



The Effect of Daily Use of Plantar Mechanical Stimulation Through Micro-Mobile Foot Compression Device Installed in Shoe Insoles on Vibration Perception, Gait, and Balance in People With Diabetic Peripheral Neuropathy

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Abstract

Objective: People with diabetic peripheral neuropathy (DPN) have impaired gait and balance performance. The aim of this study is to investigate therapeutic effectiveness of mechanical stimulation through a wearable foot compression device equipped in a shoe insole on vibration perception, balance control and gait performance in people with DPN.

Methods: Using a single-arm 4-week intervention study design, we examined effectiveness of daily use of shoes equipped with the foot compression device (Footbeat™, AVEX, Grand Junction, CO, USA) on improving vibration perception threshold (VPT_{max}), skin perfusion pressure (SPP), ankle brachial index (ABI), lower extremities edema (circumferences in the calf and ankle), and motor performance (postural sway with eyes open and closed conditions, and gait performance during normal, dual-task and fast walking). Thirty people with type 2 diabetes and symptoms of PN completed the experimental protocol.

Results: Improvements in VPT_{max} (before = 27.4 V, after = 23.3 V, $P = .007$, $d = 0.33$, where d denotes effect size), center-of-mass sway in the mediolateral direction with both eyes open and closed conditions (before = 0.94 cm, after = 0.76 cm, $P = .020$, $d = 0.47$; before = 1.10 cm, after = 0.83 cm, $P = .033$, $d = 0.66$, respectively), and stride velocity for normal walking, dual-task walking and fast walking tasks (before = 0.87 m/s, after = 0.96 m/s, $P = .017$, $d = 0.41$; before = 0.75 m/s, after = 0.91 m/s, $P = .001$, $d = 0.77$; before = 1.10 m/s, after = 1.20 m/s, $P = .043$, $d = 0.33$, respectively) were found post treatment. There was no significant improvement in SPP, ABI, and circumferences in the calf and ankle.

Conclusions: Our findings suggest the wearable foot compression device may be effective for reducing neuropathic symptoms and enhancing motor performances in people with DPN.

Keywords

diabetes, diabetic peripheral neuropathy, vibration perception threshold, gait, balance

In the United States, more than 30 million people suffer from diabetes, and every year 1.5 million people are newly diagnosed with diabetes.¹ Diabetic peripheral neuropathy (DPN), nerve damage, is a major diabetic complication, affecting between 30 and 50% of people with diabetes at all ages,² and a leading risk factor for foot ulcer, infection, and amputation.³ One common problem in DPN is diminished sensation particularly in the lower extremity due to damaged nerve.⁴ This results in lack of sensorimotor communication with the central nervous system during locomotor tasks such as gait and balance control during quiet standing. In fact, several studies

have documented gait abnormalities and postural instability associated with DPN.^{5–10} For example, people with DPN have

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Table 1. Inclusion/Exclusion Criteria for Participants.

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> • Male or female, age ≥ 18 years old • Diagnosis of type 2 diabetes confirmed by patient's physician • Ambulatory • History of peripheral neuropathy according to patient electronic record • Able and willing to provide informed consent • Able and willing to complete the full protocol (eg, living in a long distance from clinic limiting the ability to participate in follow up visit) 	<ul style="list-style-type: none"> • Severe peripheral vascular disease (ABI < 0.5 or ABI > 1.30) according to the International Working Group on the Diabetic Foot (IWGDF) guidelines³⁴ • Active wound, or wound infection, or untreated osteomyelitis according to the IWGDF guidelines³⁴ • Charcot foot or other deformities that won't fit in the shoes • Foot amputation including people with transmetatarsal amputation. People with minor amputation (eg, few digits) would be still eligible based on the judgement of our clinical experts who assessed the safety of participants during walking with the proposed footwear • Unable to independently walk with or without walking assistance for approximately 12 meters • Unable or unwilling to complete the full protocol • Use of immunosuppressive drugs • Pregnancy or breast feeding

larger postural sway during quiet standing compared to people with diabetes and no neuropathy, and healthy people.⁵ Also, people with DPN have slower gait speed compared to healthy people.⁷ These impairments in locomotor tasks are likely to indicate increase in risk of injury during locomotion such as falling,^{11,12} and low quality of life and high morbidity and mortality in people with diabetes.¹³ Therefore, it is important to treat DPN properly and prevent worsening of its symptoms.

It is well established that nonsurgical and nonpharmacological interventions may be an effective adjunct to pathophysiological and/or motor symptoms of DPN. It was reported that, in people with DPN, aerobic exercise intervention improves balance control and gait speed,¹⁴ and exercise intervention specifically focusing on ankle movement (ie, balance training) improved balance control.^{15,16} In addition, previous studies demonstrated that use of ankle-foot orthoses or off-loading devices improves wound healing,¹⁷⁻¹⁹ balance control,²⁰ and gait stability.²¹ Also, several studies investigated the effect of electrical stimulation as an adjunctive therapy,^{12,22,23} and reported improvement in wound healing,²² plantar sensation in the foot and balance control,^{12,23} and gait speed¹² in people with DPN after receiving electrical stimulation. Although these studies reported positive results for the management of DPN, fundamental barriers such as reluctance to exercise,²⁴ discomfort in wearing an exoskeleton^{25,26} and electrical stimulation devices,²⁶ and the relatively high cost of electrical stimulation may limit the effectiveness of such treatments.

In addition to these interventions, a few studies have reported that mechanical stimulation applied to the bottom of the foot through vibrating insoles may be effective for enhancing plantar sensation in the foot²⁷⁻²⁹ and balance control for people with DPN.^{30,31} These studies only reported the effect of mechanical stimulation on plantar sensation or balance control. However, their findings together with its effectiveness on gait and balance in healthy older adults reported in another study³² have predicted the possibility of potent effects of mechanical stimulation on sensation, gait

and balance control in people with DPN. Furthermore, recent development in micro-mobile compression devices installed in shoe insoles has enabled mechanical stimulation on the plantar surface of the foot during day-to-day activities without additional discomfort.³³ However, its effectiveness on pathophysiology and motor symptoms in people with DPN has not yet been tested. Therefore, the aim of this study was to evaluate the effect of mechanical stimulation through micro-mobile foot compression devices installed in shoe insoles on vibration perception, balance control, and gait performance in people with diabetes. Based on prior findings, we hypothesized that daily use of the wearable foot compression device would improve vibration perception. In addition, it was hypothesized that the improvements in vibration perception would lead to improvements in balance outcomes and gait parameters.

Methods

Participants

We recruited a convenience sample of 30 people with type 2 diabetes in this study. Potential participants were screened for eligibility based on the inclusion and exclusion criteria described in Table 1.³⁴ We recruited participants from the Baylor College of Medicine, outpatient clinics and senior centers in the greater Houston area via their physicians' referrals or advertisements. All participants provided written informed consent approved by the Baylor College of Medicine Institutional Review Board prior to participating in the experimental protocol. This study was registered in ClinicalTrials.gov, identifier NCT03135535.

Device

In this study, an FDA cleared micro-mobile foot compression device installed in shoe insoles (Footbeat, AVEX LLC, Grand Junction, CO, USA) was used (Figure 1). The foot

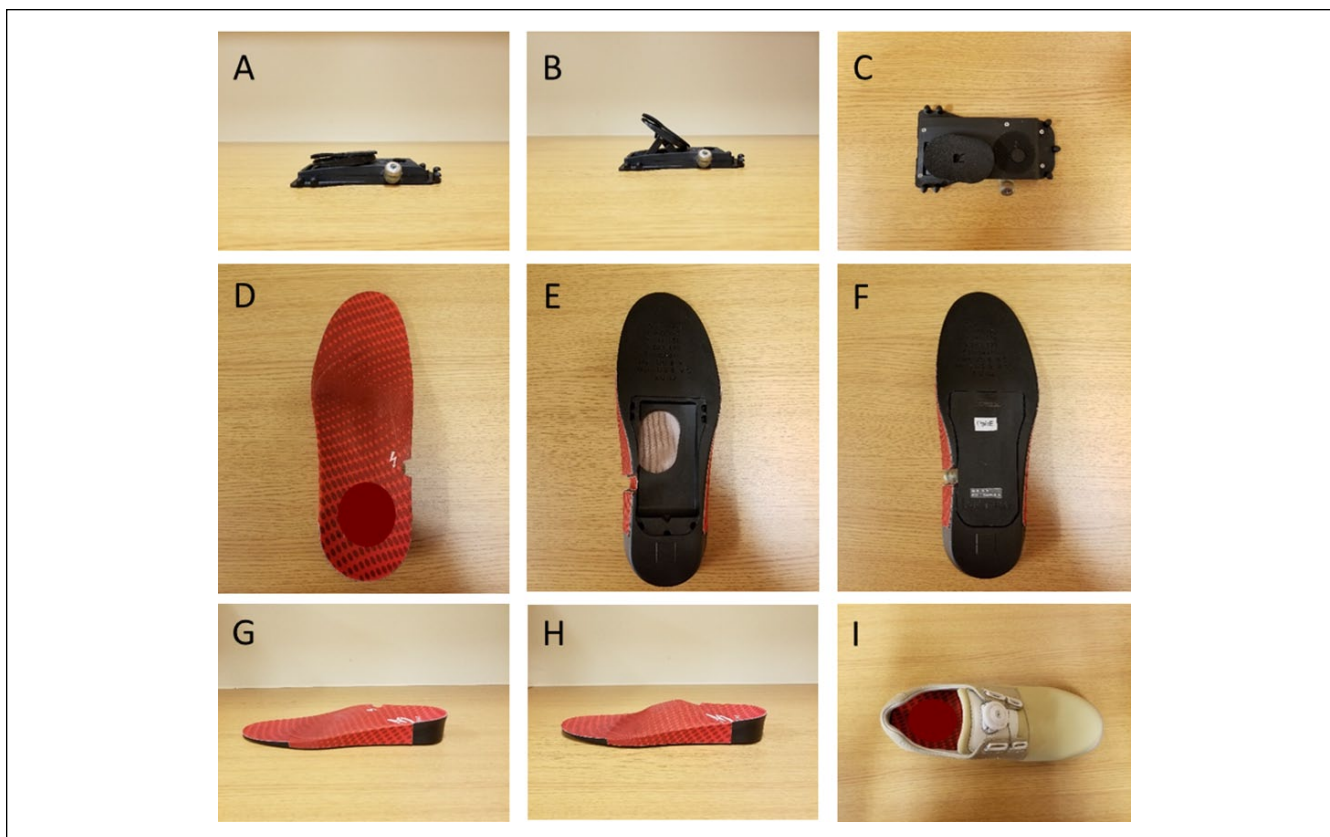


Figure 1. Illustrations of the foot compression device, insole and shoe that were used in this study: (A) side view of the foot compression device with the thrusting arm and pressure pad when resting; (B) side view of the foot compression device with the thrusting arm and pressure pad when pushing; (C) top view of the foot compression device with the thrusting arm and pressure pad when pushing; (D) top view of the top side of the insole; (E) top view of the bottom side of the insole before installing the foot compression device; (F) top view of the bottom side of the insole after installing the foot compression device; (G) side view of the insole with the thrusting arm and pressure pad when resting; (H) side view of the insole with the thrusting arm and pressure pad when pushing; and (I) top view of the shoe equipped with the insole.

compression device is composed of a rechargeable motorized thrusting arm and pressure pad (18.6 cm²). It was designed to push the arch of the plantar surface of the foot with a pressure of 3.76 N/cm² every 35 seconds while participants were sitting or lying down, which empties the plantar venous plexus and accelerates blood flow in the lower extremity (Figure 1).³³ The foot compression device was automatically deactivated when it senses standing or walking (ie, when it senses more plantar pressure). We provided each participant with a pair of shoes (Dr. Comfort LLC, Mequon, WI, USA) equipped with the insoles with the micro-mobile foot compression device. The tightness of the shoes was adjusted using a reel clutch (BOA Technology Inc, Denver, CO, USA).³⁵ We asked participants to wear the shoes for at least four hours a day for a period of four weeks based on the minimum battery life of the foot compression device when the system was continuously activated. The average time of wearing the shoes and the average time of the compression device activation across participants were 5.4 ± 2.0 and 5.2 ± 2.0 hours, respectively.

Experimental Protocol and Outcomes

We used a single-arm 4-week intervention study design of daily use of plantar mechanical stimulation. At baseline, we collected participant characteristics including age, body mass index (BMI), sex, the number of prescribed and over-the-counter medications, comorbidities, and deformities in the foot, skin (eg, flaky, calluses, warts) and nail (discolored, missing, dystrophic/fungal).³⁶ In addition, we assessed each participant's depressive state using the Center for Epidemiological Studies Depression Scale (CES-D),³⁷ cognitive function using the Montreal Cognitive Assessment (MoCA)³⁸ and frailty status using the Fried Frailty Criteria.³⁹ Functional characteristics such as fall history, daily activities level and mobility-related fatigue were assessed using self-disclosure, the Barthel Index of Activities of Daily Living (ADL)⁴⁰ and the Mobility Tiredness Scale, respectively. Other functional characteristics such as timed up and go test (TUG) and four step square test (FSST) were assessed using two wearable sensors

(LegSys™, BioSensics, Watertown, MA, USA). Also, we assessed fear of falling using the Falls Efficacy Scale–International (FES-I)⁴¹ and pain level in the foot using the Virtual Analog Scale (VAS).

We performed several clinical assessments at baseline and conclusion of the intervention. We measured vibration perception threshold (VPT) for assessing severity of neuropathic symptoms, skin perfusion pressure (SPP) and ankle brachial index (ABI) for assessing peripheral vascular status, and circumferences in the calf and ankle for assessing lower extremity edema. We measured VPT at the first and fifth metatarsal head and heel in the plantar surface of both feet using a Biothesiometer (Bio-Medical Instrument Co, Newbury, OH, USA) as indicated in previous studies.^{12,42} Briefly, we had placed the probe of the Biothesiometer on one of the sites in the plantar surface of the foot for a participant, and had gradually increased the magnitude of electrical vibration from 0 V until the participant responded “I am feeling the vibration now”. To confirm the threshold for perception of sensation, we had increased the voltage from the participant self-reported value and then gradually reduced until the participant responded “I am not feeling the vibration now”. If the two values were close (< 2 V difference), the max value was considered as VPT. Otherwise, the process was repeated. Then, we repeated this method for the other sites for the participant. We defined VPT_{max} as maximum measured VPT values from all sites from both feet. A cutoff of equal or greater than 25 V⁴³⁻⁴⁵ was used to distinguish between those with severe (severe PN: $VPT \geq 25$ V) and mild PN (mild PN: $VPT < 25$ V). We measured ABI and SPP using PAD-IQ (VÄSAMED, Eden Prairie, MN, USA).

We measured balance characteristics using two validated wearable sensors (BalanSens™, BioSensics, Watertown, MA, USA) attached on the shank in the dominant leg and lower back.⁴⁶ For balance assessment, participants were asked to stand as quietly as possible for 30 seconds while the feet stay close together but no touching (ie, double stance), and the dominant foot stays half step behind the nondominant foot (ie, semitandem stance). For each stance, participants performed balance tasks with eyes open (EO) and eyes closed (EC) conditions. For each balance task, we measured total sway areas (cm²) in the ankle, hip, and center of mass (CoM), and mediolateral (ML) sway (cm) in the CoM.

We measured gait characteristics using five validated wearable sensors (LegSys™, BioSensics, Watertown, MA, USA) attached on the middle of the thigh and distal shank in both legs, and lower back.⁴⁷ For gait assessment, participants were asked to walk 10 meters at their normal and fast paces (ie, normal walking and fast walking). In addition, participants were asked to perform a cognitive task (eg, counting backward by twos) while walking (ie, dual-task walking). For each gait task, we measured stride velocity (m/s), stride length (m), stride time (seconds) and double limb support (%).

Statistical Analysis

Descriptive results are expressed as mean \pm standard deviation (SD). To compare outcome values between baseline and 4-week follow-up (ie, repeated measurements at two time points), we used a linear mixed model with random effects of participants and fixed effects of two time points (ie, baseline and follow-up), and age and BMI (ie, covariates). P values $< .05$ were considered significant differences in 4-week follow-up assessment compared to baseline assessment after Bonferroni correction. We estimated effect size for quantifying the difference in outcome values between baseline and follow-up using Cohen's d , and denoted it as d in the results section. We classified the magnitude of effect size in the following categories: $d < 0.20$ as no noticeable effect, $0.20 \leq d < 0.50$ as small effects, $0.50 \leq d < 0.79$ as medium effects and $0.80 \leq d < 1.29$ as a large effects.⁴⁸ All statistical analyses were performed using SPSS® version 25 (IBM, Armonk, NY, USA).

Results

Thirty people with type 2 diabetes met the inclusion and exclusion criteria, and completed the full protocol. We summarized baseline characteristics for all participants in Table 2. We summarized characteristics of pathophysiology for baseline and follow-up for all participants in Table 3. We found significant improvement in neuropathic symptom. All participants received the same mechanical stimulation to the arch of the plantar surface of the foot through the wearable foot compression device. Across all participants, VPT_{max} reduced significantly in follow-up compared to baseline (before = 27.4 ± 12.6 V, after = 23.3 ± 11.9 V, 15.0% decrease, $P = .007$, $d = 0.33$). When participants were divided into two subgroups of severe PN ($VPT_{max} \geq 25$ V) and mild PN ($VPT_{max} < 25$ V) in baseline evaluation, the subgroup of severe PN had significant reduction in VPT_{max} in follow-up evaluation compared to baseline evaluation (before = 36.5 ± 7.6 V, after = 30.5 ± 10.5 V, 16.4% decrease, $P = .005$, $d = 0.65$). VPT_{max} in follow-up evaluation tended to reduce compared to baseline evaluation in the subgroup of mild PN, however the reduction was not significant (before = 15.5 ± 5.8 V, after = 14.0 ± 5.2 V, 9.7% decrease, $P = .496$, $d = 0.27$). There were no significant changes in lower extremity vascular status as measured by SPP and ABI, and lower extremity edema as measured by calf and ankle circumferences between baseline and follow-up (all $P > .05$).

We summarized balance characteristics for baseline and follow-up for all participants in Table 4. Across all participants, there were no significant improvements in ankle (deg²), hip (deg²) and CoM sway (cm²), however we found significant improvement in some characteristics for balance control during quiet standing with double stance. Importantly, CoM sway in the ML direction reduced significantly for double

Table 2. Participant Characteristics.

	All participants (N = 30)	Severe PN (n = 17)	Mild PN (n = 13)
Demographic characteristics			
Age, years	68.1 ± 9.7	69.6 ± 9.3	66.2 ± 10.2
BMI, kg/m ²	33.4 ± 6.1	33.3 ± 4.9	33.4 ± 7.5
Women	19 (63.3%)	10 (58.8%)	9 (69.2%)
Clinical characteristics			
Prescribed medications, n	6.6 ± 4.5	6.9 ± 3.8	6.1 ± 5.6
Over-the-counter medications, n	1.5 ± 1.6	2.1 ± 1.7	0.6 ± 0.8
Comorbid disorders, n	3.1 ± 1.5	3.1 ± 1.2	3.1 ± 2.0
Foot deformity, n	18 (60.0%)	10 (58.8%)	8 (61.5%)
Skin deformity, n	23 (76.7%)	12 (70.6%)	11 (84.6%)
Nail deformity, n	21 (70.0%)	12 (70.6%)	9 (69.2%)
Psychocognitive characteristics			
Depression (CES-D), 0-60	8.2 ± 8.3	7.5 ± 5.7	9.2 ± 11.3
Depressed (CES-D ≥ 16), n	5 (16.7%)	2 (11.8%)	3 (23.1%)
Cognition (MoCA), 0-30	23.3 ± 3.6	22.9 ± 4.1	23.8 ± 2.9
Impaired (MoCA < 26), n	15 (50.0%)	10 (58.8%)	5 (38.5%)
Frailty characteristics			
Frail, n	4 (13.3%)	1 (5.9%)	3 (23.1%)
Pre-frail, n	15 (50.0%)	9 (52.9%)	6 (46.2%)
Robust, n	10 (33.3%)	6 (35.3%)	4 (30.8%)
Functional characteristics			
Fall incidence during the last year	13 (43.3%)	7 (41.2%)	6 (46.2%)
Number of falling during the last year	0.8 ± 1.2	0.7 ± 0.9	1.1 ± 1.4
Barthel ADL Index, 0-100	94.0 ± 8.0	93.8 ± 9.4	94.3 ± 6.1
Mobility tiredness scale, 0-6	2.5 ± 2.0	2.6 ± 2.1	2.4 ± 2.0
Timed up and go (TUG), s	10.7 ± 4.9	11.1 ± 5.7	10.0 ± 3.7
At risk of falling (TUG ≥ 13.5 s)	4 (13.3%)	2 (11.8%)	2 (15.4%)
Four step square test (FSST), s	12.1 ± 3.4	11.9 ± 3.8	12.3 ± 3.1
At risk of falling (FSST ≥ 15 s)	5 (16.7%)	3 (17.6%)	2 (15.4%)
Quality of life			
Fear of falling (FES-I), 0-64	34.8 ± 15.7	29.7 ± 16.0	41.2 ± 13.4
High fear of falling (FES-I ≥ 23), n	20 (66.7%)	8 (47.1%)	12 (92.3%)
Foot pain (VAS), 0-10	1.0 ± 1.9	1.1 ± 1.7	1.0 ± 2.3

Table 3. Characteristics of Pathophysiology for Baseline and 4-Week Follow-Up for All Participants.

	Baseline	Week 4	P value	Effect size
Neuropathy				
VPT _{max} , volts	27.4 ± 12.6	23.3 ± 11.9	.007*	0.33
Severe PN	36.5 ± 7.6	30.5 ± 10.5	.005*	0.65
Mild PN	15.5 ± 5.8	14.0 ± 5.2	.496	0.27
Vascular status				
SPP, mmHg	75.1 ± 15.8	75.7 ± 11.1	.783	0.04
ABI, no unit	1.20 ± 0.18	1.16 ± 0.16	.587	0.23
Edema, circumference				
Calf, cm	37.7 ± 3.6	37.3 ± 4.0	.200	0.11
Ankle, cm	23.1 ± 2.6	23.0 ± 2.4	.952	0.04

Note: Asterisks indicate significant differences between baseline and 4-week follow-up. * $P < .05$.

stance with EO and EC conditions in follow-up compared to baseline (before = 0.94 ± 0.43 cm, after = 0.76 ± 0.32 cm, 21.3% decrease, $P = .020$, $d = 0.47$; before = 1.10 ± 0.45 cm, after = 0.83 ± 0.37 cm, 24.5% decrease, $P = .033$, $d = 0.66$, respectively). Similar to the results for VPT_{max}, the subgroup of severe PN in baseline evaluation had significant reduction in CoM sway in the ML direction for double stance with EO and EC conditions in follow-up evaluation (before = 0.94 ± 0.35 cm, after = 0.75 ± 0.37 cm, 20.2% decrease, $P = .024$, $d = 0.53$; before = 1.22 ± 0.55 cm, after = 0.83 ± 0.36 cm, 32.0% decrease, $P = .041$, $d = 0.84$, respectively). Although CoM sway in the ML direction for double stance with EO and EC conditions tended to decrease in the subgroup of mild PN but the decrease was not significant.

We summarized gait characteristics for baseline and follow-up for all participants in Table 5. We found significant

Table 4. Characteristics for Balance Control for Baseline and 4-Week Follow-Up for All Participants.

	Baseline	Week 4	P value	Effect size
Double stance—Eyes open				
Ankle sway, deg ²	4.48 ± 4.49	3.97 ± 4.41	.955	0.11
Hip sway, deg ²	4.13 ± 3.17	3.46 ± 2.37	.525	0.24
CoM sway, cm ²	0.93 ± 0.59	0.92 ± 0.83	.692	0.01
ML CoM sway, cm	0.94 ± 0.43	0.76 ± 0.32	.020*	0.47
Severe PN	0.94 ± 0.35	0.75 ± 0.37	.024*	0.53
Mild PN	0.94 ± 0.52	0.78 ± 0.28	.256	0.38
Semitandem stance—Eyes open				
Ankle sway, deg ²	5.17 ± 4.47	6.72 ± 7.72	.282	0.25
Hip sway, deg ²	4.63 ± 3.03	4.34 ± 3.18	.167	0.09
CoM sway, cm ²	1.17 ± 0.84	1.08 ± 0.62	.773	0.12
ML CoM sway, cm	0.98 ± 0.36	0.93 ± 0.34	.620	0.14
Double stance—Eyes closed				
Ankle sway, deg ²	6.28 ± 4.11	6.07 ± 4.68	.822	0.05
Hip sway, deg ²	5.87 ± 3.33	4.85 ± 3.58	.135	0.30
CoM sway, cm ²	1.39 ± 0.79	1.24 ± 0.90	.356	0.18
ML CoM sway, cm	1.10 ± 0.45	0.83 ± 0.37	.033*	0.66
Severe PN	1.22 ± 0.55	0.83 ± 0.36	.041*	0.84
Mild PN	0.98 ± 0.29	0.84 ± 0.40	.260	0.40
Semitandem stance—Eyes closed				
Ankle sway, deg ²	11.17 ± 6.90	10.59 ± 8.13	.744	0.08
Hip sway, deg ²	8.71 ± 4.23	7.08 ± 5.03	.333	0.35
CoM sway, cm ²	2.73 ± 2.08	2.12 ± 1.61	.199	0.33
ML CoM sway, cm	1.56 ± 0.44	1.31 ± 0.45	.087	0.56

Note: Asterisks indicate significant differences between baseline and 4-week follow-up. * $P < .05$.

improvement in several gait variables for all walking tasks. Most importantly, across all participants, stride velocity increased significantly from baseline to follow-up for all walking tasks (before = 0.87 ± 0.21 m/s, after = 0.96 ± 0.23 m/s, 12.6% increase, $P = .017$, $d = 0.41$ for normal walking; before = 0.75 ± 0.18 m/s, after = 0.91 ± 0.23 m/s, 21.3% increase, $P = .001$, $d = 0.77$ for dual-task walking; before = 1.10 ± 0.33 m/s, after = 1.20 ± 0.27 m/s, 9.1% increase, $P = .043$, $d = 0.33$ for fast walking). In addition to improvement in stride velocity, we found significant improvement in stride length for normal walking and dual-task walking tasks (before = 1.05 ± 0.21 m, after = 1.13 ± 0.20 m, 7.6% increase, $P = .030$, $d = 0.35$; before = 1.03 ± 0.19 m, after = 1.14 ± 0.24 m, 10.7% increase, $P = .009$; $d = 0.51$, respectively), and marginal improvement in stride length for fast walking task (before = 1.15 ± 0.27 m, after = 1.24 ± 0.24 m, 7.8% increase, $P = .050$, $d = 0.35$). Also, stride time decreased in follow-up compared to baseline for dual-task walking (before = 1.41 ± 0.16 s, after = 1.28 ± 0.15 s, 9.2% decrease, $P < .001$, $d = 0.84$), and double limb support decreased in follow-up compared to baseline for dual-task walking and fast walking (before = 31.02 ± 6.23 %, after = 28.22 ± 5.48 %, 9.0% decrease, $P = .004$; $d = 0.48$; before = 23.96 ± 7.61 %, after = 22.14 ± 5.84 %, 7.6% decrease, $P = .031$, $d = 0.27$, respectively).

After dividing into two subgroups, both subgroups had significant increase in stride velocity for dual-task walking in follow-up compared to baseline (before = 0.72 ± 0.21 m/s, after = 0.85 ± 0.26 m/s, 18.1% increase, $P = .023$, $d = 0.55$ for the subgroup of severe PN; before = 0.79 ± 0.13 m/s, after = 0.97 ± 0.19 m/s, 22.8% increase, $P = .022$, $d = 1.11$ for the subgroup of mild PN). Also, the subgroup of mild PN in baseline evaluation had significant increase in stride velocity for fast walking in follow-up (before = 1.14 ± 0.25 m/s, after = 1.27 ± 0.19 m/s, 11.4% increase, $P = .017$, $d = 0.59$). Both subgroups' stride velocity tended to increase for normal walking and the subgroup of severe PN tended to walk faster for fast walking, however the increase was not significant. For all other gait parameters, significant improvements were found for stride length for the subgroup of mild PN, stride time for both subgroups and double limb support for the subgroup of mild PN for dual-task walking, and double limb support for the subgroup of mild PN for fast walking.

Discussions

We demonstrated that daily use of plantar mechanical stimulation through a micro-mobile foot compression device installed in a shoe insole is effective for improving vibration perception, which likely results in improvements in some balance outcomes and some gait parameters. Key findings were improvements in plantar sensation in the foot, CoM sway in the ML direction during quiet standing, and stride velocity and other spatiotemporal gait parameters after using the wearable foot compression devices for four weeks. These findings highlight the potential of plantar mechanical stimulation as an adjunctive therapy for treating symptoms related to DPN. To our knowledge, this is the first trial that investigated therapeutic effectiveness of daily use of mechanical stimulation under natural circumstances on neuropathic symptoms, vascular status, lower extremity edema, balance and gait in people with DPN.

In this study, as hypothesized, we found 15% reduction in VPT_{max} in the foot after receiving 4 weeks of the treatment. In addition, as hypothesized, we found significant improvements in gait and balance in this study. A possible explanation for the recovery in plantar sensation is accelerated local blood flow in the foot due to the mechanical stimulation. The association between diabetic neuropathic foot and reduced microvascular blood flow (ie, reduced oxygenation) is well established,⁴⁹ and improving local blood flow is recommended for clinical management of diabetic foot.^{2,34} Together with the results from previous studies,²⁷⁻²⁹ our findings support that mechanical stimulation through wearable foot compression device may be a potential clinical option for neuropathic symptoms. Sensory information that is delivered

Table 5. Characteristics for Gait Performance for Baseline and 4-Week Follow-Up for All Participants.

	Baseline	Week 4	P value	Effect size
Normal walking				
Stride velocity, m/s	0.87 ± 0.21	0.96 ± 0.23	.017*	0.41
Severe PN	0.85 ± 0.24	0.94 ± 0.27	.081	0.35
Mild PN	0.89 ± 0.16	0.99 ± 0.16	.081	0.62
Stride length, m	1.05 ± 0.21	1.13 ± 0.24	.030*	0.35
Severe PN	1.04 ± 0.25	1.11 ± 0.28	.169	0.26
Mild PN	1.06 ± 0.14	1.17 ± 0.17	.081	0.71
Stride time, s	1.23 ± 0.14	1.21 ± 0.12	.115	0.15
Double limb support, %	28.15 ± 6.43	27.00 ± 6.81	.187	0.17
Dual-task walking				
Stride velocity, m/s	0.75 ± 0.18	0.91 ± 0.23	.001*	0.77
Severe PN	0.72 ± 0.21	0.85 ± 0.26	.023*	0.55
Mild PN	0.79 ± 0.13	0.97 ± 0.19	.022*	1.11
Stride length, m	1.03 ± 0.19	1.14 ± 0.24	.009*	0.51
Severe PN	1.01 ± 0.23	1.10 ± 0.28	.096	0.35
Mild PN	1.05 ± 0.14	1.18 ± 0.18	.033*	0.81
Stride time, s	1.41 ± 0.16	1.28 ± 0.15	< .001*	0.84
Severe PN	1.45 ± 0.15	1.32 ± 0.16	.014*	0.84
Mild PN	1.36 ± 0.17	1.24 ± 0.12	.015*	0.82
Double limb support, %	31.02 ± 6.23	28.22 ± 5.48	.004*	0.48
Severe PN	32.26 ± 6.88	29.77 ± 6.23	.094	0.38
Mild PN	29.48 ± 5.18	26.32 ± 3.80	.007*	0.70
Fast walking				
Stride velocity, m/s	1.10 ± 0.33	1.20 ± 0.27	.043*	0.33
Severe PN	1.07 ± 0.38	1.15 ± 0.32	.609	0.23
Mild PN	1.14 ± 0.25	1.27 ± 0.19	.017*	0.59
Stride length, m	1.15 ± 0.27	1.24 ± 0.24	.050	0.35
Stride time, s	1.09 ± 0.17	1.06 ± 0.11	.152	0.21
Double limb support, %	23.96 ± 7.61	22.14 ± 5.84	.031*	0.27
Severe PN	24.22 ± 8.24	22.75 ± 7.05	.716	0.19
Mild PN	23.62 ± 5.99	21.39 ± 4.05	.004*	0.44

Note: Asterisks indicate significant differences between baseline and 4-week follow-up. * $P < .05$.

to the central nervous system plays a critical role for successful completion of gait and balance tasks.⁵⁰ People with sensory impairment such as DPN have poor performance in gait and balance.⁵⁻¹⁰ In healthy people, artificial reduction in sensory function worsens balance control,^{51,52} and also enhanced sensory information improves gait and balance tasks.^{32,53} Our findings were consistent with previous studies that reported improvements in plantar sensation, balance (ML sway) and gait (stride velocity, stride length, overall dual-task performance, and overall fast walking performance) in people with DPN after receiving electrical stimulation.^{12,23}

In addition, higher intervention response for ML sway postural balance may have been related to the specific ML baseline balance deficit in our fall prone participants, in particular among those with severe PN as described in previous studies.⁵⁴⁻⁵⁶ Similarly, we observed higher improvement during dual-task gait and fast walking, which could be also link to baseline gait and cognitive-motor deficits in particular among those with severe PN.⁵⁷⁻⁵⁹ Thus, it is suggested that

wearing the foot compression device may be also effective in treating motor impairments in DPN in particular among those with severe PN.

Among our study sample, 77% ($n = 23$) were aged 65 years and older (ie, were older adults). Increased ML CoM sway during balance tasks⁶⁰ and decreased gait speed during gait tasks⁶¹ are associated with increased risk of falling in older adults. Thus, the improvement in gait and balance that was found in this study suggests the foot compression device may be beneficial in decreasing risk of falling in people with DPN. Importantly, even after the participants were divided into two subgroups based on the baseline VPT_{max}, we found significant improvements or tendency of improvements in VPT_{max}, balance outcomes and gait parameters in both subgroups. Thus, the mechanical stimulation may be beneficial across diabetic people with varied severities in neuropathy symptoms.

In this study, we asked participants to wear the shoes four hours per day. In fact, our previous studies demonstrated the

medium values for the longest unbroken sitting bout during the daytime was less than four hours.^{8,19} Thus, we anticipate that participants will be more likely to get benefit from the foot compression device when they were sitting thus the choice of four hours may replicate the use of the system during daily activities as well.

There are several limitations in this study. First, the study design was single-arm-intervention study, and the potential training effect in balance outcomes and gait parameters were not considered. Also, we included people with type 2 diabetes in this study only, and the effectiveness of the intervention for people with type 1 diabetes needs to be investigated in future studies. Given the improvements in dual-task walking task in this study, it is likely that the treatment may improve dual-task balance control as well but it was not tested in this study. It is suggested to investigate dual-task balance control after using the wearable foot compression device in future studies. Our sample was a convenience sample, and relatively small as we were not able to find differences in several balance measurement. The relatively small sample size may also limit the generalizability of our findings. Although we asked participants to wear the shoes for at least four hours per day during four weeks, the adherence was not objectively controlled, thus there is a possibility that time of wearing would have affected the results. The baseline motor assessment has been performed while participants were wearing their own footwear, however the follow-up assessment has been performed while they were wearing the study footwear, which may have affected results for the motor tasks. However, given the improvements in VPT_{max} that is independent of footwear type, it is likely that the improvements in motor tasks are due to the treatment. In addition, potential effect of being familiar to the motor tasks in the follow-up assessment may have affected the results.

Conclusion

This study suggests mechanical stimulation applied to the arch of the foot through a micro-mobile foot compression device improves neuropathic symptoms, and gait and balance performances in people with DPN. The device is equipped in a shoe insole thus wearable and proper for daily use without additional discomfort. The technique may be considered as an alternative adjunct treatment for exercise intervention, electrical stimulation, or exoskeleton.

Abbreviations

ABI, ankle brachial index; ADL, activities of daily living; CES-D, Center for Epidemiological Studies Depression Scale; CoM, center of mass; DPN, diabetic peripheral neuropathy; EC, eyes closed; EO, eyes open; FES-I, Falls Efficacy Scale–International; FSST, Four Step Square Test; IWDGF, International Working Group on the Diabetic Foot; ML, mediolateral; MoCA, Montreal Cognitive Assessment; PN, peripheral neuropathy; PROMIS, Patient-Reported Outcomes Measurement Information System; SPP, skin

perfusion pressure; TUG, Timed Up and Go; VAS, Virtual Analog Scale; VPT, vibration perception threshold.

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References

- Centers for Disease Control and Prevention. *Prevention. National Diabetes Statistics Report, 2017*. Atlanta, GA: Centers for Disease Control and Prevention; 2017.
- Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. *JAMA*. 2005;293:217-228.
- Lavery LA, Armstrong DG, Wunderlich RP, Mohler MJ, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. *Diabetes Care*. 2006;29:1288-1293.
- Ametov AS, Barinov A, Dyck PJ, et al. The sensory symptoms of diabetic polyneuropathy are improved with α -lipoic acid. *Diabetes Care*. 2003;26:770-776.
- Simoneau GG, Ulbrecht JS, Derr JA, Becker MB, Cavanagh PR. Postural instability in patients with diabetic sensory neuropathy. *Diabetes Care*. 1994;17:1411-1421.
- Corriveau H, Prince F, Hébert R, et al. Evaluation of postural stability in elderly with diabetic neuropathy. *Diabetes Care*. 2000;23:1187-1191.
- Menz HB, Lord SR, St George R, Fitzpatrick RC. Walking stability and sensorimotor function in older people with diabetic peripheral neuropathy. *Arch Phys Med Rehabil*. 2004;85:245-252.
- Najafi B, Crews RT, Wrobel JS. Importance of time spent standing for those at risk of diabetic foot ulceration. *Diabetes Care*. 2010;33:2448-2450.
- Toosizadeh N, Mohler J, Armstrong DG, Talal TK, Najafi B. The influence of diabetic peripheral neuropathy on local postural muscle and central sensory feedback balance control. *PLOS ONE*. 2015;10:e0135255.
- Zhou H, Al-Ali F, Rahemi H, et al. Hemodialysis impact on motor function beyond aging and diabetes—objectively assessing gait and balance by wearable technology. *Sensors*. 2018;18:3939.

11. Schwartz AV, Hillier TA, Sellmeyer DE, et al. Older women with diabetes have a higher risk of falls: a prospective study. *Diabetes Care*. 2002;25:1749-1754.
12. Najafi B, Crews RT, Wrobel JS. A novel plantar stimulation technology for improving protective sensation and postural control in patients with diabetic peripheral neuropathy: a double-blinded, randomized study. *Gerontology*. 2013;59:473-480.
13. Jacobson AM, De Groot M, Samson JA. The evaluation of two measures of quality of life in patients with type I and type II diabetes. *Diabetes Care*. 1994;17:267-274.
14. Allet L, Armand S, De Bie R, et al. The gait and balance of patients with diabetes can be improved: a randomised controlled trial. *Diabetologia*. 2010;53:458-466.
15. Richardson JK, Sandman D, Vela S. A focused exercise regimen improves clinical measures of balance in patients with peripheral neuropathy. *Arch Phys Med Rehabil*. 2001;82:205-209.
16. Grewal GS, Sayeed R, Schwenk M, et al. Balance rehabilitation: promoting the role of virtual reality in patients with diabetic peripheral neuropathy. *J Am Podiatr Med Assoc*. 2013;103:498-507.
17. Armstrong DG, Nguyen HC, Lavery LA, Van Schie CH, Boulton AJ, Harkless LB. Off-loading the diabetic foot wound: a randomized clinical trial. *Diabetes Care*. 2001;24:1019-1022.
18. Katz IA, Harlan A, Miranda-Palma B, et al. A randomized trial of two irremovable off-loading devices in the management of plantar neuropathic diabetic foot ulcers. *Diabetes Care*. 2005;28:555-559.
19. Najafi B, Grewal GS, Bharara M, Menzies R, Talal TK, Armstrong DG. Can't stand the pressure: the association between unprotected standing, walking, and wound healing in people with diabetes. *J Diabetes Sci Technol*. 2017;11:657-667.
20. Wang C, Goel R, Rahemi H, Zhang Q, Lepow B, Najafi B. Effectiveness of daily use of bilateral custom-made ankle-foot orthoses on balance, fear of falling, and physical activity in older adults: a randomized controlled trial. *Gerontology*. Epub ahead of print 13 November 2018. DOI: 10.1159/000494114
21. Richardson JK, Thies SB, DeMott TK, Ashton-Miller JA. Interventions improve gait regularity in patients with peripheral neuropathy while walking on an irregular surface under low light. *J Am Geriatr Soc*. 2004;52:510-515.
22. Peters EJ, Lavery LA, Armstrong DG, Fleischli JG. Electric stimulation as an adjunct to heal diabetic foot ulcers: a randomized clinical trial. *Arch Phys Med Rehabil*. 2001;82:721-725.
23. Najafi B, Talal TK, Grewal GS, Menzies R, Armstrong DG, Lavery LA. Using plantar electrical stimulation to improve postural balance and plantar sensation among patients with diabetic peripheral neuropathy: a randomized double blinded study. *J Diabetes Sci Technol*. 2017;11:693-701.
24. Korkiakangas EE, Alahuhta MA, Laitinen JH. Barriers to regular exercise among adults at high risk or diagnosed with type 2 diabetes: a systematic review. *Health Promot Int*. 2009;24:416-427.
25. Vinci P, Gargiulo P. Poor compliance with ankle-foot-orthoses in Charcot-Marie-Tooth disease. *Eur J Phys Rehabil Med*. 2008;44:27-31.
26. Bulley C, Shiels J, Wilkie K, Salisbury L. User experiences, preferences and choices relating to functional electrical stimulation and ankle foot orthoses for foot-drop after stroke. *Physiotherapy*. 2011;97:226-233.
27. Liu W, Lipsitz LA, Montero-Odasso M, Bean J, Kerrigan DC, Collins JJ. Noise-enhanced vibrotactile sensitivity in older adults, patients with stroke, and patients with diabetic neuropathy. *Arch Phys Med Rehabil*. 2002;83:171-176.
28. Khaodhiar L, Niemi JB, Earnest R, Lima C, Harry JD, Veves A. Enhancing sensation in diabetic neuropathic foot with mechanical noise. *Diabetes Care*. 2003;26:3280-3283.
29. Zwaferink JB, Hijmans JM, Schrijver CM, Schrijver LK, Postema K, van Netten JJ. Mechanical noise improves the vibration perception threshold of the foot in people with diabetic neuropathy. *J Diabetes Sci Technol*. Epub ahead of print 17 October 2018. DOI: 10.1177/1932296818804552..
30. Priplata AA, Patritti BL, Niemi JB, et al. Noise-enhanced balance control in patients with diabetes and patients with stroke. *Ann Neurol*. 2006;59:4-12.
31. Hijmans JM, Geertzen JH, Zijlstra W, Hof AL, Postema K. Effects of vibrating insoles on standing balance in diabetic neuropathy. *J Rehabil Res Dev*. 2008;45:1441-1450.
32. Lipsitz LA, Lough M, Niemi J, Trivison T, Howlett H, Manor B. A shoe insole delivering subsensory vibratory noise improves balance and gait in healthy elderly people. *Arch Phys Med Rehabil*. 2015;96:432-439.
33. Dohm M, Williams KM, Novotny T. Micro-mobile foot compression device compared with pneumatic compression device. *Clin Orthop Relat Res*. 2011;469:1692.
34. Hinchliffe R, Brownrigg J, Apelqvist J, et al. IWGDF guidance on the diagnosis, prognosis and management of peripheral artery disease in patients with foot ulcers in diabetes. *Diabetes Metab Res Rev*. 2016;32:37-44.
35. Rahemi H, Armstrong DG, Enriquez A, Owl J, Talal TK, Najafi B. Lace up for healthy feet: the impact of shoe closure on plantar stress response. *J Diabetes Sci Technol*. 2017;11:678-684.
36. Murray HJ, Young MJ, Hollis S, Boulton AJ. The association between callus formation, high pressures and neuropathy in diabetic foot ulceration. *Diabet Med*. 1996;13:979-982.
37. Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Appl Psychol Measur*. 1977;1:385-401.
38. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53:695-699.
39. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56:M146-M157.
40. Mahoney R, Barthel DW. Functional evaluation: the Barthel Index: a simple index of independence useful in scoring improvement in the rehabilitation of the chronically ill. *Maryland State Med J*. 1965;14:61-65.
41. Yardley L, Beyer N, Hauer K, Kempen G, Piot-Ziegler C, Todd C. Development and initial validation of the Falls Efficacy Scale-International (FES-I). *Age Ageing*. 2005;34:614-619.
42. Boulton A, Armstrong D, Albert S, et al. Comprehensive foot examination and risk assessment. *Endocr Pract*. 2008;14:576-583.
43. Armstrong DG, Hussain SK, Middleton J, Peters EJ, Wunderlich RP, Lavery LA. Vibration perception threshold: are multiple sites of testing superior to single site testing on diabetic foot examination? *Ostomy Wound Manage*. 1998;44:70-74, 76.
44. Garrow AP, Boulton AJ. Vibration perception threshold—a valuable assessment of neural dysfunction in people with diabetes. *Diabetes Metab Res Rev*. 2006;22:411-419.

45. Zahiri M, Chen KM, Zhou H, et al. Using wearables to screen motor performance deterioration because of cancer and chemotherapy-induced peripheral neuropathy (CIPN) in adults—toward an early diagnosis of CIPN. *J Geriatr Oncol*. Epub ahead of print 18 January 2019. DOI: 10.1016/j.jgo.2019.01.010
46. Najafi B, Horn D, Marclay S, Crews RT, Wu S, Wrobel JS. Assessing postural control and postural control strategy in diabetes patients using innovative and wearable technology. *J Diabetes Sci Technol*. 2010;4:780-791.
47. Aminian K, Najafi B, Büla C, Leyvraz P-F, Robert P. Spatio-temporal parameters of gait measured by an ambulatory system using miniature gyroscopes. *J Biomech*. 2002;35:689-699.
48. Cohen J. A power primer. *Psychol Bull*. 1992;112:155-159.
49. Malik R, Newrick P, Sharma A, et al. Microangiopathy in human diabetic neuropathy: relationship between capillary abnormalities and the severity of neuropathy. *Diabetologia*. 1989;32:92-102.
50. Winter DA. Human balance and posture control during standing and walking. *Gait Posture*. 1995;3:193-214.
51. Magnusson M, Enbom H, Johansson R, Wiklund J. Significance of pressor input from the human feet in lateral postural control: the effect of hypothermia on galvanically induced body-sway. *Acta Otolaryngol*. 1990;110:321-327.
52. Horak F, Nashner L, Diener H. Postural strategies associated with somatosensory and vestibular loss. *Exp Brain Res*. 1990;82:167-177.
53. Qiu F, Cole MH, Davids K, et al. Enhanced somatosensory information decreases postural sway in older people. *Gait Posture*. 2012;35:630-635.
54. Maki BE, Holliday PJ, Topper AK. A prospective study of postural balance and risk of falling in an ambulatory and independent elderly population. *J Gerontol*. 1994;49:M72-M84.
55. Mohler MJ, Wendel CS, Taylor-Piliae RE, Toosizadeh N, Najafi B. Motor performance and physical activity as predictors of prospective falls in community-dwelling older adults by frailty level: application of wearable technology. *Gerontology*. 2016;62(6):654-64.
56. Najafi B, Horn D, Marclay S, Crews RT, Wu S, Wrobel JS. Assessing postural control and postural control strategy in diabetes patients using innovative and wearable technology. *J Diabetes Sci Technol*. 2010;4:780-791.
57. Wrobel JS, Najafi B. Diabetic foot biomechanics and gait dysfunction. *J Diabetes Sci Technol*. 2010;4:833-845.
58. Najafi B, Khan T, Fleischer A, Wrobel J. The impact of footwear and walking distance on gait stability in diabetic patients with peripheral neuropathy. *J Am Podiatr Med Assoc*. 2013;103:165-173.
59. Grewal GS, Bharara M, Menzies R, Talal TK, Armstrong D, Najafi B. Diabetic peripheral neuropathy and gait: does footwear modify this association? *J Diabetes Sci Technol*. 2013;7:1138-1146.
60. Schwenk M, Mohler J, Wendel C, Fain M, Taylor-Piliae R, Najafi B. Wearable sensor-based in-home assessment of gait, balance, and physical activity for discrimination of frailty status: baseline results of the Arizona frailty cohort study. *Gerontology*. 2015;61:258-267.
61. Verghese J, Holtzer R, Lipton RB, Wang C. Quantitative gait markers and incident fall risk in older adults. *J Gerontol A Biol Sci Med Sci*. 2009;64:896-901.