Washington University in St. Louis
Washington University Open Scholarship

All Theses and Dissertations (ETDs)

Spring 4-28-2014

Foot Progression Angle in Individuals with Diabetes Mellitus and Peripheral Neuropathy

Ericka Nayram Merriwether
Washington University in St. Louis

Follow this and additional works at: https://openscholarship.wustl.edu/etd

WASHINGTON UNIVERSITY IN ST. LOUIS

Program in Movement Science

Dissertation Examination Committee:

David R. Sinacore, Chair
W. Todd Cade
John H. Hollman
Michael J. Mueller
Michael J Strube
Linda Van Dillen
Dequan Zou

Foot Progression Angle in Individuals with Diabetes Mellitus and Peripheral Neuropathy

by

Ericka Nayram Merriwether

A dissertation presented to the
Graduate School of Arts and Sciences
of Washington University in
partial fulfillment of the
requirements for the degree
of Doctor of Philosophy

May 2014

St. Louis, Missouri

TABLE OF CONTENTS

Page

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

DM   diabetes mellitus, diabetes mellitus without peripheral neuropathy or prior history of a neuropathic plantar ulcer participant group

DMPN   diabetes mellitus and peripheral neuropathy

FPA   foot progression angle (degrees)

NPU   neuropathic plantar ulcer(s)

PPP   peak plantar pressure (N/cm^2)

WHO   World Health Organization

CDC   Centers for Disease Control

1st MTPJ   first metatarsophalangeal joint

CON   non-diabetic control participant group

DMPN-NPU diabetes mellitus and peripheral neuropathy without a prior history of a neuropathic plantar ulcer participant group

DMPN+NPU diabetes mellitus and peripheral neuropathy with a prior history of a neuropathic plantar ulcer

High FPA   foot with greater foot progression angle magnitude (degrees)

Low FPA   foot with lesser foot progression angle magnitude (degrees)

FPA Diff   absolute value of the difference in FPA magnitude between the High FPA and Low FPA feet

RSCP   resting calcaneal stance position

pFPA   preferred FPA walking condition

cFPA   corrected FPA walking condition

FTI force-time integral (N*s)

Med Fore medial forefoot regional mask

Lat Fore lateral forefoot regional mask

Med Mid medial mid foot regional mask

Lat Mid lateral mid foot regional mask

Inv involved foot

Uninv uninvolved foot

ACKNOWLEDGMENTS

- To all of the participants in the projects for this dissertation, I offer my sincere gratitude for your willingness to take the time to participate!

- To all of the past and present students in the Movement Science Program, thank you for your support, encouragement, and assistance with this dissertation research. I wish you all the best in your future endeavors.

Administration and Support Staff

- To the staff of the Program in Physical Therapy and physical therapy clinic, and to the security and housekeeping staff of Washington University, I sincerely thank you for ensuring the timely and correct submission of all documentation related to grant submission and accounting. Your contributions were extremely valuable, and I thank you so much for your patience (I know you needed a lot of it dealing with me☺)

Family and community

No endeavor of this magnitude occurs without the love and support of a community of family and friends.

- To my firstborn, Jade Kasui, you are more than I ever imagined you would be! From the moment you quietly entered this world, you have exhibited the grace and humility that a future queen needs to navigate your dreams in an often cold world. I love you more than life, and I truly appreciate your willingness to take this journey with me without complaint. You are all my reasons.

- To my only son, Jared Reign, I will always marvel at your gifts for humor, compassion, perseverance, and competitive fire! You boldly entered this space, and have been letting everyone in the vicinity know when and where you are ever since. I hope this journey has shown you something that will help you navigate a world that at times can

be hostile. I love you more than life, and I truly appreciate your willingness to take this journey with me without complaint. You are all my reasons.

- To my mother, Dr. Sheila Radford-Hill, you epitomize Black womanhood in a way that I demonstrate in my life today. You have been there through the laughter, the tears, the anger and frustration, and everything in-between. You gave me wings, then provided the wind at my back when I was strong enough to fly. You are simply everything.

- To my dad, Walter D. Street, III, I thank you for embracing your role as my surrogate father with grace and dignity. You and mom have been the wind beneath my wings, and I love you with everything I am and everything I have.

- To my father Dr. Lee Hill and stepmother, Dr. Brenda Mallard, thank you for allowing us the chance to share in this journey as a family. You all were there for me and the children in the best and worst of times, and I love you both very much.

- To my aunts, uncles, cousins, and friends, I want to sincerely thank you for listening, for caring, and for bringing me into a positive head space when I needed to stay grounded. I love you all.

- To the families and community at the Flynn Park Elementary School, Brittany Woods Middle School, and Crossroads College Preparatory School, I want to thank you explicitly for opening your hearts, homes, and refrigerators to me, Jade, and Jared. I am forever grateful for the community that has rallied around us to carpool to and from school and extracurricular activities. I am forever in your debt.

- To the Association of Black Biomedical Graduate Students (ABBGS), Assistant Provost Rochelle Smith, Dr. Rafia Zafar, and all of the deans and administrative staff at the Graduate School of Arts and Sciences, I thank you for your support, encouragement, and opportunities to serve on the Graduate Council and Black Graduate Council. I am forever grateful for those experiences.

Chapter 1

Introduction

Musculoskeletal impairments associated with diabetes mellitus (DM) have been disproportionately understudied though they often lead to reported functional limitations and disability. Furthermore, individuals with diabetes mellitus and peripheral neuropathy (DMPN) have nearly three times the rate of functional mobility deficits associated with lower extremity impairment than their non-diabetic counterparts[1,2]. The focus of this research is on DM and its related complications, specifically the examination of the contribution of a specific gait impairment, an excessive external foot progression angle (FPA), on the lower extremity impairment cascade of medial neuropathic plantar ulcer (NPU) development and subsequent non-traumatic lower extremity amputation in individuals with DMPN (Figure 1).

1.1. Diabetes mellitus: Healthcare burden and clinical relevance

1.1.a. Prevalence.

Diabetes mellitus (DM) is a chronic and progressive metabolic disease characterized by elevated blood glucose secondary to insufficient insulin output and insulin resistance, leading to impaired glucose uptake and suboptimal neuromuscular function[3,4]. Medical management of DM represents a major national and international healthcare burden, with total estimated costs of treatment and management of $174 billion in the United States[5]. The World Health Organization (WHO) estimates a worldwide prevalence of DM of 347 million people[4], while the Centers for Disease Control and Prevention estimate a prevalence of approximately 25.8 million Americans (8.3% of the population)[5]. In the United States, 90-95% of those with DM have type 2 diabetes (T2DM), of which Black/African American (13.1 per 1000), Hispanic/Latino (12.3 per 1000), and American Indian/Alaska Native (11.8 per 1000) race groups have a disproportionately higher prevalence compared with White Americans (8.7/1000)[5].

1.1.b. Complications of diabetes mellitus.

1.1.b.1. Peripheral neuropathy. An observed long-term complication of DM is peripheral neuropathy, defined as a clinical diagnosis of peripheral nerve impairment resulting in dysfunction affecting the sensory, motor, and autonomic nervous systems[6,7]. The proposed pathogenesis for the onset and progression of peripheral neuropathy features a complex interaction of vascular and metabolic factors that result in ischemic nerve injury[8,9]. Peripheral neuropathy follows a heterogeneous clinical course with an equally varied manifestation of progressive clinical symptoms, and is estimated to affect up to 60-70% of individuals with chronic DM in the United States [6, 7,10-12]. The most prevalent form of peripheral neuropathy is the distal symmetric polyneuropathy classification in which sensory and motor changes occur symmetrically in the lower and upper extremity [10, 13]. This is also referred to as the "stocking and glove distribution" of peripheral nerve symptoms[13]. Clinical symptoms are insidious and progressive in nature, characterized by a transition from acute sensory changes such as varying degrees of hyperalgesia (an exaggerated response to a noxious stimulus) and allodynia (a pain response to a non-noxious stimulus) to paresthesia (numbness, tingling), abnormal reflexes, and muscle performance deficits[6]. Diagnostic screening for the presence of diabetic peripheral neuropathy includes tests of protective sensation, lower extremity perfusion, and self-assessments of function[6]. The chronicity of peripheral neuropathy is purported to contribute to the development of diabetic foot disease, a cluster of lower extremity pathologies that often lead to pain, morbidity, loss of function and disability[6,14].

1.1.b.2. Diabetic foot disease. Diabetic foot disease carries a substantial economic healthcare burden. Treatment and management of diabetic foot disease in the United States costs approximately $4.6-13.7 billion annually, and often culminates in non-traumatic lower extremity amputation [6,15]. The hallmarks of diabetic foot disease are demineralization and structural malalignment of the pedal bones, excessive regional peak plantar pressure,

neuropathic plantar ulceration, and acute or chronic foot infection in individuals with DM[14]. There are more than 65,000 non-traumatic lower extremity amputations in adults with DMPN annually in the United States, 84% of which are preceded by neuropathic plantar ulcers (NPUs)[5,16]. Sinacore et al (1987) showed that 64-81% of NPUs are located on the medial side of the foot compared to the lateral side of the foot[17].

1.1.b.3. Neuropathic plantar ulceration. The development and recurrence of neuropathic plantar ulcers (NPUs) are a significant health and economic burden worldwide. In the United States, an estimated 12 to 25% of adults will develop an NPU[18,19]. Furthermore, those with a history of NPU have the highest relative risk for re-ulceration or new ulcer development (RR=2.46; 95% CI: 1.84-3.29)[20]. Peak plantar pressure (PPP) is often used as an index of risk for skin injury in individuals with DMPN[21,22]. People with DMPN with history of NPU have greater PPP in regions of the foot vulnerable to ulceration compared to those with no history of NPU[23,24]. The combined effects of elevated PPP, limited joint mobility of the foot and ankle, lack of somatic sensation in the foot, and impairments in autonomic nerve function that lead to dry skin and callus formation contribute to the relative risk of NPU development[25]. The development and recurrence of NPUs in individuals with DMPN are related to gait adaptations that compensate for limited joint mobility and impaired muscle performance of the foot and ankle joint complex [26-28].

1.1.b.4. Gait dysfunction. Individuals with DMPN often exhibit the following gait abnormalities: 1) decreased gait speed, 2) excessive external FPA or 'toe-out angle', and 3) prolonged stance time [26,28,29-32]. These gait adaptations have been linked to the protracted timing and magnitude of regional plantar stresses in areas of the foot at risk for skin injury in individuals with DMPN [27,32]. Foot progression angle, or "toe-out angle," is a spatial gait characteristic defined by the orientation of the longitudinal axis of the foot in the transverse plane with respect to the direction

of progression during gait[33,34]. Previous reports have established normative values for FPA magnitude as ranging from 5-9º in older and younger healthy adults with an accompanying degree of asymmetry (inter-limb differences) of at least 2º[32, 35]. Therefore, a reasonable criterion for classification of excessive FPA is a measured FPA of greater than 10±5º.

Lower extremity joint mobility and gait speed. Reported lower extremity joint mobility limitations related to slower gait speed include less 1st metatarsophalangeal joint (1st MTPJ) extension motion, less ankle dorsiflexion motion, less ankle plantar flexor muscle power and peak torque, and decreased hip rotation during walking compared with healthy, age and weight-matched control subjects[27-29,36-39]. In addition, Giacomozzi et al (2008) and Allet et al (2009) suggest that decreased gait speed and the associated joint mobility impairments may precede the onset or clinical detection of peripheral neuropathy in persons with diabetes mellitus[31,38].

Lower extremity joint mobility and FPA. Studies from independent groups suggest a direct relationship between external FPA and timing and magnitude of medial and lateral PPP in adults with DMPN[21,32]. However, there is a dearth of evidence identifying specific joint mobility limitations associated with excessive external FPA in individuals with DMPN. Similarly, it is not known if changes in FPA characteristics (magnitude and inter-limb asymmetry) progress in parallel with the severity of lower extremity impairments associated with DMPN, or if the changes in FPA magnitude are modifiable. Studies from the pediatric orthopedic literature provide some evidence for lower extremity joint limitations related to FPA magnitude. Ho et al (2000) and Chang et al (2004) suggest greater ankle dorsiflexion and hip external (lateral) rotation are related to increased FPA magnitude in children with and without neuromuscular disease[40,41] though these impairments have not been identified as contributors to excessive FPA in adults with DMPN.

5

1.2. Current neuropathic plantar ulcer (NPU) treatment options.

1.2.a. Bracing and custom footwear.

Many treatment options exist for offloading plantar sites to promote wound healing or to prevent re-ulceration. Commonly used pressure offloading strategies include use of custom-made insoles[42], removable cast walking boots, total contact casting, and non-weight bearing strategies such as wheelchair usage[43]. Though these interventions have been shown to successfully reduce forefoot and mid foot PPP in individuals with DMPN and a history of NPU[43,44], often there are barriers related to cost, patient compliance, and reimbursement[43,45]. Moreover, non-weight bearing offloading techniques potentially contribute to the development and progression of mobility limitations reported by individuals with diabetes[5]. Though offloading strategies may provide the proper healing environment for NPUs, excessive offloading may make the tissues vulnerable to re-injury as evidenced by the high rates of re-ulceration (~20-70%) after successful healing with offloading[46,47].

1.2.b. Gait pattern modification.

Some research groups have investigated the effects of modified gait patterns on plantar pressure distribution in healthy young adults and in adults with DMPN[45,48,49]. These modified gait patterns were proposed as preventative or healing strategies for people with DMPN at risk for first-time or recurrent NPU. Strategies for those with DMPN include walking slower, reducing push off in late stance phase of walking by exaggerating hip flexion[48], or walking with a "step-to" gait pattern[49]. Though these strategies reduce PPP in the forefoot region, reported changes in other regions of the plantar surface of the foot are variable. However, there have been no documented results as to whether an excessive external FPA is modifiable in a DM population with or without peripheral neuropathy, or the effects of such a modification.

1.3. Scope of dissertation

1.3 a. Unexplored areas of research

Despite the strong relationship between external FPA and the increased timing and magnitude of medial plantar pressure[21,32], there are no studies that have investigated the unique features of FPA in individuals with DMPN. Also, to our knowledge, there are no studies that have examined the specific joint mobility limitations associated with excessive external FPA in individuals with DMPN. Furthermore, there have been no studies probing whether excessive external FPA can be modified in adults with DMPN, thereby potentially creating a strategy for early rehabilitative intervention in the lower extremity impairment cascade which often culminates in amputation (Figure 1). Our research seeks to improve our understanding of the lower extremity alignment factors that contribute to an excessive external FPA in adults with DM with and without peripheral neuropathy, and if those factors are amenable to early intervention using modification of walking patterns.

1.3.b. Expected outcomes

Based on previous published studies, we hypothesized that limitations in foot, ankle, and hip range of motion contribute substantially to excessive external FPA in adults with DMPN[27-29,36-39]. We also hypothesized that after visual and verbal cueing and practice, adults with DMPN would be able to intentionally reduce their external FPA, resulting in concomitant decreases in PPP particularly in the medial side of the foot. Figure 1 illustrates the proposed relationship between excessive external FPA and the lower extremity impairment cascade of excessive medial PPP, medial neuropathic plantar ulceration, and non-traumatic foot amputation. The primary objective of this research was to explore how specific characteristics (magnitude and inter-limb asymmetry) of FPA change with disease progression (Aim 1), to determine static and dynamic predictors of FPA magnitude (Aim 2), and to examine the effect of

a modification of external FPA magnitude on the regional plantar pressure distribution (Aim 3).

A portion of this project was to investigate the impact of limited hip joint rotation on external FPA magnitude in individuals with DMPN (Aim 2). A particularly novel aspect of the project represents a considerable expansion of previous literature on hip joint mobility in persons with DM, which has only explored hip joint mobility limitations in the sagittal plane with respect to a decreased gait speed[39]. Given that treatment for joint limitations are within the scope of physical therapist practice, intervention(s) targeting lower extremity joint limitations could potentially serve as treatment sites to minimize risk for NPU development in DMPN.

1.4. Specific Aims and Hypotheses

Specific Aim 1. Determine the characteristics of foot progression angle in groups of participants without diabetes mellitus (CON), with diabetes mellitus <u>without</u> peripheral neuropathy (DM only), with diabetes mellitus <u>and</u> peripheral neuropathy WITHOUT a history of neuropathic plantar ulcers (DMPN-NPU) with diabetes mellitus <u>and</u> peripheral neuropathy WITH a history of neuropathic plantar ulcers (DMPN+ NPU).

Hypothesis 1. The primary external FPA characteristic of interest is magnitude, but a secondary characteristic of interest is inter-limb asymmetry (i.e., right side versus left side). We hypothesize that individuals with DMPN+NPU will demonstrate an increased external FPA magnitude compared with other groups.

Hypothesis 2. We hypothesize there will be a progressive decrease in inter-limb asymmetry of FPA across participant groups with and without DMPN and a prior history of ulceration.

Specific Aim 2. Determine ability of select lower extremity joint variables to predict FPA magnitude.

Hypothesis 3. There will be an **inverse** relationship between FPA and peak ankle plantar flexor power, as well as peak range of motion values for 1st MTPJ extension and ankle joint dorsiflexion. There will be a **direct** relationship between FPA and hip external rotation range of motion.

Hypothesis 4. Peak hip external rotation range of motion and ankle joint dorsiflexion range of motion will account for at least 50% of the variance in external FPA magnitude during the stance phase of gait.

Specific Aim 3. Determine the effect of reducing external FPA on medial peak plantar pressure in individuals with DMPN with excessive external FPA. The primary objective is to determine if reducing FPA using instruction, visual and verbal cues and practice trials results in concomitant reductions in medial peak plantar pressure in adults with DMPN.

Hypothesis 5. Adults with DMPN who reduce their FPA magnitude to 10º or less will demonstrate decreased medial peak plantar pressure compared with pre-intervention values.

REFERENCES

1. Ryerson B, Tierney EF, Thompson TJ et al. Excess physical limitations among adults with diabetes in the U.S. population, 1997-1999. *Diabetes Care* 2003;26(1):206-10

2. Hilton TN, Tuttle LJ, Bohnert KL, Mueller MJ, Sinacore DR. Excessive adipose tissue infiltration in skeletal muscle in individuals with obesity, diabetes mellitus, and peripheral neuropathy: association with performance and function. *Phys Ther* 2008; 88 (11): 1336-1344

3. Chlebowy DO, Garvin BJ. Social support, self-efficacy, and outcome expectations: impact on self-   care behaviors and glycemic control in Caucasian and African-American adults with type 2 diabetes. *Diabetes Educator.* 2006; 32, 777-786

4. World Health Organization. World Health Organization Diabetes Fact Sheet. http://www.who.int/mediacentre/factsheets/fs312/en/. Published October, 2013. Accessed February 10, 2014

5. Centers for Disease Control and Prevention. National Diabetes Fact Sheet, 2011. http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Published 2011. Accessed January 23, 2014

6. Boulton AJ. Management of diabetic peripheral neuropathy. *Clin Diabetes* 2005; 23(1): 9-15

7. Pinzur MS. Diabetic peripheral neuropathy. *Foot Ankle Clin* 2011; 16(2):345-349

8. Cameron NE, Eaton SE, Cotter MA, Testafaye S. Vascular factors and metabolic interactions in the pathogenesis of diabetic neuropathy. *Diabetologia* 2001; 44:1973-1988

9. Sytze Van Dam P, Cotter MA, Bravenboer B, Cameron NE. Pathogenesis of diabetic neuropathy: focus on neurovascular mechanisms. *Eur J Pharmacol* 2013; 719:180-186

10. Partanen J, Niskanen L, Lehtinen J, Mervaala E, Siitonen O, Uusitupa M. Natural history of peripheral neuropathy in patients with non-insulin-dependent diabetes mellitus. *N Engl J Med* 1995; 333(2), 89-94

11. Dyck PJ, O'Brien PC, Litchy WJ, Harper CM, Klein, CJ, Dyck, PJ. Monotonicity of nerve tests in diabetes: subclinical nerve dysfunction precedes diagnosis of polyneuropathy. *Diabetes Care* 2005; 28(9): 2192-2200

12. Vinik A, Ullal J, Parson HK, Casellini CM. Diabetic neuropathies: clinical manifestations and current treatment options. *Nat Clin Pract Endocrinol & Metabol* 2006; 2(5):269-281

13. Pasnoor M, Dimachkie MM, Barohn RJ. Diabetic neuropathy part 2: proximal and asymmetric phenotypes. *Neurol Clin* 2013; 31:447-462

14. Sinacore DR, Bohnert KL, Hastings MK, Johnson JE. Mid foot kinetics characterize structural polymorphism in diabetic foot disease. *Clin Biomech* 2008; 23(5):653-661

15. Gordois A, Scuffham P, Shearer A, Oglesby A, Tobian JA. The health care costs of diabetic peripheral neuropathy in the US. *Diabetes Care* 2003; 26(6):1790-1795

16. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. Basis for prevention. *Diabetes Care* 1990; 13(5):513-521

17. Sinacore DR. Mueller MJ, Diamond JE, Blair VP, Drury D, Rose SJ. Diabetic plantar ulcers treated by total contact casting. A clinical report. *Phys Ther* 1987; 67(10):1543-1549

18. Cavanagh PR, Lipsky BA, Bradbury AW, Botek G. Treatment for diabetic foot ulcers. *Lancet* 2005; 366(9498):1725-1735

19. Owings TM, Apelqvist J, Stenström A, Becker M, Bus SA, Kalpen JS et al. Plantar pressures in diabetic patients with foot ulcers which have remained healed. *Diabet Med* 2009; 26:1141-1146

20. Boyko EJ, Ahroni JH, Stensel V, Forsberg RC, Davignon DR, Smith DG. A prospective study of risk factors for diabetic foot ulcer: the Seattle Diabetic Foot Study. *Diabetes Care* 1999; 22(7):1036-1042

21. Mueller MJ, Hastings MK, Commean PK, Smith KE, Pilgram K, Robertson D et al. Forefoot structural predictors of plantar pressures during walking in people with diabetes and peripheral neuropathy. *J Biomech* 2003; 36(7):1009-1017

22. Mueller MJ, Zou D, and Lott DJ. "Pressure gradient" as an indicator of plantar skin injury. *Diabetes Care* 2005; 28(12): 2908-2912

23. Boulton AJ, Hardisty CA, Betts RP, Franks CI, Worth RC, Ward JD et al. Dynamic foot pressure and other studies as diagnostic and management aids in diabetic neuropathy. *Diabetes Care* 1983; 6(1):26-33

24. Armstrong DG, Peters EJ, Athanasiou KA, Lavery LA. Is there a critical level of plantar foot pressure to identify patients at risk for neuropathic foot ulceration? *J Foot Ankle Surg* 1998; 37(4):303-307

25. Boulton AJ, Kirsner RS, Vileikyte L. Clinical practice. Neuropathic diabetic foot ulcers. *N Engl J Med* 2004; 94(4):353-355

26. Brach JS, Talkowski JB, Strotmeyer ES, Newman AB. Diabetes mellitus and gait dysfunction: possible explanatory factors. *Phys Ther* 2008; 88 (11): 1365-1374

27. Rao S, Saltzman C, and Yack HJ. Segmental foot mobility in individuals with and without diabetes and peripheral neuropathy. *Clin Biomech* 2007; 22(4): 464-471

28. Mueller MJ, Minor SD, Sahrmann SA, Schaaf JA, Strube MJ. Difference in the gait characteristics of patients with diabetes and peripheral neuropathy compared with age-matched controls. *Phys Ther.* 1994; 74(4):299-308

29. Salsich GB, Mueller MJ. Effect of plantar flexor muscle stiffness on selected gait characteristics. *Gait Posture.* 2000; 11(3): 207-216

30. Giacomozzi C, Caselli A, Macellari V, Giurato L, Lardieri L, Uccioli L. Walking strategy in diabetic patients with peripheral neuopathy. *Diabetes Care* 2002; 25(8):1451-1457

31. Giacomozzi C, D'Ambriogi E, Cesinaro S, Macellari V, Uccioli L. Muscle performance and ankle joint mobility in long-term patients with diabetes. *BMC Musculoskelet Disord* 2008; 9:99

32. Hastings MK, Gelber JR, Isaac EJ, Bohnert KL, Strube MJ, Sinacore DR. Foot progression angle and medial loading in individuals with diabetes mellitus, peripheral neuropathy, and a foot ulcer. *Gait Posture* 2010; 32(2):237-241

33. Holden JP, Cavanaugh PR, Williams KR, Bednarski KN. Foot angles during walking and running.   1985 International Series on Biomechanics: Biomechanics IX-A. Human Kinetics Publishers, Champaign, IL

34. Lai YC, Lin HS, Pan HF, Chang WN, Hsu CJ, Renn JH. Impact of foot progression angle on the distribution of plantar pressure in normal children. *Clin Biomech* 2014; 29(2):196-200

35. Menz HB, Latt MD, Tiedemann A, Mun San Kwan M, Lord SR. Reliability of the GAITRite walkway system for the quantification of temporo-spatial parameters of gait in young and older people. *Gait Posture* 2004; 20(1): 20-25

36. Mueller MJ, Minor SD, Schaaf JA, Strube MJ, and Sahrmann SA. Relationship of plantar-flexor peak torque and dorsiflexion range of motion to kinetic variables during walking. *Phys Ther* 1995; 75(8), 684-693

37. Rao S, Saltzman C, Yack HJ. Ankle ROM and stiffness measured at rest and during gait in individuals with and without diabetic sensory neuropathy. *Gait Posture* 2006; 24(3): 295-301

38. Allet L, Armand S, de Bie RA, Golay A, Pataky Z, Aminian K *et al.* Clinical factors associated with gait alterations in diabetic patients. *Diabet Med* 2009; 26(10): 1003-1009

39. Sawacha Z, Gabriella G, Cristoferi G, Guiotto A, Avogaro A, Cobelli C. Diabetic gait and posture abnormalities: a biomechanical investigation through three-dimensional gait analysis. *Clin Biomech* 2009; 24(9): 722-728

40. Ho CS, Lin CJ, Chou YL, Su FC, Lin SC. Foot progression angle and ankle joint complex in preschool children. *Clin Biomech* 2000; 15(4): 271-277

41. Chang WN, Tsirikos AI, Miller F, Schyler J, Glutting J. Impact of changing foot progression angle on foot pressure measurement in children with neuromuscular disease. *Gait Posture* 2004; 20(1): 14-19

42. Bus SA, Ulbrecht JS, Cavanagh PR. Pressure relief and load redistribution by custom-made insoles in diabetic patients with neuropathy and foot deformity. *Clin Biomech* 2004; 19(6): 629-638

43. Wu SC, Jensen JL, Weber AK, Robinson DE, Armstrong DG. Use of pressure offloading devices in diabetic foot ulcers: do we practice what we preach? *Diabetes Care* 2008; 31(11):2118-2119

44. Gutekunst DJ, Hastings MK, Bohnert KL, Strube MJ, Sinacore DR. Removable cast walker boots yield greater forefoot off-loading than total contact casts. *Clin Biomech* 2011; 26(6): 649-654

45. Kwon OY, Mueller MJ. Walking patterns used to reduce forefoot plantar pressures in people with diabetic neuropathies. *Phys Ther* 2001; 81(2): 828-835

46. Apelqvist J, Larsson J, Agardh CD. Long-term prognosis for diabetic patients with foot ulcers. *J Intern Med* 1993; 233(6):485-491

47. Mueller MJ, Maluf KS. Tissue adaptation to physical stress: a proposed "Physical Stress Theory" to guide physical therapist practice, education, and research. *Phys Ther* 2002; 82(4) 383-403

48. Mueller MJ, Sinacore DR, Hoogstrate S, Daly L. Hip and ankle walking strategies: effect on peak plantar pressures and implications for neuropathic ulceration. *Arch Phys Med Rehabil* 1994; 75(11):1196-2000

49. Brown HE, Mueller MJ. A "step to" gait decreases pressures on the forefoot. *J Orthop Sports Phys Ther* 1998; 28(3):139-145
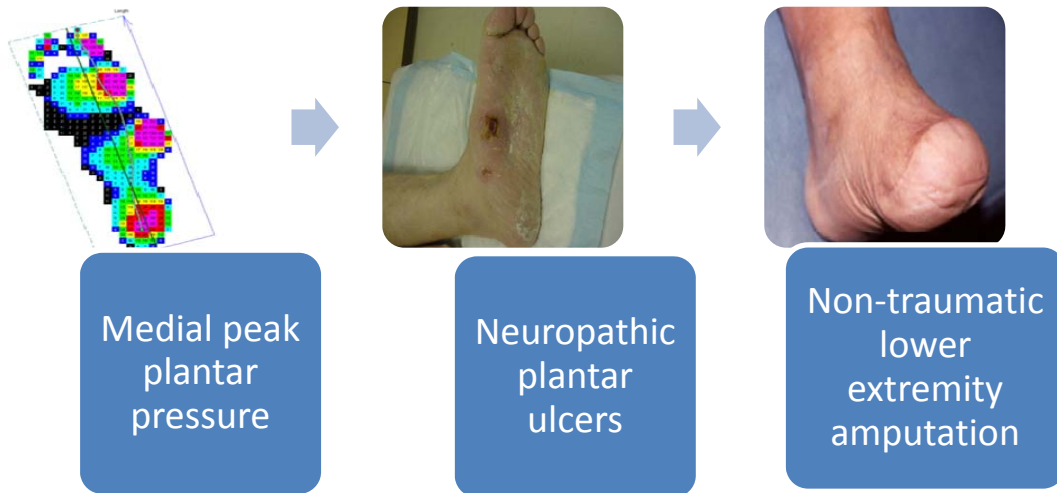
Figure 1.1. Impairment cascade of non-traumatic lower extremity amputation

Chapter 2

Characteristics of foot progression angle in individuals with diabetes mellitus and

peripheral neuropathy

Status of resulting manuscript: in preparation, *The Foot*

2.1   Abstract

In the United States, an estimated 15% of patients with diabetes mellitus and peripheral neuropathy (DMPN) have a lifetime risk of neuropathic plantar ulcer (NPU) development, which often precedes non-traumatic lower extremity amputation. Despite evidence of the relationship between excessive external foot progression angle (FPA or "toe-out angle") and plantar ulceration risk in individuals with DMPN, specific characteristics of FPA, e.g. magnitude and inter-limb asymmetry have not been examined. The primary purposes of this study were to describe the magnitude and inter-limb asymmetry (the difference in FPA between sides). Forty-five participants with and without diabetes participated, and were classified into one of four groups: 1) non-diabetic control (CON), 2) diabetes mellitus **without** peripheral neuropathy (DM), 3) diabetes mellitus and peripheral neuropathy without a prior history of a neuropathic plantar ulcer (DMPN-NPU), and 4) diabetes mellitus and peripheral neuropathy with a prior history of a neuropathic plantar ulcer (DMPN+NPU).   The foot with the higher external FPA value was designated the High FPA foot for all groups, while the foot with the lower FPA value was designated as the Low FPA foot. The DMPN+NPU group had a greater FPA on the High FPA foot than the other groups (DMPN+NPU=-21±5°; DMPN-NPU=-13±7°; DM=-14±5°; CON=-15±6°, p=.03), with no group difference in FPA on the Low FPA foot (DMPN+NPU=-15±9°; DMPN-NPU=-9±5°; DM=-10±5°; CON=-8.7±4.8°, p=.07). There was no group difference in degree of inter-limb asymmetry (FPA Diff). These results indicate that it may be useful to include measurement of FPA magnitude as part of a clinical gait assessment for individuals with DMPN with a prior history of ulceration.

2.2   Introduction

In the United States, an estimated 15% of patients with diabetes mellitus and peripheral neuropathy (DMPN) have a lifetime risk of neuropathic plantar ulcer (NPU) development[1].

Recent data show more than 65,000 non-traumatic lower extremity amputations in adults with DMPN occur annually in the United States, with 84% preceded by the development of a NPU[2,3]. The development and recurrence of NPUs in individuals with DMPN have been linked to the protracted duration and magnitude of regional peak plantar pressure (PPP) in areas of the foot at risk for skin injury secondary to altered gait characteristics[4,5]. Foot progression angle (FPA), or "toe-out angle," is a spatial gait variable defined by the orientation of the longitudinal axis of the foot in the transverse plane with respect to the direction of progression during gait[6,7]. Previously established normative values for FPA magnitude range from 5-9º in older and younger healthy adults[5,8]. Therefore, an accepted criterion for classification of excessive external FPA ('toe-out angle') is a measured FPA of greater than 10±5º. Chang et al reported a direct relationship between an excessive external FPA and the increased duration and magnitude of medial PPP in children with neurological pathology[9]. Other investigators have established FPA as a predictor of elevated medial PPP, a proxy measure of dermal injury risk in adults with DMPN with a history of plantar ulceration[5,10]. However, findings from this previous work have been conducted primarily on the affected limb. Despite evidence of the direct relationship between increased external FPA and PPP in individuals with DMPN, it is unknown if FPA magnitude during the stance phase of walking changes in parallel with the severity of lower extremity impairments associated with DMPN.

Inter-limb symmetry of gait patterns is becoming more widely accepted as a measure of functional lower extremity motor control and coordination[11-13]. Though there is evidence to support asymmetry in spatiotemporal gait parameters, muscle performance measures, and joint mobility as indicators of gait pathology, there is equally compelling evidence to support asymmetry of these variables as a normal feature of gait[14]. In a review by Sadeghi et al (2000), several investigators have reported asymmetries in step and stride lengths, external FPA, and joint kinematics and kinetics in healthy people without lower extremity pathologies[14].

Researchers have often attributed the presence of any minor inter-limb asymmetry in gait variables to "limb dominance" and to the differential functions of braking and propulsion, or the deceleration and acceleration of the body during gait[14]. Researchers have reported values of inter-limb asymmetry in FPA ranging from 2-4º in healthy young and older adults[8,15]. However, it is unknown if inter-limb asymmetry in FPA is a feature of normal gait in adults with DMPN compared to adults without diabetes. Furthermore, it is also unclear if there is a similar FPA magnitude in both feet of individuals with DMPN at risk for NPU development. Given the evidence supporting the link between excessive increased FPA (an FPA of >10±5º) and increased medial PPP in adults with DMPN, we wanted to characterize FPA across a spectrum of older adults with and without DMPN or a prior history of neuropathic plantar ulceration. Therefore, the purposes of this study were to describe the magnitude and inter-limb asymmetry in adults with and without DMPN and a prior history of plantar ulceration. We hypothesized there would be a progressive increase in FPA magnitude and a progressive decrease in the inter-limb asymmetry in FPA across a spectrum of participants with and without DMPN and accompanying history of prior ulceration.

2.3. Methods

2.3.a. Participants

Forty-five participants with and without diabetes (21 M, 24 F; age, 60±11 yrs; height, 1.7±0.1 m; BMI, 36±8) participated, and provided written informed consent as approved by the local Institutional Review Board. Participants were classified into one of four groups: 1) age-matched non-diabetic control participants (CON), 2) diabetes mellitus *without* peripheral neuropathy (DM), 3) diabetes mellitus and peripheral neuropathy without a prior history of a neuropathic plantar ulcer (DMPN-NPU), and 4) diabetes mellitus and peripheral neuropathy with a prior history of a neuropathic plantar ulcer (DMPN+NPU). The presence or absence of

18

peripheral neuropathy was assigned based on the presence or absence of protective sensation, and ulcer classification was based on any prior history of plantar ulceration. Peripheral neuropathy was assessed using a 5.07 (10 gram) Semmes-Weinstein monofilament at seven sites on the plantar surface of the foot[16]. In addition, we measured vibration perception threshold (VPT) using a 120 V bioesthesiometer (Bio-medical Instrument Co., Newbury, OH, 44065, USA) to assess large fiber peripheral nerve function. Those who were unable to perceive vibration of the bioesthesiometer at threshold of 25 V or greater were classified as having peripheral neuropathy. A VPT $\geq$25 V is associated with incidence of foot ulceration in individuals with Type 2 diabetes mellitus[17]. The combination of these tests for protective sensation has been shown to increase specificity of risk identification and disease severity without diminution in sensitivity[17]. Twelve participants were classified as CON, twelve were classified as DM, eleven were classified as DMPN-NPU, and ten were classified as DMPN+NPU with 8 reporting a history on one foot and 2 participants reporting a history of plantar ulcers on both feet (8 unilateral, 2 bilateral). Participants classified as DMPN+NPU did not have an open ulcer at the time of testing. Those identified as non-ambulatory or with lower extremity amputations proximal to the digits were excluded from the study.

2.3.b. Gait Analysis

2.3.b.1. Data collection. Three-dimensional kinematic and kinetic data were collected during gait for the pelvis and bilateral lower extremities while participants walked at a self-selected speed over a walkway within the capture volume. Kinematic data were acquired using an infrared 8-camera, 200 Hz motion capture system (Vicon MX, Los Angeles, CA, USA), and kinetic data were collected using a Bertec K80301 force plate with a resolution of 500 Hz (Bertec Corporation, Columbus, OH, USA).

2.3.b.2. Marker placement. All participants were fitted with 10 mm diameter retro-reflective markers affixed directly to the skin or to pre-molded rigid plate in a non-collinear arrangement to establish segment coordinate systems for the foot, shank, thigh, pelvis, and trunk. A modification of the "obesity-specific marker set", described by Lerner et al for the trunk, pelvis, and thigh, was used in this study in an effort to account for potential motion artifact secondary to adiposity[18,19]. Briefly, single markers for the trunk were placed on the body of the sternum, the C7 spinous process, right and left acromion processes, and the inferior angle of the scapula. Markers on the pelvis included single markers on the right and left posterior superior iliac spines, with an accompanying marker cluster placed on the sacrum. Marker clusters on the pelvis have been shown to have greater repeatability and less movement variability during non-sagittal plane motion of the pelvis in overweight and obese individuals[20]. To correct for marker displacement secondary to adiposity, digitized markers were created for the anterior superior iliac spines and iliac crests with a static digitizing wand (C-Motion, Germantown, MD) using procedures described by Lerner et al[18,19]. Additional corrections were made using measurements of inter-ASIS distance using a skinfold caliper in subject-specific models. Lerner et al reported that use of marker clusters and digitized markers on the thigh and pelvis minimized overestimation of lower extremity kinematics and kinetics[19]. Single thigh markers were placed proximally on the greater trochanter and distally on the medial and lateral femoral epicondyles, with a 4-marker cluster for tracking on the distal thigh superior to the lateral epicondyle.

We utilized a marker configuration for the foot and shank described by Carson et al (2001) and modified by Hastings et al (2013). Individual shank markers were placed on the fibular head, tibial tuberosity, and malleoli, with a 4-marker cluster placed on the distal shank superior to the lateral malleolus[22]. To determine FPA magnitude and inter-limb asymmetry, we modeled the foot as a single, rigid body segment using three markers in a non-collinear

arrangement. The foot segment was defined by virtual markers created from projected midpoints between the lateral and medial malleoli at the proximal end, and between the first and fifth metatarsal heads at the distal end. The hind foot segment was defined by calcaneal marker placement on the sustentaculum tali, fibular trochlea, and by three mounted markers on a molded plastic plate applied to the posterior calcaneal bisection—a vertical line between the sustentaculum tali and the fibular trochlea[42]. The forefoot segment was defined distally by a marker placed at the midpoint between the second and third metatarsals, and by markers at the first and fifth metatarsal heads. The proximal forefoot was defined by the base of the first and fifth metatarsals. The hallux segment was defined by a plate with three mounted markers arranged parallel with the long axis of the proximal phalanx of the great toe[22].

All participants were asked to walk barefoot at a self-selected speed. All were given at least 1-2 practice trials prior to recording. To minimize risks associated with barefoot walking in participants in the DMPN-NPU and DMPN+NPU groups, walking distance was truncated to include the steps on and at least 10 cm beyond the force plate.   A maximum of five trials in which participants were able to contact the force plate without "targeting" were collected. A minimum of three trials were included in the analysis if FPA values were within one standard deviation of the within-trial mean for each participant. Stride speed was calculated in the Visual 3D software as the time for the foot opposite the one contacting the force plate to complete one full stride[21].

2.3.c. Data Processing and Analysis.

2.3.c.1. Processing. All marker trajectories and tri-axial force data were processed using a fourth-order, low-pass filter in Visual 3D software (C-Motion, Inc, Rockville, MD). Marker trajectories were filtered at 6Hz, and tri-axial force data were filtered at 20Hz. Inter-segmental and global orientation angles were derived using Cardan angle sequences, and parallel

alignment of the segmental axes represent neutral position[22]. FPA was calculated as the magnitude of transverse plane rotation of the foot segment around the local superior-inferior axis at mid stance (i.e., 50% of the stance phase)[23]. Kinematic convention for all FPA measurements was to designate external FPA (toe-out angle) as negative and internal FPA (toe-in angle) as positive.

2.3.c.2. Statistical analyses. Prior to all analyses, we conducted the Shapiro-Wilk test of normality to verify that continuous data for both FPA and FPA Diff was normally distributed. Each foot for all participants was classified as High FPA or Low FPA based on the FPA magnitude. The foot with the greater FPA was classified as High FPA for all groups, while the foot with the lesser FPA was classified Low FPA.

Based on previous work investigating asymmetry in lower extremity variables during gait[24,25] we initially performed a two-way analysis of variance (Group [4 levels] X Side [2 levels]) to determine the main and interaction effects of group and side. We then quantified the degree of inter-limb asymmetry (FPA Diff) as the absolute value of the difference in FPA magnitude between the High FPA and Low FPA feet (|High-Low|), and performed a univariate analysis of variance to determine group differences.. Based on previous work[8,15], the criterion for having a clinically meaningful measure of FPA Diff have reported degrees of asymmetry was 4°. Statistical analyses were performed using IBM SPSS Statistics software, version 21.0 (SPSS Inc, Chicago, IL, USA). Post-hoc analyses for main and interaction effects were conducted using a Bonferroni correction, with statistical significance for all analyses set at $p<.05$.

2.4. Results

2.4.a. Participant Characteristics

The mean (SD) age for all participants (N=45) was 60 (10) years (range: 44-85 years). There were no group differences in age, height or body mass index (BMI)(Table 2.1). The

DMPN+NPU group had diabetes for a longer duration and had greater loss of vibration perception than the DM group (Disease duration in years): DM=8±5, DMPN-NPU=11±9, DMPN+NPU= 24±8; p<.01). The DMPN-NPU and DMPN+NPU groups had a significantly greater vibration perception threshold than the DM and CON groups (DMPN+NPU=34 V; DMPN-NPU=37 V, p<.01). There were no between-group differences in stride speed (p=.80) (Table 2.1).

2.4.b. FPA magnitude

The DMPN+NPU group had a greater FPA magnitude on the High FPA foot (DMPN+NPU=-21±5º; DMPN-NPU=-13±7º; DM=-14±5º; CON=-15±6º, p=.03), with a trend toward a greater FPA magnitude in the Low FPA foot compared with the other groups (DMPN+NPU=-15±6º; DMPN-NPU=-9±7º; DM=-10±5º; CON=-9±5º, P=.07). Posthoc testing showed a greater FPA for the High FPA foot in the DMPN+NPU group compared to the DMPN-NPU group (p=.03). Values for the High and Low FPA feet for each group are presented in Table 2.2. Statistical analysis revealed the presence of outlier values for FPA on both feet in the control group (CON=-32º) and for the DMPN-NPU group (DMPN-NPU=1º). Values for FPA on either foot were considered outliers if they were two or more standard deviations from the group mean FPA value. Results from analysis *with outliers excluded* revealed enhanced group differences in the High FPA foot (DMPN+NPU-21±5º; DMPN-NPU=-15±5º; DM=-14±5º; CON=-13±3º, p=.01) and Low FPA foot (DMPN+NPU-15±9º; DMPN-NPU=-9±4º; DM=-10±5º; CON=-8±3º, p=.03). Values for both feet for each group with outliers excluded are shown in Table 2.3. Time series motion graphs of FPA excursion during the stance phase of gait is illustrated in Figure 2.1.

2.4.c. FPA asymmetry

There was a main effect of side, with the High FPA foot having a greater FPA magnitude than the Low FPA foot (p<.01). There was no interaction effect of group x side (p=.76), which was confirmed by the lack of FPA Diff between the groups (DMPN+NPU=6±6º; DMPN-NPU=5±4º; DM=3±6º; CON=6±4º, p=.36). When outliers were removed from the analysis, there were no group differences in FPA Diff. FPA Diff for all groups is shown in Table 2.2.

2.5   Discussion

This is the first investigation to determine the characteristics of FPA in individuals with and without diabetes mellitus. One of the key findings from this investigation is that external FPA on the High FPA and Low FPA feet of the DMPN+NPU were greater in magnitude than the other participant groups. Additionally, there were no between-group differences in inter-limb asymmetry (FPA Diff).

The FPA values for the High FPA foot of all participant groups were greater than 10º, and would therefore be classified as excessive compared to young adults[15]. Findings of greater FPA values in both feet of participants with DMPN with a prior history of ulceration compared with adults without DM is consistent with previous findings from other research groups[5,10]. Hastings et al reported an FPA of greater than 10º in both feet of individuals with DMPN with a history of ulceration[5]. This group also stated that FPA magnitude for both feet explained 35-45% of the variance in the duration of medial load in adults with DMPN with a prior history of neuropathic plantar ulceration[5]. In addition, Mueller et al reported that FPA predicted up to 15% of the variance in medial and lateral forefoot peak plantar pressure on the involved foot of individuals with DMPN having a prior history of neuropathic plantar ulcers[10]. These findings suggest that an excessive FPA in the presence of peripheral neuropathy potentially exposes individuals with DMPN with a prior history of ulceration to elevated regional peak plantar pressure sustained for longer duration on the medial side of the foot and subsequently, to an

elevated risk for NPU development. Therefore, it may be clinically useful to observe and measure FPA in one or both feet of adults with DMPN with a prior history of ulceration as part of an assessment of risk for elevated regional stresses and loads that often lead to the development of new NPUs or recurrent NPUs in the same location on the plantar surface of the foot. Future studies could identify predictors of FPA magnitude in a cohort of older adults with and without DMPN.

In the present study, we observed no group differences in FPA inter-limb asymmetry. These results may indicate that FPA asymmetry in a cohort of adults with and without DMPN is not disease-specific, and may be a common spatial characteristic of gait in adults 50 years or older. Several investigators have reported inter-limb differences in movement patterns, force output, and spatiotemporal parameters as an indicator of disease progression and severity, though smaller degrees of asymmetry were also reported in groups without pathology [14,25,29-31]. However, there is also evidence to support inter-limb asymmetry in joint alignment and function as characteristics of normal gait. Sadeghi et al suggest that the cumulative effect of asymmetries in individual joint function ('local asymmetry') possibly culminate into symmetric performance of the lower extremities during gait ('global symmetry')[24.] Also, Riskowski and colleagues reported that in population-level study of older adults, greater degrees of asymmetry in foot alignment were associated with faster walking speeds and more optimal foot function[11]. These findings suggest that inter-limb asymmetry of FPA may contribute to optimal gait performance. Additionally, measurement of the difference in FPA between feet may not be clinically relevant for the assessment of risk for elevated regional stresses and loads, and subsequently, the development or recurrence of NPUs in adults with and with DMPN with a prior history of ulceration.

There are limitations associated with this study. One limitation is the small sample size of the individual groups. Additionally, our selection criteria for study participation were primarily

based on disease status, and not on FPA magnitude or inter-limb asymmetry.   Refinement of our selection criteria plus inclusion of additional participants may have potentially resulted in more robust differences in FPA magnitude. Finally, we selected one of many possible methods of quantifying asymmetry which we believed was appropriate given the purpose of the study. The variation in determining inter-limb asymmetry for spatiotemporal gait variables may be challenging to compare across studies.

2.6.   Conclusion

Results from this investigation highlight the differences in FPA magnitude across a cohort of adults with and without DMPN and a prior history of ulceration. These findings suggest that an excessive FPA in the presence of peripheral neuropathy potentially exposes individuals with DMPN with a prior history of ulceration to elevated regional stresses and loads on the plantar surface of the foot. Therefore, it may be clinically useful to observe and measure FPA in one or both feet of adults with DMPN with a prior history of ulceration as part of an assessment of risk for elevated regional stresses and loads that often lead to the development of new NPUs or recurrent NPUs in the same location on the plantar surface of the foot. Findings from this study also suggest that FPA inter-limb asymmetry is not disease-specific, and may be a common spatial characteristic of walking patterns in adults 50 years or older.

REFRENCES

1. Owings TM, Apelqvist J, Stenström A, Becker M, Bus SA, Kalpen JS et al. Plantar pressures in diabetic patients with foot ulcers which have remained healed. *Diabet Med* 2009; 26:1141-1146

2. Centers for Disease Control and Prevention. National Diabetes Fact Sheet, 2011. http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Published 2011. Accessed January 23, 2014

3. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. Basis for prevention. *Diabetes Care* 1990; 13(5):513-521

4. Rao S, Saltzman C, Yack HJ. Segmental foot mobility in individuals with and without diabetes and peripheral neuropathy. *Clin Biomech* 2007; 22(4): 464-471

5. Hastings MK, Gelber JR, Isaac EJ, Bohnert KL, Strube MJ, Sinacore DR. Foot progression angle and medial loading in individuals with diabetes mellitus, peripheral neuropathy, and a foot ulcer. *Gait Posture* 2010; 32:237-241

6. Holden JP, Cavanaugh PR, Williams KR, Bednarski KN. Foot angles during walking and running.   1985 International Series on Biomechanics: Biomechanics IX-A. Human Kinetics Publishers, Champaign, IL

7. Lai YC, Lin HS, Pan HF, Chang WN, Hsu CJ, Renn JH. Impact of foot progression angle on the distribution of plantar pressure in normal children. *Clin Biomech* 2014; 29(2):196-200

8. Menz GH, Latt MD, Tiedermann A, Mun San Kwan M, Lord SR. Reliability of the GAITRite walkway system for the quantification of temporo-spatial parameters of gait in young and older people. *Gait Posture* 2004; 20(1): 20-25

9. Chang WN, Tsirikos AI, Miller F, Schyler J, Glutting J. Impact of changing foot progression angle on foot pressure measurement in children with neuromuscular disease. *Gait Posture* 2004; 20(1): 14-19

10. Mueller MJ, Hastings MK, Commean PK, Smith KE, Pilgram,TK, Robertson D et al. Forefoot structural predictors of plantar pressures during walking in people with diabetes and peripheral neuropathy. *J Biomech* 2003; 36(7):1009-1017

11. Riskowkski JL, Hagedorn TJ, Dufour AB, Hannan MT. Functional foot symmetry and its relation to lower extremity physical performance in older adults: the Framingham Foot Study. *J Biomech* 2012; 45(10):1796-1802

12. Kodesh E, Kafri M, Dar G Dickstein R. Walking speed, unilateral leg loading, and step symmetry in young adults. *Gait Posture* 2012; 35(1):66-69

13. Patterson KK, Nadkarni NK, Black SE, McIlroy WE. Gait symmetry and velocity differ in their relationship to age. *Gait Posture* 2012; 35(4): 590-594

14. Sadeghi H, Allard P, Prince F, Labelle H. Symmetry and limb dominance in able-bodied gait: a review. *Gait Posture* 2000; 12(1): 34-45

15. Boenig DD. Evaluation of a clinical method of gait analysis. *Phys Ther* 57(7):795-798

16. Diamond JE, Mueller MJ, Delitto A, Sinacore DR. Reliability of diabetic foot evaluation. *Phys Ther* 1989; 69(10):797-802

17. Kästenbauer T, Sauseng S, Brath H, Abrahamian H, Irsigler K. The value of the Rydel-Seiffer tuning fork as a predictor of diabetic polyneuropathy compared with a neurothesiometer. *Diabet Med* 2004; 21(6): 563-567

18. Lerner, ZF, Board, WJ, Browning, RC. Effects of obesity on lower extremity muscle function during walking at two speeds. *Gait Posture* 2013; pii: S0966-6362(13)00715-7. doi:10.1016/j.gaitpost.2013.12.020

19. Lerner ZF, Board WJ, Browning RC. Effects of an obesity-specific marker set on estimated muscle and joint forces in walking. *Med Sci Sports Exerc* 2014; PMID: 24518193

20. Borhani M, McGregor AH, Bull AM. An alternative technical marker set for the pelvis is more repeatable than the standard pelvic marker set. *Gait Posture* 2013; 38(4):1032-1037

21. Carson MC, Harrington ME, Thompson N, O'Connor JJ, Theologis TN. Kinematic analysis of a multi-segment foot model for research and clinical applications: a repeatability analysis. *J Biomech* 2001; 34(10): 1299-1307

22. Hasting MK, Sinacore DR, Woodburn J, Paxton ES, Klein SE, Bohnert KL *et al*. Kinematics and kinetics after the Bridle procedure for treatment of traumatic foot drop. *Clin Biomech* 2013; 28(5): 555-561

23. Raspovic, A. Gait characteristics of people with diabetes-related peripheral neuropathy, with and without a history of ulceration. *Gait Posture* 2013; 38(4):723-728

24. Sadeghi, H. Local or global asymmetry in gait of people without impairments. *Gait Posture* 2003; 17(3): 197-204

25. Mills, K, Hettinga, BA, Pohl, MB, Ferber, R. Between-limb kinematic asymmetry during gait in unilateral and bilateral mild to moderate knee osteoarthritis. *Arch Phys Med Rehabil* 2013; 94(11): 2241-2247

26. Mueller MJ, Zou D, and Lott DJ. "Pressure gradient" as an indicator of plantar skin injury. *Diabetes Care* 2005; 28(12): 2908-2912

27. Rao S, Saltzman C, Yack HJ. Ankle ROM and stiffness measured at rest and during gait in individuals with and without diabetic sensory neuropathy. *Gait Posture* 2006; 24(3): 295-301

28. Giacomozzi C, D'Ambriogi E, Cesinaro S, Macellari V, Uccioli L. Muscle performance and ankle joint mobility in long-term patients with diabetes. *BMC Musculoskelet Disord* 2008; 9:99

29. Perry MC, Carville SF, Smith CH, Rutherford OM, Newham DJ. Strength, power output and symmetry of leg muscles: the effect of age and history of falling. *Eur J Appl Physiol* 2007; 100(5): 527-533

30. Briem K, Snyder-Mackler L. Proximal gait adaptations in medial knee OA. *J Orthop Res* 2009; 27(1): 78-83

31. Laroche DP, Cook SB, Mackala K. Strength asymmetry increases gait asymmetry and variability in older women. *Med Sci Sports Exerc* 2012; 44(11): 2172-2181

	CON (N=12)	DM (N=12)	DMPN-NPU (N=11)	DMPN+NPU (N=10)	p
Age (years)	60 (12)	58 (9)	63 (11)	58 (11)	.80
Height (meters)	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)	.79
Sex (M:F)	7:5	5:7	4:7	5:5	.95
BMI (kg/m^2)	33 (5)†	34 (8)$^#$	39 (9)	41 (9)	.08
Disease duration (years)	N/A	8 (5)$^#$	11 (9)§	24 (8)	<.01
Great Toe VPT (Volts)	20 (9)	15 (6)	37 (11)	34 (17)	<.01
Walking Speed (m/s)	1.1 (0.1)	1.1 (0.1)	1.1 (0.1)	1.1 (0.1)	.80
Side of greater FPA (R:L)	11R:1L	9R:3L	9R:3L	6R:4L	--

Table 2.1. Participant characteristics. Values are expressed in mean (SD). VPT: vibration perception threshold (Volts). Side with greater FPA magnitude (R:L): Number of right feet (R) or left feet (L). †,#,§ :significance values for between-group differences in participant characteristics. †: CON versus DMPN-NPU and DMPN+NPU; #: DM versus DMPN-NPU and DMPN+NPU; §:DMPN-NPU versus DMPN+NPU

	CON (N=12)		DM (N=12)		DMPN-NPU (N=11)		DMPN+NPU (N=10)		p
	High	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	
FPA (deg)	-15 (6)*	-9 (5)*	-14 (5)*	-10 (5)*	-13 (7)[#]*	-9 (5)*	-21 (5)*	-15 (9)*	.03
FPA Diff	6(4)		3(7)		5(4)		6(6)		.36

Table 2.2. Foot progression angle (FPA) magnitude for each foot for all participants. Values are expressed in degrees, mean (SD). High: foot with the higher FPA magnitude (High FPA). Low: foot with the lower FPA magnitude (Low FPA). FPA Diff: the absolute difference in FPA magnitude between the High FPA and Low FPA feet (|High-Low|). [#]: Between-group differences in FPA magnitude of the High foot. DMPN-NPU versus DMPN+NPU. *: Paired mean differences in FPA for all groups, p<.01.

	CON (N=12)		DM (N=12)		DMPN-NPU (N=11)		DMPN+NPU (N=10)		p
	High	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	
FPA (deg)	-13 (3)[†]*	-8 (3)*	-14 (5)[#]*	-10 (5)*	-15 (5)*	-9 (4)*	-21 (5)[#]*	-15 (2)*	<.01
FPA Diff (|High-Low|)	6(4)		3(6)		5(4)		6(6)		.40

Table 2.3. Foot progression angle (FPA) magnitude for each foot **with outliers excluded from the analysis**. Values are expressed in degrees, mean (SD). High: foot with the higher FPA magnitude (High FPA). Low: foot with the lower FPA magnitude (Low FPA). FPA Diff: the absolute difference in FPA magnitude between the High and Low feet. †,#,§ : Between-group differences in FPA magnitude of the High foot. [†]: CON versus DMPN+NPU; [#]: DM versus DMPU+NPU; [§]: DMPN-NPU versus DMPN+NPU. *: Paired mean differences in FPA for all participant groups, p<.01
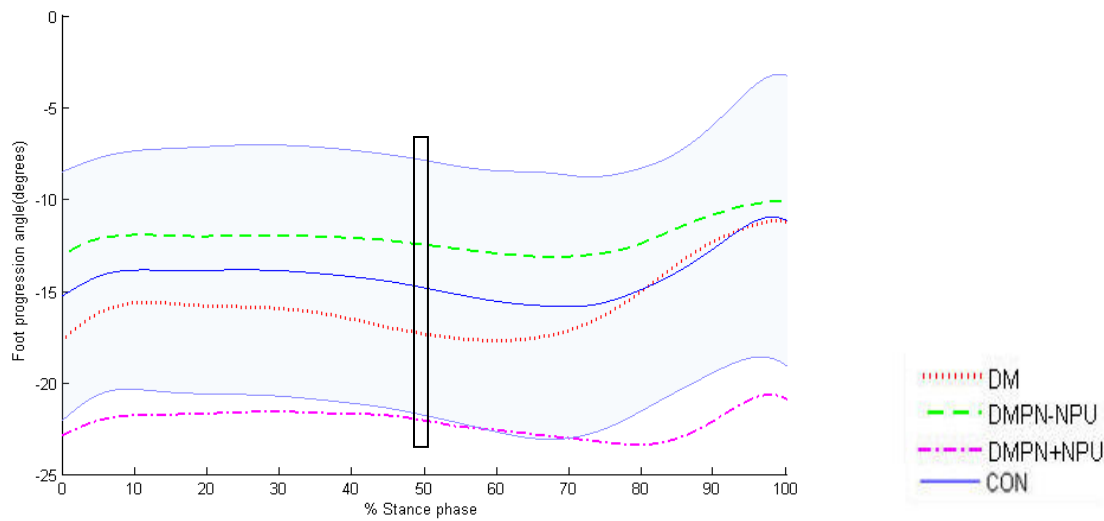
Figure 2.1. Time series motion graph of foot progression angle (FPA) during the stance of gait. The blue line and shaded region represents the mean±1 standard deviation of the motion for the CON group. Boxed regions represent values used in the analysis. **Figure legend**. CON: non-diabetic control participants; DM: diabetes mellitus without peripheral neuropathy group; DMPN-NPU: diabetes mellitus with peripheral neuropathy without a previous neuropathic plantar ulcer; DMPN+NPU: diabetes mellitus with peripheral neuropathy with a previous neuropathic plantar ulcer

Chapter 3

Static and dynamic predictors of foot progression angle in individuals with diabetes

mellitus and peripheral neuropathy

Status of resulting manuscript: in preparation, *Clinical Biomechanics*

3.1 Abstract

The development and recurrence of neuropathic plantar ulcers (NPU) are a significant health and economic burden worldwide. In the United States, an estimated 12 to 25% of adults with diabetes mellitus and peripheral neuropathy (DMPN) have a lifetime risk of NPU development. Foot progression angle (FPA or "toe-out angle") has been identified as a predictor of elevated medial and lateral plantar loading in individuals with DMPN. Despite FPA being reported as a predictor of regional plantar stress in individuals with DMPN, there have been no identified static or dynamic predictors of FPA magnitude. The primary purpose of this study was to determine static (goniometric) and dynamic (gait kinematics and kinetics) predictors of FPA magnitude in adults with DMPN. In a hierarchical multiple regression analysis of static predictor variables, total hip excursion, ankle dorsiflexion range of motion, and resting calcaneal stance position (RSCP) accounted for 29% of FPA variance. However, the unique contribution of these variables was not statistically significant ($p > .05$). In a hierarchical multiple regression analysis of the dynamic predictor variables, the overall contribution of all dynamic predictor variables to FPA was 48%. Thigh and shank external (lateral) rotation accounted for 37% of the variance in FPA ($p < .01$). These findings suggest that external rotation of proximal segments during gait better predict FPA than static (goniometric) measures of limited joint mobility and joint position at the hip, ankle, and subtalar joints in individuals with DMPN. Identification of dynamic predictors of FPA could inform areas for clinical assessment and targets for treatment of lower extremity impairments earlier in the lower extremity impairment cascade to minimize risk of elevated plantar stresses and loads that often lead to NPU development.

3.2 Introduction

In the United States, an estimated 15% of patients with diabetes mellitus and peripheral neuropathy (DMPN) have a lifetime risk of neuropathic plantar ulcer (NPU) development[1,2]. Recent statistics show more than 65,000 non-traumatic lower extremity amputations in adults with DMPN occur annually in the United States, with 84% preceded by the development of a NPU[3,4]. Elevated regional peak plantar pressure is an established index of risk dermal injury in adults with DMPN[6,7], and is thought to initiate a lower extremity impairment cascade of NPU development and subsequent non-traumatic lower extremity amputation in individuals with DMPN.

Selected measures of gait performance and of foot and ankle function during gait have been identified as dynamic (gait kinematic or kinetic) predictors of elevated regional stresses and loads in adults with DMPN with and without a history of ulcer [6,8,9]. Adults with DMPN often exhibit the following spatiotemporal gait abnormalities: 1) slower gait speed, 2) larger external foot progression angle (FPA) or 'toe-out angle', and 3) prolonged stance time compared with healthy control participants[10-14]. Several investigators have reported specific lower extremity kinematic and kinetic impairments associated with spatiotemporal gait abnormalities in adults with DMPN. Slower gait speed is associated with decreases in 1st metatarsophalangeal joint (MTPJ) extension motion, ankle dorsiflexion motion, ankle plantar flexor muscle power, and hip rotation motion in adults with DMPN compared with healthy control subjects[12,15-18]. Foot progression angle is a spatial gait variable defined by the orientation of the longitudinal axis of the foot in the transverse plane with respect to the direction of gait progression[19,20]. Studies from independent groups report external FPA as a dynamic predictor of elevated regional plantar stresses and loading in individuals with DMPN[6,8]. However, there is limited available evidence identifying dynamic predictors of FPA. In studies from pediatric orthopedic literature, Ho et al suggest that the degree of ankle dorsiflexion motion during gait is related to FPA magnitude in healthy children[21]. Lee et al report that inter-segmental external (lateral) rotation of the pelvis (r=-49, p<.01) and knee (shank to thigh) during gait (r=.38, p=.03) is significantly

correlated with FPA, whereas hip (thigh to pelvis) is not significantly correlated with FPA in children with cerebral palsy (r=.33, p=.06)[22]. Yet it is unknown if these are dynamic predictors of FPA in individuals with DMPN with and without a history of prior NPU.

Limited joint mobility of the foot and ankle is often measured during clinical assessment of lower extremity function. Selected goniometric measures of alignment and limited joint mobility of the foot and ankle have been reported as static predictors of elevated regional peak plantar pressure in adults with DMPN with and without a history of ulcer[23,24]. Zimny et al reported that decreased ankle dorsiflexion and 1st MTPJ extension motions were inversely correlated with forefoot plantar loads in participants with DMPN without a history of a prior NPU[23]. Turner and associates also noted a correlation between 1st MTPJ extension motion and peak plantar pressure[24]. Despite the reported impairments in motion and alignment of the 1st MTPJ and ankle joints as static predictors of elevated plantar stresses and loads, it is unclear if these impairments predict FPA.

Foot progression angle and selected measures of joint alignment and mobility in the foot and ankle are static and dynamic predictors of elevated regional plantar stresses and loads in adults with DMPN. However, there are no reported static or dynamic predictors of external FPA in individuals with DMPN despite FPA being an established predictor of regional plantar stresses and loads. Therefore, the purposes of this study were to: 1) determine static and dynamic predictors of FPA in individuals with and without DMPN, and 2) determine the between-group differences in select lower extremity static and dynamic measures of foot, ankle, and hip rotation. We hypothesized that select static and dynamic predictor variables would explain a significant portion of the variance in FPA. Additionally, we hypothesized a hierarchical model of dynamic predictor variables would explain a greater portion of FPA variance compared with a hierarchical regression model of static predictor variables.

3.3   Methods

3.3. a. Participants

Forty-five participants with and without diabetes (21 M, 24 F; age, 60±11 yrs; height, 1.7±0.1 m; BMI, 36±8) participated, and provided written informed consent as approved by the local Institutional Review Board. Participants were classified into one of four groups: 1) age-matched control (CON), 2) diabetes mellitus *without* peripheral neuropathy (DM), 3) diabetes mellitus and peripheral neuropathy without a prior history of a neuropathic plantar ulcer (DMPN-NPU), and 4) diabetes mellitus and peripheral neuropathy with a prior history of a neuropathic plantar ulcer (DMPN+NPU) . The presence or absence of peripheral neuropathy was assigned based on the presence or absence of protective sensation, and ulcer classification was based on any prior history of plantar ulceration. Peripheral neuropathy was assessed using a 5.07 (10 gram) Semmes-Weinstein monofilament at seven sites on the plantar surface of the foot[25]. In addition, we measured vibration perception threshold (VPT) using a 120 V bioesthesiometer (Bio-medical Instrument Co., Newbury, OH, 44065, USA) to assess large fiber peripheral nerve function. Those who were unable to perceive vibration of the bioesthesiometer at threshold of 25 V or greater were classified as having peripheral neuropathy. A VPT $\geq$25 V is associated with incidence of foot ulceration in individuals with Type 2 diabetes mellitus[26]. The combination of these tests for protective sensation has been shown to increase specificity of risk identification and disease severity without diminution in sensitivity[26]. Twelve participants were classified as CON, twelve were classified as DM, eleven were classified as DMPN-NPU, and ten were classified as DMPN+NPU with 8 reporting having had a prior ulcer on one foot and 2 participants reporting having had a prior ulcer on both feet (8 unilateral, 2 bilateral). Participants classified as DMPN+NPU did not have an open ulcer at the time of testing.

3.3.b. Static predictor measurement

3.3.b.1. Data collection. Static predictors in this investigation were operationally defined as goniometric measures of motion and position of select lower extremity joints. Hip (coxafemoral) joint internal (medial) and external (lateral) rotation were measured using a bubble inclinometer (Medical Research Ltd, Leeds LS124JF, United Kingdom) with a precision of 1° using the methods described by Elllison et al (1990)[27]. Hip rotation was selected for measurement because of the reported kinematic link between hip rotation and FPA magnitude in children[28,]. The reported intra-rater reliability for hip internal and external rotation measurement using the procedures outlined by Ellison et al ranges from .95-.99 in both directions in subjects with and without low back pain dysfunction[27]. Total hip rotation range of motion is the sum of hip internal (medial) rotation and hip external (lateral) rotation.

Ankle (talocrural) joint dorsiflexion excursion was measured in two positions using a standard goniometer with a precision of 2°, while ankle plantar flexion was measured in the prone position. Ankle joint dorsiflexion excursion was measured with each participant lying prone using previously described procedures[25]. Measurement of ankle joint dorsiflexion excursion in non-weight bearing is performed with the subtalar joint held in palpated neutral alignment while the calcaneus moves into dorsiflexion[25]. Ankle joint dorsiflexion excursion was also measured in the standing position with the axis of the goniometer aligned with the lateral malleolus, the moveable arm aligned with the axis of the lateral malleolus and fibular head, and the stationary arm aligned parallel to the floor. Measurement of ankle joint dorsiflexion in standing allows for dorsiflexion motion without manual fixation of the talus. Limited ankle dorsiflexion motion is reported to contribute to elevated regional plantar pressures and localized skin breakdown on the plantar surface of the forefoot[6,29]. The reported intra-rater reliability for ankle joint ROM measurement using the procedures outlined by Diamond et al (1989) ranges from .89-.96[25].

First metatarsophalangeal joint (1st MTPJ) extension was measured in sitting with a standard goniometer using procedures described by Menz et al[30]. First metatarsophalangeal joint (1st MTPJ) range of motion was also measured in the standing position with the axis of the goniometer aligned over the medial aspect of the 1st metatarsal head, the moveable arm aligned with the first ray, and the stationary arm aligned with the floor.

Calcaneal position in the frontal plane was measured with the participant in the weight bearing and non-weight bearing positions using a modified procedure described by Picciano et al (1993)[31]. For the non-weight bearing measurement of calcaneal frontal plane motion, participants were in the prone position with the knee of the foot being measured in the extended position. Using a water-soluble marker, a line of bisection of the lower one-third of the leg was drawn[31]. In a similar fashion, a line was drawn between the lateral and medial malleoli representing a bisection of the calcaneus[31]. Then, the angle between the lines of bisection on the lower leg and calcaneus were measured using a standard 2° goniometer[31]. The axis of the goniometer was aligned a midpoint between the malleoli, and the stationary and moveable arms aligned with the line of bisection for the lower leg and calcaneus, respectively[31]. We also measured resting calcaneal stance position (RSCP), a weight bearing measurement of calcaneal position using modified measurement procedures described by Picciano et al[31]. With participants in standing, RCSP values represent the alignment of the calcaneus determined as the angle formed between the lines of the bisection of the posterior calcaneus and the floor using a standard 2° goniometer[31].

3.3.c. Dynamic predictor measurement

3.3.c.1. Data collection. Dynamic predictors in this investigation were operationally defined as lower extremity segmental and inter-segmental positions and orientations at select points during the stance phase of gait. Three-dimensional kinematic and kinetic data were collected during

gait for the trunk, pelvis, and bilateral lower extremities while participants walked at a self-selected speed over a 4 m distance. Kinematic data were acquired using an infrared 8-camera, 200 Hz motion capture system (Vicon MX, Los Angeles, CA, USA), and kinetic data were collected using a Bertec K80301 force plate with a resolution of 500 Hz (Bertec Corporation, Columbus, OH, USA).

3.3.c.2. Marker placement. All participants were fitted with 10 mm diameter retro-reflective markers affixed directly to the skin or to pre-molded rigid plate in a non-collinear arrangement to establish segment coordinate systems for the foot, shank, thigh, pelvis, and trunk. A modification of the "obesity-specific marker set", described by Lerner et al for the trunk, pelvis, and thigh, was used in this study in an effort to account for potential motion artifact secondary to central adiposity[32,33]. Briefly, single markers for the trunk were placed on the body of the sternum, the C7 cervical spinous process, right and left acromion processes, and the inferior angle of the right scapula. Markers on the pelvis included single markers on the right and left posterior superior iliac spines, with an accompanying marker cluster placed on the sacrum. Marker clusters on the pelvis have been shown to have greater repeatability and less movement variability during non-sagittal plane motion of the pelvis in overweight and obese individuals[34]. To correct for marker displacement secondary to central adiposity, digitized markers were created for the anterior superior iliac spines and iliac crests with a static digitizing wand (C-Motion, Germantown, MD) using procedures described by Lerner et al[32,33]. Additional corrections were made using measurements of inter-ASIS distance using skinfold caliper in subject-specific models. Lerner et al reported that use of marker clusters and digitized markers on the thigh and pelvis minimized overestimation of lower extremity kinematics and kinetics[32]. Single thigh markers were placed proximally on the greater trochanter and distally on the medial and lateral femoral epicondyles, with a 4-marker cluster for tracking on the distal thigh superior to the lateral epicondyle.

We utilized a marker configuration for the foot and shank described by Carson et al[35] and modified by Hastings et al[36], which included a single, rigid body foot segment[36]. Individual shank markers were placed on the fibular head, tibial tuberosity, and malleoli, with a 4-marker cluster placed on the distal shank superior to the lateral malleolus. The hind foot segment was defined by calcaneal marker placement on the sustentaculum tali, fibular trochlea, and by three mounted markers on a molded plastic plate applied to the posterior calcaneal bisection—a vertical line between the sustentaculum tali and the fibular trochlea[36]. The forefoot segment was defined distally by a marker placed at the midpoint between the second and third metatarsals, and by markers at the first and fifth metatarsal heads. The proximal forefoot was defined by the base of the first and fifth metatarsals. The hallux segment was defined by a plate with three mounted markers arranged parallel with the long axis of the proximal phalanx of the great toe[36].

Participants were asked to walk barefoot at a self-selected speed. All were given at least 1-2 practice trials prior to recording. To minimize risks associated with barefoot walking in participants in the DMPN-NPU and DMPN+NPU groups, walking distance was truncated to include the steps on and at least 10 cm beyond the force plate. A minimum of five trials in which participants were able to contact the force plate without "targeting" was collected. A minimum of three trials were included in the analysis if values were within one standard deviation of the within-trial mean for each participant. Walking speed was calculated as stride length time of the foot contralateral to the limb contacting the force plate[36].

3.3.d. Data Processing and Statistical Analysis.

3.3.d.1. Kinematic and kinetic variables. All marker trajectories and tri-axial force data were processed using a fourth-order, low-pass filter in Visual 3D software (C-Motion, Inc, Rockville, MD). Marker trajectories were filtered at 6Hz, and tri-axial force data were filtered at 20Hz.

Inter-segmental and global orientation angles were derived using Cardan angle sequences, and

parallel alignment of the segmental axes represent neutral position[36]. Foot progression angle

was the value of transverse plane rotation of the foot segment around the local superior-inferior

axis at the mid stance of the gait cycle (i.e., 50% of the stance phase of walking)[37].

3.3.d.2. Group comparisons. Prior to all analyses, we conducted the Shapiro-Wilk test of

normality to verify that continuous data for both FPA and all static and dynamic predictor

variables were normally distributed[38]. Each foot for all participants was classified as either a

High FPA or Low FPA based on the FPA magnitude. The foot with the greater FPA was

classified as High FPA for all groups, while the foot with the lesser FPA was classified Low FPA.

All static and dynamic predictor variables for the High FPA foot were analyzed using a

multivariate analysis of variance (MANOVA) to determine group differences. This analysis was

performed to determine if group assignment should be included into a hierarchical multiple

regression analyses for both static and dynamic predictor variables. Post-hoc analyses were

conducted using a Bonferroni correction, with statistical significance for all analyses set at

$p<.05$. Statistical analyses were performed using IBM SPSS Statistics software, version 21.0

(SPSS Inc, Chicago, IL, USA).

3.3.d.3. Hierarchical multiple regression analyses. The following hierarchical multiple

regression analyses were conducted, and are summarized below. Variables were considered

predictors of FPA in the multiple regression analyses if they met the following *a priori* criteria: 1)

the predictor variable had a unique contribution to FPA variance of at least 5%, and 2) the

statistical significance of the change in the overall F value for the coefficients was less than

$.05^{6,39}$.

      Hierarchical multiple regression model of static predictors. Because we had no *a*

priori hypothesis of specific static predictors of FPA, we analyzed the relationship between all

static predictor variables and FPA on the High FPA foot using Pearson product moment correlation coefficient (r)[6,38] and coefficients of determination (R^2). Three of fourteen candidate static predictor variables plus group predictor variables were selected for inclusion into a hierarchical multiple regression analysis based on preliminary bivariate correlation and coefficient of determination analyses. Static predictor variables entered into the model were total hip rotation range of motion, ankle joint dorsiflexion range of motion in non-weight bearing, and RSCP. Order for model entry for the static predictor variables was based on the proximal to distal location of the joint in the lower extremity.

Hierarchical multiple regression model of dynamic predictors. Two hierarchical multiple regression analyses were performed for the dynamic predictor variables for the High FPA foot. Predictor variables for the first dynamic hierarchical multiple regression analysis (Dynamic Model A) were thigh to lab external (lateral) rotation, peak hind foot on shank (ankle) dorsiflexion, peak hallux on forefoot (1st MTPJ) extension, and peak ankle plantar flexor power. Dynamic Model A predictor variables were selected *a priori* based on previously reported relationships between slower gait speed and limited dynamic forefoot on hind foot (1st MTPJ) extension, of the hind foot on shank (ankle) dorsiflexion, and decreased ankle plantar flexor power in adults with DMPN[10-14,16]. Group variables were also included into the model. Order for model entry for dynamic predictor variables was based on the proximal to distal location of the joint in the lower extremity.

To further assess any potential contribution of other candidate dynamic predictor variables not selected *a priori* for inclusion into a multiple regression analysis, we performed an additional hierarchical multiple regression analysis (Dynamic Model B). We analyzed the relationship between all candidate dynamic predictor variables of FPA on the High FPA foot using Pearson product moment correlation coefficient (r)[6,38] and coefficients of determination (R^2). To determine the unique contributions of inter-segmental foot motion during walking to

44

FPA, hind foot on shank (calcaneal) eversion at mid stance as an indicator of frontal plane subtalar joint position, and forefoot on hind foot abduction at mid stance as an indicator of transverse plane forefoot position were also included into the multiple regression analysis of dynamic predictor variables. Selection of these variables was based on previously reported decreases in frontal plane hind foot motion[41], and fixed forefoot deformities (i.e., hammer toe deformity, hallux abducto-valgus, forefoot abduction on hind foot) in adults with DMPN[39,42]. The dynamic predictor variables measured at mid stance included in Dynamic Model B were thigh to lab external (lateral) rotation, shank to lab external (lateral) rotation, hind foot on shank (calcaneal) eversion, and forefoot on hind foot abduction. Group variables were also included into the model. Order for model entry for dynamic predictor variables was based on the proximal to distal location of the joint in the lower extremity.

3.4.   Results

3.4.a. Participant Characteristics

The mean± SD age for all participants (N=45) was 60±10 years (range: 44-85 years). There were no group differences in age or height or body mass index (BMI)(Table 3.1). The DMPN+NPU group had been diagnosed with diabetes earlier and had greater loss of vibration perception than the DM group. The DMPN-NPU and DMPN+NPU groups had a significantly greater vibration perception threshold than the DM and CON groups. There were no between-group differences in walking speed (p=.80). The mean and standard deviations are shown in Table 3.1.

3.4.b. Group comparisons

The DMPN+NPU group had a greater FPA on the High FPA foot than the other groups (DMPN+NPU= -21±5º; DMPN-NPU=-13±7º; DM=-14±5º; CON=-15±6º, P=.03). Posthoc testing revealed a difference between the DMPN-NPU and DMPN+NPU groups (p=.04), as well as a

trending difference between the DM and DMPN+NPU groups (p=.09). The means and standard deviations are shown in Table 3.3.

For the static predictor variables, the DMPN+NPU group had less total hip rotation and standing 1st MTPJ extension range of motion than the other participant groups (DMPN+NPU$_{total}$ $_{hip}$= 58±17°; DMPN-NPU$_{total\ hip}$= 69±16°; DM$_{total\ hip}$= 80±12°; CON$_{total\ hip}$ =77±19°, p=.01; DMPN+NPU $_{1st\ MTPJ}$= 35±18°; DMPN-NPU $_{1st\ MTPJ}$ = 55±11°; DM$_{1st\ MTPJ}$ = 61±7°; CON$_{1st\ MTPJ}$ =53±11°, p=.01). There were no group differences in range of motion or position for the other static predictor variables. The means and standard deviations for all static predictor variables are shown in Table 3.2.

For the dynamic predictor variables, the DMPN+NPU group had less peak ankle plantar flexor power (p=.01) and peak hallux on forefoot (1st MTPJ) extension during the stance phase of gait compared to the other participant groups (p=.02). There were no group differences in the other inter-segmental motion variables. The means and standard deviations for all dynamic predictor variables are shown in Table 3.3.

3.4.c. Hierarchical multiple regression analyses

Static model. Selection of static predictor variables for inclusion into a hierarchical multiple regression analysis was based on the results of bivariate correlation and coefficient of determination analyses for the static predictor variables. The coefficients of determination that associate static predictor variables with FPA in this model are shown in Table 3.4. Total hip rotation and ankle dorsiflexion range of motion explained 8-10% of the variance in FPA. Resting calcaneal stance position (RSCP) explained 6% of FPA variance, a unique contribution that had a trend toward statistical significance (p=.05), and was therefore included into the model.

Table 3.6 illustrates the hierarchical multiple regression model for static predictor variables. Four variables (total hip rotation range of motion, ankle dorsiflexion range of motion, RSCP, group) were selected for inclusion into the hierarchical multiple regression model for static predictor variables. Multiple regression analysis for these four static predictors explain 29% of FPA variance, but the unique contribution of each variable was not statistically significant (R^2=.29, p>.05). Additionally, the group differences in FPA and total hip rotation range of motion are not significant after the static predictors are partialed out. Based on our criteria, none of the static predictor variables contribute to FPA variance.

Dynamic model A. Dynamic predictor variables for inclusion into a hierarchical multiple regression analysis were selected *a priori*. Table 3.7 illustrates the dynamic multiple regression analysis of the *a priori* variables (Dynamic Model A). Multiple regression analysis for the dynamic predictors explain 37% of FPA variance (R^2=.37, p<.05), but the unique contribution of thigh external (lateral) rotation at mid stance explains 23% of FPA variance (p<.01). The combined contribution of the remaining predictor variables was 14%, but their unique contribution to FPA was not significant (p>.05).

Dynamic Model B. The coefficients of determination that associate the dynamic predictor variables with FPA in this model are shown in Table 3.5. Thigh external (lateral) rotation and shank external (lateral) rotation at mid stance explained 20-33% of FPA variance. Table 3.8 illustrates the dynamic multiple regression analysis of the added dynamic predictor variables. Multiple regression analysis for the dynamic predictors in this model explain 48% of FPA variance (R^2=.48, p<.05). The unique contribution of thigh and shank external (lateral) rotation at mid stance accounts for 37% of FPA variance (p<.01). Shank to lab external (lateral) rotation uniquely contributed 16% of FPA variance (R^2 change=.16, p=.01). The addition of hind foot on shank eversion, forefoot on hind foot abduction, and group classification did not predict FPA.

3.5   Discussion

This is the first investigation to determine static and dynamic predictors of FPA in a population of adults with and without DMPN. Additionally, this study is the first to determine the unique and collective contribution of goniometric measurements of hip rotation to a spatiotemporal gait variable across a spectrum of individuals with and without diabetes mellitus. Key findings from this study are that in adults with DMPN, static goniometric measures of lower extremity alignment and joint mobility do not predict FPA. However, dynamic inter-segmental external (lateral) rotation of the thigh and shank obtained at the mid stance phase of gait predicted 37% of variance in FPA in adults with DMPN. Furthermore, inter-segmental foot motion did not predict FPA in either dynamic hierarchical multiple regression model (Dynamic Model A, Dynamic Model B).

3.5.a. Static predictors. Static predictors of FPA in the current study are select goniometric measures of alignment and mobility of select lower extremity joints. One of the purposes of this study was to identify impairment-based predictor variables that contribute to FPA at mid stance in participants with and without DMPN and a prior history of ulceration. Static predictors did not contribute to FPA variance despite limitations in hip rotation and ankle dorsiflexion in the DMPN+NPU group compared with the other participant groups. These findings suggest that static measures of alignment and limited joint mobility at the foot and ankle are not predictive of foot placement during gait in adults with or without DMPN and a prior history of ulceration. Static measures of limited joint mobility (LJM) are often used to assess risk for elevated regional plantar stresses and loads in individuals with DMPN[23,24]. Given the previously reported relationship between static measures of LJM at the foot and ankle and elevated regional PPP[11,23,24], static measurement of LJM in individuals with DMPN may better predict regional plantar stresses than FPA.

3.5.b. Dynamic predictors. In the current investigation, thigh and shank external (lateral) rotation position at mid stance predicted 37% of the variance in FPA. Shank external (lateral) rotation position at mid stance was the strongest predictor of FPA, having a unique contribution of 16% to FPA variance. Furthermore, dynamic measures of inter-segmental foot mobility, namely hind foot on shank (ankle dorsiflexion, hind foot on forefoot (calcaneal) eversion, forefoot on hind foot abduction, and hallux on forefoot (1st MTPJ extension) did not predict FPA in either hierarchical multiple regression analysis. Lee et al reported that knee (shank on thigh) external rotation during gait was moderately correlated with FPA in children with cerebral palsy[22]. Our findings are similar in that external rotation of the thigh and shank segments best predict FPA in adults with and without DMPN and a prior history of ulceration. Ho et al reported that healthy children with a large external FPA demonstrated greater ankle dorsiflexion motion during gait compared with children with "normal" FPA[21]. In this study, hind foot on shank (ankle) dorsiflexion motion during gait did not predict FPA in adults with and without DMPN and a prior history of ulceration. These findings suggest that rotation of the proximal segments may better predict FPA than distal lower extremity segments in adults with DMPN. Rao et al reported that dynamic measures of dynamic 1st MTPJ extension accounts for 20% of plantar stresses under the hallux in adults with DMPN[43]. Although there is considerable evidence identifying foot motion variables as dynamic predictors of elevated regional plantar stresses and loads, inter-segmental foot motion variables do not predict FPA.

In the current study, dynamic measures of hind foot on shank (ankle) dorsiflexion, hind foot on shank (calcaneal) eversion, forefoot on hind foot abduction, and hallux on shank (1st MTPJ) extension did not predict FPA. A possible explanation could be the moderate to strong associations of shank external (lateral) rotation with peak ankle plantar flexor power, hind foot on shank (calcaneal) eversion at mid stance, forefoot on hind foot abduction at mid stance, and peak hallux on forefoot (1st MTPJ) extension. The association between shank external (lateral)

rotation and hind foot on shank eversion is illustrative of the coupled motions of shank external (lateral) rotation with hind foot eversion during the stance phase of gait reported in previous investigations[44-46]. Rao et al (2007) reported no differences in segmental motion of the shank during the stance phase of gait between participants with and without diabetes, which they suggest augments the differences in hind foot eversion and fore foot sagittal plane motion[41]. Findings from the current study suggest that transverse plane motion of the shank at mid stance is greater in the DMPN+NPU, and is moderately correlated with proximal and distal inter-segmental foot motion. The correlation between shank external (lateral) rotation and dynamic predictor variables manifests as more robust contribution of transverse plane shank motion to FPA variance.

Interventions that target static and dynamic impairments in foot alignment and motion structural deformities within the scope of physical therapist practice are limited, and are often cost prohibitive[22]. Identifying predictors of FPA could inform areas for clinical assessment and targets for treatment of lower extremity impairments earlier in the lower extremity impairment cascade to minimize risk of elevated plantar stresses that often lead to NPU development. Also, simple cost-effective rehabilitative interventions, like gait modification strategies, which incorporate movement of proximal lower extremity segments (i.e., the thigh and shank) could be effective in reducing plantar stresses in areas of the foot vulnerable to ulceration in adults with DMPN. Future studies should examine the efficacy of physical therapy interventions such as gait modification, which may serve as a cost-effective strategy to reducing FPA magnitude, and subsequently lowering risk for NPU development in adults with DMPN.

There are limitations associated with this study. The first of these limitations is small sample size using a four-group design. A larger sample size would allow a more thorough exploration of the many alignment and position variables that might predict FPA magnitude. Similarly, we did not include radiographic measures in the protocol primarily due to a lack of

50

previous indication for their utility in predicting FPA. Given the reported relationship between radiographic alignment measures of the foot and ankle and elevated regional plantar stresses in adults with DMPN[6,42], static alignment and bony abnormalities of the lower extremity may also be static predictors of FPA in adults with and without DMPN and a prior history of ulceration.

3.6.   Conclusions

In adults with and without DMPN and a prior history of ulceration, dynamic (gait) variables best predict FPA. External (lateral) rotation of the proximal segments (thigh and shank) at the mid stance phase of gait explained 37% of the variance in FPA. Shank external (lateral) rotation had a unique contribution of 16% to FPA variance, therefore making it the strongest predictor of FPA. Foot motion variables did not predict FPA in either hierarchical multiple regression model of dynamic variables, despite group differences in 1st MTPJ extension and ankle plantar flexor power. Static, goniometric measures of limited joint mobility of the foot and ankle joints do not predict FPA in individuals with DMPN. These findings suggest that identifying predictors of FPA could be clinically useful in informing where to focus assessments and interventions earlier in the lower extremity impairment cascade to minimize risk of elevated regional plantar stresses and load in adults with DMPN with and without a prior history of ulceration.

REFERENCES

1. Cavanagh PR, Lipsky BA, Bradbury AW, Botek G. Treatment for diabetic foot ulcers. *Lancet* 2005; 366(9498):1725-1735

2. Owings TM, Apelqvist J, Stenström A, Becker M, Bus SA, Kalpen JS et al. Plantar pressures in diabetic patients with foot ulcers which have remained healed. *Diabet Med* 2009; 26:1141-1146

3. Centers for Disease Control and Prevention. National Diabetes Fact Sheet, 2011. http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Published 2011. Accessed January 23, 2014

4. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. Basis for prevention. *Diabetes Care* 1990; 13(5):513-521

5. Sinacore DR. Mueller MJ, Diamond JE, Blair VP, Drury D, Rose SJ. Diabetic plantar ulcers treated by total contact casting. A clinical report. *Phys Ther* 1987; 67(10):1543-1549

6. Mueller MJ, Hastings MK, Commean PK, Smith KE, Pilgram K, Robertson D *et al.* Forefoot structural predictors of plantar pressures during walking in people with diabetes and peripheral neuropathy. *J Biomech* 2003; 36(7):1009-1017

7. Mueller MJ, Zou D, and Lott DJ. "Pressure gradient" as an indicator of plantar skin injury. *Diabetes Care* 2005; 28(12):2908-2912

8. Hastings MK, Gelber JR, Isaac EJ, Bohnert KL, Strube MJ, Sinacore DR. Foot progression angle and medial loading in individuals with diabetes mellitus, peripheral neuropathy, and a foot ulcer. *Gait Posture* 2010; 32:237-241

9. Ko M, Hughes L, Lewis H. Walking speed and peak plantar pressure distribution during barefoot walking in persons with diabetes. Physio Res Int. 2012; 17(1):29-35

10. Brach JS, Talkowski JB, Strotmeyer ES, Newman AB. Diabetes mellitus and gait dysfunction: possible explanatory factors. *Phys Ther* 2008; 88 (11): 1365-1374

11. Mueller MJ, Minor SD, Sahrmann SA, Schaaf JA, Strube MJ. Difference in the gait characteristics of patients with diabetes and peripheral neuropathy compared with age-matched controls. *Phys Ther*. 1994; 74(4):299-308

12. Salsich GB, Mueller MJ. Effect of plantar flexor muscle stiffness on selected gait characteristics. *Gait Posture.* 2000; 11(3): 207-216

13. Giacomozzi C, Caselli A, Macellari V, Giurato L, Lardieri L, Uccioli L. Walking strategy in diabetic patients with peripheral neuropathy. *Diabetes Care* 2002; 25(8):1451-1457

14. Giacomozzi C, D'Ambriogi E, Cesinaro S, Macellari V, Uccioli L. Muscle performance and ankle joint mobility in long-term patients with diabetes. *BMC Musculoskelet Disord* 2008; 9:99

15. Mueller MJ, Minor SD, Schaaf JA, Strube MJ, and Sahrmann SA. Relationship of plantar-flexor peak torque and dorsiflexion range of motion to kinetic variables during walking. *Phys Ther* 1995; 75(8), 684-693

16. Rao S, Saltzman C, Yack HJ. Ankle ROM and stiffness measured at rest and during gait in individuals with and without diabetic sensory neuropathy. *Gait Posture* 2006; 24(3): 295-301

17. Allet L, Armand S, de Bie RA, Golay A, Pataky Z, Aminian K *et al.* Clinical factors associated with gait alterations in diabetic patients. *Diabet Med* 2009; 26(10): 1003-1009

18. Sawacha Z, Gabriella G, Cristoferi G, Guiotto A, Avogaro A, Cobelli C. Diabetic gait and posture abnormalities: a biomechanical investigation through three-dimensional gait analysis. *Clin Biomech* 2009; 24(9): 722-728

19. Holden JP, Cavanaugh PR, Williams KR, Bednarski KN. Foot angles during walking and running.   1985 International Series on Biomechanics: Biomechanics IX-A. Human Kinetics Publishers, Champaign, IL

20. Lai YC, Lin HS, Pan HF, Chang WN, Hsu CJ, Renn JH. Impact of foot progression angle on the distribution of plantar pressure in normal children. *Clin Biomech* 2014; 29(2):196-200

21. Ho CS, Lin CJ, Chou YL, Su FC, Lin SC. Foot progression angle and ankle joint complex in preschool children. *Clin Biomech* 2000; 15(4): 271-277

22. Lee KM, Chung CY, Sung KH, Kim TW, Lee SY, Park MS. Femoral anteversion and tibial torsion only explain 25% of the variance in regression analysis of foot progression angle in children with diplegic cerebral palsy. *J Neuroengineering Rehabilitation* 2013; 15; doi: 10.1186/1743-0003-10-56

23. Zimny S, Schatz H, Pfolhl M. The role of limited joint mobility in diabetic patients with an at-risk foot. *Diabetes Care.* 2004; 27(4):942-946

24. Turner DE, Helliwell PS, Burton AK, Woodburn J. The relationship between passive range of motion and range of motion during gait and plantar pressure measurements. *Diabet Med* 2007; 24(11):1240-1246

25. Diamond JE, Mueller MJ, Delitto A, Sinacore DR. Reliability of diabetic foot evaluation. *Phys Ther.* 1989; 69(10):797-802

26. Kästenbauer, T, Sauseng, S, Brath, H, Abrahamian, H, and Irsigler, K. The value of the Rydel-Seiffer tuning fork as a predictor of diabetic polyneuropathy compared with a neurothesiometer. *Diabet Med* 2004; 21(6):563-567

27. Ellison, JB, Rose, SJ, and Sahrmann, SA. Patterns of hip rotation range of motion: a comparison between healthy subjects and patients with low back pain. *Phys Ther* 1990; 70(9): 537-541

28. Chang WN, Tsirikos AI, Miller F, Schyler J, Glutting J. Impact of changing foot progression angle on foot pressure measurement in children with neuromuscular disease. *Gait Posture* 2004; 20(1): 14-19

29. Mueller MJ, Sinacore DR, Hastings MK, Strube MJ, Johnson JE. Effect of Achilles tendon lengthening on neuropathic plantar ulcers. A randomized clinical trial. J Bone Joint Am 2003; 85-A(8):1436-1145

30. Menz HB, Morris ME. Clinical determinants of plantar forces and pressures during walking in older people. *Gait Posture* 2006; 24(2):229-236

31. Picciano AM, Rowlands MS, Worrell T. Reliability of open and closed chain subtalar joint neutral position and navicular drop test. *J Orthop Sports Phys Ther* 1993; 18(4):553-558

32. Lerner, ZF, Board, WJ, Browning, RC. Effects of obesity on lower extremity muscle function during walking at two speeds. *Gait Posture* 2013; pii: S0966-6362(13)00715-7. doi:10.1016/j.gaitpost.2013.12.020

33. Lerner ZF, Board WJ, Browning RC. Effects of an obesity-specific marker set on estimated muscle and joint forces in walking*. Med Sci Sports Exerc* 2014; PMID: 24518193

34. Borhani M, McGregor AH, Bull AM. An alternative technical marker set for the pelvis is more repeatable than the standard pelvic marker set. *Gait Posture* 2013; 38(4):1032-1037

35. Carson MC, Harrington ME, Thompson N, O'Connor JJ, Theologis TN. Kinematic analysis of a multi-segment foot model for research and clinical applications: a repeatability analysis. *J Biomech* 2001; 34(10): 1299-1307

36. Hasting MK, Sinacore DR, Woodburn J, Paxton ES, Klein SE, Bohnert KL *et al.* Kinematics and kinetics after the Bridle procedure for treatment of traumatic foot drop. *Clin Biomech* 2013; 28(5): 555-561

37. Raspovic, A. Gait characteristics of people with diabetes-related peripheral neuropathy, with and without a history of ulceration. *Gait Posture* 2013; 38(4):723-728

38. Cornwall MW, McPoil TG. Relationship between static foot posture and foot mobility. *J Foot Ankle Res* 2011; 18 4:4 doi: 10.1186/1757-1146-4-4.

39. Cavanagh PR, Morag E, Boulton AJ, Deffner KT, Pammer SE. The relationship of static foot structure to dynamic foot function. *J Biomech* 1997; 30(3): 243-250

40. Salsich GB, Mueller MJ. Relationships between measures of function, strength, and walking speed in patients with diabetes and transmetatarsal amputation. Clin Rehabil 1997; 11(1):60-67

41. Rao S, Saltzman C, and Yack HJ. Segmental foot mobility in individuals with and without diabetes and peripheral neuropathy. *Clin Biomech* 2007; 22(4): 464-471

42. Morag E, Cavanagh PR. Structural and functional predictors of regional peak pressures under the foot during walking. *J Biomech* 1999; 32(4):359-370

43. Rao S, Song J, Kraszewski A, Backus S, Ellis SJ, Deland JT, Hillstrom HJ. The effect of foot structure on 1st metatarsophalangeal joint flexibility and hallucal loading. *Gait Posture* 2011; 34:131-137

44. Pohl MB, Messenger N, Buckley JG. Forefoot, rearfoot, and shank coupling: effect of variations in speed and mode of gait. *Gait Posture* 2007; 25(2): 295-302

45. Preece SJ, Graham-Smith P, Nester CJ, Howard D, Hermens H, Herrington L. *et al. Gait Posture* 2008; 27(4):616-621

46. Khamis S, Yizhar Z. Effect of hyperpronation on pelvic aligment in a standing position. *Gait Posture* 2007; 25(1):127-134

	CON (N=12)	DM (N=12)	DMPN-NPU (N=11)	DMPN+NPU (N=10)	p
Age (years)	60 (12)	58 (9)	63 (11)	58 (11)	.80
Height (m)	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)	.79
Sex (M:F)	7:5	5:7	4:7	5:5	.95
BMI (kg/m^2)	33 (5)[†]	34 (8)[#]	39 (9)	41 (9)	.08
Disease duration (years)	N/A	8 (5)[#]	11 (9)[§]	24 (8)	<.01
Great Toe VPT (V)	20 (9)[†]	15 (6)[#]	37 (11)	34 (17)	<.01
Walking Speed (m/s)	1.1 (0.1)	1.1 (0.1)	1.1 (0.1)	1.1 (0.1)	.80
Side of greater FPA (R:L)	11R:1L	9R:3L	9R:3L	6R:4L	--

Table 3.1. Participant characteristics, mean (SD). VPT: vibration perception threshold (Volts);
Side of greater FPA (R:L): Number of right feet (R) or left feet (L) having a greater foot
progression angle. †,#,§:significance values for group differences. Disease duration (years): [†]:
CON versus DMPN-NPU and DMPN+NPU; [#]: DM versus DMPN+NPU; [§]: DMPN-NPU versus
DMPN+NPU. Great Toe VPT (V): [†]: CON versus DMPN-NPU and DMPN+NPU; [#]DM versus
DMPN-NPU and DMPN+NPU;

	CON (N=12)	DM (N=12)	DMPN-NPU (N=11)	DMPN+NPU (N=10)	p
Total hip rotation ROM*	77 (19)†	80 (12)$^\#$	69 (16)§	58 (17)	.01
Ankle dorsiflexion ROM	8 (5)	9 (5)	8 (4)	5 (4)	.20
RCSP	4 (2)	2 (4)	4 (5)	4 (5)	.78
1st MTPJ extension	53 (11)†	61 (7)$^\#$	55 (11)§	35 (18)	.01

Table 3.2. Static (goniometric) measures for the foot with the greater foot progression angle (High FPA). Values are expressed in degrees, mean (SD). **Motion variables**. Total hip rotation ROM is the sum of range of motion values for hip internal and external rotation. Ankle dorsiflexion ROM is goniometric ankle dorsiflexion range of motion measurement in non-weight bearing (prone lying). Resting calcaneal stance position (RCSP) is measure of calcaneal position relative to the floor in standing. 1st metatarsophalangeal joint is extension range of motion measurement assessed in standing. Reported significance values (p) are overall group comparisons; †,#,§:significance values for group differences. Total hip excursion: †: CON versus DMPN+NPU; $^\#$: DM versus DMPN+NPU; §: DMPN-NPU versus DMPN+NPU. Standing 1st MTPJ extension: †: CON versus DMPN+NPU; $^\#$: DM versus DMPN+NPU; §: DMPN-NPU versus DMPN+NPU

	CON (N=12)	DM (N=12)	DMPN-NPU (N=11)	DMPN+NPU (N=10)	p
FPA	-15 (6)	-14 (5)	-13 (7)[§]	-21 (5)	.03
Thigh rotation	-1 (9)	-6 (9)	-4 (13)	-9 (7)	.30
Shank rotation	-4 (13)	-8 (9)	-9 (14)	-16 (8)	.17
Peak HF on Shank DF	9 (5)	9 (5)	8 (5)	13 (3)	.13
Peak ankle PF power	2 (1)[†]	2 (1)[#]	2 (1)[§]	1 (1)	.01
HF on Shank EV	-7 (9)	-4 (6)	-6 (6)	-2 (5)	.22
Peak hallux on FF EXT	34 (7)[†]	31 (9)[#]	33 (6)[§]	23 (9)	.02
FF on HF ABD	-6 (7)	-3 (6)	-3 (9)	-5 (8)	.71
Walking speed (m/s)	1.1 (0.1)	1.1 (0.1)	1.1 (0.1)	1.0 (0.4)	.74

Table 3.3. Dynamic (gait kinematic and kinetic) measures for the foot with the greater foot progression angle (High FPA). Kinematic values are expressed in degrees, mean (SD). Peak ankle plantar flexor power is expressed in Watts/kg, mean (SD). **Motion variables**. FPA is the foot progression angle on the High FPA foot, (-)=toe-out angle; Thigh rotation: Thigh segment external rotation (-) value at mid stance; Shank rotation: Shank segment external (-) rotation value at mid stance; Peak HF on Shank DF: the peak value of hind foot on shank (ankle) dorsiflexion (+) during stance; Peak ankle PF power: the peak value of ankle plantar flexor power generation (+) during stance; HF on Shank EV: hind foot on shank (calcaneal) eversion (-) value at mid stance; Peak hallux on FF EXT: the peak value of hallux on forefoot (1st MTPJ) extension (+) during stance; FF on HF ABD: forefoot on hind foot abduction (-) at mid stance. Reported significance values (p) are overall group comparisons. †,#,§:significance values for group differences. FPA: §: DMPN-NPU versus DMPN+NPU; Peak Ankle PF Power: †: CON versus DMPN+NPU; #: DM versus DMPN+NPU; §: DMPN-NPU versus DMPN+NPU; Peak Hallux on FF EXT: †: CON versus DMPN+NPU; #: DM versus DMPN+NPU; §: DMPN-NPU versus DMPN+NPU

	FPA	Total hip rotation ROM	Ankle dorsiflexion ROM	RSCP	1st MTPJ extension
FPA	-	.08*	.10*	.06	.01
Total hip rotation ROM	.08*	-	.25**	.00	.18**
Ankle dorsiflexion ROM	.10*	.25**	-	.00	.16**
RSCP	.06	.00	.00	-	.00
1st MTPJ extension	.01	.18**	.02	.00	-

Table 3.4. Coefficients of determination (R^2) values between the static predictor variables and foot progression angle (FPA) for the foot with the greater foot progression angle (High FPA). **Motion variables**. Total hip rotation ROM is the sum of range of motion values for hip internal and external rotation. Ankle dorsiflexion ROM is goniometric ankle dorsiflexion range of motion measurement in non-weight bearing (prone lying). Resting calcaneal stance position (RCSP) is measure of calcaneal position relative to the floor assessed in standing. 1st metatarsophalangeal joint is extension range of motion measurement assessed in standing. *: significance level (1-tailed), p<.05; **: p<.01

	FPA	Thigh rotation	Shank rotation	Peak HF on Shank DF	Peak ankle PF power	HF on Shank EV	Peak hallux on FF EXT	FF on HF ABD
FPA	-	.45**	.58**	-.26	.32	-.27	.15	.01
Thigh rotation	.20**	-	.86**	-.22	.37*	-.32*	.32	-.17
Shank rotation	.34**	.86**	-	-.23	.40**	-.37*	.33*	-.34*
Peak HF on Shank DF	.07	-.22	-.23	-	-.40**	.21	-.24	-.05
Peak ankle PF power	.10	.37*	.40**	-.40**	-	-.36*	.48*	-.05
HF on Shank EV	.07	-.32*	-.37*	.21	-.36*	-	-28	-.01
Peak hallux on FF EXT	.02	.32	.33*	-.24	.48*	-28	-	-.29
FF on HF ABD	.00	-.17	-.34*	-.05	-.05	-.01	-.29	-

Table 3.5. Coefficients of determination (R^2) values between the dynamic predictor variables and foot progression angle (FPA) for the foot with the greater foot progression angle (High FPA). **Motion variables**. FPA: the foot progression angle on the High FPA foot, (-)=toe-out angle; Thigh rotation: Thigh segment external rotation (-) value at mid stance; Shank rotation: Shank segment external (-) rotation value at mid stance; Peak HF on Shank DF: the peak value of hind foot on shank (ankle) dorsiflexion (+) during stance; Peak ankle PF power: the peak value of ankle plantar flexor power generation (+) during stance; HF on Shank EV: hind foot on shank (calcaneal) eversion (-) value at mid stance; Peak hallux on FF EXT: the peak value of hallux on forefoot (1st MTPJ) extension during stance; FF on HF ABD: forefoot on hind foot abduction (-) at mid stance.

Variables	Unstandardized beta (95% CI)	Standardized beta	R^2	R^2 change	Sig. F Change
(Constant)	-18.73 (-30.52,-15.00)	N/A	N/A	N/A	<.01
Total hip rotation ROM	.03 (-.09, .15)	.09	.08	.08	.07
Ankle dorsiflexion ROM	.15 (-.22, .52)	.13	.12	.04	.18
RSCP	-.41 (-.91, .09)	-.25	.18	.06	.10
d_1 (DM)	.38 (-4.67, 5.42)	.03			
d_2 (DMPN-NPU)	2.55 (-2.89, 7.99)	.17			
d_3 (DMPN+NPU)	-4.02 (-10.04, 1.99)	-.27	.29	.11	.15

Table 3.6. Hierarchical multiple regression analysis of static (goniometric) predictors of foot progression angle (FPA) on the foot with the greater FPA (High FPA). Variables are listed in the order of entry. **Motion variables**. Total hip rotation ROM is the sum of range of motion values for hip internal and external rotation. Ankle dorsiflexion ROM is goniometric ankle dorsiflexion range of motion measurement in non-weight bearing (prone lying). Resting calcaneal stance position (RCSP) is measure of calcaneal position relative to the floor assessed in standing. 1st metatarsophalangeal joint is extension range of motion measurement assessed in standing.

Variables	Unstandardized beta (95% CI)	Standardized beta	R^2	R^2 change	Sig. F Change
(Constant)	-15.47 (-26.01,-4.80)	N/A	N/A	N/A	<.01
Thigh rotation	.24 (.06, .45)	.37	.23*	.23	<.01
Peak HF on Shank DF	-.02 (-.52, .30)	-.08	.25	.05	.26
Peak hallux on FF EXT	.04 (-.15, .88)	.05	.26	.03	.45
Peak ankle PF power	.08 (-2.14, 3.39)	.19	.29	.03	.25
d_1 (DM)	1.92 (-2.89, 6.74)	.14			
d_2 (DMPN-NPU)	2.58 (-2.26, 7.41)	.18			
d_3 (DMPN+NPU)	-3.01 (-8.85, 2.83)	-.20	.37	.08	.30

Table 3.7. Hierarchical multiple regression analysis of dynamic (gait kinematic and kinetic) predictors of foot progression angle (FPA) on the High FPA foot (Dynamic Model A). Variables are listed in the order of entry. **Motion variables**. Thigh rotation: Thigh segment external rotation (-) value at mid stance; Peak HF on Shank DF: the peak value of hind foot on shank (ankle) dorsiflexion (+) during stance; Peak hallux on FF EXT: the peak value of hallux on forefoot (1st MTPJ) extension (+) during stance; Peak ankle PF power: the peak value of ankle plantar flexor power generation (+) during stance. d_1,d_2,d_3: Coding for group classification with CON participants as the reference group. d_1: DM group; d_2: DMPN-NPU group; d_3: DMPN+NPU group

Variables	Unstandardized beta (95% CI)	Standardized beta	R^2	R^2 change	Sig. F Change
(Constant)	-13.63 (-15.0,-12.2)	N/A	N/A	N/A	<.01
Thigh rotation	-.15 (.46, .16)	-.24	.21*	.23	<.01
Shank rotation	.40 (.10, .70)	.75	.37*	.16	<.01
HF on Shank EV	-.10 (-.16, .29)	-.11	.39	.05	.32
FF on HF ABD	.06 (-1.45, 7.05)	.08	.41	.03	.26
d_1 (DM)	1.62 (-2.60, 5.84)	.12			
d_2 (DMPN-NPU)	2.80 (-1.45, 7.05)	.20			
d_3 (DMPN+NPU)	-1.84 (-6.48, 2.79)	-.13	.48	.07	.20

Table 3.8. Hierarchical multiple regression analysis of dynamic (gait kinematic and kinetic) predictors of foot progression angle (FPA) on the High FPA foot (Dynamic Model B). Variables are listed in the order they were entered into the multiple regression analysis. **Motion variables**. Thigh rotation: Thigh segment external rotation (-) value at mid stance; Shank rotation: Shank segment external (-) rotation value at mid stance; HF on Shank EV: hind foot on shank (calcaneal) eversion (-) value at mid stance; FF on HF ABD: forefoot on hind foot abduction (-) at mid stance. d_1,d_2,d_3: Coding for group classification with CON participants as the reference group. d_1: DM group; d_2: DMPN-NPU group; d_3: DMPN+NPU group

A . FPA

B.   Thigh rotation

C. Shank rotation

D.   HF on Shank (ankle)

E.   Ankle PF Power

F.   Hallux on FF (1st MTPJ)

G.   HF on Shank (calcaneal)

H.   FF on HF (forefoot)

.... DM
 — — DMPN-NPU
 —··— DMPN+NPU
 —— CON
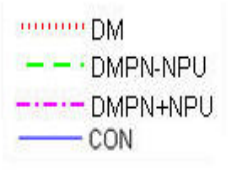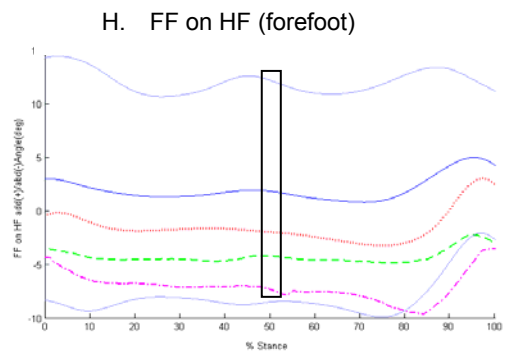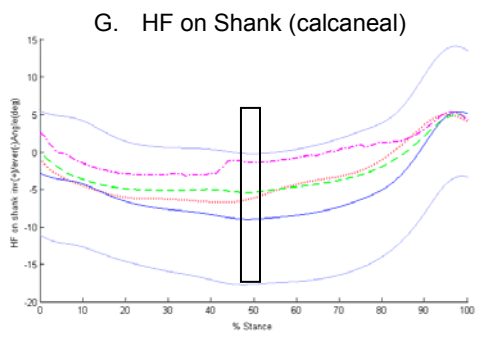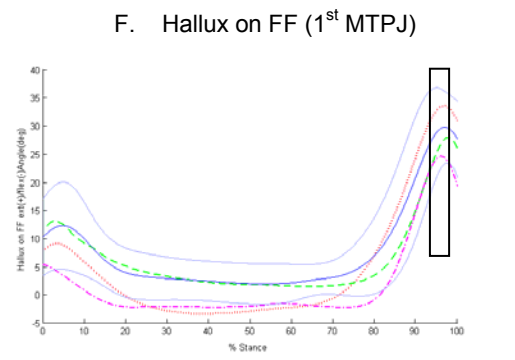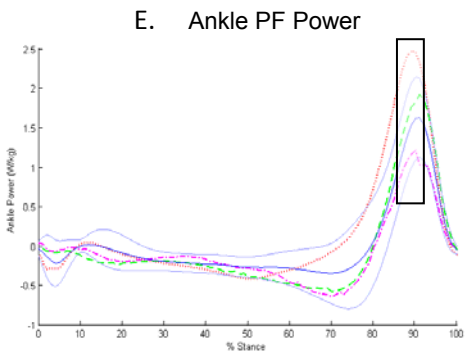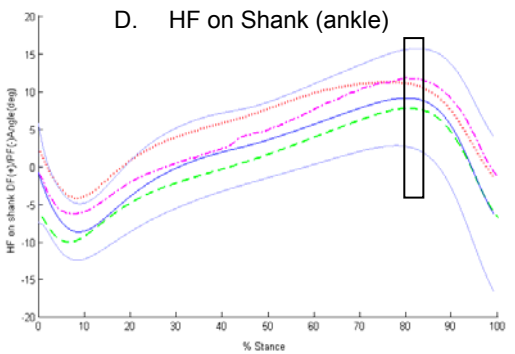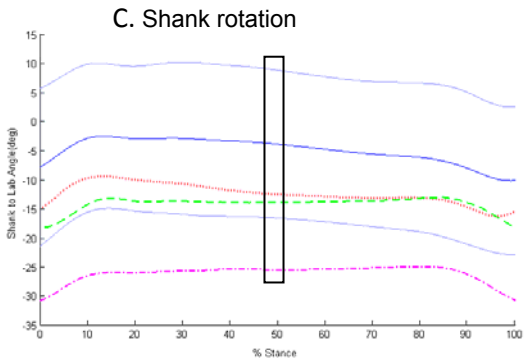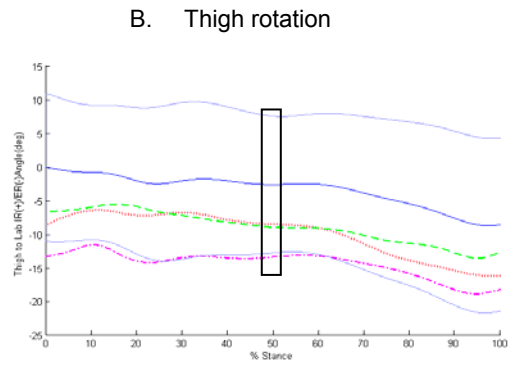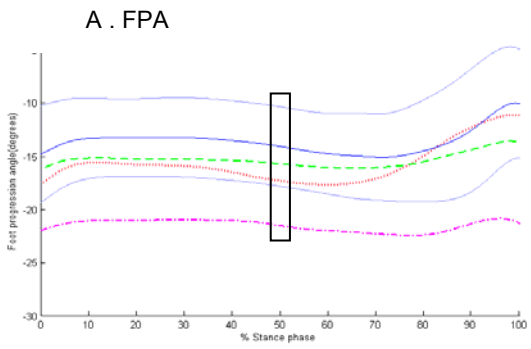
Figure 3.1. Time series motion graphs of dynamic predictor variables during the stance of walking. The blue line and shaded region represents the mean± 1 standard deviation of the motion for the CON group. Boxed regions represent values used in the analysis. **Figure legend**. CON: non-diabetic control participants; DM: diabetes mellitus without peripheral neuropathy group; DMPN-NPU: diabetes mellitus with peripheral neuropathy without a previous neuropathic plantar ulcer; DMPN+NPU: diabetes mellitus with peripheral neuropathy with a previous neuropathic plantar ulcer. **Motion variables**. A. FPA: FPA on the High FPA foot (-)=toe-out angle; B. Thigh rotation: Thigh segment internal (+)/external rotation (-) ; Shank rotation: C. Shank segment internal(+)/external(-) rotation; D. HF on Shank (ankle): Hind foot on shank (ankle) dorsiflexion (+)/plantarflexion (-); E. Ankle PF power: Ankle plantar flexor power generation (+)/absorption(-); F. Hallux on forefoot (1st MTPJ) extension (+)/flexion (-); G. HF on Shank (calcaneal): Hind foot on shank inversion (+)/eversion (-); H. FF on HF (forefoot): Forefoot on hind foot adduction (+)/abduction (-).

Chapter 4

Impact of foot progression angle modification on plantar loading in individuals

with diabetes mellitus and peripheral neuropathy

Status of resulting manuscript: in preparation, *Gait & Posture*

4.1.   Abstract

In the United States, an estimated 12 to 25% of patients with diabetes mellitus and peripheral neuropathy (DMPN) have a lifetime risk of neuropathic plantar ulcer (NPU) development.   Peak plantar pressure (PPP) is often used as an index of risk for NPU development in individuals with DMPN. Previous groups have reported a direct relationship between an excessive external foot progression angle (FPA) and the magnitude of regional PPP in adults with DMPN. However, it is unknown if FPA is modifiable in diabetes mellitus, or the effects of such a modification on regional PPP. The purposes of this study were to determine: 1) if participants with diabetes mellitus can reduce FPA, and 2) the impact of the reduction of FPA on the magnitude of PPP. Twenty-one individuals with diabetes were classified as having: 1) diabetes mellitus without peripheral neuropathy (DM), and 2) DMPN with a prior history of NPU (DMPN+NPU). Participants walked at their preferred FPA (pFPA), and with their foot in a corrected, or reduced, FPA position (cFPA). The cFPA was reduced from the pFPA in both groups, but only significant for the DM group (Mean±SE; DM_{pFPA}=-13±2º, DM_{cFPA}=4±3º, p=<.01; $DMPN+NPU_{pFPA}$=-16±2º; $DMPN+NPU_{cFPA}$=-11±4º, p=.13). The DM group demonstrated a 32% reduction in medial forefoot PPP in the cFPA versus the pFPA condition that trended toward statistical significance (Mean±SE; DM_{pFPA}=44±11 N/cm^2, DM=30±14 N/cm^2, p=.07). Our findings highlight the potential utility for FPA modification in adults with diabetes mellitus as a therapeutic intervention for offloading areas of the foot at risk for NPU development.

4.2.   Introduction

The development and recurrence of neuropathic plantar ulcers (NPUs) are a significant health and economic burden worldwide. In the United States, an estimated 12 to 25% of individuals with diabetes mellitus and peripheral neuropathy (DMPN) have a lifetime risk of NPU development[1,2]. Previous studies have shown that individuals with DMPN with history of NPU

have greater peak plantar pressure (PPP) in the forefoot region compared to those who did not[3,4]. Those with a history of NPU have the highest relative risk for re-ulceration of the previous healed NPU or ulcer development in an alternative location (RR=2.46; 95% CI: 1.84-3.29)[5] Over 65,000 non-traumatic lower extremity amputations in adults with DMPN are performed annually in the United States, 84% of which are preceded by NPUs[6,7].

Numerous treatment strategies have been employed for offloading plantar sites to promote NPU healing and to prevent re-ulceration. Commonly used offloading strategies include use of custom-made insoles or other shoe modifications[8], removable cast walking boots, total contact casting, and non-weight bearing strategies such as wheelchair usage[9]. Though custom made insoles, total contact casts, and removable cast walking boots have been shown to successfully reduce forefoot and mid foot peak plantar pressure in individuals with DMPN and a history of NPU [8,10], there are often barriers related to cost, patient compliance, and reimbursement [9,11]. Much of the previous research reports the efficacy of these interventions as treatment strategies for healing *existing* NPUs[12]. Moreover, non-weight bearing offloading techniques potentially contribute to the development and progression of mobility limitations reported by individuals with diabetes[6]. Though offloading strategies may provide the proper healing environment for NPUs, extensive periods of offloading may make the skin on the plantar surface of the foot vulnerable to re-injury, as evidenced by the high rates of re-ulceration (~20-70%) after successful healing with offloading[13,14].

In addition to casting, orthotics, and footwear treatment options, researchers have also examined the effectiveness of modifying gait patterns on reduction of PPP in healthy young adults and in adults with DMPN[11,15,16]. Gait modification strategies for older adults with DMPN include walking slower, reducing push off in late stance phase of walking by exaggerating hip flexion[15], or walking with a "step-to" gait pattern[16]. Though these strategies reduce PPP in the forefoot, reported changes in other regions of the plantar surface of the foot are variable[15,16]. Foot progression angle (FPA), or "toe-out angle," is the orientation of the longitudinal axis of the

foot in the transverse plane with respect to the direction of progression during gait[17,18]. Investigators have reported a direct relationship between excessive external FPA and elevated medial PPP in children with neurological impairments, and with the timing and magnitude of medial and lateral PPP in adults with DMPN[19-21]. However, there have been no reports as to whether an excessive FPA is modifiable in individuals with diabetes mellitus with or without peripheral neuropathy, or the effects of such a modification on regional PPP. Therefore, the purposes of this study were to: 1) determine if participants with diabetes mellitus with and without peripheral neuropathy and a history of NPU can reduce their excessive FPA with a simple intervention of verbal and visual cueing, and 2) determine the impact of FPA reduction on regional PPPs in adults with diabetes. We hypothesized that reduction of FPA in both groups would result in concomitant decreases in the magnitude of PPP on the medial forefoot mask on the plantar surface of the foot.

4.3.   Methods

4.3.a. Subjects

Twenty-one individuals with diabetes (10 men, 11 women; Mean±SE; age, 59±2.0 years; height, 1.7±0.1 m; BMI, 37±2 kg/m^2) participated, and provided written informed consent as approved by our university's Institutional Review Board. Participants were classified into one of two groups: 1) diabetes mellitus without peripheral neuropathy (DM), and 2) diabetes mellitus and peripheral neuropathy with a prior history of a neuropathic plantar ulcer (DMPN+NPU). The purpose for selecting these groups was to determine the effect of reducing FPA in a population of adults with diabetes that demonstrated mild and severe impairment in sensation and foot function. The presence or absence of peripheral neuropathy was assigned based on the presence or absence of protective sensation, and ulcer classification was based on any prior history of plantar ulceration. Peripheral neuropathy was assessed using a 5.07 (10 gram)

Semmes-Weinstein monofilament at seven sites on the plantar surface of the foot[22]. In addition, we measured vibration perception threshold (VPT) using a 120 V bioesthesiometer (Bio-medical Instrument Co., Newbury, OH, 44065, USA) to assess large fiber peripheral nerve function. Those who were either unable to feel the 10 gram monofilament on at least one of the seven sites on the foot, or were unable to perceive vibration of the bioesthesiometer at threshold of 25 V or greater were classified as having peripheral neuropathy. A VPT $\geq$25 V is associated with incidence of foot ulceration in individuals with Type 2 diabetes mellitus[23]. The combination of these tests for protective sensation has been shown to increase specificity of risk identification and disease severity without diminution in sensitivity[23]. Eleven participants were classified as DM, and ten were classified as DMPN+NPU. Of the DMPN+NPU participants, 8 reported a history of unilateral ulceration and 2 reported a history of bilateral ulceration. Participants classified as DMPN+NPU were not ulcerated at the time of testing. Those identified as non-ambulatory or with lower extremity amputations proximal to the digits were excluded from the study.

4.3.b. Procedure

Dynamic plantar pressures were collected using an EMED-ST-P-2 pedobarograph (Novel Inc., St. Paul, MN, USA). System specifications include a sampling frequency of 50Hz and resolution of 2 sensors/cm^2 for a network of 2736 sensors. Participants were selected to walk under two conditions using the 2-step method[24]. Participants were first asked to walk over a 3.6 m walkway at their self-selected speed and preferred FPA (pFPA). Participants were then verbally directed to align their foot along the 2nd ray (representing the longitudinal axis of the foot) on a thickened black line in the floor parallel with the line of gait progression and walk with their foot in this corrected position (cFPA) over the walkway their self-selected speed. Participants were also given verbal instructions to "keep their feet turned straight" prior to practice trials. Walking speed was measured using a stopwatch over a predetermined distance,

and is expressed in meters/min. Participants performed three walking trials with each foot

contacting the EMED platform during each condition. All participants were allowed 1-2 practice

trials prior to recording.

4.3.c. Data processing and statistical analysis

4.3.c.1. FPA measurement. *FPA* was calculated as measured angle between the line

of progression (a line drawn parallel to the printed paper) and the line representing the anterior-

posterior bisection of the foot extending from the center of the hind foot through the 2nd/3rd rays

obtained from the plantar pressure map using a 2^0 increment goniometer[20]. A change of ≥4º

was considered a meaningful corrected change in FPA based on reported ranges of 5-9º for

FPA magnitude and 1-2º for FPA asymmetry in young and older adults[25]. The threshold of ≥4º

was, therefore, the desired response to visual and verbal cues with several practice trials.

4.3.c.2. Masks of Pressure map. The pressure map of each foot step was first divided

into two regions using a 50% vertical bisector approximately between the 2nd and 3rd rays,

creating medial (Med) and lateral (Lat) vertical masks using Percent Mask software (Novel Inc.,

St. Paul, MN, USA). The plantar map was further divided into three horizontal regions at 33%

and 63% of foot length creating masks at the heel (Heel), mid foot (Mid) and forefoot (Fore).

The vertical and horizontal bisections of the foot created six distinct masks: the medial and

lateral forefoot (Med Fore, Lat Fore), the medial and lateral mid foot (Med Mid, Lat Mid), and the

medial and lateral heel (Med Heel, Lat Heel).   The variable of interest was peak plantar

pressure (PPP) which we use to operationally define stress based on previous work[8]. PPP is

the peak pressure recorded within a mask region during stance phase of the gait cycle[8]. PPP

has been accepted as an index of risk for dermal injury on the foot plantar surface because

elevated regional PPP values occur at areas of skin breakdown in individuals with diabetes that

have a lack of protective sensation and a history of neuropathic ulceration[19]. Force-time integral

(FTI) is a description of force expressed as a calculated sum of the product of pressure recorded from each sensor multiplied by the area and contact time of each sensor ($\sum$(pressure X area X time)) for each region of the plantar surface of the foot[8]

4.3.c.3. Statistical analysis. Participants' feet were designated as Involved (Inv) for the DMPN+NPU group based on the foot with an ulcer history. If DMPN+NPU participants had a history of bilateral involvement, the foot with the most recent ulceration was classified as the Inv foot. Comparisons were made between the Inv foot of the DMPN+NPU group and a randomly assigned foot of participants in the DM group. Statistical analyses were performed using IBM SPSS Statistics software, version 21.0 (SPSS Inc, Chicago, IL, USA).

PPP and FTI for the Inv foot was averaged over three trials, and statistically analyzed using a repeated measures, mixed-model analysis of covariance (ANCOVA). There was no difference in walking speed between conditions for either group, but there was a between-group difference in walking speed for both conditions. Therefore, an average walking speed (mean walking speed=49 m/min) was used as a covariate to account for the established influence of walking speed on PPP as well as the between-group differences in walking speed (Table 1)[26]. The between-groups factor was group (DM versus DMPN+NPU), and the repeated measures factors were condition (pFPA versus cFPA), mediolateral mask location (Mask A: Lat versus Med), and anteroposterior mask location (Mask B: Fore versus Mid). Only the forefoot and mid foot masks were included in the analyses because these regions are most vulnerable to NPU development[11,27]. Post-hoc analyses for main and interaction effects were conducted using a Bonferroni correction, with statistical significance for all analyses set at p<.05.

4.4. Results

4.4.a. Participant Characteristics

The mean ± SE age for all participants (N=21) was 59±2 years (range: 43-76 years). There were no group differences in age, DM, height, or body mass index (BMI) (Table 1). The DMPN+NPU group had a longer duration of diabetes and greater vibration perception threshold (VPT) on the Inv foot than the DM group, confirming the presence of peripheral neuropathy. There were between-group differences in walking speed, with the DM group walking faster than the DMPN+NPU group under both conditions (Table 4.1).

4.4.b. Foot Progression Angle

The DM group showed a significant reduction in FPA between conditions (Mean±SE; pFPA=-13±2°, cFPA=4±3°; p<.01). Though the DMPN+NPU group overall achieved the meaningful corrected change in FPA magnitude of at least 4°, the reduction in FPA was not statistically significant (pFPA=-16±2°, cFPA=-11±4°; p=.13). Nine participants out of eleven (82%) in the DM group and seven of ten participants (70%) in the DMPN+NPU group were able to achieve the meaningful corrected change in FPA magnitude. Two of eleven participants (18%) in the DM group and five of ten participants (50%) in the DMPN+NPU had a FPA of ≥10° in the cFPA condition. Of the five DMPN+NPU participants with an FPA of ≥10° in the cFPA condition, three of them did not achieve the meaningful corrected change of 4°. There were participants in both groups that demonstrated reductions in FPA that resulted in the development of an internal FPA ("toe-in" angle), a positive numeric value. The DM group had a greater magnitude of absolute change between conditions compared to the DMPN(+)NPU group, but these differences were not statistically significant (DM: 16±3°, DMPN+NPU: 9±2°, p=.14). Values are shown in Table 4.2.

4.4.c. Peak Plantar Pressure

73

Values for PPP in each mask region are in Table 4.3. There was a statistically significant four-way interaction of Condition x Group x Mask A (Lat versus Med) x Mask B (Fore versus Mid) (p=.0.02). Figure 4.1 illustrates the peak plantar pressure profiles for the DM and DMPN+NPU groups. DM participants reduced PPP in the medial forefoot and increased PPP in the lateral mid foot in the cFPA condition compared with the pFPA condition. The DMPN+NPU group showed very little change in pressure in any region as a function of FPA correction. Post hoc comparisons verified this pattern, albeit only at marginally significant levels. There was a 32% decrease in the Med Fore mask in the DM group (pFPA=44 N/cm^2, cFPA=30 N/cm^2; p=.07), with an accompanying 62% increase in the Lat Mid mask (pFPA=21 N/cm^2, cFPA=35 N/cm^2; p=.07). Regional changes in PPP in the DM group demonstrated trends toward statistical significance.

4.4.d. Force-Time Integral

There was a significant Condition X Mask B interaction (Fore versus Mid, p=.04). There was a decrease in FTI in the forefoot from the pFPA to the cFPA condition (pFPA=139 N/cm^2, cFPA=130 N/cm^2, p=.02), with an increase in FTI in the mid foot (pFPA=68 N/cm^2, cFPA=76 N/cm^2, p=.01). No other effects were statistically significant. Values are shown in Table 4.4.

4.5.   Discussion

This is the first investigation to determine the impact of FPA modification on plantar loading in participants with diabetes with and without peripheral neuropathy and plantar ulceration. One of the key findings from this investigation was that both groups overall achieved a clinically meaningful reduction of at least 4º in their FPA with visual and verbal cueing. Another key finding was that both groups had a characteristic pressure shift from the medial forefoot (Med Fore) mask, a region shown to be at risk for ulceration in adults with DMPN, to the

74

lateral mid foot (Lat Mid) mask as a result of the reduction in FPA. However, larger differences in PPP were observed in the DM group. These findings indicate that use of a simple gait modification strategy of reducing FPA may be a potentially effective therapeutic strategy to modify plantar stresses in areas of the foot vulnerable to dermal injury in adults with diabetes mellitus prior to the onset of peripheral neuropathy and the development of a neuropathic plantar ulcer.

In the current study, we observed a pattern of reduction in medial forefoot PPP (DM=32%; DMPN+NPU=8%), with a notable increase in lateral mid foot PPP in both groups (DM=62%; DMPN+NPU=21%). Other research groups have reported similar patterns of reduction in forefoot PPP using various gait modification strategies. Mueller and colleagues have reported reductions in in-shoe forefoot PPP by 27-53% and increases in heel PPP by 24% using "hip flexion" and "step-to" gait modification strategies[15,16]. The authors, however, acknowledge these types of gait modifications impair movement symmetry and gait speed. Rosenbaum (2013) reported that manipulation of FPA yielded a 54% decrease in medial forefoot PPP and a 75% increase in lateral mid foot PPP as a result of in-toeing[28]. The current investigation expands these findings by investigating the effects of implementing a similar gait modification in participants with diabetes with and without peripheral neuropathy. In our study, both groups experienced a shift in PPP from the medial forefoot to the lateral mid foot, though participants in the DM groups had a greater magnitude of these changes compared to the DMPN+NPU group. The differences in the magnitude of the regional changes in PPP between groups could be attributed to limitations in hip and ankle range of motion[29,30]. Additionally, the increase in regional PPP in the lateral mid foot in both groups were well below PPP values reported by Sinacore et al (2008) for classifications of lateral column foot deformities in individuals with DMPN[27].

In recent years, there has been an expansion in the number of treatment options for offloading areas of the foot vulnerable to NPU development in individuals with DMPN. In a review by Bus et al (2008), there is evidence supporting the efficacy of custom made insoles, total contact casts, and removable cast walkers for reducing forefoot PPP compared to standard footwear. Percentages of reduction in forefoot PPP range from 10-19% for custom made insoles[13]. In the current investigation, we observed greater reductions in medial forefoot PPP using FPA reduction as a gait modification strategy. Findings from this investigation demonstrate the potential for achieving similar decreases in areas of the foot vulnerable to dermal injury in adults with diabetes using a movement strategy as a cost-effective therapeutic intervention within the scope of physical therapist practice.

One of the limitations associated with this study is the small sample size. Inclusion of additional participants would have potentially brought the trending differences in the lateral mid foot to statistical significance. Another limitation is the heterogeneity of reported NPU location in the DMPN+NPU group. Ulcer location may be indicative of the onset of rigid structural foot deformities, thereby potentially limiting the magnitude of PPP reductions in the regions of interest. In addition, FPA modification consisted of single session instruction, with measurements taken over several single steps. Future studies could expand these findings by assessing the effects of changing FPA over multiple steps, and determining the effects of modifying FPA on other parts of the lower extremity kinetic chain. Finally, we examined the effect of modifying FPA under barefoot conditions to observed changes in PPP without the influence of footwear. Therefore, we cannot generalize these findings to the effect of FPA modification to in-shoe pressure measurements. Future studies should confirm the impact of this type of gait modification strategy on in-shoe measurements of PPP.

4.6.   Conclusion

Our findings highlight the potential utility for FPA modification in adults with diabetes mellitus as a therapeutic intervention aimed at offloading areas of the plantar surface of the foot at risk for NPU development. Furthermore, we were able to reduce medial forefoot loading without creating excessive loads in other regions of the forefoot and mid foot. Therefore, using FPA reduction as a treatment strategy for offloading areas of the foot at risk for NPU development could be safely implemented in a physical therapist clinical practice.

REFERENCES

1. Cavanagh PR, Lipsky BA, Bradbury AW, Botek G. Treatment for diabetic foot ulcers. *Lancet* 2005; 366(9498):1725-1735

2. Owings TM, Apelqvist J, Stenström A, Becker M, Bus SA, Kalpen JS et al. Plantar pressures in diabetic patients with foot ulcers which have remained healed. *Diabet Med* 2009; 26:1141-1146

3. Boulton AJ, Hardest CA, Betts RP, Franks CI, Worth RC, Ward JD *et al*. Dynamic foot pressure and other studies as diagnostic and management aids in diabetic neuropathy. *Diabetes Care* 1983; 6(1): 26-33

4. Armstrong DG, Peters EJ, Athanasius KA, Livery LA. Is there a critical level of plantar foot pressure to identify patients at risk for neuropathic foot ulceration? *J Foot Ankle Surge* 1998; 37(4): 303-307

5. Boyce EJ, Apron JH, Stengel V, Forsberg RC, Avignon DR, Smith DG. A prospective study of risk factors for diabetic foot ulcer. The Seattle Diabetic Foot Study. *Diabetes Care* 1999; 22(7):1036-1042

6. Centers for Disease Control and Prevention. National Diabetes Fact Sheet, 2011. http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Published 2011. Accessed January 23, 2014

7. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. *Diabetes Care* 1990; 13(5):513-521

8. Bus SA, Ulbricht JS, Cavanagh PR. Pressure relief and load redistribution by custom-made insoles in diabetic patients with neuropathy and foot deformity. *Clin Biomech* 2004; 19(6): 629-638

9. Wu SC, Jensen JL, Weber AK, Robinson DE, Armstrong DG. Use of pressure offloading devices in diabetic foot ulcers: do we practice what we preach? *Diabetes Care* 2008; 31(11):2118-2119

10. Gutekunst DJ, Hastings MK, Bohnert KL, Strube MJ, Sinacore DR. Removable cast walker boots yield greater forefoot off-loading than total contact casts. *Clin Biomech* 2011; 26(6): 649-654

11. Kwon OY, Mueller MJ. Walking patterns used to reduce forefoot plantar pressures in people with diabetic neuropathies. *Phys Ther* 2001; 81(2): 828-835

12. Bus SA, Val GD, van Duren RW, Armstrong DG, Caravaggio C, Hlaváček P *et al*. The effectiveness of footwear and offloading interventions to prevent and heal foot ulcers and reduce plantar pressure in diabetes: a systematic review. *Diabetes Metab Res Rev* 2008; 24 Suppl 1: S162-S180

13. Apelqvist J, Larsson J, Agardh CD. Long-term prognosis for diabetic patients with foot ulcers. *J Intern Med* 1993; 233(6):485-491.

14. Mueller MJ, Maluf KS. Tissue adaptation to physical stress: a proposed "Physical Stress Theory" to guide physical therapist practice, education, and research. *Phys Ther* 2002; 82(4) 383-403

15. Mueller MJ, Sinacore DR, Hoogstrate S, Daly L. Hip and ankle walking strategies: effect on peak plantar pressures and implications for neuropathic ulceration. *Arch Phys Med Rehabil* 1994; 75(11):1196-2000

16. Brown HE, Mueller MJ. A "step to" gait decreases pressures on the forefoot. *J Orthop Sports Phys Ther* 1998; 28(3):139-145

17. Holden JP, Cavanaugh PR, Williams KR, Bednarski KN. Foot angles during walking and running.   1985 International Series on Biomechanics: Biomechanics IX-A. Human Kinetics Publishers, Champaign, IL

18. Lai YC, Lin HS, Pan HF, Chang WN, Hsu CJ, Renn JH. Impact of foot progression angle on the distribution of plantar pressure in normal children. *Clin Biomech* 2014; 29(2):196-200

19. Mueller MJ, Hastings MK, Commean PK, Smith KE, Pilgram K, Robertson D et al. Forefoot structural predictors of plantar pressures during walking in people with diabetes and peripheral neuropathy. *J Biomech* 2003; 36(7):1009-1017

20. Hastings MK, Gelber JR, Isaac EJ, Bohnert KL, Strube MJ, Sinacore DR. Foot progression angle and medial loading in individuals with diabetes mellitus, peripheral neuropathy, and a foot ulcer. *Gait Posture* 2010; 32(2):237-241

21. Chang WN, Tsirikos AI, Miller F, Schyler J, Glutting J. Impact of changing foot progression angle on foot pressure measurement in children with neuromuscular disease. *Gait Posture* 2004; 20(1): 14-19

22. Diamond JE, Mueller MJ, Delitto A, Sinacore DR. Reliability of diabetic foot evaluation. *Phys Ther* 1989; 69(10):797-802

23. Kästenbauer T, Sauseng S, Brath H, Abrahamian H, Irsigler K. The value of the Rydel-Seiffer tuning fork as a predictor of diabetic polyneuropathy compared with a neurothesiometer. *Diabet Med* 2004; 21(6):563-567

24. Meyers-Rice B, Sugars L, McPoil, T, Cornwall MW. Comparison of three methods for obtaining plantar pressures in non-pathologic subjects. *J Am Podiatr Med Assoc,* 84(10): 499-504

25. Menz HB, Latt MD, Tiedemann A, Mun San Kwan M, Lord SR. Reliability of the GAITRite walkway system for the quantification of temporo-spatial parameters of gait in young and older people. *Gait Posture* 2004; 20(1): 20-25

26. Ko M, Hughes L, Lewis H. Walking speed and peak plantar pressure distribution during barefoot walking in persons with diabetes. Physio Res Int. 2012; 17(1):29-35

27. Sinacore DR, Bohnert KL, Hastings MK, Johnson JE. Mid foot kinetics characterize structural polymorphism in diabetic foot disease. *Clin Biomech* 2008; 23(5):653-661

28. Rosenbaum D. Foot loading can be changed by deliberately walking with in-toeing or out-toeing gait modifications. *Gait Posture* 2013; 38(4): 1067-1069

29. Mueller MJ, Minor SD, Sahrmann SA, Schaaf JA, Strube MJ. Difference in the gait characteristics of patients with diabetes and peripheral neuropathy compared with age-matched controls. *Phys Ther.* 1994; 74(4):299-308

30. Sawacha Z, Gabriella G, Cristoferi G, Guiotto A, Avogaro A, Cobelli C. Diabetic gait and posture abnormalities: a biomechanical investigation through three-dimensional gait analysis. *Clin Biomech* 2009; 24(9): 722-728

	DM (N=11) Mean (SE)	DMPN+NPU (N=10) Mean (SE)	p
Age (years)	59 (3)	58 (3)	.80
Height (m)	1.7 (0.1)	1.7 (0.1)	.70
BMI (kg/m^2)	34 (3)	40 (3)	.09
Duration of disease (years)	7 (2)*	24 (2)	<.01
R Great Toe VPT (volts)	15 (4)*	34 (4)	<.01
Walking speed (m/min)	58 (2)*	38 (3)	<.01

Table 4.1. Participant characteristics, mean (SE). VPT: vibration perception threshold

(Volts); participants with a VPT greater than 25 Volts. *:p<.05

	DM (N=11)	DMPN+NPU (N=10)	p
Preferred FPA (pFPA, deg)	-13 (2)	-16 (2)	.15
Corrected FPA (cFPA, deg)	4 (3)	-11 (4)	<.01
FPA change (deg)	16 (3)	9 (2)	.14
# able to correct >4º	9	7	--
#with ≥10º cFPA	2	5	--

Table 4.2. Foot progression angle (FPA) magnitude on the involved (Inv) foot in both

conditions for both groups. Values are expressed in degrees, mean (SE).   Absolute

FPA change (deg): the absolute difference in FPA between conditions on the involved

(Inv) foot; #able to correct: the number of participants able to achieve a clinically

meaningful corrected change in FPA; # with ≥10º in cFPA condition: the number of

participants with an FPA ≥10º for the cFPA condition.

	Group	pFPA	cFPA	p (condition)	95% CI (Mean difference)
		Mean (SE)	Mean (SE)		
Walking Speed (m/min)					
	DM	58 (2)*	57 (2)*	.32	-2 to 4
	DMPN+NPU	39 (5)	38 (4)	.58	-3 to 6
	p (Group)	<.01	<.01		
FPA (deg)					
	DM	-13 (2)*	4 (3)*	<.01	-23 to -10
	DMPN+NPU	-16 (2)	-11(4)	.13	-13 to 2
	p (Group)	.15	<.01		
Absolute FPA change (deg)					
	DM	16 (3)	N/A		-2 to 15
	DMPN+NPU	9 (2)	N/A		-2 to 14
	p (Group)	.14			
PPP Med Fore (N/cm^2)					
	DM	44 (11)	30 (14)	.07	-2 to 30
	DMPN+NPU	64 (9)	59 (11)	.24	-7 to 18
	p (Group)	.16	.12		
PPP Lat Fore (N/cm^2)					
	DM	36 (10)	30 (10)*	.37	-5 to 17
	DMPN+NPU	60 (8)	57 (8)	.57	-6 to 11
	p (Group)	.08	.04		
PPP Med Mid (N/cm^2)					
	DM	10 (1)	10 (6)	.99	-12 to 12
	DMPN+NPU	8 (1)	11 (5)	.55	-12 to 7
	p (Group)	.39	.88		
PPP Lat Mid (N/cm^2)					
	DM	21(10)	35 (12)	.07	-28 to 1
	DMPN+NPU	26 (8)	31 (10)	.32	-17 to 6
	p (Group)	.74	.83		

Table 4.3. Foot progression angle (FPA) and peak plantar pressure (PPP) covariance-corrected means for the four-way interaction effect of Condition (pFPA versus cFPA) x Group (DM versus DMPN+NPU) x Mask A (Fore versus Mid) x Mask B (Lat versus Med) (p=.0.02). Columns represent the condition effect (within-group differences) in all variables, expressed in mean (SE). Rows represent the group effect (between-group difference) in all variables, expressed in mean (SE). pFPA: preferred FPA walking condition; cFPA: corrected FPA walking condition. **Mask descriptions**. Med Fore=medial forefoot; Lat Fore=lateral forefoot; Med Mid=medial mid foot; Lat Mid=lateral mid foot. **Variable descriptions**. FPA: the value of foot

progression angle on the involved (Inv) foot for both groups under both walking conditions.

Absolute FPA change: Absolute difference in FPA between conditions on the involved (Inv) foot.

PPP: peak plantar pressure for each mask.   p (condition): significance values for the condition

main effect, 95% CI of the average difference. p (group): significance values for the group main

effect, p<.05.

	Group	pFPA	cFPA	p value (condition)	95% CI (Mean difference)
		Mean (SE)	Mean (SE)		
FTI Med Fore (N*s)					
	DM	138 (42)	119 (40)	.86	-15 to 53
	DMPN+NPU	189 (33)	181(31)	.54	-19 to 18
	p (group)	.35	.24		
FTI Lat Fore (N*s)					
	DM	93 (22)	94 (21)	.98	-33 to 32
	DMPN+NPU	136 (17)	128 (16)	.54	-18 to 33
	p (group)	.15	.20		
FTI Med Mid (N*s)					
	DM	14 (8)	17 (19)	.87	-44 to 38
	DMPN+NPU	9 (6)	21 (15)	.45	-44 to 20
	p (group)	.60	.89		
FTI Lat Mid (N*s)					
	DM	116 (37)	128 (35)	.48	-47 to 23
	DMPN+NPU	133 (29)	138 (28)	.32	-17 to 6
	p (group)	.35	.23		

Table 4.4. Force-time integral (FTI) covariance-corrected means for the four-way interaction effect of Condition (pFPA versus cFPA) x Group (DM versus DMPN+NPU) x Mask A (Fore versus Mid) x Mask B (Lat versus Med) (p=.0.02). Columns represent the condition effect (within-group differences) in all variables, expressed in mean (SE). Rows represent the group effect (between-group difference) in all variables, expressed in mean (SE). pFPA: preferred FPA walking condition; cFPA: corrected FPA walking condition. **Mask descriptions**. Med Fore=medial forefoot; Lat Fore=lateral forefoot; Med Mid=medial mid foot; Lat Mid=lateral mid foot. **Variable descriptions**. FPA: the value of foot progression angle on the involved (Inv) foot for both groups under both walking conditions. Absolute FPA change: Absolute difference in FPA between conditions on the involved (Inv) foot. PPP: peak plantar pressure for each mask. p (condition): significance values for the condition main effect, 95% CI of the average difference. p (group): significance values for the group main effect, p<.05.

Figure 4.1. Regional peak plantar pressure (PPP) in DM (A) and DMPN+NPU (B) participant groups. pFPA: preferred FPA walking condition; cFPA: corrected FPA walking condition. **Mask descriptions**. Med Fore=medial forefoot; Lat Fore=lateral forefoot; Med Mid=medial mid foot; Lat Mid=lateral mid foot.

Chapter 5

Summary and Conclusions

5.1.   Summary

Elevated regional peak plantar pressure (PPP) is an established index of risk dermal injury in adults with diabetes mellitus and peripheral neuropathy (DMPN)[1,2], and is thought to initiate a lower extremity impairment cascade of medial neuropathic plantar ulcer (NPU) development and subsequent non-traumatic lower extremity amputation in individuals with DMPN. Foot progression angle (FPA) is a predictor of elevated regional PPP, a proxy measure of dermal injury risk in adults with DMPN with and without a history of plantar ulceration[1,3]. Prior to this series of investigations, there were no longitudinal or cross-sectional studies that investigated specific characteristics of FPA in adults with DMPN. Also, to our knowledge there were no studies that identifying static or dynamic predictors of FPA in adults with DMPN. Finally, there were no studies probing whether excessive FPA is modifiable in adults with DMPN, thereby potentially creating a strategy for early rehabilitative intervention to interrupt the cascade of lower extremity impairment leading to amputation[4]. The primary objectives of this research were to determine if specific characteristics of FPA (magnitude and asymmetry) were altered with disease progression and increasing severity of impairments (Aim 1), to identify static and dynamic predictors of FPA magnitude (Aim 2), and to examine the effect of reducing FPA on the regional plantar pressure distribution (Aim 3) in adults with and without DMPN. Our first hypothesis was there would be a progressive increase in FPA magnitude and a progressive decrease in the inter-limb FPA asymmetry across a spectrum of participants with and without DMPN and accompanying history of prior ulceration. Our second hypothesis was that select static and dynamic predictor variables would explain a significant portion of the variance in FPA. Our third hypothesis was reduction of FPA in both groups would result in concomitant decreases in the magnitude of both regional force-time integral (FTI) and regional peak plantar pressure (PPP) on the medial forefoot mask on the plantar surface of the foot. The following is a summary of the key findings and clinical relevance from each investigation.

5.1.a. Specific Aim 1.

5.1.a.1. Key findings. A detailed description of this investigation is outlined in Chapter 2. One of the key findings from Aim 1 is that participants with diabetes mellitus and peripheral neuropathy with a reported history of prior ulceration (DMPN+NPU) had a greater FPA magnitude on both feet than other participant groups of older adults with and without DMPN. Another key finding from this investigation is there is no difference in the degree of asymmetry between groups, indicating that FPA asymmetry is not disease-specific, and may be a common spatial characteristic of normal gait in adults 50 years or older.

5.1.a.2. Clinical relevance. FPA is an established predictor of elevated regional plantar stress, a proxy measure of neuropathic plantar ulceration risk, in adults with DMPN with and without a history of NPU development[1,3].   Although all groups met the criterion for having an excessive FPA (FPA>10º) in this study, a large FPA in the presence of peripheral neuropathy potentially exposes individuals with DMPN to elevated regional PPP and, subsequently, to risk for NPU development. Therefore, there may be more clinical utility in the observation and measurement of FPA of *both* feet in adults with DMPN with and without a prior history of NPU development as part of an assessment of risk of NPU development or recurrence.

5.1.b. Specific Aim 2.

5.1.b.1. Key findings. A detailed description of all findings is outlined in Chapter 3. One of the key findings from this study is that static (goniometric) measures of limited joint mobility of lower extremity joint motion are not predictors of FPA, whereas dynamic (gait kinematic and kinetic) variables 37% of FPA. Additionally, dynamic measures of the thigh and shank transverse plane motion during the mid stance phase of gait are better predictors of FPA than dynamic measures of inter-segmental foot motion.

5.1.b.2. Clinical relevance. These findings suggest rotation of segments proximal to the foot during gait may better predict FPA in older adults with DMPN. Current interventions that target static and dynamic predictors of regional PPP within the scope of physical therapist practice are limited, and are often cost prohibitive[5]. Identification of predictors of FPA could be clinically useful in assessing risk for elevated PPPs earlier in the lower extremity impairment cascade using tools that are widely available in most rehabilitation clinical settings (i.e., goniometers, inked-moleskin method of gait analysis).

5.1.c. Specific Aim 3.

5.1.c.1. Key findings. A detailed description of all findings is outlined in Chapter 4. In this investigation, two groups of participants with diabetes mellitus were able to achieve a clinically meaningful reduction of FPA magnitude using a simple gait modification as the therapeutic strategy. Another key finding of this study is the observed decrease in stress and load from the medial forefoot, an area of the foot vulnerable to NPU development, and concomitant increase in mid foot stress and load in both groups. This shift in regional stress is more pronounced in the DM group, which indicates that this particular gait modification strategy may more efficacious prior to the onset of peripheral neuropathy.

5.1.c.1. Clinical relevance. In clinical practice, there are numerous treatment strategies for offloading plantar sites to promote wound healing or to prevent re-ulceration. Results from this investigation demonstrate the potential for achieving similar patterns of regional offloading in areas of the foot vulnerable to dermal injury in adults with DMPN using a cost-effective therapeutic intervention within the scope of physical therapist practice.

5.2.　　Study Limitations and Future Directions

5.2.a. FPA magnitude and asymmetry. FPA magnitude, not inter-limb asymmetry, is disease-specific in a cross-section of individuals with and without diabetes, peripheral neuropathy, and a

prior history of ulceration. Future studies should employ a longitudinal study design with more participants to better determine if there is a progressive increase in FPA magnitude in adults with DMPN with and without a prior history of ulceration. Determination of the onset of the development of an excessive FPA could possibly facilitate treatment optimally before the initiation of the lower extremity impairment cascade of excessive medial peak plantar pressure (PPP), medial neuropathic plantar ulceration, and non-traumatic amputation.

5.2.b. Predictors of FPA. Our investigation identified transverse rotation position of the thigh and shank segments during the stance phase of gait as being the strongest predictors of FPA magnitude, irrespective of disease severity. However, our study did not include radiographic measures of lower extremity measures of static alignment. Future studies could potentially extend these findings by examining the radiographic static alignment factors in the proximal and distal segments of the lower extremity to determine if they also contribute to FPA.

5.2.c .Gait modification. This study was the first to address the utility of reducing FPA (or positioning the foot closer to midline) as a gait modification strategy using simple visual and verbal cues. However, this gait instruction and modification was performed over a very brief series of single steps. Future studies could expand these findings by assessing the effects of changing FPA over multiple steps, and determining the effects of longer durations of modifying FPA on other parts of the lower extremity kinetic chain. Finally, we assessed the effect of modifying FPA under barefoot conditions in order to measure FPA under similar conditions. We cannot generalize our findings related to the effect of FPA modification to impact of footwear assessing in-shoe pressures and forces. Future studies should examine the effects of this type of gait modification strategy on in-shoe measures of stress and load.

5.3. Conclusions

This dissertation research has identified specific characteristics and predictors of FPA. FPA is a predictor of elevated regional plantar stresses and loads in adults with and without DMPN. This is the first series of investigations to characterize FPA in adults with increasing severity of impairments attributed to DMPN. This dissertation research provides new information on characteristics and predictors of FPA, a risk factor for elevated regional PPP in adults with DMPN. The clinical relevance of the findings from this dissertation research is the earlier identification of targets for earlier assessment and intervention in the lower extremity impairment cascade that often culminates in non-traumatic lower extremity amputation in individuals with DMPN. Furthermore, future studies could examine the efficacy of targeted physical therapy assessment tools and treatment strategies that may potentially address prevention versus treatment of NPU based on the unique features of FPA identified in this dissertation.

REFERENCES

1. Mueller MJ, Hastings MK, Commean PK, Smith KE, Pilgram K, Robertson D *et al.* Forefoot structural predictors of plantar pressures during walking in people with diabetes and peripheral neuropathy. *J Biomech* 2003; 36(7):1009-1017

2. Mueller MJ, Zou D, and Lott DJ. "Pressure gradient" as an indicator of plantar skin injury. *Diabetes Care* 2005; 28(12):2908-2912

3. Hastings MK, Gelber JR, Isaac EJ, Bohnert KL, Strube MJ, Sinacore DR. Foot progression angle and medial loading in individuals with diabetes mellitus, peripheral neuropathy, and a foot ulcer. *Gait Posture* 2010; 32:237-241

4. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. Basis for prevention. *Diabetes Care* 1990; 13(5):513-521

5. Kwon OY, Mueller MJ. Walking patterns used to reduce forefoot plantar pressures in people with diabetic neuropathies. *Phys Ther* 2001; 81(2):828-835
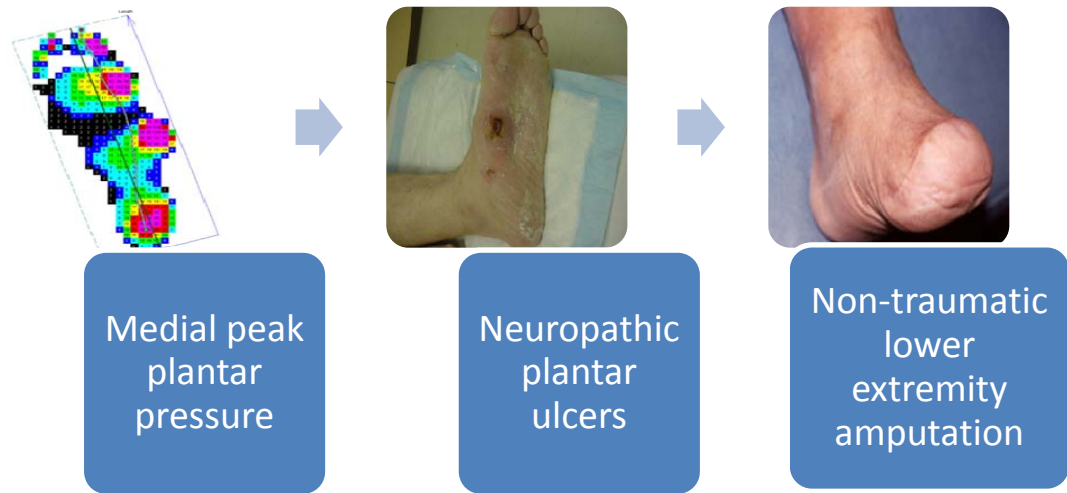
Figure 5.1. Impairment cascade of non-traumatic lower extremity amputation

Appendix

Appendix 1. Mean (SD) and univariate correlation of foot progression angle (FPA) measurement using motion capture (Aim 1, Aim 2) and EMED pedobarograph (Aim 3) for a subset of participants in the current study (N=21).

	EMED/MoCap (right)	EMED/MoCap (left)	p
r	0.79	0.73	<.01

<u>**Table 1A.**</u> Pearson product moment correlation (r) between foot progression angle (FPA) values derived using EMED pedobarograph (EMED) and motion capture (MoCap). EMED/MoCap (right): the correlation coefficient for FPA values derived using the EMED pedobarograph and motion capture (MoCap) for the right foot. EMED/MoCap (left): the correlation coefficient for FPA values derived using the EMED pedobarograph and motion capture (MoCap) for the left foot.

	EMED (right)	MoCap (right)	p (right)	EMED (left)	MoCap (left)	p (left)
FPA (deg)	-13 (4)	-14 (7)	0.17	-10 (4)	-10 (5)	0.58

<u>**Table 1B.**</u> Mean (SD) of FPA values derived using the EMED pedobarograph and motion capture. EMED (right): the mean (SD) for FPA values derived using the EMED pedobarograph. MoCap (right): the mean (SD) for FPA values using motion capture (MoCap) for the right foot. EMED (left): the mean (SD) for FPA values using motion capture (MoCap) for the left foot. MoCap (left): the mean (SD) for FPA values using motion capture (MoCap) for the left foot.
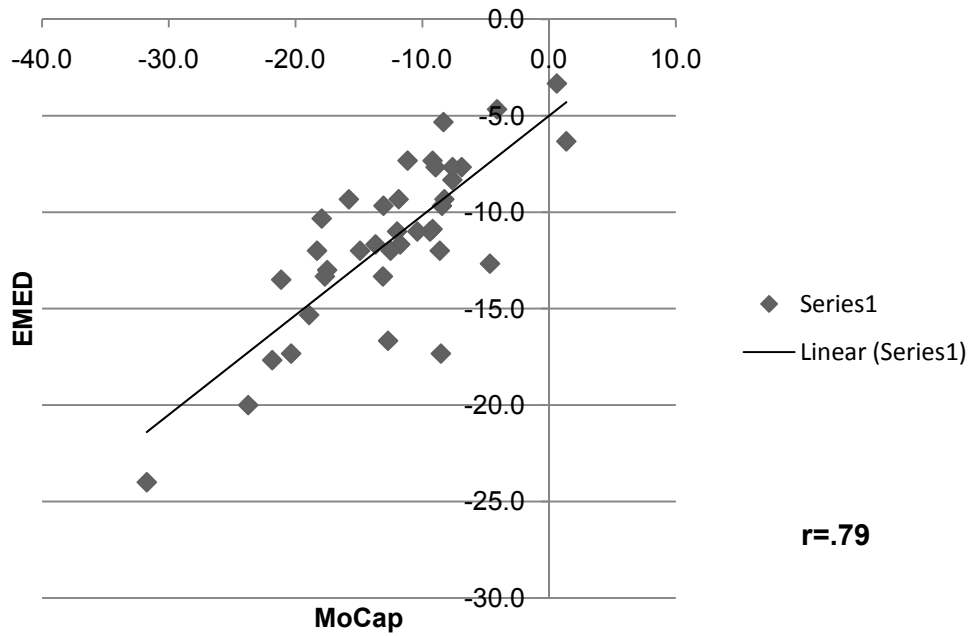
Figure 1A. Scatter plots of average FPA values for both feet derived using the EMED pedobarograph (EMED) and using motion capture (MoCap) in the study population for all dissertation projects (N=21).

Curriculum Vitae

Ericka Nayram Merriwether, PT, DPT, ATC, CSCS

Ph.D. candidate, Washington University in St. Louis, USA

6647 Washington Ave.   Office phone: (314) 747-0648
Saint Louis, MO 63130   Home phone: (314) 875-0089
                                             E-mail: emerriwether@wustl.edu

SUMMARY OF QUALIFICATIONS

Doctoral candidate in Movement Science with emphasis on lower extremity biomechanics in individuals with diabetes mellitus and peripheral neuropathy. Diverse background in biomechanics, including experience with 3D motion capture, isokinetic dynamometry, and plantar pressure measurement. Extensive knowledge of foot and ankle mechanics in individuals with diabetes mellitus and peripheral neuropathy. Clinical experience with youth, young adult, and older adult populations as a licensed physical therapist and certified athletic trainer.

HIGHLIGHTS

- Collaborated on the development and implementation of a protocol for measurement of lower extremity joint kinematics and kinetics in an overweight/obese population using 3D motion capture
- Investigating alignment factors that contribute to the magnitude of foot progression angle, a spatial gait variable associated with increased risk of plantar ulceration in people with diabetes mellitus and peripheral neuropathy
- Testing a pilot treatment protocol to address prevention of neuropathic plantar ulcers in individuals with diabetes mellitus and peripheral neuropathy
- Promotion of Doctoral Studies (PODS) I and II/Laura K. Smith Award recipient, Foundation for Physical Therapy
- NIH Individual Fellowship Award (F31) recipient

EDUCATION

Ph.D. candidate Movement Science (Biomechanics focus)
Washington University in St. Louis, Saint Louis, Missouri, USA   2008-present
Doctor of Physical Therapy
Mayo Clinic School of Health Sciences, Rochester, Minnesota, USA   2008
Bachelor of Science (B.S.) Kinesiology
University of Illinois at Urbana-Champaign, Urbana, Illinois, USA   1999

RESEARCH EXPERIENCE

Graduate Research Assistant, Applied Kinesiology Laboratory
Washington University in St. Louis   2008-present
Dissertation Title: Foot Progression Angle in Individuals with Diabetes Mellitus
and Peripheral Neuropathy
- Measuring the magnitude of foot progression angle in individuals with diabetes
  mellitus and peripheral neuropathy across a spectrum of impairments
- Determining alignment factors that contribute to foot progression angle magnitude
- Determining the effect of reducing foot progression angle magnitude via
  single-session intervention on plantar pressure distribution

PUBLICATIONS

Manuscripts

1. Hollman JH, Beckman BA, Brandt RA, Merriwether EN, Williams RT, Nordrum JT.
   Minimum detectable change in gait velocity during acute rehabilitation following hip
   fracture. 2008. *J Geriatr Phys Ther*, 31, 2: 8, 53-56

2. Merriwether EN, Host HH, Sinacore DR. Sarcopenic indices in community-dwelling
   older adults. *J Geriatr Phys Ther,* 2012 Jul-Sep; 35(3): 118-25

Manuscripts in Preparation

1. Merriwether EN, Hastings MK, Bohnert KL, Sinacore DR. Characteristics of foot
   progression angle in individuals with diabetes mellitus and peripheral neuropathy. In
   preparation, *Foot*

2. Merriwether EN, Hastings MK, Mueller MJ, Strube MJ, Bohnert KL, Sinacore DR. Static
   and dynamic predictors of foot progression angle in individuals with diabetes mellitus
   and peripheral neuropathy. In preparation, *Clinical Biomechanics*

3. Merriwether EN, Hastings MK, Strube MJ, Bohnert KL, Sinacore DR. Impact of foot
   progression angle modification on plantar loading in individuals with diabetes mellitus
   and peripheral neuropathy. In preparation, *Gait & Posture*

Abstracts and Conference Proceedings

1. Merriwether EN (Abstract and presentation only). 2009. Factors influencing the
   automaticity of gait. Abstract for podium presentation at the Luther College Black
   History Month Conference, Decorah, IA

2. Merriwether EN, Host HH, Sinacore DR. 2009. Sarcopenic indices of physical frailty.
   Abstract for poster presentation, American Physical Therapy Association Section on
   Research (SOR) Retreat, Pacific Groves, CA.

3. Merriwether EN, Host HH, Sinacore DR. 2010. Sarcopenic indices and isokinetic peak
   torque measures as indicators of physical frailty. Abstract for poster presentation at the
   American Physical Therapy Association Combined Sections Meeting, Las Vegas, NV.

4. <u>Merriwether EN</u>, Host HH, and Sinacore DR. 2010. Sarcopenic indices and isokinetic peak torque measures as indicators of physical frailty. Abstract for poster presentation at the Exercise and Physical Activity in Aging conference (EXPAAC), Indianapolis, IN.

5. <u>Merriwether EN</u>, Hastings MK, Bohnert KL, Penelton K, Sinacore DR. 2011. Foot progression angle measurement using the Oxford Foot Model. Abstract accepted for podium presentation at Gait and Clinical Movement Analysis Society Annual Meeting, Bethesda, MD.

6. <u>Merriwether EN,</u> Hastings MK, Bohnert KL, Penelton K, Sinacore DR. 2011. Comparison of three methods for measurement of foot progression angle (FPA) magnitude and asymmetry. Abstract accepted for poster presentation, American Society of Biomechanics.

7. <u>Merriwether, EN,</u> Hastings MK, Bohnert KL, Sinacore DR. 2013. Impact of modification of foot progression angle on forefoot plantar loading. Abstract accepted for podium presentation, American Physical Therapy Association Combined Sections Meeting, San Diego, CA.

8. <u>Merriwether EN,</u> Hastings MK, Bohnert KL, Sinacore DR. 2013. Asymmetry and modification of foot progression angle and their impact on plantar loading. Abstract accepted for poster presentation at the Gait and Clinical Movement Analysis Society Annual Meeting, Cincinnati, OH.

RESEARCH SUPPORT

Current

1F31DK-088512   Merriwether (PI)   7/2012-6/2014
NIH/NIDDK $58,848
Title: Foot progression angle in individuals with diabetes mellitus and peripheral neuropathy
The objective of this research is to determine the contribution of foot progression angle, a spatial gait variable that represents foot rotation in the transverse plane, to the development of neuropathic plantar ulcers in adults with diabetes mellitus and peripheral neuropathy.
Role: Principal Investigator

Promotion of Doctoral Studies (PODS) II   8/31/2013-9/01/2013
Foundation for Physical Therapy $15,000
Role: Principal Investigator

Completed

Promotion of Doctoral Studies (PODS) I   8/31/2009-9/1/2011
Foundation for Physical Therapy $15,000
This project sought to identify specific measures of foot and ankle motion during walking that could potentially be used to classify patients with diabetes mellitus and peripheral neuropathy as being at risk for the development of plantar ulcers and non-traumatic lower extremity amputation.
Role: Principal Investigator

CLINICAL EXPERIENCE

Board Certifications
- Certified Athletic Trainer, National Athletic Trainers' Association
- Certified Strength and Conditioning Specialist, National Strength and Conditioning Association

Licensure
- Missouri   Physical Therapist #2008030517

POSITIONS HELD

- **Staff Athletic Trainer**, Trident Sports Medicine and Rehabilitation.
  North Charleston, South Carolina, USA   2002-2005
  Provided injury evaluation, treatment, and referral for high school sports teams.
- **Physical Therapist Aide**, Summerville Medical Center
  Summerville, South Carolina, USA   2005
  Assisted in-patient physical therapists with transport and treatment.

- **Supplemental Athletic Trainer**, Mayo Clinic Sports Medicine
  Rochester, Minnesota, USA   2005-2008
  Provided injury evaluation, treatment, and referral for select youth and adult sporting events.

HONORS AND AWARDS

2012	Edward Bouchet Graduate Honors Society, Washington University
2012	Promotion of Doctoral Studies (PODS) II Scholarship, Foundation for Physical Therapy
2010	Laura K. Smith Promotion of Doctoral Studies (PODS) I Scholarship, Foundation for Physical Therapy
2009	Promotion of Doctoral Studies (PODS) I Scholarship, Foundation for Physical Therapy
2008	Mayo Clinic Physical Therapy Alumni Association Academic Scholarship, Mayo Clinic
2007-2008	Dr. Robert Waller Foundation Academic Scholarship/Clarence Day Foundation, Mayo Clinic
1999	Applied Life Studies Continuation Academic Scholarship, University of Illinois at Urbana-Champaign

PROFESSIONAL MEMBERSHIPS

American Physical Therapy Association
American Society of Biomechanics
Gait & Clinical Movement Analysis Society
International Society of Biomechanics

SERVICE

Manuscript Reviewer, Gait & Posture   2013-present

Executive Committee Member, Washington University in St. Louis Graduate Council	2011, 2013
Member, Policies and Services Committee, Washington University in St. Louis	2010-present
Vice-President, Black Graduate Council, Washington University in St. Louis	2011-present
Departmental Student Representative, Graduate Council, Washington University	2009-present
Minority and International Affairs liaison, Student Assembly, American Physical Therapy Association	2007
Chair/Co-founder, Student Diversity Network, Mayo Clinic School of Health Sciences	2006-2008
Representative, Student Alliance, Mayo Clinic School of Health Sciences	2006-2008
Rochester Branch Secretary/Youth Advisor, National Association for the Advancement of Colored People (NAACP)	2007-2008