater Sway Velocity compared to both the T2D cohort ( $p = 0.002$ ) and healthy controls ( $p \leq 0.001$ ). Additionally, the T2D cohort exhibited significantly greater Sway Velocity than the healthy cohort ( $p = 0.002$ ).

ii. *Surface Condition* × *Cohort*

When investigating Sway Velocity across surface conditions and between cohorts, a significant main effect for both EO ( $F_{1, 39} = 49.71, p \leq 0.001, \eta^2 = 0.56$ ) and EC ( $F_{1, 39} = 49.35, p \leq 0.001, \eta^2 = 0.56$ ) surface conditions, indicating that Sway Velocity differed between firm and foam conditions on both surface condition. Significant interaction effects were also observed between visual condition and cohort for each postural outcome measure ( $F_{2, 39} = 6.27, p = 0.004, \eta^2 = 0.24$ ;  $F_{2, 39} = 6.48, p = 0.004, \eta^2 = 0.25$ ). Planned comparisons during the eyes open condition revealed that the healthy cohort exhibited significantly lower Sway Velocity compared to both the T2D cohort ( $p = 0.010$ ) and the DPN cohort ( $p = 0.002$ ). However, no significant difference was observed between the T2D and DPN cohorts ( $p = 0.50$ ). In contrast, under the eyes closed condition, planned comparisons revealed significant differences between all cohorts: healthy vs. T2D ( $p = 0.002$ ), healthy vs. DPN ( $p \leq 0.001$ ), and T2D vs. DPN ( $p = 0.004$ ), indicating that increased postural challenge exacerbates differences in Sway Velocity among groups

A mixed-design repeated-measures ANCOVA [2 (Vision) × 2 (Surface) × 3 (Diagnosis Group)] was conducted for both Sway Area and Sway Velocity to account for potential confounding variables: BMI, Years Since Clinical Diagnosis of T2D, and Age.

*BMI*

**Table 3.4.** Interaction effects of rmANCOVA after controlling for effects of body mass index (BMI) on postural sway ( $n = 42$ )

<b>Dependent Variable</b>	<b>Effect</b>	<b><i>F</i></b>	<b><i>p</i>-value</b>	<b><math>\eta^2</math></b>
<b>Sway Area</b>	Vision × Clinical Diagnosis	$F_{2,38} = 3.94$	0.028	0.172
	Surface × Clinical Diagnosis	$F_{2,38} = 1.02$	0.372	0.051
	Vision × Surface × Diagnosis	$F_{2,38} = 0.38$	0.690	0.019
	Clinical Diagnosis	$F_{2,38} = 9.16$	$\leq 0.001$	0.325

**Table 3.4** (Continued)

	BMI	$F_{1,38} = 0.001$	0.976	0.000
<b>Sway Velocity</b>	Vision × Clinical Diagnosis	$F_{2,38} = 3.35$	0.046	0.150
	Surface × Clinical Diagnosis	$F_{2,38} = 1.34$	0.273	0.066
	Vision × Surface × Diagnosis	$F_{2,38} = 0.86$	0.433	0.043
	Clinical Diagnosis	$F_{2,38} = 11.58$	$\leq 0.001$	0.379
	BMI	$F_{1,38} = 1.42$	0.241	0.036

For Sway Area (see Table 3.4), within-subjects effects demonstrated Vision × Diagnosis interaction remained significant ( $F_{2,38} = 3.94, p = 0.028, \eta^2 = 0.17$ ), though the effect size was reduced from the original rmANOVA ( $\eta^2 = 0.45$ ) after controlling for BMI ( $\eta^2 = 0.17$ ). However, Surface × Diagnosis indicated that BMI ( $\eta^2 = 0.051$ ) potentially accounts for the differences in group means detected by the ANOVA, reducing the effect from the original rmANOVA ( $\eta^2 = 0.24$ ). Aligned with the ANOVA, the three-way interaction between Vision × Surface × Diagnosis remained nonsignificant, and the effect size was reduced ( $\eta^2 = 0.08$  vs.  $0.02$ ). As demonstrated by the between-group effects, BMI did not account for a significant amount of variance ( $F_{1,38} = 0.001, p = 0.976, \eta^2 = 0.00$ ) in the dependent measure. Post hoc analyses revealed that group differences in Sway Area were maintained between the Healthy vs. T2D ( $p = 0.004$ ) and DPN ( $p \leq 0.001$ ). However, the initially significant difference between the T2D and DPN groups ( $p = 0.01$ ) was no longer statistically significant after controlling for BMI ( $p = 0.077$ ), though it is trending towards significance.

When investigating Sway Velocity (see Table 3.4), within-subjects effects demonstrated that the Vision × Diagnosis interaction remained significant ( $F_{2,38} = 3.35, p = 0.046, \eta^2 = 0.15$ ), though the effect size was reduced from the original rm ANOVA ( $\eta^2 = 0.40$ ) after controlling for BMI. Similar to Sway Area, the Surface × Diagnosis interaction resulted in not significant ( $F_{2,38} = 1.34, p = 0.273, \eta^2 = 0.07$ ) after controlling

for BMI. Aligned with the ANOVA, the three-way interaction between Vision  $\times$  Surface  $\times$  Diagnosis remained nonsignificant, although the effect size was reduced ( $\eta p^2 = 0.36$  vs. 0.04). As demonstrated by the between-group effects, BMI did not account for a significant amount of variance ( $F_{1, 38} = 1.42, p = 0.241, \eta p^2 = 0.04$ ) in the dependent measure. Post hoc analyses revealed that group differences in Sway Velocity were maintained between the Healthy vs. T2D ( $p = 0.001$ ) and DPN ( $p \leq 0.001$ ). However, the initially significant difference between the T2D and DPN control groups ( $p = 0.05$ ) was no longer statistically significant after controlling for BMI ( $p = 0.064$ ), though it is trending towards significance.

*Age*

**Table 3.5.** Interaction effects of rmANCOVA after controlling for effects of age on postural Sway ( $N=42$ )

<b>Dependent Variable</b>	<b>Effect</b>	<b><i>F</i></b>	<b><i>p</i>-value</b>	<b><math>\eta p^2</math></b>
<b>Sway Area</b>	Vision $\times$ Clinical Diagnosis	$F_{2,38} = 6.08$	0.005	0.242
	Surface $\times$ Clinical Diagnosis	$F_{2,38} = 1.58$	0.219	0.077
	Vision $\times$ Surface $\times$ Diagnosis	$F_{2,38} = 0.67$	0.517	0.034
	Clinical Diagnosis	$F_{2,38} = 12.83$	$\leq 0.001$	0.403
	Age	$F_{1,38} = 3.54$	0.068	0.085
<b>Sway Velocity</b>	Vision $\times$ Clinical Diagnosis	$F_{2,38} = 7.54$	0.002	0.284
	Surface $\times$ Clinical Diagnosis	$F_{2,38} = 2.07$	0.138	0.099
	Vision $\times$ Surface $\times$ Diagnosis	$F_{2,38} = 0.80$	0.457	0.040
	Clinical Diagnosis	$F_{2,38} = 11.32$	$\leq 0.001$	0.373
	Age	$F_{1,38} = 0.90$	0.349	0.023

After controlling for age (see Table 3.5), there was a significant two-way interaction preserved between Vision and Diagnosis Group ( $F_{2, 39} = 6.08, p \leq 0.005, \eta p^2 = 0.24$ ) when investigating Sway Area, though the effect size was reduced from the original rm ANOVA ( $\eta p^2 = 0.45$ ) after controlling for Age ( $\eta p^2 = 0.24$ ). However, Surface  $\times$  Diagnosis indicated that Age may potentially account for the differences in group means detected by the ANOVA. Aligned with the ANOVA, the three-way interaction between

Vision  $\times$  Surface  $\times$  Diagnosis remained nonsignificant, although the effect size was reduced ( $\eta p^2 = 0.08$  vs.  $0.03$ ). As demonstrated by the between-group effects, Age did not account for a significant amount of variance ( $F_{1,38} = 3.54$ ,  $p = 0.068$ ,  $\eta p^2 = 0.09$ ) in the dependent measures. Post hoc analyses revealed that group differences in Sway Area were maintained between the Healthy vs. T2D ( $p = 0.003$ ) and DPN ( $p \leq 0.001$ ). However, the initially significant difference between the T2D and DPN control groups ( $p = 0.01$ ) was no longer statistically significant after controlling for Age ( $p = 0.077$ ), though it is trending towards significance.

When investigating Sway Velocity, within-subjects effects demonstrated Vision  $\times$  Diagnosis interaction remained significant ( $F_{2,38} = 7.54$ ,  $p = 0.002$ ,  $\eta p^2 = 0.284$ ), though the effect size was reduced from the original rm ANOVA ( $\eta p^2 = 0.40$ ) after controlling for Age. Similar to Sway Area, the Surface  $\times$  Diagnosis interaction resulted in not significant ( $F_{2,38} = 2.09$ ,  $p = 0.138$ ,  $\eta p^2 = 0.10$ ) after controlling for Age. Aligned with the ANOVA, the three-way interaction between Vision  $\times$  Surface  $\times$  Diagnosis remained nonsignificant, although the effect size was reduced ( $\eta p^2 = 0.36$  vs.  $0.04$ ). As demonstrated by the between-group effects, Age did not account for a significant amount of variance ( $F_{1,38} = 0.90$ ,  $p = 0.349$ ,  $\eta p^2 = 0.023$ ) in the dependent measure. Post hoc analyses revealed that group differences in Sway Velocity were maintained between the Healthy vs. T2D ( $p = 0.003$ ) and DPN ( $p \leq 0.001$ ). However, the T2D and DPN control groups ( $p = 0.148$ ) were not statistically significant after controlling for Age.

*Time Since T2D Diagnosis*

**Table 3.6.** Interaction effects of rmANCOVA after controlling for effects of Time Since Diagnosis of T2D on postural Sway ( $n = 28$ )

<b>Dependent Variable</b>	<b>Effect</b>	<b><i>F</i></b>	<b><i>p</i>-value</b>	<b><math>\eta p^2</math></b>
<b>Sway Area</b>	Vision $\times$ Clinical Diagnosis	$F_{1,25} = 7.26$	0.012	0.23
	Surface $\times$ Clinical Diagnosis	$F_{1,25} = 2.10$	0.160	0.08
	Vision $\times$ Surface $\times$ Diagnosis	$F_{1,25} = 0.68$	0.416	0.03
	Clinical Diagnosis	$F_{1,25} = 2.11$	0.159	0.08
	Time Since T2D Diagnosis	$F_{1,25} = 0.30$	0.588	0.01
<b>Sway Velocity</b>	Vision $\times$ Clinical Diagnosis	$F_{1,25} = 11.91$	0.002	0.32
	Surface $\times$ Clinical Diagnosis	$F_{1,25} = 7.37$	0.012	0.23
	Vision $\times$ Surface $\times$ Diagnosis	$F_{1,25} = 5.67$	0.025	0.19
	Clinical Diagnosis	$F_{1,25} = 0.17$	0.688	0.01
	Time Since T2D Diagnosis	$F_{1,25} = 2.78$	0.108	0.10

*Note:* Only those with a clinical diagnosis of Type 2 Diabetes ( $n = 14$ ) and Diabetic Peripheral Neuropathy ( $n = 14$ ) were including in the analysis

After controlling for Time Since T2D Diagnosis (see Table 3.6), there was a significant two-way interaction between Vision  $\times$  Diagnosis Group ( $F_{1,25} = 7.26, p = 0.012, \eta p^2 = 0.23$ ), while no significant interaction was observed between Surface  $\times$  Diagnosis Group for Sway Area. Additionally, the three-way interaction between Vision  $\times$  Surface  $\times$  Diagnosis demonstrated no significant interactions. As shown by the between-group effects, Time Since Diagnosis of T2D and Clinical Diagnosis did not account for a significant amount of variance in the dependent measures.

Sway Velocity demonstrated significant interactions between Vision  $\times$  Diagnosis Group ( $F_{1,25} = 11.91, p = 0.002, \eta p^2 = 0.32$ ) and Surface  $\times$  Diagnosis Group ( $F_{1,25} = 7.37, p = 0.012, \eta p^2 = 0.23$ ). Additionally, the three-way interaction between Vision  $\times$  Surface  $\times$  Diagnosis demonstrated significant interactions ( $F_{1,25} = 5.67, p = 0.025, \eta p^2 = 0.19$ ) when adjusting for Time Since Diagnosis of T2D. Interestingly, when examining the within-subjects effects, no significant differences were observed for the between-group

comparison of Clinical Diagnosis of T2D and DPN, or for the cofounder Time Since Diagnosis of T2D.

## Discussion

The present study demonstrates the feasibility of using a validated smartphone application capable of detecting subtle postural changes across different diagnostic groups, specifically in identifying significant differences between those with and without DPN. Consistent with our hypothesis, these findings provide a foundation for enhancing clinical decision-making by introducing an accessible and objective tool to support DPN assessment beyond conventional diagnostic methods.

Through the present research, three factors were identified as important in supporting postural instability as a viable indicator of diagnosis progression associated with DPN. First, we successfully replicated previous findings that demonstrate an increase in postural sway as postural conditions become more challenging. Consistent with prior literature, balance performance deteriorated when visual input was removed, regardless of cohort, reflecting the central role of vision in spatial orientation and movement correction.<sup>153,154</sup> Similarly, standing on a foam surface disrupted somatosensory feedback from the feet and ankles, leading to increased postural sway, a finding supported by studies showing that altered proprioceptive input challenges the postural control system.<sup>153–155</sup> These effects were believed to occur because postural control relies on the integration of visual, somatosensory, and vestibular inputs. When one system is compromised, such as by closing the eyes or standing on an unstable surface, the body must rely more heavily on the remaining sensory systems.<sup>136</sup> The findings show both significant main effects of visual condition, surface condition, and cohort, as well as significant interaction effects. This

postural decline pattern was consistent across all participants, regardless of diagnostic cohort (see Table 3.2). However, the effect was more pronounced in individuals with DPN, who already suffer from diminished somatosensory input when compared to the T2D and healthy controls.<sup>44,52,156,157</sup>

Secondly, subtle differences in postural behaviors across diagnostic groups, differentiating individuals with and without DPN using postural outcome measures, were observed. This is particularly important to Aim 2, as significant interactions between cohorts underscore the critical role of sensory input in postural control and suggest that individuals with and without DPN respond differently to balance demands. The significant three-way interaction among vision, surface, and diagnosis group emphasizes that Sway Velocity is highly responsive to combined sensory and contextual challenges, making it a robust indicator of balance dysfunction in this population. Between-group differences and contrast analyses further confirmed that DPN participants exhibited significantly greater Sway Velocity than both T2D and healthy individuals, and that even T2D individuals showed subtle but significant increases compared to healthy controls. These findings suggest that Sway Velocity may be a sensitive marker for the early detection of postural instability in diabetes, even before neuropathy is clinically diagnosed. Additionally, Sway Area demonstrated significant interactions between vision and diagnosis group and between surface and diagnosis group, indicating that individuals with DPN exhibit exaggerated sway when sensory input is reduced. Although the three-way interaction was not significant, the between-group effect was substantial, with large effect sizes, and contrasts confirmed distinct group differences. Notably, Sway Area differentiated all three

groups, reinforcing its clinical utility in assessing balance impairment progression across the diabetes spectrum.

To provide further granularity, Sway Area and Sway Velocity were analyzed independently, allowing for a more detailed examination of how diagnostic group differences were influenced by each postural condition. Consistent with Dixit et al. (2015),<sup>155</sup> the present study found that individuals with DPN exhibited significantly greater sway across all conditions compared to controls; however, sway increased progressively from EO to EC, and further on foam surfaces, with the highest instability observed in the EC Foam condition.

Interestingly, no significant cohort differences were observed during Sway Velocity (Visual  $\times$  Cohort) when measured on the firm surface, indicating that compensatory mechanisms may be sufficient under conditions with minimal postural demands. However, on the foam surface, where proprioceptive input is further reduced, the DPN cohort exhibited significantly greater Sway Velocity than both the T2D and healthy groups. This aligns with the notion that DPN impairs peripheral somatosensory processing, reducing sensitivity to pressure, joint position, and surface changes, and weakening the ability to respond to postural disturbances, especially when somatosensory input is limited.<sup>155</sup> As a result, individuals with DPN may be forced to rely more heavily on slower (vision) or less precise (vestibular) compensatory systems, leading to increased postural instability, especially in the absence of firm surface cues.

Additionally, no significant differences were observed between the T2D and DPN cohorts under postural conditions involving lower levels of challenge, specifically, in Sway Area (Surface  $\times$  Cohort) and Sway Velocity (Surface  $\times$  Cohort) when visual input was

available (i.e., EO). However, significant differences between the T2D and DPN groups emerged across all postural conditions once visual input was removed, highlighting the inability of those with DPN to effectively use somatosensory inputs when vision is removed. Furthermore, those with DPN likely compensate for this deficit when vision is available, as well as supplementing with vestibular input.

Despite the absence of a clinical diagnosis of neuropathy, the T2D cohort exhibited emerging trends and significant differences when compared to healthy controls, particularly under more challenging postural conditions.<sup>65,143–146</sup> These findings suggest that, while overt postural impairments may not yet be present in T2D, subtle disruptions to balance control may already be emerging. This could be important, especially for tracking the progression of T2D through postural changes before the onset of DPN occurs.

Finally, controlling for covariates, BMI, Time Since Diagnosis of T2D, and Age, helped to further understand postural outcomes measures across Healthy, T2D, and DPN individuals. The significant Vision  $\times$  Diagnosis interaction for both Sway Area and Sway Velocity remained robust after adjusting for each covariate, though the effect sizes were consistently reduced. Specifically, when observing partial eta squared values for Vision  $\times$  Cohort in Sway Area, which were weakened in strength from 0.45 in the unadjusted model to 0.17 (BMI), 0.24 (Age), and 0.23 (Time Since Diagnosis of T2D) for each confounder. Similarly, Sway Velocity exhibited reduced strength from 0.40 to 0.15 (BMI), 0.28 (Age), and 0.32 (Time Since Diagnosis of T2D).

These reductions in effect sizes suggest that while these covariates account for some of the variance in postural measures, they do not eliminate the diagnostic group differences, particularly between the Healthy controls and those with T2D and DPN.

Importantly, BMI and Age did not account for a statistically significant amount of differences in the between-subject effects of dependent measures (BMI:  $p = 0.976$  and Age:  $p = 0.068$ ) for Sway Area, and (BMI:  $p = 0.349$  and Age:  $p = 0.241$ ) for Sway Velocity. This suggests that although these factors are correlated with postural control, their influences are not strong enough to overshadow the disease-related effects on the postural control system.

The inclusion of Time Since Diagnosis as a covariate provided insight into the role of disease duration in impairments of postural control. As T2D progresses, it is associated with an increase in the clinical manifestation of DPN, which in turn impairs sensory feedback and motor coordination needed for balance. Neither Time Since Diagnosis (Sway Area:  $p = 0.59$ ; Sway Velocity:  $p = 0.11$ ) nor Clinical Diagnosis (Sway Area:  $p = 0.16$ ; Sway Velocity:  $p = 0.69$ ) independently accounted for significant between-group differences in postural control. This suggests that balance impairments may not be solely driven by diagnostic category or disease duration alone. However, its inclusion revealed within-subject interaction effects, particularly for Sway Velocity. These findings suggest that longer disease duration may exacerbate postural challenges under combined sensory conditions, particularly in those with DPN. These findings underscore the importance of considering disease duration as a potential covariate or moderating factor when evaluating balance impairments in individuals with diabetes.

Although Age and BMI modestly reduce the observed group effects and likely interact with clinical status to influence balance, they do not fully explain the deficits seen in individuals with T2D and DPN. The emergence of a three-way interaction when adjusting for Time Since Diagnosis suggests an interesting, progressive influence of

disease duration on Sway Velocity, potentially reflecting sensorimotor decline. These findings reinforce the conclusion that diabetic diagnosis, particularly the presence of peripheral neuropathy, remains a primary driver of postural instability, even after accounting for common clinical and demographic confounders. That being said, clinicians and researchers should consider the nuanced role of the preceding confounders when measuring balance and postural control in those with T2D and DPN populations.

While this study provides valuable evidence for the use of a novel smartphone application to detect postural instability in those with DPN, it is important to acknowledge its limitations. The study design consisted of a single session in which participants were asked to complete the postural task protocol under varying visual and surface conditions. Although the participant provided demographic and clinical information, this single session provided a snapshot of their diabetes and functional abilities. However, T2D and DPN symptoms can be variable on a day-to-day basis. As such, future studies should evaluate postural stability over time using a longitudinal study design to illustrate further the effect diagnosis may have on postural outcome measures as T2D and DPN progresses.

### Conclusion

Taken together, current findings indicate that both Sway Velocity and Sway Area can differentiate diagnostic groups, showing heightened sensitivity under multi-sensory challenge conditions and reflecting broader group-level differences. These results support the utility of postural sway measures as a functional measure for identifying and tracking balance impairments in individuals with diabetes and neuropathy using a validated smartphone device. The observed differences highlight the importance of early screening for postural instability in clinical settings, even among individuals with T2D who do not

yet exhibit neuropathic symptoms, in addition to those with DPN, to reduce poor outcomes. Incorporating balance assessments, especially one that is portable, objective, and accessible, into routine diabetes care could enhance early detection and inform targeted interventions to reduce fall risk and improve quality of life.

## **CHAPTER 4: VALIDATION OF POSTURAL INSTABILITY AS AN EARLY MARKER OF DIABETIC PERIPHERAL NEUROPATHY USING A SMARTPHONE BALANCE APPLICATION AND A CLINICAL REFERENCE STANDARD**

### Introduction

Diabetic Peripheral Neuropathy (DPN) is a common and progressive complication of diabetes that causes neurodegeneration of the small and large nerve fibers of the extremities,<sup>12,15-19</sup> and traditionally presents itself in a “glove and stocking” distribution. It develops gradually, often beginning with subtle symptoms such as tingling, numbness, or burning sensations in the feet, and can progress to sharp pain, muscle weakness, and even complete loss of sensation. Additionally, DPN negatively affects postural control and balance,<sup>158</sup> significantly increasing the risk of falls due to its impact on the sensory and motor nerves of the lower extremities.<sup>61-63,65,153</sup> As the condition progresses, individuals may experience severe complications such as foot ulcers, infections, and, in extreme cases, amputations.<sup>24-29</sup> These physical impairments not only diminish the quality of life and functional ability of the individual but also contribute substantially to broader healthcare burdens, requiring ongoing medical management, increased hospitalization rates, care for fall-related injuries, and long-term support services.<sup>6,7,159</sup>

In the United States, the total annual cost of treating DPN and its complications was estimated to be \$10.91 billion and has continued to rise since.<sup>159</sup> One in 2 people diagnosed with Type 2 Diabetes (T2D) is said to develop DPN within 25 years of their initial diagnosis.<sup>14</sup> In a study conducted in 2023, it was estimated that individuals with T2D accounted for 93.1% of the total costs associated with DPN.<sup>159</sup> This is primarily due to the

medical assistance of poor outcomes attributed to the disease, such as diabetic foot ulcerations, amputations, and falls.<sup>160,161</sup>

Two primary factors are crucial for diagnosing DPN: a thorough history and a comprehensive physical examination.<sup>78</sup> Poor outcomes attributed to DPN can be prevented with early diagnosis, management, and treatment.<sup>32–34</sup> Commonly used clinical tools to assess nerve function include the gold standard, Nerve Conduction Velocity (NCV) test, and other clinically validated assessments<sup>79</sup> such as the Semmes Weinstein Monofilament Examination, the vibration perception threshold test, which uses a 128-Hz tuning fork, the Achilles tendon reflex assessment, and physical examinations of the foot. These assessments are often combined to determine the severity of sensory deficits that may exist in the foot or limb, and the combination of more than one has demonstrated a sensitivity of 87% in detecting DPN.<sup>80,81</sup>

The Utah Early Neuropathy Scale (UENS) is a physical examination scale specifically designed to quantify the early stages of DPN and detect modest changes in the severity and distribution of sensory loss.<sup>33</sup> It incorporates a combination of validated clinical measures for both large and small fiber neurodegeneration. Among subjects with existing neuropathy, the UENS closely correlates with that of the established scales of the Michigan Neuropathy Screening Instrument (MNSI)<sup>40</sup> and the Neuropathy Impairment Score–Lower Leg (NIS-LL),<sup>82</sup> providing further support for its validity. In a study conducted by Singleton et al., the UENS demonstrated a high level of interrater reliability, with an intraclass correlation coefficient of 0.94. Confirmatory tests were used to diagnose neuropathy, including NCV studies of the sural and peroneal nerves, skin biopsy for intraepidermal nerve fiber density (IENFD), quantitative sudomotor axon reflex testing

(QSART), and quantitative sensory testing (QST). When compared, the confirmatory tests were more strongly correlated with the UENS than with either the MDNS or NIS-LL.<sup>33</sup> Furthermore, within these cohorts, the UENS outperformed both the MDNS and NIS-LL in receiver operating characteristic (ROC) analysis, achieving a sensitivity of 92%, which was higher than that of the MDNS (67%) and NIS-LL (81%), without compromising specificity.<sup>33</sup>

Despite the availability of sensitive diagnostic tools, many pitfalls currently exist in the diagnosis and management of DPN. Some of the biggest factors to consider are that these diagnostic tools and techniques require a clinical setting with a trained specialist to perform the examination and specialized equipment that is not always available in general care facilities.<sup>40,83,84</sup> Additionally, in general care facilities, both patients and providers often lack awareness of DPN symptoms and lack the time during appointments to perform the examination,<sup>39-41</sup> making it challenging to detect DPN in its early stages. As it currently stands, DPN is underdiagnosed and undertreated in US primary care settings,<sup>85-87</sup> missing potential opportunities for early intervention and prevention of poor outcomes.<sup>87</sup> Additionally, in many of the commonly used diagnostic measures and tools, there is an emphasis on subjective clinical expertise. In a study investigating general physicians' perceptions of diagnosing DPN, there was only a 14% concordance between the monofilament testing and visual examination of the foot. Furthermore, doctors achieved minimal success in diagnosing mild/moderate neuropathy compared to severe neuropathy.<sup>87</sup>

DPN diagnostic and management methods have several barriers that aren't always accessible or feasible to the individuals who suffer from the disease. At the national level,

the American Diabetes Association (ADA) recommends annual diabetes foot examinations and neuropathy screenings for individuals with T2D beginning after diagnosis.<sup>37</sup> However, the CDC found only a 52% compliance rate among general care clinics in 2019.<sup>38</sup> Failure to comply with the ADA's preventive measure recommendations is due to a lack of awareness of DPN symptoms, lack of training to utilize instrumentation, lack of appropriate equipment, and a lack of time during appointments to perform the examination.<sup>39-41</sup> Due to its insidious nature, DPN is often unnoticed by both the patient and physician until irreversible nerve damage has already occurred.<sup>16,17,35,36</sup>

The heightened risk of falls and postural instability among those with DPN stems from the profound sensorimotor impairments that disrupt balance, muscular strength,<sup>46-49</sup> and protective reflexes.<sup>45</sup> These symptoms have a detrimental effect on one's functional ability, as large afferent (1A/B) fibers are critical inputs involved in producing complex patterns to control and counteract external forces during postural control.<sup>53,137</sup> Among neurological populations, those with peripheral neuropathy report to be categorized as the third highest rate of falls.<sup>66</sup> However, individuals with diabetes do not always report their unsteadiness as a clinical problem because they do not recognize it to be potentially caused by DPN, but rather a byproduct of age. Vileikyte et al. found that 23% of 484 patients with DPN perceived themselves as being unsteady only when asked specifically about it.<sup>77</sup> However, when evaluated, individuals with T2D, with and without DPN, demonstrated greater postural instability during quiet stance compared to healthy controls.<sup>65,143-146</sup> Lai et al (2025) recently conducted a cross-sectional study involving 146 adults who underwent clinical neuropathy evaluations alongside instrumented postural (eyes open on a force plate) examinations. Results indicated that sway velocity achieved an AUC of 0.76,

indicating moderate to good accuracy for identifying individuals with DPN during quiet stance.<sup>162</sup>

Interestingly, diagnostic methods and management do not currently include tests that evaluate postural decline in clinical settings, despite the vast research that supports this claim,<sup>64,73–76,162</sup> and physicians must rely on subjective recollections of falls and instability. If postural stability could be shown to have criterion validity relative to an established diagnostic method for DPN, this could create the possibility of a quantitative method to assess degeneration of the peripheral nerves that doesn't initially require a trained professional or specialized equipment.

The primary goal of this study is to establish postural instability as an early indicator of DPN, compared to a validated early neuropathy screening tool (UENS) that evaluates sensitivity and motor responses in the lower extremities using a battery of examinations commonly used in clinical settings to assess DPN. If postural instability is validated to the UENS using a smartphone application and has the ability to discriminate between diagnosis groups, it could enhance clinical judgment and broaden clinical examinations to include balance in the diagnosis and management of individuals with T2D and DPN.

## Methodology

Forty-two participants (see Table 3.1 for demographic data) were classified into three groups ( $n = 14$  per group): Control (healthy), Type 2 Diabetes (T2D), and Diabetic Peripheral Neuropathy (DPN), to participate in a single-session repeated-measures design study. Group assignments were determined at the beginning of the study based on clinical diagnosis by a trained physician. To be eligible, participants had to be: 1) Between 30-60

years of age, 2) Able to give informed consent, 3) Have a clinical diagnosis of Type 2 Diabetes or no history of diabetes (clinical diagnosis is based on HbA1C levels exceeding 6.5), 4) Able to ambulate without an assistive device. Exclusion Criteria was as followed: 1) lower limb or musculoskeletal injury or amputation which affects balance, 2) clinically significant orthopedic, muscular, or neurological (excluding peripheral neuropathy) disability that affect their ability to perform the postural task protocol, 3) inability to stand independently for at least 10 minutes, 4) individuals who suffer from substance abuse, 5) currently pregnant, 6) vitamin B deficiency.

Two factors were considered in selecting age parameters: 1) Postural decline due to age, and 2) the onset of diabetes and DPN. With respect to these factors outlined in Chapter 3's Methodology, we limited our recruitment age range between 30 and 60 years.

The Temple University Institutional Review Board approved the procedures, and all participants provided informed consent prior to participating in the study. Participants were recruited from the Philadelphia community and compensated for time and travel. Individuals with a clinical diagnosis of T2D and/or DPN received a one-time \$50.00 gift card as compensation. Individuals who served as healthy controls for the study received a one-time \$25.00 gift card as compensation.

The sample size estimate for the present dissertation is based on the present study, which assesses the discrimination of a smartphone application for early detection of DPN when compared to the Utah Early Neuropathy Scale (UENS), a validated early diagnostic functional assessment. The prevalence of DPN has been reported as approximately 50% of all individuals diagnosed with T2D.<sup>14</sup> The predictive accuracy of the novel smartphone application for the presence of DPN will be assessed using a Receiver Operating

Characteristic (ROC) analysis. Currently, the UENS has provided an 88% diagnostic accuracy in detection,<sup>33</sup> so we will estimate a necessary sample size to achieve no less than 10% of this diagnostic accuracy (AUC = 0.78). Sample size estimation was performed with a two-sided z-test using PASS software, resulting in a recruitment target of 28 participants.<sup>116,117,152</sup> Of the total sample population, 14 diabetic individuals with DPN and 14 diabetic individuals without DPN (assuming an allocation ratio DPN/no DPN of 1:1) would suffice with 80% power to detect a difference of 0.29 between the area under the curve (AUC), under the null hypothesis of AUC = 0.5 (no diagnostic accuracy) and the alternative hypothesis of AUC = 0.78 (moderate diagnostic accuracy), at a significance level of 0.05.

#### *Postural Task & Protocol*

The following study utilizes the methodology and postural data obtained from Aim 2 (see Chapter 3: *Postural Task & Protocol*).

The Utah Early Neuropathy Scale is designed as a simple and quick examination to identify early-stage DPN. The UENS is based on assessments of first toe extension vibration, proprioception, and an extended examination of pinprick sensation, including assessments in six different segments of the foot and lower limb. Allodynia and ankle reflexes are also assessed. The UNES has a maximum score of 42 points. All participants were assessed using the UENS (see Table 3.1).

### *Statistical Analysis*

The primary purpose of Aim 3 is to assess and validate the accuracy of a smartphone application for detecting postural instability in three cohorts when compared to the Utah Early Neuropathy Scale. A Sensitivity and Specificity Analysis using ROC Curves were used on the entire cohort ( $N = 42$ ) to derive a positive (indicating DPN,  $n = 14$ ) or negative (no signs of DPN,  $n = 28$ ) diagnostic conclusion<sup>114,115</sup> Additionally, ROC Curves were used to derive categorical accuracy for each sub-cohort (i.e., healthy vs. T2D, healthy vs. DPN, and T2D vs. DPN) using each postural outcome measure as the dependent variable.

A “known-groups” analysis was used to test the accuracy of the smartphone and functional assessments. To establish these “known” groups, T2D and DPN were clinically assessed by a trained clinician, and these patients were then referred to the study based on having met the inclusion/exclusion criteria. ROC curve analysis was used on the known-groups to calculate the AUCs. The AUC can be used to determine the accuracy (i.e. sensitivity and specificity) of the UENS and the smartphone postural measures (Sway Area and Sway Velocity) separately. We further compared the AUCs of the smartphone application postural outcome measures and UENS using a modified version of DeLong’s test based on the difference in paired AUC curves estimated by the non-parametric method,<sup>116</sup> to establish “non-inferiority” of the postural measures to the UENS.<sup>117</sup>

Non-inferiority was confirmed if the  $p$ -value derived from DeLong’s test was non-significant and greater than 0.05 (i.e., no statistical difference exists between the two AUC curves when compared), indicating that the smartphone postural measures’ ability to discriminate between positive and negative diagnoses was statistically no worse than the

established clinical standard. This would suggest that smartphone-based sway metrics offer comparable diagnostic accuracy to traditional clinical assessments, supporting their potential utility as accessible and portable screening tools for early neuropathy detection.

Singleton et al. found the UENS provided an 88% diagnostic accuracy in detecting DPN.<sup>33</sup> Hence, using the ROC curve analysis for sensitivity and specificity, we predicted the AUC would be greater than an AUC = 0.78 (moderate diagnostic accuracy) at a significance level of 0.05, indicating that the measure is clinically useful and not due to chance ( $AUC \leq 0.50$ ). The following analysis aims to demonstrate that the smartphone is a sufficient diagnostic indicator of early-stage large fiber degeneration caused by DPN.

Statistical significance was confirmed with  $p \leq 0.05$ . Data handling and statistical analyses were performed using RStudio (R Foundation for Statistical Computing, Vienna, Austria).

## Results

Demographic information for all participants ( $N = 42$ ) was previously presented in Table 3.1, as the same cohorts completed all testing in a single session, repeated measures design. Postural outcome measures were evaluated to assess differences across visual conditions (EO – eyes open and EC– eyes closed) and surface types (firm and foam), as shown in Table 4.1.

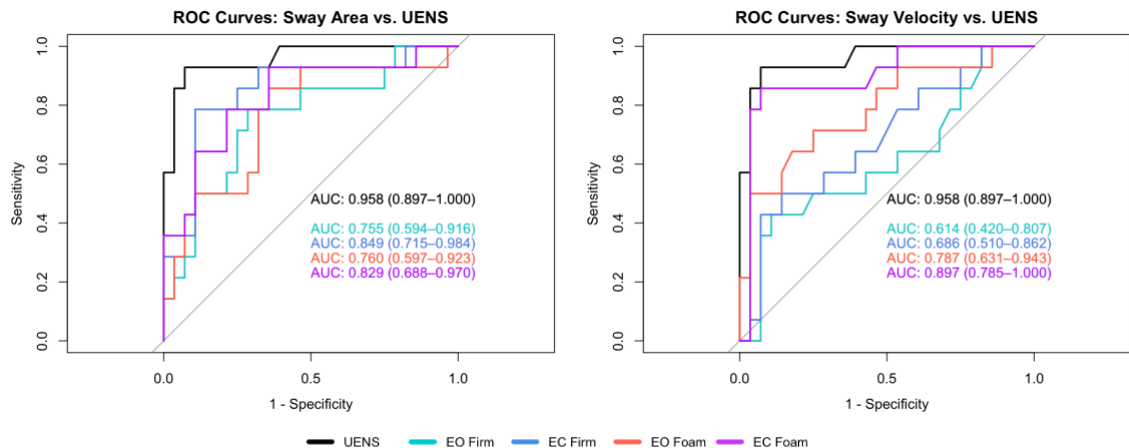
**Table 4.1.** Delong’s Method comparing ROC Curves of the smartphone application and UENS for each postural outcome measure in individuals with and without DPN

	Postural Condition	z-Score	p-value	Non-Inferiority
Sway Area	EO, Firm	2.99	0.003	Not Observed
	EC, Firm	2.32	0.020	Not Observed
	EO, Foam	3.14	0.002	Not Observed
	EC, Foam	2.43	0.050	Not Observed
Sway Velocity	EO, Firm	3.68	< 0.001	Not Observed

**Table 4.1** (Continued)

EC, Firm	3.10	0.002	Not Observed
EO, Foam	1.98	0.048	Not Observed
EC, Foam	0.94	0.345	Observed

Across all Sway Area and Sway Velocity postural conditions, the AUC was observed to be higher for the UENS compared to the smartphone tool (see Figure 4.1). Additionally, with the exception of Sway Velocity EC/Foam, all postural outcome measures for Sway Area and Velocity indicated that non-inferiority was not demonstrated in these comparisons with z-scores ranging from 1.98 to 3.68 and corresponding p-values below the conventional threshold of 0.05 (see Table 4.1). However, under the EC/Foam condition for Sway Velocity ( $z = 0.94$ ,  $p = 0.345$ ) no significant differences between the two AUC values were demonstrated. This non-significant result confirmed non-inferiority, suggesting that the smartphone postural outcome performs comparably to the UENS in discriminating between individuals with and without neuropathy.



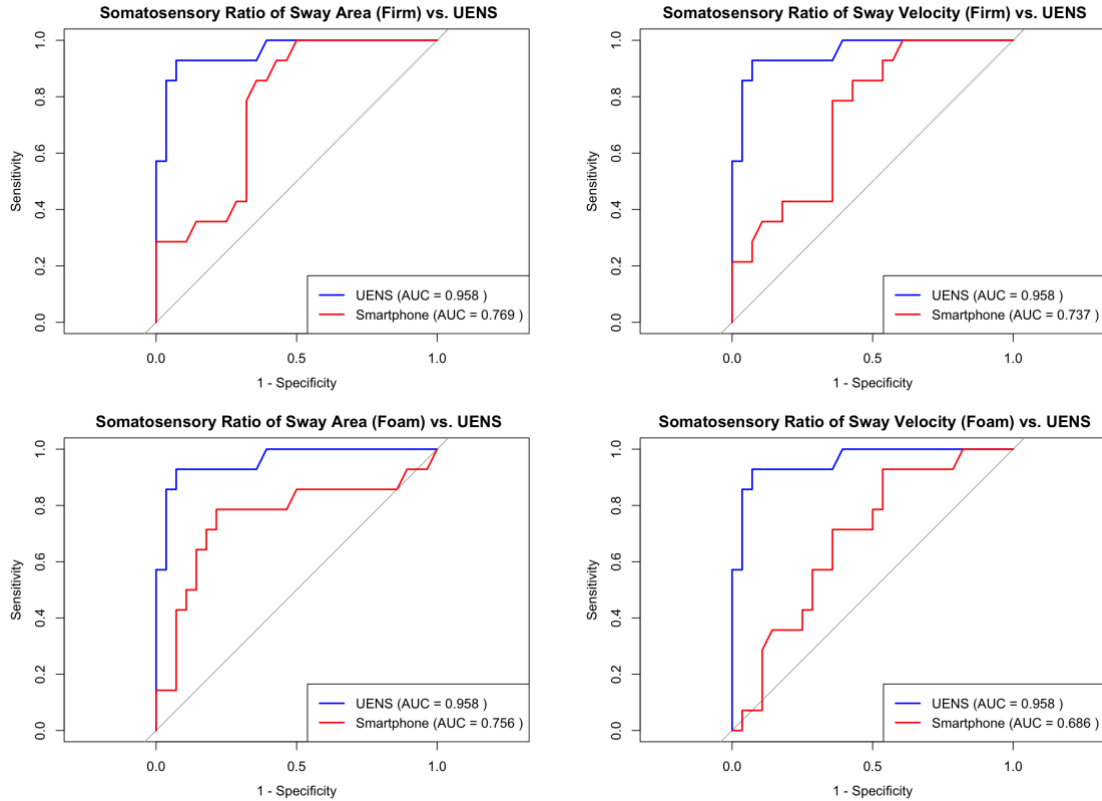
**Figure 4.1.** Illustrates ROC curves of each postural outcome measure, collected using the novel smartphone application compared to the validated UENS to derive a positive (indicating DPN) or negative (no signs of DPN) diagnostic conclusion. Sway velocity in EC-Foam (purple) was non-inferior to UENS.

The accuracy of the smartphone Somatosensory Ratios (see Chapter 2, equation 3) across Sway Area and Sway Velocity outcomes under different surface conditions all showed significant AUC's ( $p < 0.04$ ); however, when evaluated in comparison to the UENS using Delong's methods, non-inferiority was not confirmed (Table 4.2). In other words, the Somatosensory ratios calculated from postural variables measured by the smartphone were inferior to the UENS assessment.

**Table 4.2.** ROC Curve analysis comparing the diagnostic accuracy of the novel smartphone application and the validated UENS for detecting DPN, based on the somatosensory ratio across postural outcome measures.

	<b>Surface Condition</b>	<b>z-Score</b>	<b>p-value</b>	<b>Non-Inferiority</b>
Sway Area	Firm	2.52	0.012	Not Observed
	Foam	2.06	0.040	Not Observed
Sway Velocity	Firm	2.57	0.010	Not Observed
	Foam	2.86	0.004	Not Observed

*Note:* Analysis based on  $N = 42$ ; individuals with neuropathy = 14, individuals without neuropathy = 28)



**Figure 4.2.** ROC curves of the Somatosensory Ratios for Sway Area and Sway Velocity are illustrated per surface condition using the novel smartphone application and compared to the validated Utah Early Neuropathy Scale.

In addition, ROC Curves were used to derive categorical accuracy for each sub-cohort (i.e., healthy vs. T2D, healthy vs. DPN, and T2D vs. DPN) using each postural outcome measure as the dependent variable (see Table 4.3). Across comparisons, the UENS consistently exhibited high diagnostic accuracy, with AUC values ranging from 0.918 (T2D vs. DPN) to 0.997 (Healthy vs. DPN), affirming its established role in clinical neuropathy detection when comparing cohort sensitivity.

**Table 4.3.** ROC Curves showing the accuracy of the novel smartphone application for each postural outcome measure across cohorts.

	Postural Condition	z-Score	p-value	AUC for smartphone	Non-Inferiority
<b>Healthy vs. T2D (n = 28)</b>					
<i>UENS</i>				<i>0.957</i>	
Sway Area	EO, Firm	2.26	0.024	0.768	Not Observed
	EC, Firm	1.89	0.059	0.804	Observed
	EO, Foam	2.73	0.006	0.730	Not Observed
	EC, Foam	1.87	0.062	0.796	Observed
Sway Velocity	EO, Firm	2.66	0.001	0.656	Not Observed
	EC, Firm	2.24	0.021	0.658	Not Observed
	EO, Foam	1.24	0.213	0.885	Observed
	EC, Foam	1.17	0.243	0.888	Observed
<b>Healthy vs. DPN (n = 28)</b>					
<i>UENS</i>				<i>0.997</i>	
Sway Area	EO, Firm	2.09	0.037	0.847	Not Observed
	EC, Firm	1.26	0.208	0.939	Observed
	EO, Foam	1.83	0.067	0.852	Observed
	EC, Foam	1.44	0.149	0.898	Observed
Sway Velocity	EO, Firm	2.95	0.003	0.696	Not Observed
	EC, Firm	2.50	0.012	0.776	Not Observed
	EO, Foam	1.58	0.113	0.903	Observed
	EC, Foam	1.03	0.301	0.974	Observed
<b>T2D vs. DPN (n = 28)</b>					
<i>UENS</i>				<i>0.918</i>	
Sway Area	EO, Firm	2.87	0.004	0.663	Not Observed
	EC, Firm	2.26	0.024	0.760	Not Observed
	EO, Foam	3.05	0.002	0.668	Not Observed
	EC, Foam	2.07	0.039	0.760	Not Observed
Sway Velocity	EO, Firm	3.31	< 0.001	0.531	Not Observed
	EC, Firm	2.79	0.005	0.597	Not Observed
	EO, Foam	1.92	0.056	0.671	Observed
	EC, Foam	0.86	0.392	0.819	Observed

*Note:* Healthy vs. T2D = AUC of the UENS was 0.957; Healthy vs. DPN = AUC of the UENS was 0.997; T2D vs. DPN = AUC of the UENS was 0.918.

### *Healthy vs. T2D*

The UENS achieved an AUC of 0.957, confirming a high accuracy in distinguishing healthy individuals from those with T2D (see Table 4.3). For Sway Area, the smartphone application demonstrated non-inferiority to the UENS under the EC/Firm ( $z = 1.89$ ,  $p = 0.059$ , AUC = 0.804) and EC/Foam ( $z = 1.87$ ,  $p = 0.062$ , AUC = 0.796)

conditions. For Sway Velocity, non-inferiority was demonstrated in the EO/Foam ( $z = 1.24$ ,  $p = 0.213$ ,  $AUC = 0.885$ ) and EC/Foam ( $z = 1.17$ ,  $p = 0.243$ ,  $AUC = 0.888$ ) conditions.

#### *Healthy vs. DPN*

In this comparison, the UENS demonstrated a high accuracy ( $AUC = 0.997$ ) in distinguishing cohorts when compared to the smartphone AUC (see Table 4.3). The smartphone application showed non-inferiority in three of the four Sway Area conditions: EC/Firm ( $z = 1.26$ ,  $p = 0.208$ ,  $AUC = 0.939$ ), EO/Foam ( $z = 1.83$ ,  $p = 0.067$ ,  $AUC = 0.852$ ), and EC/Foam ( $z = 1.44$ ,  $p = 0.149$ ,  $AUC = 0.898$ ). However, non-inferiority was denied for the EO/Firm condition ( $z = 2.09$ ,  $p = 0.037$ ,  $AUC = 0.847$ ). Sway Velocity additionally confirmed non-inferiority in the EO/Foam ( $z = 1.58$ ,  $p = 0.113$ ,  $AUC = 0.903$ ) and EC/Foam ( $z = 1.03$ ,  $p = 0.301$ ,  $AUC = 0.974$ ) conditions.

#### *T2D vs. DPN*

The UENS demonstrated strong diagnostic accuracy in differentiating between individuals with T2D and those with DPN ( $AUC = 0.918$ ). In this cohort comparison, the AUCs for the smartphone were significant, but smaller when the smartphone and UENS AUC's were compared. Non-inferiority of the smartphone application was confirmed only under the Sway Velocity EO/Foam ( $z = 1.92$ ,  $p = 0.056$ ,  $AUC = 0.671$ ) and EC/Foam ( $z = 0.86$ ,  $p = 0.392$ ,  $AUC = 0.819$ ) conditions (see Table 4.3).

## Discussion

The primary objective of the present study was to assess the diagnostic accuracy of a novel smartphone-based postural application in comparison to a criterion measure, UENS. Current diagnostic tools for detecting DPN primarily investigate mechanisms related to sensory detection. Despite the fact that the large fiber degeneration associated with DPN is known to cause postural instability, balance assessments are not typically components of DPN diagnosis or management.<sup>76,88-90</sup> To the author's knowledge, this is the first study to establish postural instability as a potential diagnostic measure for the early detection of DPN using smartphone-based metrics. By demonstrating non-inferiority in the present study in several of the postural outcome measures between different stages of neuropathy, the present study creates a foundation for the implementation of the smartphone in clinical settings, allowing for potentially earlier identification of individuals at risk, and enabling timely referral for further evaluation.

To establish diagnostic rigor, a “known group” analysis was used to compare the accuracy of our novel instrumented smartphone approach with the validated Utah Early Neuropathy Scale. DeLong’s method was used to detect non-inferiority by determining whether the smartphone was not significantly worse than the criterion measure (UENS) in distinguishing between healthy, T2D, and DPN individuals. As such, in the present study, several postural conditions demonstrated non-inferiority. This was especially evident during the more challenging balance conditions, notably on the EC/Foam condition. In Table 4.1, Sway Velocity under EC/Foam was the only condition where non-inferiority was confirmed when investigating individuals with and without neuropathy. However, in

the sub-cohort analyses, the smartphone performed well relative to the UENS across many postural conditions.

Notably, in the sub-cohort analyses presented in Table 4.3, the smartphone application demonstrated strong performance in differentiating healthy individuals from those with T2D and DPN independently. In the Healthy vs. DPN group, the smartphone achieved high AUC values (up to 0.974) in several postural conditions, showing no significant differences when compared to the UENS, indicating robust discrimination of neuropathy. Similarly, in the Healthy vs. T2D comparisons, the smartphone detected subtle impairments in postural control, even when neuropathic symptoms were not clinically apparent yet. These findings highlight the smartphone application's potential role in the early screening of individuals at risk of sensory motor loss.

In the sub-cohort analysis comparing T2D vs DPN, the UENS demonstrated a strong AUC of 0.918. While the smartphone application still showed AUCs significantly greater than chance across postural tasks, they were relatively smaller when compared to the other AUC sub-cohort analyses involving healthy individuals (see Table 4.3). This may be due to the fact that T2D vs. DPN is a more complex and clinically challenging differentiation because of overlapping symptomology. Regardless of this, the smartphone successfully confirmed non-inferiority when measuring Sway Velocity in the EO/Foam and EC/Foam conditions. This is a promising outcome, as Sway Velocity proved to be a meaningful biomarker in distinguishing individuals with T2D from those with DPN by simply using this 1-minute smartphone-based postural measurement, which required minimal assistance and equipment.

These findings highlight two key themes. First, for the majority of the results showing non-inferiority, postural tasks that were more challenging—such as standing on an unstable (foam) surface with eyes closed—appear to improve the accuracy of the smartphone tool. This likely reflects the nature of DPN, which impairs sensory integration, making individuals more susceptible to postural instability when visual and surface cues are less available or reliable. In such conditions, balance relies more heavily on the vestibular system, which becomes the primary source of spatial orientation. For individuals with DPN, this increased demand on vestibular input, while somatosensory and visual inputs are compromised, exposes deficits in sensory compensation, thereby enhancing the tool's sensitivity to detect neuropathic changes. Second, sway velocity appears to be a more consistently informative measure when using smartphone sensors, suggesting that velocity-based metrics may better capture subtle postural adjustments in these populations. This finding aligns with previous research. For example, Lai et al. (2025) identified postural sway velocity as a strong, predictor of DPN, showing clear differences between affected and healthy individuals when analyzing both gait and posture.<sup>162</sup> However, Lai et al. also emphasized, in their limitations, the need for simpler, more scalable technologies, such as wearable inertial sensors or smartphone-based balance tools, to replace the research-grade systems they used. They highlighted the importance of low-cost, portable solutions to confirm the utility of sway velocity metrics in true low-resource settings. Accordingly, the current study aimed to develop an accessible, portable, and quantitative method for detecting DPN without the limitations posed by existing technologies.

Other findings revealed that the accuracy of the smartphone-based postural assessment varied widely based on postural condition and cohort comparisons. Under less

challenging tasks, such as standing with eyes open on a firm surface, the smartphone tool showed inferior discrimination compared to the UENS in all postural conditions. This likely reflects the body's ability to rely on visual input to maintain balance, compensating for somatosensory deficits commonly demonstrated in T2D and DPN populations. In contrast, when visual information was removed, and especially when the support surface was made unstable, balance primarily depended on vestibular input, revealing greater postural deficits that corresponded to the sensory and motor deficits depicted by the UENS. However, an unstable surface inherently makes somatosensory input less reliable for both healthy and neuropathic individuals, forcing greater reliance on vestibular and central integration mechanisms. This suggests that the observed impairments in individuals with DPN may not be due solely to peripheral sensory loss. There may be additional contributions from vestibular processing deficits or slowed spinocerebellar responses within our cohort, which can further disrupt postural control under these conditions. Nonetheless, sensory-challenging conditions significantly enhanced the tool's diagnostic accuracy, likely because they unmask more complex deficits in multisensory integration and motor coordination beyond the periphery.

Interestingly, the somatosensory ratios for neither Sway Area nor Sway Velocity were suitable metrics for discriminating between our cohort of individuals with and without neuropathy when compared to the UENS (see Table 4.2), although AUC values demonstrated moderate to good strength (see Figure 4.2). This was surprising, as the Somatosensory Ratio is commonly used to evaluate an individual's reliance on somatosensory input for postural control, particularly under conditions where visual cues are absent.

Several clinically significant implications emerged from this research and warrant consideration. First, the adoption of this novel application could offer several practical advantages to diabetes management, including reduced healthcare costs, enhanced portability, and at-home quantitative monitoring. Second, establishing non-inferiority supports the wider deployment of this tool in various healthcare settings, including those with limited access to preventive healthcare. This opens up the potential for clinical adoption, promoting broader access to reliable testing and screening to enhance clinical judgment.

While the findings are encouraging, the study has limitations. Although non-inferiority was demonstrated in a handful of postural conditions, those in which it was consistently observed would currently require materials such as a foam or an unstable surface, along with a guard, to ensure patient safety while performing the postural task. Future research should aim to investigate EO and EC visual conditions on a firm surface using a broader sample size. Additionally, the current study employed a single-session repeated-measures research design, essentially capturing a snapshot of each individual's disease state. By implementing a longitudinal research design, future studies can potentially gain a more comprehensive understanding of how T2D and DPN progression affects balance over time, when compared to a validated clinical measure. All of which provides further evidence to support its integration into routine clinical practice.

## Conclusion

The smartphone-based postural assessment tool demonstrated clinically relevant diagnostic accuracy, particularly under conditions that challenge sensory integration, such as eyes-closed or foam surface conditions. Taken together, these findings support the

integration of the smartphone-based tool into clinical practice as a supplement to traditional diagnostic methods. By enabling frequent, low-cost, and accessible screening, the tool could facilitate proactive management, improve patient convenience, and reduce delays in diagnosis. Its portability and usability make it ideal for use in telehealth, community outreach, and routine primary care visits.

## CHAPTER 5: CONCLUSION

### Summary and Review of Specific Aims

The overarching goal of this work was to investigate postural instability as an indicator for the early detection of large fiber degeneration associated with Diabetic Peripheral Neuropathy (DPN). To measure postural instability, a novel smartphone application was developed and validated against gold-standard posturography instrumentation (i.e., motion capture and force plate systems) and a validated clinical assessment (i.e., Utah Early Neuropathy Scale – UENS) for assessing lower limb somatosensory function. In this experimental setup, participants were instructed to perform quiet stance during various visual (eyes open –EO and eyes closed–EC) and surface (Firm and Foam) conditions. A total of 12, 30-second trials were administered in the same prescribed order (see Figure 2.3), while data from the three posturography instruments were collected synchronously. Postural outcome measures were used in each of our three aims to test the validity, reliability, and sensitivity to visual and surface conditions, as well as the ability of the novel smartphone application to distinguish between diagnostic groups (Healthy controls, Type 2 Diabetes (T2D), and DPN). This investigation was organized with the following three aims:

**Aim 1: Develop and validate a novel smartphone application relative to the validated research-grade posturography techniques.**

**H1.1:** There will be test-retest reliability of the smartphone application within and across devices and criterion-related validity when compared to the gold-standard force plate and motion capture systems.

**H1.2:** The smartphone application will be sensitive to differences in postural stability known to occur when comparing eyes closed to eyes open quiet stance.

**Aim 2: Determine normalized postural control values for individuals with and without type 2 diabetes (T2D) using the novel smartphone application.**

**H2.1:** Individuals with diabetes will have statistically more postural instability across conditions when compared to age-matched healthy controls.

**Aim 3: Validate the smartphone application for early detection of DPN when compared to a validated early diagnostic functional assessment.**

**H3.1:** There will be a strong correlation between the sensitivity of the lower extremities, as measured by the Utah Early Neuropathy Scale (UENS), and postural outcome measures, as measured by the smartphone application.

By leveraging smartphone accelerometers, Aim 1 demonstrated both construct and criterion-related validity of a custom application in relation to force plate center of pressure (COP) and motion capture system center of mass (COM) postural data. Within the approach outlined in Aim 1, the following study supports both proposed hypotheses. First, H1.1 was confirmed, demonstrating strong test-retest reliability of the smartphone application both within a single device and across different devices. Furthermore, the application showed high criterion-related validity when compared to established gold-standard systems. Secondly, H1.2 was supported, as the application proved sensitive to

known differences in postural stability, effectively distinguishing between visual and surface conditions during quiet stance.<sup>112</sup>

By adjusting the level of difficulty of various standing tasks and eliciting a range of postural responses, the current study provided insight into whether the novel smartphone application can serve as a stand-alone balance measurement device. Our findings suggest that, regardless of the surface or visual condition, the devices were more or less equal, in that no statistically significant differences were found in the postural measurements among the three devices. Moreover, when analyzing the sensitivity of the smartphone device, statistically significant differences were observed in both vision and surface conditions. This is particularly important for the long-term goal of the application, as the smartphone is sensitive to a wide range of postural movements, including something as small as closing one's eyes. This level of sensitivity enables the ability to track postural decline over time quantitatively, rather than relying on subjective accounts of falls and postural instability. In clinical settings, this is a selling point, where many conditions involve the progressive deterioration of postural control systems (i.e., neuropathy), resulting in decreased balance and increased fall risk.

Overall, the smartphone application demonstrated reliability in postural outcome measures, both across devices (raters) and within individual trials per device. Demonstrating both inter-rater reliability against gold-standard measures and intra-rater for test-retest reliability is essential for the smartphone application to be accepted and trusted by clinicians and researchers. Furthermore, it promotes standardized practices in healthcare settings and home use, ultimately enhancing patient care and quality.

The validation of the smartphone application against gold-standard systems, such as motion capture and force plates, represents a crucial step in demonstrating its clinical and research utility. These traditional systems are known for their high accuracy and reliability in measuring postural control in quiet stance, and thus serve as a benchmark for evaluating emerging technologies. The smartphone application's ability to produce comparable results affirms its role as a validated alternative for postural assessment. This is particularly significant given the widespread availability and affordability of smartphones, which make them a practical tool for use in diverse settings, including clinics, community environments, and even patient homes. The portability and ease of use of the application also enables frequent and remote monitoring, which may support earlier identification of postural impairments and more timely intervention. These advantages highlight the value of integrating validated smartphone technologies into broader efforts to enhance access to postural health monitoring, especially in underserved or resource-limited populations.

Building upon this, Aim 2 demonstrated the feasibility of using a validated smartphone application capable of detecting subtle postural changes across different diagnostic groups, specifically differentiating individuals with and without DPN using postural outcome measures. Within the approach outlined in Aim 2, the following study supports the proposed hypothesis, as individuals with diabetes demonstrated statistically more postural instability across visual and surface conditions when compared to age-matched healthy controls. Furthermore, the findings demonstrate that postural instability, quantified by Sway Area and Sway Velocity, is a viable and sensitive indicator for

detecting balance impairments throughout the progression of diabetes, particularly in individuals with DPN.

By replicating and extending prior research, the following study confirmed that balance performance declines as sensory input is reduced or removed, with the most pronounced impairments observed under combined visual and proprioceptive challenges. This is primarily due to how the body utilizes and integrates visual, somatosensory, and vestibular information to produce motor responses in order to keep us upright and stable.<sup>56</sup> Aim 2 reinforces the critical role of multisensory integration in postural control and highlights the progressive impact that diabetes, particularly DPN, has on balance function.<sup>61-65</sup> As postural demands increase through the removal of visual input or destabilization of somatosensory cues through an unstable surface, individuals with DPN exhibited significantly greater sway compared to those with T2D and healthy controls.<sup>90,113</sup> Notably, individuals with T2D also demonstrated postural instability under challenging conditions, suggesting that balance impairments may precede clinically diagnosed neuropathy.

These findings underscore the utility of sway metrics, particularly under eyes-closed and unstable surface conditions, for differentiating between healthy individuals, T2D, and DPN cohorts. Sway Velocity was especially responsive to sensory manipulation, revealing group differences and potentially serving as an early diagnostic marker. Moreover, the observed interaction effects suggest that individuals with DPN rely more heavily on vision and other compensatory mechanisms due to diminished somatosensory input. Controlling for covariates such as BMI, age, and time since diabetes diagnosis did not eliminate the observed group differences, reinforcing the conclusion that disease-

related factors primarily drive postural control deficits. Although these covariates modestly attenuated effect sizes, they did not account for the significant differences attributed to diagnostic status.

Taken together, these findings provide strong support for incorporating postural sway assessment into clinical protocols for evaluating balance dysfunction in diabetic populations. Early identification of subtle balance impairments may enable timely interventions to prevent falls and slow the progression of T2D and neuropathic complications.

Finally, guided by the findings of the first two aims, Aim 3 demonstrated that a novel smartphone-based postural assessment has the potential to serve as an effective and accessible screening method for the early detection of DPN. By comparing the postural outcome measures for diagnostic performance against the established UENS in a “known groups” analysis, this investigation provides evidence supporting postural instability, particularly under sensory-challenging conditions, as a viable biomarker for early neuropathic dysfunction.

A key finding was the confirmation of non-inferiority in several postural metrics, particularly Sway Velocity, during conditions designed to challenge sensory integration (e.g., standing on foam with eyes closed). This suggests that the smartphone tool is capable of detecting the proprioceptive deficits that characterize early DPN with an AUC that is not statistically different from that of the UENS. Importantly, these results support previous research indicating that postural Sway Velocity is a sensitive indicator of neuropathic progression<sup>162</sup> and further advances the field by demonstrating the feasibility of capturing such metrics using a relatively low-cost, portable smartphone technology.

The tool performed especially well in distinguishing between healthy individuals and those with either T2D or DPN, achieving high AUC values in several conditions as well as non-inferiority to the UENS. These findings are important because they suggest the smartphone can detect subtle postural changes even in individuals without overt neuropathic symptoms, indicating the potential for early screening and prevention without the current barriers of management and diagnostic tools. While discrimination between individuals with T2D and those with established DPN was more difficult, an expected outcome due to overlapping symptomology and gradual disease progression, the smartphone application, nevertheless, confirmed non-inferiority in several postural conditions, reinforcing the clinical relevance of these measures.

While these findings are encouraging, we did find that under less challenging balance conditions, such as standing with eyes open on a firm surface, the smartphone tool showed inferior performance relative to the UENS. This highlights the body's ability to compensate for sensory loss via visual input, which may mask subtle deficits in neuropathy. Furthermore, the Somatosensory Ratio, a commonly used comparative metric to evaluate an individual's reliance on somatosensory input for postural control, did not offer enhanced discriminative value in this study.

Overall, Aim 3 supports the integration of smartphone-based postural assessments into clinical workflows for neuropathy screenings. The tool's portability, low cost, and ease of use make it particularly suited for resource-limited environments or for remote assessments to enhance clinical judgment and early intervention of DPN and the poor outcomes associated with it.

## Limitations and Future Directions

While this study provides valuable evidence supporting the integration of postural control in the diagnosis, management, and early detection of DPN, several limitations must be acknowledged, which, when considered appropriately, can be helpful in guiding future research and development. Some of these limitations were previously discussed and are further expanded upon here.

A primary limitation is the exclusive use of a single iPhone 14 for all data collections. This limits the generalizability of the findings, as performance may vary across different smartphone models. Future research should evaluate intra-device reliability to determine whether the application yields consistent results across a range of devices. Furthermore, the application was developed solely for Apple's iOS platform. To enhance its accessibility and adoption, future iterations should aim for cross-platform compatibility, allowing for broader use among individuals with Android or other operating systems. Additional validation is also needed to assess how smartphone positioning and orientation may impact sensor accuracy, especially when used across various makes and models.

Another notable limitation is the study's single-session design, which restricts insights into how postural control changes over time. A longitudinal research approach would offer a deeper understanding of the progression of postural instability in individuals with T2D and DPN. Future studies could ask participants to download the application and complete the postural assessment protocol regularly over an extended period. This would not only allow for the tracking of disease progression but also serve as a real-world test of the application's usability without the presence of trained professionals, enhancing its practical value for both patients and clinicians.

The study also did not collect data on whether participants were on pharmaceutical drugs to help treat their T2D. Some medications or combinations of medications are known to have interactions or side effects, which have been shown to influence neuromuscular function and postural stability, dizziness being one notable side effect.<sup>163,164</sup> Although medications known to affect balance were initially screened through a chart review by a trained physician, detailed medication use was not systematically documented in this study. Future studies should include detailed medical histories and current medications to evaluate the potential confounding effects of these treatments.

An important future direction involves the collection of fall-related data. Falls are a common and serious complication among individuals with T2D and DPN and understanding the relationship between postural stability and fall risk is critical for advancing both clinical care and patient outcomes. Future studies could incorporate self-reported fall histories and prospective fall monitoring alongside postural stability assessments collected through the smartphone application. Linking device-derived stability measures with fall outcomes would provide valuable insight into the predictive validity of the tool. Moreover, the development of a fall risk score, derived from postural metrics tracked longitudinally, could offer both clinicians and patients a meaningful and easy-to-interpret indicator of fall risk. Such a score would enhance the clinical utility of the application by supporting earlier interventions, while also empowering patients to monitor changes in their own stability then take proactive steps in reducing fall risk over time.

One of the long-term goals of this project is to make the postural assessment application viable for at-home use, enabling remote monitoring without the need for a trained professional, thereby enhancing patient convenience and accessibility for those

with limited access to preventive healthcare. In the current study, postural data was collected using an iPhone 14 secured at the L5 region of the lower back (the estimated location of COM during quiet stance) with a modified running belt (see Figure 2.2) to ensure consistency and minimize external sources of error, such as device tilt or improper placement. While this setup helped standardize data collection, the reliance on a harness may limit user-friendliness. Additionally, current results demonstrate that posturally challenging tasks using unstable surfaces absent of visual cues were the most accurate in discriminating between cohorts. However, these tasks may increase the risk of falls for individuals who already have somatosensory dysfunction. Future development should focus on eliminating the need for such equipment to improve ease of use and accessibility in unsupervised settings.

Building on the application's core capabilities, future directions may also include integrating educational and self-management tools on the application's user interface. These could involve educational videos and notifications on T2D management and foot care, as well as reminders for blood sugar monitoring, foot inspections, and routine medical appointments. Much like social media platforms, the vision is to make the application an integral part of users' daily lives. One of the greatest challenges faced by individuals with T2D and DPN is limited access to education and care, often resulting in poor outcomes and irreversible complications. Despite decades of research and clinical guidelines, many individuals at risk for or living with T2D do not receive recommended care, underscoring a persistent public health challenge driven by barriers in healthcare delivery, disparities in access, and the growing population-level burden of diabetes. By combining diagnostic tools with accessible educational content, the application could serve as a critical bridge

between clinical and at-home care, ultimately aiming to improve health outcomes and reduce the burden of DPN.

## Conclusion

The presented dissertation developed and validated a novel smartphone application capable of measuring postural instability in individuals with type 2 diabetes and diabetic peripheral neuropathy. Through the achievement of each specific aim, this dissertation demonstrated the application's validity, reliability, and sensitivity in assessing postural stability, both in comparison to gold-standard posturography equipment, as well as using a validated clinical tool (UENS) designed for the early detection of DPN by evaluating motor and sensory function in the lower extremities. By collecting postural data from healthy controls, individuals with T2D, and individuals with DPN, the study not only established normative postural control values for each group but also assessed the potential of postural stability as a metric for distinguishing individuals with DPN from those without. This dissertation and the developed application provide a strong foundation for remote balance monitoring and enhanced patient engagement, both critical components for the early detection and effective management of DPN, particularly in populations with limited access to preventive care and treatment.

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