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Foot and ankle mechanics in individuals with diabetes mellitus and neuropathy

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FOOT AND ANKLE MECHANICS IN INDIVIDUALS WITH DIABETES MELLITUS AND NEUROPATHY

by

Smita Rajshekhar Rao

An Abstract

Of a thesis submitted in partial fulfillment
of the requirements for the Doctor of
Philosophy degree in Physical Rehabilitation Science
in the Graduate College of
The University of Iowa

July 2006

Thesis Supervisor: Associate Professor H. John Yack

ABSTRACT:

With over 7% (20 million) people in the United States affected by diabetes mellitus (DM), DM has emerged as a significant health problem. The hallmark of DM is multi-system involvement and the lower limbs are frequently involved in the form of foot ulcers. Inability to heal foot ulcers and maintain healing contributes to the high rate of amputation seen in individuals with DM.

The development of foot ulcers has been strongly linked with mechanical stress. Changes in muscle characteristics and segmental foot mobility have been postulated to limit forward progression of the leg on the fixed foot during walking. This in turn may result in prolonged and excessive loading on the ball of the foot. However the extent and site of the impairments and their functional consequences are not well understood. The purpose of this work is to examine determinants of dynamic foot function and plantar loading in individuals with DM.

Our results revealed that in spite of differences in passive ankle dorsiflexion and stiffness, subjects with DM demonstrated ankle motion, stiffness and plantar pressures, similar to control subjects, while walking at the identical speed, 0.89 m/s (2 mph). In terms of segmental mobility, reductions were particularly dramatic in the calcaneus (20%) compared to the forefoot and first metatarsal. Decreases in frontal plane calcaneal motion were accompanied by reduced midfoot mobility. Sagittal motion of the first metatarsal and forefoot, and frontal motion of the calcaneus, in subjects with DM, was negatively associated with the magnitude of plantar loading under the respective segment. This information is important because it may help elucidate underlying mechanisms and add to our understanding of the disease process and its effects. In addition, these results may help develop more focused intervention strategies.

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CERTIFICATE OF APPROVAL

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PH.D. THESIS

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This is to certify that the Ph.D. thesis of

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To

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ABSTRACT

With over 7% (20 million) people in the United States affected by diabetes mellitus (DM), DM has emerged as a significant health problem. The hallmark of DM is multi-system involvement and the lower limbs are frequently involved in the form of foot ulcers. Inability to heal foot ulcers and maintain healing contributes to the high rate of amputation seen in individuals with DM.

The development of foot ulcers has been strongly linked with mechanical stress. Changes in muscle characteristics and segmental foot mobility have been postulated to limit forward progression of the leg on the fixed foot during walking. This in turn may result in prolonged and excessive loading on the ball of the foot. However the extent and site of the impairments and their functional consequences are not well understood. The purpose of this work is to examine determinants of dynamic foot function and plantar loading in individuals with DM.

Our results revealed that in spite of differences in passive ankle dorsiflexion and stiffness, subjects with DM demonstrated ankle motion, stiffness and plantar pressures, similar to control subjects, while walking at the identical speed, 0.89 m/s (2 mph). In terms of segmental mobility, reductions were particularly dramatic in the calcaneus (20%) compared to the forefoot and first metatarsal. Decreases in frontal plane calcaneal motion were accompanied by reduced midfoot mobility. Sagittal motion of the first metatarsal and forefoot, and frontal motion of the calcaneus, in subjects with DM, was negatively associated with the magnitude of plantar loading under the respective segment. This information is important because it may help elucidate underlying mechanisms and add to our understanding of the disease process and its effects. In addition, these results may help develop more focused intervention strategies.

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CHAPTER I: INTRODUCTION:

Overview:

Diabetes Mellitus (DM), with its escalating prevalence and incidence, has emerged as a significant health problem: over 6% of the adult population in the United States (18.2 million) is affected by DM and one million new cases are diagnosed annually (NIDDK, 2004).

The hallmark of pathology in DM is longstanding hyperglycemia, which has been linked to increased protein glycation and concomitant generation of free radicals (Dickinson, Carrington et al. 2002). The excess free radicals have been postulated to create oxidative stress leading to increased low-density lipoprotein oxidation, glycation of collagen in extracellular matrix, decreased nerve conduction velocity and decreased endoneural blood flow, thus predisposing the patient to neuropathy, atherosclerosis and increased tissue stiffness. This pathology manifests clinically in the musculoskeletal system as muscle weakness, loss of sensation, loss of range of motion and increased joint stiffness. The triumvirate of neuropathy, stiffness and repetitive loading complete a casual chain that may eventually culminating in plantar ulceration (Stokes, Faris et al. 1975; Cavanagh, Simoneau et al. 1993; Birke, Patout et al. 2000; McPoil, Yamada et al. 2001).

Plantar ulcers develop in an estimated 15% of patients with DM (Gordois, Scuffham et al. 2003). The inability to heal foot ulcers or prevent recurrence contributes to progression of the tissue degradation leading to the high rate of amputation seen in individuals with DM. Over 50% of non-traumatic lower limb amputations are performed on individuals with DM (Gordois, Scuffham et al. 2003). Along with grave consequences in terms of health and functional abilities (Price 2004), foot ulcers and amputation are often harbingers of personal and financial hardship. Factors contributing to increased

loading on the plantar aspect of the foot and thus the potential development of foot ulcers are therefore of considerable interest.

Changes in plantarflexor characteristics:

Changes in plantar flexor characteristics, specifically, limitations in ankle range of motion (ROM) and increased ankle stiffness have been postulated to limit forward progression of the leg on the fixed foot during walking, which in turn may result in prolonged and excessive loading on the ball of the foot (Van Gils and Roeder 2002). However, several issues obscure the theorized relationship between ankle characteristics and plantar loading including technical differences in the methods used to quantify stiffness, differences in criteria for determining passive end ROM and natural variations in the extent of pathology in subjects with DM (Sauseng, Kastenbauer et al. 1999; Salsich, Mueller et al. 2000; Trevino, Buford et al. 2004). A review of the literature examining functional consequences of ankle hypomobility and stiffness during walking reveals that evidence in support of the postulated relationship between ankle flexibility and plantar loading is lacking and is clouded by confounding factors (Lin, Lee et al. 1996; Armstrong, Stacpoole-Shea et al. 1999; Lavery, Armstrong et al. 2002; Mueller, Sinacore et al. 2003).

In an attempt to clarify issues (diff word? factors) that contribute to the development of ulcers two investigations were completed. In the first investigation, 25 subjects with DM were compared to a normal population of 64 adults with similar age and gender profile. Our results showed that subjects with DM have both significantly lower peak dorsiflexion ROM and higher passive ankle stiffness than non-diabetic individuals (Chapter 2). This hypomobility may have potential functional consequences in gait where 10º of dorsiflexion is normally observed (Inman, Ralston et al. 1981).

Having confirmed the existence of limitations in ROM and stiffness during static testing, a second investigation was undertaken to address the functional consequences of

these issues. We examined the relationship between ankle DF ROM and stiffness measured at rest (passively) and plantar loading during gait in individuals with DM and without DM and neuropathy. Our results showed that in spite of differences in passive ankle DF ROM and passive stiffness, dynamic measures of ankle DF ROM, stiffness and plantar pressure did not differ between groups while walking at a similar speed, 0.89 m/s (2 mph). Despite utilizing strategies such as reduced push-off (Mueller, Minor et al. 1994) and shortened stride length subjects with DM sustained plantar loads similar to control subjects suggesting the concomitant existence of other factors which may render individuals with DM vulnerable to increased plantar loading.

Changes in foot function:

Clinical studies have reported an association between factors intrinsic to the foot and plantar loading. Structural (Cavanagh, Morag et al. 1997) as well as dynamic factors (Delbridge, Perry et al. 1988; Mueller, Diamond et al. 1989; Fernando, Masson et al. 1991) have been implicated in the development of foot ulcers. Limited joint mobility and increased stiffness of the small joints of the foot have been hypothesized to limit excursion and lessen the ability of the foot to attenuate shock (Glasoe, Allen et al. 2004). These factors may contribute to the development of foot ulcers by causing abnormal pressures at susceptible sites (Delbridge, Perry et al. 1988; Fernando, Masson et al. 1991; Glasoe, Allen et al. 2004).

Gait places widely divergent demands on the foot that require it to transition from a flexible structure that dissipates impact as the foot contacts the ground to a rigid structure that allows for efficient propulsion during push-off (Saltzman and Nawoczenski 1995). To reconcile both these demands, the foot acts as a twisted osteo-ligamentous plate (Sarrafian 1987), where hindfoot eversion is accompanied by unlocking of the midfoot and concomitant first ray dorsiflexion. Due to the complex interdependence

between joints of the foot, motion at one joint can significantly impact the function/orientation of neighboring joints.

In early stance during gait, when the foot acts to attenuate shock, progressive hindfoot eversion is noted (Levangie and Norkin 2001; Neumann 2002). Hindfoot eversion serves to align the axes of the talonavicular and calcaneocuboid joints parallel to each other, increasing the amount of motion possible though the midfoot for shock absorption (Elftman 1969). At terminal stance, subtalar inversion occurs though the coupled motions of tibial rotation, ankle dorsiflexion and tightening of the plantar fascia. This in turn, effectively locks the midfoot and creates a stable platform for push-off. Inadequate hindfoot eversion has been documented in subjects with DM (Delbridge, Perry et al. 1988; Mueller, Diamond et al. 1989; Fernando, Masson et al. 1991; Arkkila, Kantola et al. 1997; Fernando and Vernidharan 1997; Duffin, Donaghue et al. 1999; Frost and Beischer 2001; Glasoe, Allen et al. 2004) and may have significant biomechanical consequences (Rosenbaum, Bauer et al. 1996) including increases in transverse tarsal joint rigidity predisposing to arthritis and lateral column over-weighting leading to stress fractures of the 4^{th} and 5^{th} metatarsals.

While the first ray is an important component of the twisted plate model of the foot, first ray mechanics in gait are still controversial. Current studies suggest that the first ray is plantarflexed during early stance and continues to dorsiflex about 10 degrees relative to the hindfoot until 70% of stance (Cornwall and McPoil 1999; Cornwall and McPoil 2002; MacWilliams, Cowley et al. 2003). However, recent evidence demonstrates minimal lowering of the proximal first metatarsal during stance (Wilken 2006) and suggesting that the excursion between the first ray and hindfoot comes predominantly from hindfoot motion. Dynamic first ray motion may be particularly important in individuals with DM because limited first ray mobility, documented in individuals with DM (Birke, Franks et al. 1995; Glasoe, Allen et al. 2004) has been hypothesized to result

in excessive loading under the medial metatarsal heads (Glasoe, Yack et al. 1999) thus predisposing to the development of foot ulcers.

Evidence confirming the functional consequences of limited joint mobility and increased stiffness in the foot is limited, partly due to the lack of biomechanical models that afford the opportunity to track segmental motion of the foot in 3D during gait. In the absence of multi-segment foot models, regression based statistical models have been implemented to determine predictors of loading (Cavanagh, Sims et al. 1991; Morag and Cavanagh 1999; Payne, Turner et al. 2002; Mueller, Hastings et al. 2003). These models provide valuable insights and help identify etiological factors on the basis of how much variance they explain in the dependent variable. However, they do not shed light on the mechanisms of action. These models often provide information that is open to interpretation and indeed may be explained in different ways. The success of this approach is predicated on the investigator's ability to offer critical variables to the regression process (Morag and Cavanagh 1999).

Results from the few studies that have used multisegment models (Nawoczenski, Baumhauer et al. 1999; Allen, Cuddeford et al. 2004) have not addressed the relationship between foot mobility and plantar loading during gait. Further, these studies were conducted on non-DM subjects with intact sensation, their extrapolation to subjects with DM who have different impairments in terms of foot structure and mobility may not be valid.

Thus, while foot mobility has been identified as an important potential contributor to foot function and loading, especially in individuals with DM, its role in gait remains poorly understood. The purpose of our study is to examine segmental foot mobility and its consequences during gait in subjects with and without DM. This work is based on a theoretical construct similar to our previous work where we sought to test a clinical hypothesis using experimental evidence. This work includes additional factors which may influence plantar loading with the intent of providing a more complete picture.

SPECIFIC AIMS, HYPOTHESES AND RATIONALE:

Specific Aim 1:

To examine hindfoot function during gait in subjects with and without DM, using a multisegment foot model.

Hypotheses:

In the first 20% of stance, compared to non-diabetic control subjects, subjects with DM will demonstrate reduced hindfoot frontal plane (eversion) range of motion.

Rationale:

Subjects with DM have reduced passive subtalar joint mobility (Mueller, Diamond et al. 1989; Fernando, Masson et al. 1991), as a result of which, they may be expected to demonstrate reduced eversion range of motion. Hindfoot eversion allows the foot to attenuate shock (Root, Orien et al. 1977; Hunt and McPoil 1995) and loss of hindfoot motion may serve as an important functional marker of loss of foot flexibility.

Specific Aim 2:

To examine first ray kinematics during gait in subjects with and without DM, using a multisegment foot model.

Hypothesis:

I. Compared to non-diabetic control subjects, subjects with DM will demonstrate reduced first ray sagittal plane (dorsiflexion) range of motion during gait.

II. Magnitude and timing of first ray motion during stance will be related to plantar fascia thickness.

Rationale:

Subjects with DM have reduced first ray motion (Birke, Franks et al. 1995; Glasoe, Allen et al. 2004). Reduction in first ray mobility has been attributed, in part to

increased plantar fascia thickness in subjects with DM (D'Ambrogi, Giurato et al. 2003; Bolton, Smith et al. 2005; Giacomozzi, D'Ambrogi et al. 2005). Increased plantar fascia thickness and reduced first ray mobility may be expected to manifest during as reduced first ray dorsiflexion.

Specific Aim 3:

To uncover differences in foot loading between subjects with and without DM.

Hypothesis:

I. Subjects with DM will demonstrate increased plantar loading compared to non-DM subjects.
II. In subjects with DM, the magnitude of hindfoot loading will be negatively associated with hindfoot range of motion in early stance, while in terminal stance, the magnitude of first metatarsal head loading will be negatively associated with first ray range of motion.

Rationale:

Subjects with DM may be expected to have impaired control of deceleration of the foot during initial contact resulting in higher energy absorption demands placed on the heel. Changes in foot-floor contact patterns and plantar soft tissues (Gooding, Stess et al. 1986; Hsu, Wang et al. 2000; Hsu, Lee et al. 2002) may be anticipated to result in impaired impact attenuation leading to higher hindfoot loading.

Limitations in first ray mobility and thickened plantar fascia may hinder the progression of body weight over the fixed foot resulting in increased loads sustained under the head of the first metatarsal.

SIGNIFICANCE:

Participation in regular physical activity such as walking offers considerable health benefits to subjects with DM (Gregg, Gerzoff et al. 2003; Laaksonen, Lindstrom et

al. 2005). It is imperative to realize however, that repetitive plantar loading sustained during everyday dynamic activities such as walking may predispose individuals with DM to tissue injury at susceptible sites.

The goal of our study is to bridge the gaps in our understanding related to dynamic foot function and plantar loading in individuals with DM. By integrating imaging and kinematic modeling technology we seek to use an intuitive and innovative approach to obtain original and valuable insights into mechanisms underlying plantar loading.

These results are important because they may help clarify coexistent changes that vary by site and in magnitude. The ability to uncover changes in foot function may provide a powerful tool to evaluate discrete factors contributing independently to plantar loading in individuals with DM. This approach may also be used to evaluate changes in the foot function over time, and in response to intervention. Delineating the site and magnitude of factors affecting foot function may further our understanding of their potential role in foot loading and ulcer formation. Our findings may be applied to help develop more focused intervention and prevention strategies, specific to the underlying tissue and its magnitude of involvement.

Assumptions and Limitations:

1. The kinematic model is based on the assumption that segments of the skeletal system can be modeled as rigid bodies and tracked using surface markers. To address this issue, we seek to apply a previously validated multi-segment foot model that allows us to capture key features of interest.
2. Since the study deals with a clinical population, results are generalizeable only to the extent that the sample represents the population of interest.

CHAPTER II:

DIABETES MELLITUS SUBJECTS HAVE HIGHER PASSIVE ANKLE STIFFNESS AND LOWER DORSIFLEXION RANGE OF MOTION

Introduction:

Just over 6% (18.2 million) people in the United States are affected by diabetes mellitus (DM) (National Institute of Diabetes and Digestive and Kidney Diseases 2004). The disease impacts many organ systems and often has dire consequences associated with substantial morbidity and mortality (Price 2004). Involvement of the lower extremity typically starts in the plantar sole of the foot where ulcers develop in an estimated 15% of patients (Gordois, Scuffham et al. 2003) The inability to effectively treat foot ulcers contributes substantially to the high rate of amputations seen in this population (Reiber, Lipsky et al. 1998).

Foot ulcers have been hypothesized to result from repetitive mechanical stress imposed on insensitive and often morphologically changed feet. Repetitive, abnormally high loading may overwhelm the ability of the soft tissue to respond and may culminate in ulceration (Brand 1981; Reiber, Vileikyte et al. 1999). Understanding factors contributing to excessive loads on the plantar aspect of the foot is therefore of considerable interest.

Loss of dorsiflexion range of motion (ROM) at the ankle and increased stiffness in the triceps surae musculature have been implicated as potential factors contributing to increased loading of the forefoot (Fernando, Masson et al. 1991). According to this theory, changes in muscle characteristics limit forward progression of the tibia over the

fixed foot during the stance phase of gait, resulting in early heel rise and increased loading on the metatarsal heads (Van Gils and Roeder 2002). Attempts to document changes in soft tissue associated with DM have had mixed results. Limitations in dorsiflexion ROM (Salsich, Mueller et al. 2000) or increased ankle stiffness (Trevino, Buford et al. 2004) have been reported in subjects with DM. However, technical differences in the methods used to quantify stiffness, differences in criteria for determining passive end ROM and natural variations in the extent of pathology in subjects with DM, may account for ostensible differences in the reported results (Sauseng, Kastenbauer et al. 1999; Salsich, Mueller et al. 2000; Trevino, Buford et al. 2004).

An additional confounding factor that likely influences ankle ROM and stiffness is knee position at the time of measurement. Salsich et al measured ankle characteristics with the knee in 10 degrees of flexion while Trevino et al. held the knee in 20-25 degrees of flexion. With the knee fully extended the biarticular gastrocnemius contributes maximally to end range control of passive dorsiflexion. However, as the knee flexes the contribution of the gastrocnemius muscle is reduced and the passive contribution of the soleus muscle increases (Sale, Quinlan et al. 1982). Varying degrees of knee flexion may capture varying combinations of gastrocnemius and soleus contributions to ankle stiffness.

The purpose of our study was to compare ankle ROM and stiffness, in individuals with DM and non-diabetic control subjects, and to document the effect of knee flexion and the severity of the pathology on ankle ROM and stiffness. Examining ankle motion in light of some of the factors that may confound the interpretation of muscle function

will enable us to obtain a clearer impression of mechanical changes that are associated with DM.

Methods:

Subjects:

In accordance with Institutional Review Board and HIPAA guidelines, Informed Consent was sought and study procedures were instituted. Twenty five individuals with diabetes mellitus and 64 non-diabetic individuals with similar age and gender profile participated in this study. Inclusion criteria for subjects with DM: Diagnosis of DM, No current or previous ipsilateral foot ulcer, great toe or transmetatarsal amputation, Absence of ipsilateral or contralateral Charcot neuroarthropathy. Inclusion criteria for subjects in the control group: Non-diabetic, No lower extremity pain or musculoskeletal pathology or history thereof in the last six months. Subject characteristics are summarized in Table 2.1.

Ankle ROM and stiffness testing:

Passive ankle ROM was measured at specific torque levels with the "IAROM" device. This device has been shown to be valid and reliable. Detailed description of the device and methods are provided in Wilken et al (Wilken, Saltzman et al. 2004). Briefly, subjects were positioned supine with the knee extended; their leg was supported by a base plate and a foam block; and secured by Velcro straps. The sole of their foot was positioned so contact was maintained to a translucent Plexiglas foot plate throughout testing. The axis of rotation of the device was then adjusted in the antero-posterior and

superior/inferior directions to approximate the ankle axis of rotation determined by palpation of the distal tips of the medial and lateral malleoli (Hicks 1953).

Torques of 15, 20 and 25 Nm were applied using a hand held force gauge (FDK 40, Wagner Instruments, Greenwich, CT) and resultant angular kinematics were measured using a digital inclinometer (Checkpoint Inc., Torrance, CA). Figure 2.1 shows the apparatus and setup. The inclinometer was referenced to the tibial crest and then mounted on the foot plate which was parallel to the sole of the foot. Three cycles of testing were performed in ascending order of force application and resultant peak DF ROM was recorded at each force level. Next, the knee was flexed to approximately 20 degrees by raising the leg plate by about 3 inches. This inclined position of the leg plate was maintained and ROM testing was repeated at the three force levels. Knee flexion to about 20 degrees was selected since it represents the magnitude of knee flexion utilized during walking (Winter 1984). Ankle stiffness was calculated as the slope of the resultant curves over the 15-25 Nm intervals.

Statistical testing:

A two sample t test was used to assess differences between the two groups (α=0.05). Pearson product moment correlation was used to assess the relationship between variables of interest. Statistical significance (H_o: ρ=0) and equality of correlations (H_o: $\rho_1=\rho_2$) were assessed using approximate tests based on Fisher's Z transformation (α=0.05).

Results:

Subjects with DM attained considerably lower peak dorsiflexion ROM and higher passive ankle stiffness than non-diabetic controls. These results were seen at all three force levels and with the knee flexed as well as extended (Table 2.2).

Within group analyses showed that women without DM had greater peak DF than men without DM, subjects with DM showed similar trends. Ankle stiffness did not differ between genders in either group (Table 2.3).

Knee flexion, in both groups, was accompanied by a significant increase in peak dorsiflexion ROM at all three force levels but not in stiffness. (Data from Table 2.2: For subjects with DM: at 15, 20 and 25 Nm, $p < 0.004$, $p < 0.003$, $p < 0.002$, stiffness: $p = 0.35$. For non-diabetic subjects, at 15, 20 and 25 Nm, $p < 0.001$, $p < 0.001$, $p < 0.001$, stiffness: $p = 0.642$)

Ankle stiffness with the knee extended was significantly associated with ankle stiffness with the knee flexed in subjects with DM, as well as in non-diabetic individuals ($r^2 = 0.57$ and 0.52 in subjects with and without DM, respectively, $p < 0.01$).

Ankle stiffness in subjects with DM was not associated with body mass ($r^2 = 0.21$ and 0.15 with knee extended and flexed, $p = 0.45$ and 0.38 respectively), age ($r^2 = 0.25$ and 0.22 with knee extended and flexed, $p = 0.52$ and 0.48 respectively) or height ($r^2 = 0.13$ and 0.23 with knee extended and flexed, $p = 0.87$ and 0.73 respectively). Similarly, in non-diabetic controls: ankle stiffness was not associated with body mass ($r^2 = 0.06$ and 0.01 with knee extended and flexed, p = 0.89 and 0.77 respectively), age ($r^2 = 0.01$ and 0.00 with knee extended and flexed, $p = 0.95$ and 0.97 respectively) or height ($r^2 = 0.16$ and 0.21 with knee extended and flexed, $p = 0.65$ and 0.78 respectively).

In subjects with DM, HbA1c levels and duration of DM showed fair association with ankle stiffness in the knee extended position (r^2 = 0.48 and 0.24 respectively, p <0.01 for both).

Discussion:

The key findings of our study demonstrate that subjects with DM have both significantly lower peak dorsiflexion range of motion and higher passive ankle stiffness than non-diabetic individuals. While it might be speculated that there would be an association between decrements in ROM and increased stiffness in the DM population, as far as we know this study is the first to confirm this association. In subjects with DM, we also found a positive association between the extent of the pathology and the magnitude of changes in the mechanical characteristics of the plantarflexors. In both study groups, knee flexion was accompanied by an increase in peak dorsiflexion ROM but not in ankle stiffness highlighting the importance of controlling knee flexion when testing ankle range of motion.

Our results, demonstrating significant limitations in dorsiflexion range of motion in subjects with DM, are comparable with previous investigations (Salsich, Mueller et al. 2000; Moseley, Crosbie et al. 2001). In addition, by using measures with established validity and inter-rater reliability we believe we were better able to establish the strength of this relationship and minimize any potential risk due to experimental bias 15. Salsich et al., documented peak dorsiflexion of 10±5 and 17±4 degrees in subjects with and without DM respectively. The limitations in ROM distinguish the DM patient population as having many more individuals who are classified as hypomobile. Using a conventional clinical criterion of limitation of ankle ROM to 10 degrees of dorsiflexion or less (Riddle

1994) 12.5% of control subjects and 56% of subjects with DM would be classified as hypomobile. Alternatively, using norm-referenced values of dorsiflexion (Moseley, Crosbie et al. 2001), (collected at 12 Nm compared to our values collected at 15 Nm), indicates that our control group would be classified as follows: hypomobile (6.25%), inflexible (30%), normal (58.75%) and flexible (2.5%) categories, while our subjects with DM would be classified as: hypomobile (40%), inflexible (44%), normal (12%), and flexible (4%). This hypomoblity has potential functional consequences in gait where 10º of dorsiflexion is normally observed (Inman, Ralston et al. 1981).

Given the mean 41% loss in dorsiflexion excursion documented in this study, it seems likely that changes in the muscle account for part, if not most of the lost ROM. Deficit in range of ankle motion has been explained as a consequence of shortened plantar flexors, with the gastrocnemius having a dominant role as the knee approaches full extension (Salsich, Mueller et al. 2000). Within the gastrocnemius muscle tendon unit, sites of limited excursion could be either in the tendon or in the muscle belly. Estimating a muscle-tendon excursion of 2.3 cm through 25 degrees of angular ankle movement (Maganaris, Baltzopoulos et al. 2000; Maganaris 2004) tendon elongation would contribute less than 30% of the total length change (Muraoka, Muramatsu et al. 2002). Muscle changes are more likely the predominant cause of dorsiflexion limitation in DM. Individuals with DM may lose contractile protein due to the protein catabolic effect of ineffective insulin action and diabetic neuropathy with subsequent muscle atrophy (Powers 2004). Evidence for loss of sarcomeres in parallel comes from studies that have documented reduction of peak torque generating capacity of the plantarflexors in individuals with DM and a concomitant positive association between plantarflexor

strength and stiffness (Mueller, Minor et al. 1994). Reduction in the number of sarcomeres in parallel would tend to reduce passive stiffness but may be accompanied by a change in the ratio of connective to contractile tissue. The increase in the proportion of connective tissue is a quantitative change, which, accompanied by qualitative changes such as increased collagen cross-linking may contribute to increased passive stiffness documented in our results. Subjects with DM often use less ankle motion during functional activities (Mueller, Minor et al. 1994) suggesting that their plantarflexors may function in a smaller range compared to non-diabetic individuals and that this may lead to associated muscle accommodations such as fiber shortening.

Our findings of increased stiffness at the ankle in subjects with DM are consistent with the findings of other studies that have measured foot and ankle stiffness in this patient population (Birke, Franks et al. 1995; Glasoe, Allen et al. 2004; Trevino, Buford et al. 2004). The increased stiffness in our DM subjects as compared with Trevino et al (0.016 versus 0.0118 Nm/kg.degree, units express ankle stiffness normalized to body mass to allow for comparison between studies) may reflect intrinsic differences in our study groups, where Trevino at al were more exclusive, screening their subjects for vascular and neurological dysfunction or may be due to differences in methodology.

Higher passive ankle stiffness in subjects with DM indicates that the plantarflexors are more resistant to elongation. Resistance to passive elongation is attributed to changes in the properties of the contractile element and elastic elements of the plantarflexors. Increased fibril density has been documented in the series elastic element (Achilles tendon) and has been hypothesized to lead to increased tendon stiffness (Grant, Sullivan et al. 1997). A stiffer tendon will result in a greater proportion of the

applied torque being taken up by the contractile and parallel elastic elements. Abnormal collagen cross-linking secondary to nonenzymatic glycosylation has been shown in subjects with DM (Kesava Reddy 2003) and may be another way in which subjects with DM manifest as increased stiffness.

Ankle stiffness appears influenced by diabetic control. We found that glycemic control and duration of diabetes account for 48 and 24% of the variance in ankle stiffness respectively. These findings are consistent with the work of Lavery et al who showed that presence of equinus was positively associated with duration of diabetes (Lavery, Armstrong et al. 2002).

Our results revealed that ankle stiffness with the knee extended explained 60 per cent of the variance in ankle stiffness with the knee flexed. The gastrocnemius, therefore, emerges as the predominant factor influencing the mechanical behavior of the plantarflexors in the 0-20 degree range of knee flexion. Further studies seeking to examine the association between ankle stiffness with knee extended and in varying degrees of knee flexion are needed.

In conclusion, our results demonstrated that subjects with DM have significantly lower peak dorsiflexion ROM and higher passive ankle stiffness than non-diabetic individuals. The gastrocnemius emerged as the predominant factor responsible for ankle stiffness in 0-20 degree range of knee flexion in both groups. Further studies are required to examine the relationship between passive ROM and stiffness and the contribution of these variables to the formation of plantar ulcers in patients with diabetes mellitus.

	DM	***Control***
	Mean± SD	Mean± SD
N	25	64
Age	54±11	53±9
Gender F:M	10:15	26:38
Height (m)	1.71±0.09	1.71±0.11
Mass (kg)	96.4±26.0	86.6±15.2
HbA1C	8.2±1.8	
Type 2	20 (80%)	
Duration (yrs)	13±11	

Table 2.1: Demographic data from study and control groups.

		DM		*Control*		
		Mean	***SD***	***Mean***	***SD***	***p values***
Knee extended						
Peak	15 Nm	5.1	8.2	11.5	5.4	*<0.001*
Dorsiflexion	20 Nm	9.8	8.1	17.5	6.2	*<0.001*
	25 Nm	13	8.3	20.8	5.7	*<0.001*
Ankle stiffness		1.505	0.388	1.012	0.138	*<0.001*
Knee flexed						
Peak	15 Nm	11.6	8.1	18.3	6.3	*<0.001*
dorsiflexion	20 Nm	16.5	8.0	24	6.1	*<0.001*
	25 Nm	20	8.0	27.5	5.9	*<0.001*
Ankle stiffness		1.282	0.442	0.990	0.126	*<0.001*

Table 2.2: Between group comparison of peak dorsiflexion and passive ankle stiffness. Units: Peak dorsiflexion: degrees, Ankle stiffness: Nm/degree.

	Group	DM Female	DM Male	*P value*	CTRL Female	CTRL Male	*P value*
Knee extended							
Peak	15 Nm	8.2±9.0	2.1±7.0	*0.059*	13.4±4.6	10.2±5.6	*<0.001*
dorsi	20 Nm	12.8±8.6	6.6±7.3	*0.064*	18.7±4.4	16.6±7.1	*0.009*
flexion	25 Nm	16.0±9.1	9.6±7.2	*0.07*	22.8±4.6	19.1±6.1	*0.004*
Ankle stiffness		1.59±0.22	1.43±0.51	*0.319*	1.01±0.10	1.02±0.13	*0.909*
Knee flexed							
Peak	15 Nm	15.4±8.8	6.0±6.6	*0.026*	20.7±5.4	16.7±6.4	*0.001*
dorsi	20 Nm	19.5±9.1	11.3±6.7	*0.068*	26.3±5.6	22.5±6.1	*0.001*
flexion	25 Nm	22.1±9.0	14.6±7.1	*0.143*	29.6±5.5	26.2±5.8	*0.02*
Ankle stiffness		1.36±0.33	1.21±0.52	*0.433*	0.92±0.11	0.90±0.13	*0.704*

Table 2.3: Within group analysis of peak dorsiflexion and passive ankle stiffness in subjects with and without DM. Units: Peak dorsiflexion: degrees, Ankle stiffness: Nm/degree.

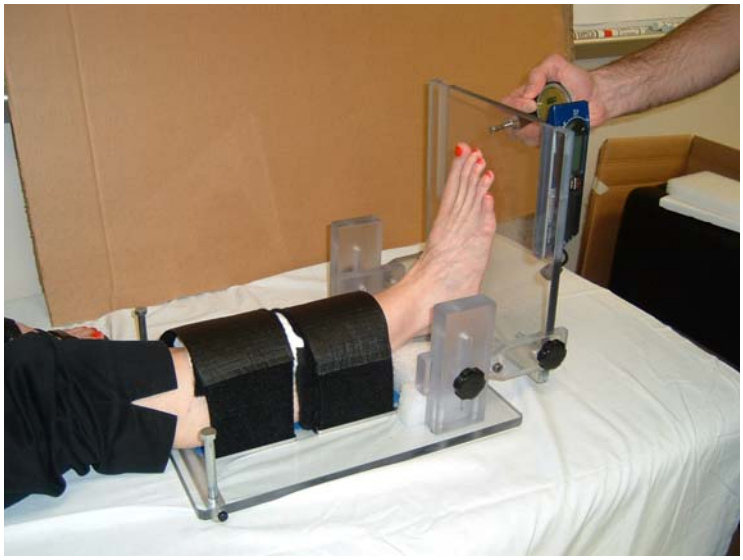


Figure 2.1: Apparatus and set up for Ankle ROM and stiffness testing

CHAPTER III:

ANKLE ROM AND STIFFNESS MEASURED AT REST AND DURING GAIT IN INDIVIDUALS WITH AND WITHOUT DIABETES AND NEUROPATHY

Introduction:

Abnormal plantar loading (Veves, Murray et al. 1992) is thought to contribute to the development of foot ulcers in individuals with diabetes mellitus (DM) where the estimated incidence is up to 20% of all individuals with DM (Reiber, Lipsky et al. 1998). Inability to heal foot ulcers or prevent recurrence contributes to progression of the local pathology, leading to the high rate of amputation seen in individuals with DM. Over 50% of non-traumatic lower limb amputations are performed on individuals with DM (Gordois, Scuffham et al. 2003). Along with grave consequences in terms of health and functional abilities (Price 2004), foot ulcers and amputation are often harbingers of personal and financial hardship. Factors contributing to increased loading on the plantar aspect of the foot and thus the potential development of foot ulcers are therefore of considerable interest.

Recent studies have implicated limited dorsiflexion (DF) range of motion (ROM) and increased ankle stiffness as key factors contributing to increased plantar loading (Lin, Lee et al. 1996; Armstrong, Stacpoole-Shea et al. 1999; Hastings, Mueller et al. 2000; Lavery, Armstrong et al. 2002; Lavery, Armstrong et al. 2003; Mueller, Sinacore et al. 2003). Limited ankle DF ROM and/or increased stiffness have been hypothesized to restrain forward progression of the tibia on the fixed foot during the stance phase of walking. This in turn may result in prolonged and excessive weight bearing stress under the metatarsal heads.

Evidence in support of the postulated relationship between ankle flexibility and plantar loading is limited, and predominantly comes from studies demonstrating improved ulcer healing following Achilles tendon lengthening surgery (Lin, Lee et al. 1996; Armstrong, Stacpoole-Shea et al. 1999; Hastings, Mueller et al. 2000). These studies have reported 9-18 degrees improvement in DF ROM with concomitant 27-46% reduction in forefoot plantar pressure 2-7 months following tendo-Achilles lengthening (Armstrong, Stacpoole-Shea et al. 1999; Mueller, Sinacore et al. 2003). However, after surgery, subjects may modulate foot pressures by altering their gait using different approaches, such as preferentially loading the non-operated limb, changing walking strategy, and reducing walking speed. In these circumstances, factors other than intervention may influence the reported relationship between ankle DF ROM and plantar loading. Further, longitudinal studies of subjects who have undergone tendon Achilles lengthening demonstrate that while improvements in ankle DF ROM are maintained seven months post-operatively (Mueller, Sinacore et al. 2003), plantar loading increased to values close to those measured preoperatively suggesting a disconnect between ankle DF ROM and loading.

Cross-sectional studies seeking to examine the relationship between mechanical properties of the ankle and plantar loading have found that subjects with reduced passive ankle ROM sustain significantly higher plantar pressures during walking (Salsich and Mueller 2000; Lavery, Armstrong et al. 2002; Zimny, Schatz et al. 2004). However, these studies did not control walking speed, which has been shown to influence both, ankle motion (Kirtley, Whittle et al. 1985; van der Linden, Kerr et al. 2002) as well as plantar loading during gait (Burnfield, Few et al. 2004; Segal, Rohr et al. 2004; Warren, Maher et al. 2004). Walking speed thus emerges as a confounding factor, rendering interpretation of purported results difficult.

Experimental studies investigating structural and functional predictors of regional plantar loading have revealed that subjects who tend to walk with larger dynamic ankle

ROM experience higher forefoot plantar pressures (Morag and Cavanagh 1999). These findings, albeit from non-diabetic individuals, highlight the importance of dynamic ROM; however they do not relate dynamic ROM to available (passive) ROM. The relationship between dynamic ROM utilized in gait and passive ROM thus emerges as an important potential factor contributing to plantar loading but has not been elucidated in individuals with DM.

The purpose of our study was to examine the relationship between ankle DF ROM and stiffness measured at rest (passively) and plantar loading during gait in individuals with DM and without DM and neuropathy. Specifically, we sought to address three questions: i. Does peak passive DF ROM predict ankle DF ROM used during gait? ii. Does passive ankle stiffness predict ankle stiffness used during gait? iii. Are any of the passive or gait ankle measures associated with plantar loading? We hypothesized that passive ankle DF ROM and stiffness would predict ankle DF ROM and stiffness during gait in individuals with DM but not in non-diabetic individuals. We expected that passive ankle DF, ROM and passive ankle stiffness would be associated with plantar loading in subjects with DM but not in non-diabetic individuals.

Methods:

All procedures were approved by the Institutional Review Board at the University of Iowa Hospitals and Clinics. Inclusion criteria for subjects with DM: diagnosis of DM, no current or history of previous ipsilateral foot ulcer, great toe or transmetatarsal amputation, absence of ipsilateral or contralateral Charcot neuroarthropathy. Presence of neuropathy was documented using 5.07 Semmes-Weinstein monofilaments. Subjects in the non-diabetic control group were matched in age and gender to subjects with DM and were screened for lower extremity pain or musculoskeletal pathology or history thereof in the last six months. Ten subjects with DM (mean age: 56±11 years, mean body mass: 96.6±31.2 kg, mean height: 1.74±0.1 m, M:F ratio: 6:4) and ten non-diabetic control

subjects (mean age: 54±8 years, mean body mass: 76±14.8 kg, mean height: 1.71±0.09 m, M:F ratio: 6:4) participated in this study. The study and control groups did not differ in age (p=0.52), body mass (p=0.09) or height (p=0.53). Subject characteristics documented in the DM group included: Average duration of DM (20±11 years), Type of DM: 80% Type 2 DM and glycemic control (most recent HbA1C: 8.1±1.2 %).

Passive testing:

Passive ankle ROM and stiffness at specific torque levels was measured using the Iowa Ankle ROM device which has been shown to be valid and reliable (Wilken, Saltzman et al. 2004). Detailed description of the device and methods are provided in Wilken et al (2004). Briefly, subjects were positioned supine with the knee extended; their leg was supported by a base plate and a foam block; and secured by Velcro straps. The sole of their foot was positioned so contact was maintained with a translucent Plexiglas foot plate throughout testing. The axis of rotation of the device was then adjusted in the antero-posterior and superior/inferior directions to approximate the ankle axis of rotation determined by palpation of the distal tips of the medial and lateral malleoli (Hicks 1953). Torques of 15, 20 and 25 Nm was applied using a hand held force gauge and resultant angular kinematics were measured using a digital inclinometer. Three cycles of testing were recorded at each force level. Next, the knee was flexed to approximately 20 degrees and ROM testing was repeated at the three force levels. Passive ankle stiffness was calculated as the slope of the resultant curves over the 15-25 Nm intervals.

Gait testing:

Kinematic and kinetic data were recorded as subjects walking along 10 m walkway at 0.89 m/s (2 mph) in their customary footwear. Previous studies have documented walking velocities between 0.77-1.26 m/s in subjects with DM (Mueller, Minor et al. 1994; Salsich and Mueller 2000; Maluf, Mueller et al. 2004), therefore 0.89

m/s (2 mph) was chosen as a comfortable walking speed, representative of preferred walking speed in subjects with DM. Kinematic data were recorded at 60 Hz using an active marker system (Optrotrak, NDI, Waterloo, Canada). Three infra-red markers were placed in a non collinear arrangement on the subject's foot (over shoe), leg and thigh segments. Kinetic data were collected at 240 Hz using a forceplate embedded in the walkway (Kistler Inc, NY). Plantar pressure data were collected at 50 Hz using pressure sensitive insoles (Pedar, Novel Inc, Minneapolis, MN).

Kinematic and kinetic data were processed using Kingait (Mishac Kinetics, University of Waterloo, Canada) software. Data were low pass filtered with a cut-off frequency of 6 Hz using a fourth order butterworth filter. Anatomical coordinate systems were established using standard criteria (Wu, Siegler et al. 2002). Sagittal ankle kinematics and kinetics were calculated. Peak dorsiflexion achieved during gait was obtained using sagittal ankle kinematics. Duration of second rocker was identified. Ankle stiffness during second rocker was defined using the method defined by (Davis and DeLuca 1996).

Data analysis:

A two sample t test was used to assess differences between the two groups (α=0.05). Pearson product moment correlation (r) was used to assess the relationship between variables of interest. Statistical significance (H_o: ρ=0) and equality of correlations (H_o: $\rho_1=\rho_2$) were assessed using approximate tests based on Fisher's Z transformation (α=0.05).

Results:

Passive testing:

Subjects with DM showed significantly lower peak passive dorsiflexion and higher passive ankle stiffness compared to age matched control subjects (Table 3.1).

Peak passive ankle dorsiflexion was not associated with peak ankle dorsiflexion attained during gait in either group, (H_o: $\rho=0$, $p=0.67$ and $p=0.98$, DM and control groups respectively, H_o: $\rho_1=\rho_2$, $p=0.49$, Figure 2). Passive ankle stiffness was not significantly associated with ankle stiffness during second rocker (H_o: $\rho=0$, $p=0.84$ and $p=0.17$, DM and control groups respectively, H_o: $\rho_1=\rho_2$, $p=0.20$, Figure 3.3).

Associations between passive ankle measures and subject characteristics are summarized in Table 3.2.

Gait testing:

Peak dorsiflexion attained during gait, ankle stiffness during second rocker and peak plantar pressure at the forefoot did not differ between groups as they walked at identical speed (Table 3.1). Subjects in the control group showed trends towards higher peak plantarflexor moment and peak ankle power generation in the sagittal plane (Figure 3.1).

Passive ankle stiffness, peak passive dorsiflexion, peak dorsiflexion used in gait and ankle stiffness used in gait associated did not show a significant relationship with peak forefoot plantar pressures in either group (Table 3.3). Stride length was associated with plantar pressure in both groups. Stride length was associated with ankle stiffness during second rocker and total ankle ROM utilized during gait in subjects with DM but not in non-diabetic control subjects (Table 3.3).

Discussion:

The main findings of our study demonstrated that subjects with DM have reduced ankle DF ROM and increased stiffness compared to non-diabetic control subjects. To our knowledge this is the first reported study showing both increased stiffness and reduced dorsiflexion ROM in subjects with DM. However, in spite of differences in passive ankle DF ROM and stiffness, subjects with DM demonstrated ankle motion, stiffness and

plantar pressures, similar to control subjects, while walking at the same speed, 0.89 m/s (2 mph).

Clinical measures of ankle DF ROM and stiffness obtained in this study are consistent with previous reports documenting reduced ankle DF ROM (Mueller, Minor et al. 1994; Lavery, Armstrong et al. 2002) and increased stiffness (Trevino, Buford et al. 2004) in subjects with DM. Changes in ankle DF ROM and stiffness in individuals with DM have been attributed to disease-dependent as well as use-dependent processes. Disease-dependent mechanisms involve non-enzymatic glycation of collagen due to the underlying metabolic disorder (Grant, Sullivan et al. 1997). Use-dependent mechanisms allude to adaptive fiber shortening within the triceps surae (Mueller, Minor et al. 1994), 1994). Qualitative changes in connective tissue stiffness as well as quantitative changes related to changes in the ratio of connective tissue to contractile tissue may contribute to increased ankle stiffness in individuals with DM.

In spite of differences in passive ankle DF ROM and passive stiffness, we found that dynamic measures of ankle DF ROM, stiffness and plantar pressure did not differ between groups while walking at a similar speed, 0.89 m/s (2 mph). However, subjects with DM walked with significantly shorter stride lengths and showed trends towards lower plantar flexor moments and peak power generation compared to non-diabetic control subjects. Shorter stride lengths decrease the forward excursion of the center of pressure (Giacomozzi, Caselli et al. 2002) which will effectively reduce the ankle moment and the ankle power. Reduced plantar flexor moment and power at push off have also been described in subjects with DM as an attempt to provide the major positive work at push-off using their hip flexors (Mueller, Minor et al. 1994). In agreement with previous reports, our results suggest that subjects with DM may utilize different strategies, such as shortened stride length and reduce push-off, compared to non-diabetic control subjects to achieve identical functional goals, in this case, to ambulate at a given speed.

Dynamic ankle motion, stiffness and plantar loading measures obtained in our study agree with previous reports of dynamic ankle DF ROM (Maluf, Mueller et al. 2004), ankle stiffness (Salsich and Mueller 2000) and plantar pressures, at comparable walking speeds ranging from 0.77- 0.89 m/s. In an attempt to recreate subjects' habitual walking performance and improve external validity, all testing was performed with customary footwear. In contrast to previous studies, walking speed was controlled in this study because preferred speed in subjects with DM may be significantly slower compared to non-diabetic controls (Mueller, Minor et al. 1994; Katoulis, Ebdon-Parry et al. 1997; Salsich and Mueller 2000). Walking speed influences ankle kinematics and kinetics (Kirtley, Whittle et al. 1985; van der Linden, Kerr et al. 2002) and also differentially affects plantar pressures in different regions of the foot (Burnfield, Few et al. 2004; Segal, Rohr et al. 2004; Warren, Maher et al. 2004).

Contrary to our hypotheses, passive ankle DF ROM and stiffness did not predict peak DF ROM and ankle stiffness utilized during gait. While passive ankle DF ROM varied between subjects, during gait, similar to previous studies (Riddle 1994), all subjects attained approximately 10 degrees peak DF ROM (range: 5-15 degrees). Analysis of ankle stiffness revealed similar findings. These results indicate that clinical measures of heel cord tightness and stiffness do not represent ankle motion or stiffness utilized during functional activities of daily living such as gait.

To evaluate the possibility that subjects may alter the contribution of the biarticular gastrocnemius muscle to ankle DF ROM and stiffness through knee flexion (Orendurff, Rohr et al. 2005), we examined peak knee flexion attained in early and midstance. Our data, consistent with previous reports (Katoulis, Ebdon-Parry et al. 1997), showed that subjects with DM and neuropathy utilize similar ranges of knee motion in early stance compared to non-diabetic controls. Further, associations between passive ankle measures obtained with the knee flexed (~15-20 degrees) and gait measures were similar to those documented with the knee in an extended position. These findings argue

against the role of limited passive DF on alterations in stance phase knee flexion as a potential mechanism that may influence the contribution of the biarticular gastrocnemius muscle on ankle stiffness or motion utilized during walking.

A second purpose of this study was to examine whether passive or gait ankle measures are associated with plantar loading. We found that while neither passive nor dynamic DF ROM or ankle stiffness were significantly associated with plantar loading, stride length was positively associated with plantar pressure in both groups. Our findings underscore the role of stride length (Zhu, Wertsch et al. 1995; Brown and Mueller 1998) as a mechanism influencing forefoot loading, even when walking velocity is controlled. We also found that longer stride lengths were accompanied by increased dynamic ankle motion and gait stiffness in subjects with DM but not in non-diabetic controls. Thus, while we found evidence for a hip strategy, our data suggest that ankle parameters are potentially linked with stride length in subjects with DM.

In summary, we found that in spite of differences in passive ankle DF ROM and stiffness, subjects with DM demonstrated ankle motion, stiffness and plantar pressures, similar to control subjects, while walking at the identical speed, 0.89 m/s (2 mph). These data indicate that clinical measures of heel cord tightness and stiffness do not represent ankle motion or stiffness utilized during functional activities of daily living such as gait. Our findings suggest that subjects with DM utilize strategies such as short stride length and reduced push off to modulate plantar loading. Further studies are needed to explore the relationship between ankle flexibility and plantar loading in a wide spectrum of subjects with DM in whom ulcer formation may be problematic.

	DM	*Ctrl*	*P value*
Peak passive DF (degrees)	6.4±6.9	19.3±3.9	<0.001
Peak passive DF ^{KF} (degrees)	13.1±4.2	24.1±5.5	<0.001
Peak DF during gait (degrees)	9.9±2.0	11.8±2.7	0.099
Peak knee flexion in mid-stance (degrees)	12.5±6.6	14.8±8.8	0.167
Passive ankle stiffness (Nm/degree)	1.5±0.49	1.042±0.56	0.001
Passive ankle stiffness ^{KF} (Nm/degree)	1.508±0.43	1.021±0.47	0.04
Ankle stiffness during second rocker (Nm/degree)	6.526±1.3	6.161±1.753	0.603
Stride length (m)	1.06±0.1	1.21±0.07	0.001
Peak Pressure (N/cm^2)	27.2±6.1	24.6±1.5	0.207
Peak plantar flexor moment (Nm/kg)	1.21±0.18	1.40±0.25	0.06
Peak dorsiflexor moment (Nm/kg)	0.19±0.12	0.15±0.04	0.383
Peak ankle sagittal power (Nm/kg*s)	1.64±0.47	2.00±0.43	0.08
Walking velocity (m/s)	0.91±0.07	0.92±0.05	0.343

Table 3.1: Summary of passive and gait related measures, ^{KF} indicates knee flexed condition.

	DM		***Ctrl***	
	Stiffness	ROM	Stiffness	ROM
Age	r=-0.36, p=0.31	r =0.46, p=0.18	r =0.28, p=0.58	r =0.19, p=0.43
Body Mass	r =0.22, p=0.54	r =-0.15, p=0.64	r =0.41, p=0.20	r =-0.42, p=0.18
Duration of DM	r =0.55, p=0.04	r =0.33, p=0.2		
HbA1C%	r =0.54, p=0.08	r =0.28, p=0.42		

Table 3.2**:** Summary of associations between subject characteristics and passive ankle stiffness and DF ROM.

Variables of Interest		*DM* r_1	*Ctrl* r_2	$\|Z\|$
Peak passive DF	Gait DF	-0.150	-0.007	0.270
Peak passive DF ^{KF}	Gait DF	0.145	0.158	0.025
Passive stiffness	Gait Stiffness	0.075	0.472	0.843
Passive stiffness ^{KF}	Gait Stiffness	-0.017	0.14	0.295
Peak passive DF	Peak forefoot pressure	-0.512	0.457	1.981
Peak passive DF ^{KF}	Peak forefoot pressure	0.065	-0.46	1.052
Gait DF	Peak forefoot pressure	0.134	0.317	0.362
Passive Stiffness	Peak forefoot pressure	-0.501	0.433	1.897
Passive Stiffness ^{KF}	Peak forefoot pressure	-0.273	-0.13	0.279
Gait Stiffness	Peak forefoot pressure	0.020	0.588	1.225
Stride length	Peak forefoot pressure	0.708	0.656	0.182
AROM	Stride length	0.732	-0.403	2.577
Gait Stiffness	Stride length	0.769	-0.396	2.688

Table 3.3: Summary of Pearson's product moment correlation to assess relationships between variables of interest in subjects with and without DM (r_1 and r_2 respectively). ^{KF} indicates knee flexed condition. The test $|Z| \geq z_{0.025}$ has a critical value of 2.57 and assesses equality of the correlations (H_o: $\rho_1=\rho_2$).

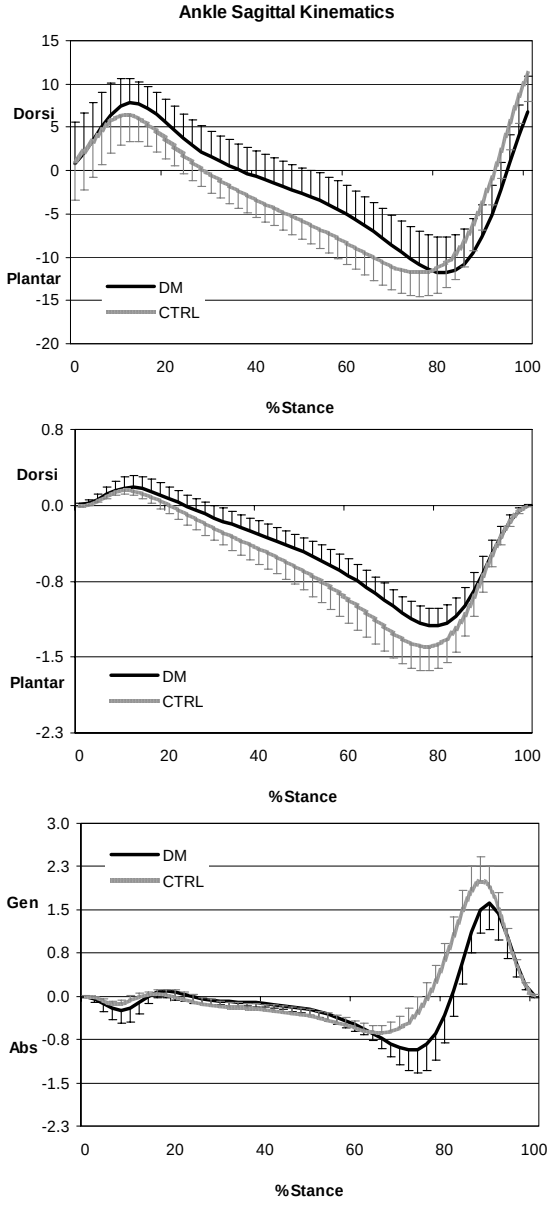


Figure 3.1: Group Mean ± SD for sagittal ankle kinematics, kinetics and power during stance phase

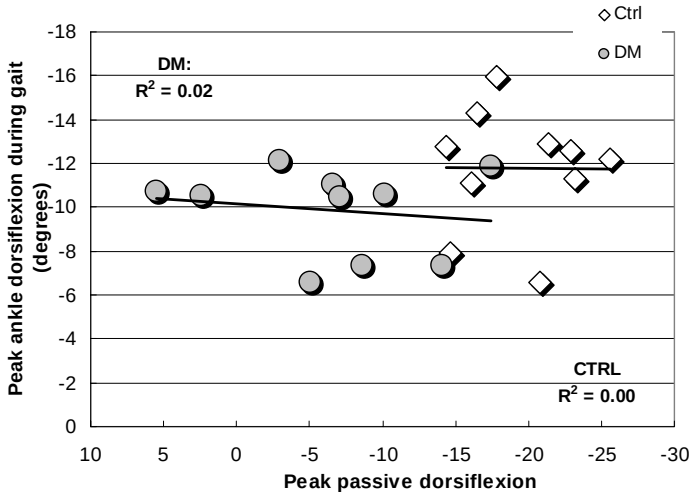


Figure 3.2: Relationship between passive ankle dorsiflexion and dorsiflexion utilized during gait

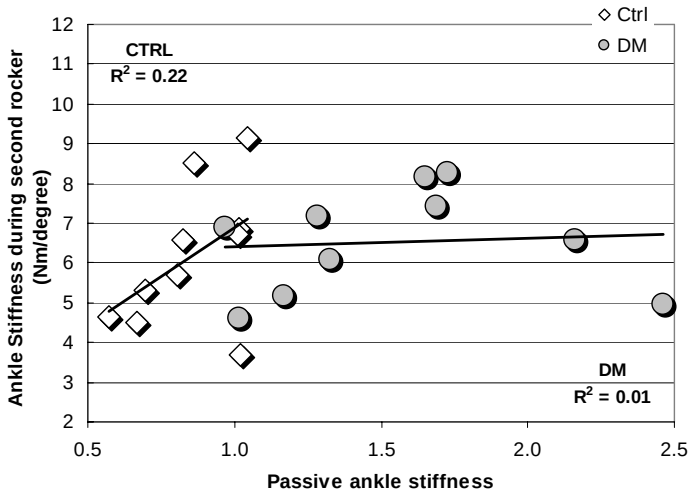


Figure 3.3: Relationship between passive ankle stiffness and ankle stiffness utilized during second rocker

CHAPTER IV:

SEGMENTAL FOOT MOBILITY IN INDIVIDUALS WITH AND WITHOUT DIABETES AND NEUROPTHY

Introduction:

Plantar ulcers develop in an estimated 15% of patients with Diabetes Mellitus (DM) (Gordois, Scuffham et al. 2003). Along with grave consequences in terms of health and functional abilities (Mueller, Sinacore et al. 2004; Price 2004), foot ulcers and amputation are often harbingers of personal and financial hardship. Factors contributing to increased loading on the plantar aspect of the foot and thus the potential development of foot ulcers are therefore of considerable interest.

Clinical studies have reported an association between factors intrinsic to the foot and plantar loading. Structural (Cavanagh, Morag et al. 1997) as well as dynamic factors (Delbridge, Perry et al. 1988; Mueller, Diamond et al. 1989; Fernando, Masson et al. 1991) have been implicated in the development of foot ulcers.

Reduced subtalar joint mobility, specifically inadequate hindfoot eversion has been documented in subjects with DM (Delbridge, Perry et al. 1988; Mueller, Diamond et al. 1989; Fernando, Masson et al. 1991; Arkkila, Kantola et al. 1997; Fernando and Vernidharan 1997; Duffin, Donaghue et al. 1999; Frost and Beischer 2001; Glasoe, Allen et al. 2004) and may have significant biomechanical consequences (Rosenbaum, Bauer et al. 1996; Sammarco 2004) including increases in transverse tarsal joint rigidity predisposing to lateral column over-weighting. Similarly, limited first metatarsal mobility, documented in individuals with DM (Birke, Franks et al. 1995; Glasoe, Allen et al. 2004) has been hypothesized to result in excessive loading under the medial metatarsal heads (Glasoe, Yack et al. 1999) thus predisposing to the development of foot ulcers.

Evidence confirming the functional consequences of limited joint mobility and increased stiffness in the foot is limited and often controversial. Current studies suggest that the first metatarsal is plantarflexed during early stance and continues to dorsiflex about 10 degrees relative to the hindfoot until 70% of stance (Wearing, Urry et al. 1998; Cornwall and McPoil 1999; Cornwall and McPoil 2002; MacWilliams, Cowley et al. 2003). However, recent evidence demonstrates minimal lowering of the proximal first metatarsal during stance (Wilken, Saltzman et al. 2005) and suggesting that the excursion between the first metatarsal and hindfoot comes predominantly from hindfoot motion.

Results from the few studies that have used multisegment models (Nawoczenski, Baumhauer et al. 1999; Allen, Cuddeford et al. 2004) have not addressed the relationship between foot mobility and plantar loading during gait. Further, these studies were conducted on non-DM subjects with intact sensation, their extrapolation to subjects with DM who have different impairments in terms of foot structure and mobility may not be valid.

Thus, while segmental foot mobility has been identified as an important potential contributor to foot function and loading, especially in individuals with DM, its role in gait remains poorly understood. The purpose of our study was to examine segmental foot mobility during gait in subjects with and without DM and neuropathy. These results are important because they may help uncover mechanisms underlying segmental foot function and plantar loading in individuals with DM.

Methods:

Subjects:

All procedures were approved by the Institutional Review Board at the University of Iowa Hospitals and Clinics. 15 subjects with DM and neuropathy and 15 non-diabetic control subjects participated in this study. Inclusion criteria for subjects with DM were: diagnosis of DM (ADA criteria (2006)), no current foot ulcer, great toe or transmetatarsal

amputation, absence of ipsilateral or contralateral Charcot neuroarthropathy. Presence of neuropathy was documented using 5.07 Semmes-Weinstein monofilaments (Mueller 1996) and VPT (Pham, Armstrong et al. 2000). Subjects in the control group were screened for diabetes and matched in age and gender to subjects with DM. Subject characteristics are summarized in Table 4.1.

Data acquisition:

Kinematic and kinetic data were acquired as subjects walked along a 10 m walkway at 0.89 m/s (2 mph). Kinematic data were collected at 120 Hz using an active marker system (Optotrak, NDI, Waterloo, Canada). Three infra-red markers were placed in a non collinear arrangement to define technical co-ordinate systems for each of the following segments: first ray, forefoot, calcaneus and leg. Kinetic data were collected at 360 Hz using a forceplate embedded in the walkway (Kistler Inc, NY).

Kinematic and kinetic data were low-pass filtered using a fourth order butterworth filter with cut-off frequencies of 6 and 8 Hz respectively and processed using Visual3D motion (C-motion Inc., NIH, MD). A threshold of 10 N was used to determine heelstrike and toe off from the force plate data. 5 successful trials were collected for each subject. A trial was considered successful if the subject made clean forceplate contact on the tested side without targeting.

Multisegment kinematic model of the foot:

A multi-segment kinematic model of the foot based on Wilken et al (Wilken, Saltzman et al. 2004) was used to examine segmental mobility of the foot. Anatomical landmarks were identified as virtual points with respect to the relevant technical co-ordinate system. Anatomically based local coordinate systems were established using the criteria defined in Appendices A and B.

Motion of the distal segment was expressed relative to the proximal segment and was calculated using Euler angles with the following sequence of rotations: sagittal,

frontal and transverse. Motion of each segment relative to the lab global co-ordinate system (GCS) was also examined. While the former convention has widespread clinical relevance, the latter allows us to examine the contribution of each moving segment to relative motion between the two. Processed kinematic data were time normalized to 100 percent stance. Stance phase mean was subtracted from pattern to correct for systematic offsets (Hunt, Smith et al. 2001). While the application of this correction may eliminate systematic offsets between groups, it helps reduce between-subject variability and allows for comparisons of range, timing and pattern of motion between the study and control groups.

Statistical Analysis:

A two-sample t-test was used to assess differences between the two groups (α=0.05).

Results:

Subjects in both groups walked with similar speed (0.89±0.13 and 0.93±0.11 m/s, DM and Ctrl respectively, p=0.169) and stride length (1.08±0.15 and 1.12±0.10 m, DM and Ctrl respectively, p=0.166).

Segmental kinematics expressed relative to the proximal segment:

Subjects with DM showed decreased excursion of the first metatarsal relative to the calcaneus in the frontal plane (Figure 4.1-b) as well as transverse plane (Figure 4.1-c) along with reductions in peak inversion and adduction (Table 4.2). Trends towards reduced frontal plane excursion of the forefoot relative to the calcaneus (Figure 4.1-e) and trends towards decreased inversion and adduction were noted in subjects with DM (Table 4.2). Subjects with DM showed reduced sagittal plane excursion (Figure 4.1-g) of the calcaneus relative to the tibia. The reduction in peak plantarflexion was more dramatic than the reduction in peak dorsiflexion (Table 4.2). Reduced frontal plane

excursion of the calcaneus relative to the tibia (Figure 4.1-h), in subjects with DM was accompanied by reduced peak eversion as well as inversion.

Segmental kinematics expressed relative to the lab:

The first metatarsal as well as the forefoot in subjects with DM showed less peak dorsiflexion at heelstrike and less peak plantarflexion at push off, resulting in less sagittal plane excursion through stance (Figure 4.2-a, d). In addition, the forefoot showed decreased excursion in the frontal plane in subjects with DM (Figure 4.2-e). Similar trends were noted in the transverse plane (Table 4.3). Subjects with DM showed trends towards less dorsiflexion of the calcaneus at heel strike, less plantar flexion at push off and less sagittal plane excursion (Figure 4.2-g). Reduced calcaneal excursion in the frontal plane (Figure 4.2-h) was accompanied by reduction in peak eversion.

Discussion:

We applied a novel multi-segment kinematic model with established validity and reliability to examine foot function in individuals with DM and neuropathy compared to non-diabetic control subjects. Our results revealed significant differences in patterns of segmental mobility between the two groups, with DM subjects showing lower magnitudes of motion. The reductions in motion were not generalized – they were particularly dramatic in the calcaneus (20%) compared to the forefoot and first metatarsal. Our results underscore the complexity of segmental foot function during gait; motion at one joint has important consequences on motion at neighboring joints. Our findings provide new insights on the nature of impairments in segmental foot function in individuals with DM.

During gait, foot-floor interaction begins with heel contact which places significant demands on the subtalar joint in terms of mobility and shock absorption (Saltzman and Nawoczenski 1995). In agreement with reports based on surface markers (Leardini, Benedetti et al. 1999; Hunt, Fahey et al. 2000; Hunt, Smith et al. 2001;

Levangie and Norkin 2001; Neumann 2002; MacWilliams, Cowley et al. 2003; Allen, Cuddeford et al. 2004) as well as bone pins (Westblad, Hashimoto et al. 2002), our results showed that the calcaneus undergoes rapid pronation in early stance. Calcaneal pronation, manifest as calcaneal eversion and abduction, was accompanied by first metatarsal and forefoot eversion in early stance, supporting the argument that the foot is flexible and 'splays' during this interval. In subjects with DM, we found a reduction in the magnitude of peak calcaneal eversion (~28%) and trends towards reduced abduction.

The reduction in calcaneal motion is important because subtalar pronation has important consequences on joints proximal as well as distal to it. Subtalar motion reduces rotational stresses that would otherwise be transferred proximally (Perry 1983). Lack of eversion at the subtalar joint may be expected to render the axes of the transverse tarsal joints out of alignment thus decreasing the amount of motion possible though the midfoot for shock absorption (Elftman 1969; Blackwood, Yuen et al. 2005). This phenomenon may help explain the reduced forefoot eversion noted in subjects with DM.

Loss of frontal plane mobility of the calcaneus may be attributed to several discrete yet coexisting processes in subjects with DM. While it is unlikely that subjects in either group approximated end range-of-motion of the subtalar joint (Mueller, Diamond et al. 1989; Duffin, Donaghue et al. 1999), increased stiffness of the subtalar joint as well as reduced compliance of the calcaneal heel pad (Kao, Davis et al. 1999) may contribute to reduced excursion. The reduction of joint excursion may also be ascribed to neuropathy. Previous studies (Nurse and Nigg 2001; Giacomozzi, Caselli et al. 2002) have suggested that the absence of cutaneous feedback results in the adoption of a more conservative walking strategy. Reductions in forefoot motion may be due to lack of eversion of the subtalar joint but could also be due to factors intrinsic to the transverse tarsal joint, such as stiffness of talonavicular and calcaneocuboid joints. In subjects with DM, non-enzymatic glycosylation of collagen may contribute to increased stiffness of the

distal joints of the feet, hindering its ability of the foot to deform and transition from a rigid lever to a more flexible configuration.

Calcaneal motion, through its effect on the talonavicular joint may also influence arch mobility. Gradual arch deformation, discerned as sagittal plane motion of the first ray relative to the calcaneus (Figure 4.1-a) followed calcaneal pronation in both groups, in agreement with previous reports (Leardini, Benedetti et al. 1999; Carson, Harrington et al. 2001; Hunt, Smith et al. 2001; MacWilliams, Cowley et al. 2003). In terminal stance, calcaneal plantarflexion under the influence of the gastrocnemius-soleus complex resulted in rapid tensing of the arch, providing midfoot stability. Particularly striking in both groups, was that the finding that medial longitudinal arch deformation was accompanied by nearly static first metatarsal inclination (Figure 4.2-a) supporting the theory that calcaneal mobility is a major contributor to arch motion while the first metatarsal provides distal stability. These data support the contention that the talus and calcaneus move over the relatively fixed naviculo-cuboid unit (Levangie and Norkin 2001; Wilken 2006).

Early calcaneal pronation was followed by gradual supination in both groups. These findings agree with the traditional understanding of foot mechanics wherein swing phase of the contralateral limb facilitates external rotation of the stance limb, which in turn helps initiate subtalar supination (Inman 1993; Neumann 2002). Traditional foot models predict that forefoot pronation will accompany calcaneal supination in order for the sole of the foot to maintain contact with the ground. Consistent with this theory, our results showed that calcaneal supination was accompanied by the first ray and forefoot staying static in eversion and abduction.

At terminal stance, in agreement with previous reports (Leardini, Benedetti et al. 1999; Carson, Harrington et al. 2001; Hunt, Smith et al. 2001; Cornwall and McPoil 2002; Arndt, Westblad et al. 2004), calcaneal supination was accompanied by first ray and forefoot supination to convert the foot into a rigid lever. In subjects with DM,

decreases in calcaneal plantarflexion, first metatarsal and forefoot supination were noted. Decreased calcaneal plantarflexion may result from reduced plantarflexor contraction at push off ((Maluf, Mueller et al. 2004), Chapter 3). Decreases in first metatarsal and forefoot motion accentuate the finding that it takes less supination in the foot with DM to create a stable, rigid lever at push off. In subjects with DM, midfoot stability may be derived from soft tissue such as the plantar fascia (Giacomozzi, D'Ambrogi et al. 2005).

In summary, we applied a multisegment kinematic foot model with established reliability and validity to examine segmental foot mobility in individuals with and without DM and neuropathy. Our findings agree with the traditional understanding of foot mechanics and shed new light on patterns and magnitude of motion during gait. Decreases in frontal plane calcaneal motion (30%) were accompanied by reduced midfoot mobility, discerned as reduced first metatarsal and forefoot motion. Our findings indicate that there are dramatic differences in foot function in early stance in shock absorption and in propulsion in terminal stance.

	DM	*Control*
N	15	15
Age	58±11	56±12
Gender F:M	5:15	5:15
Height (m)	1.77±0.11	1.75±0.10
Mass (kg)	90.6±13.8	74.6±13.3
VPT	48±5	13±6
HbA1C	8.1±1.1	
Type 2	12 (80%)	
Duration (yrs)	19±6	

Table 4.1: Demographic data from study and control groups, expressed as mean ± SD.

Segment	*Plane*		*DM*	*Ctrl*	*P value*
First Ray	Sagittal	Dorsi	6.5±3.8	5.6±1.9	*0.147*
		Range	13.0±2.5	14.7±3.3	*0.270*
	Frontal	Inver	6.0±3.5	11.8±5.3	*0.001*
		Ever	-6.3±3.6	-8.6±4.6	*0.073*
		Range	9.9±3.7	12.3±3.2	*0.029*
	Trans-	Add	3.2±1.2	6.0±3.3	*0.003*
	verse	Abd	-3.9±2.7	-5.0±3.5	*0.197*
		Range	7.1±3.1	9.6±3.6	*0.026*
Forefoot	Sagittal	Dorsi	6.4±2.6	5.9±2.5	*0.302*
		Range	13.8±3.3	15.3±4.0	*0.139*
	Frontal	Inver	7.4±4.7	10.6±6.7	*0.075*
		Ever	-8.5±6.3	-11.4±6.5	*0.119*
		Range	13.6±5.3	16.7±5.2	*0.062*
	Trans-	Add	7.4±2.0	9.7±4.6	*0.056*
	verse	Abd	-4.9±2.4	-5.1±2.1	*0.396*
		Range	12.3±3.2	14.7±6.0	*0.102*
Calcaneus	Sagittal	Dorsi	5.9±2.1	6.7±2.2	*0.015*
		Plant	-7.7±3.2	-13.0±3.9	*0.000*
		Range	12.7±4.3	19.6±4.4	*0.000*
	Frontal	Ever	4.5±2.0	6.5±2.4	*0.010*
		Inver	-4.9±3.0	-8.7±3.5	*0.002*
		Range	9.5±4.3	15.0±3.9	*0.000*
	Trans-	Add	7.7±5.8	10.6±5.2	*0.084*
	verse	Abd	-6.9±4.8	-8.8±5.2	*0.164*
		Range	15.6±11.9	19.1±9.8	*0.191*

Table 4.2: Summary of segmental kinematics (Mean±SD), expressed relative to the proximal segment

Segment	*Plane*		*DM*	*Ctrl*	*P value*
First Ray	Sagittal	Dorsi	18.3±6.7	22.2±3.8	*0.032*
		Range	68.8±12.5	81.1±8.8	*0.002*
	Frontal	Inver	7.9±2.9	9.2±3.7	*0.14*
		Ever	3.3±1.2	4.0±1.2	*0.072*
		Range	11.2±3.3	13.2±4.6	*0.092*
	Transverse	Add	7.0±3.2	8.1±3.8	*0.187*
		Abd	3.1±1.5	3.9±1.9	*0.111*
		Range	10.1±3.6	12.0±5.0	*0.122*
Forefoot	Sagittal	Dorsi	19.3±6.6	23.3±4.3	*0.032*
		Range	68.4±12.4	81.4±8.7	*0.001*
	Frontal	Inver	8.3±2.5	11.9±4.5	*0.009*
		Ever	3.8±1.0	5.4±1.8	*0.005*
		Range	12.1±3.2	16.6±4.6	*0.003*
	Transverse	Add	11.3±4.1	13.8±4.2	*0.06*
		Abd	4.0±1.0	4.6±1.2	*0.08*
		Range	15.2±4.8	18.3±5.0	*0.052*
Calcaneus	Sagittal	Dorsi	22.3±5.7	24.9±4.1	*0.077*
		Plant	41.9±6.0	47.9±3.9	*0.001*
		Range	64.1±10.4	72.8±7.2	*0.006*
	Frontal	Ever	3.1±3.0	5.2±3.5	*0.037*
		Inver	5.9±3.2	6.1±2.9	*0.428*
		Range	9.7±7.5	12.6±4.6	*0.021s*
	Transverse	Add	5.6±4.9	8.6±8.3	*0.125*
		Abd	6.7±5.8	6.3±5.0	*0.433*
		Range	10.1±4.5	10.2±2.9	*0.46*

Table 4.3: Summary of segmental kinematics (Mean±SD), expressed relative to the GCS

Figure 4.1: Ensemble averaged kinematics of the first ray, forefoot and calcaneus relative to the proximal segment. Circles represent subjects with DM, Diamonds represent Ctrl subjects; Error bars represent ±1SD.

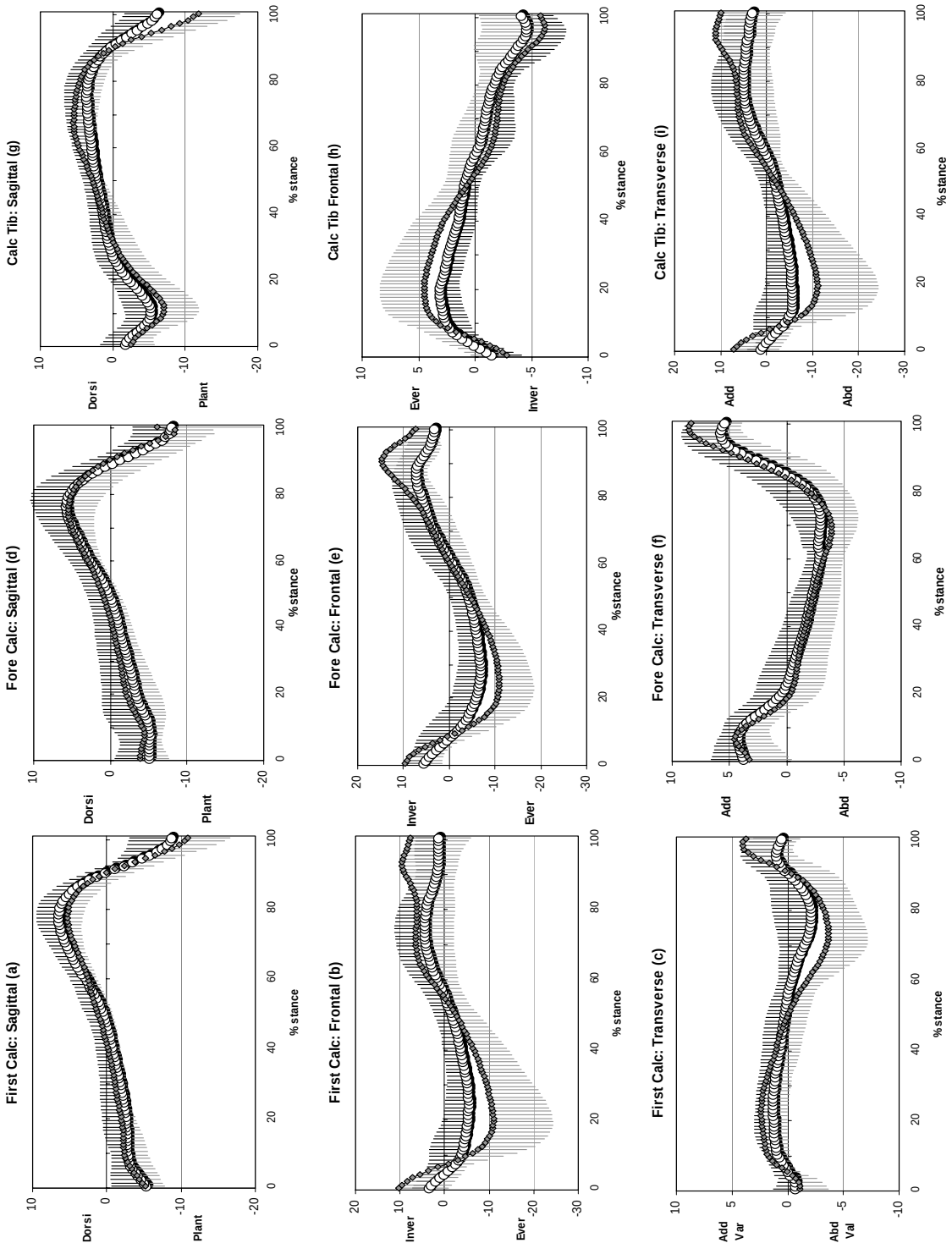
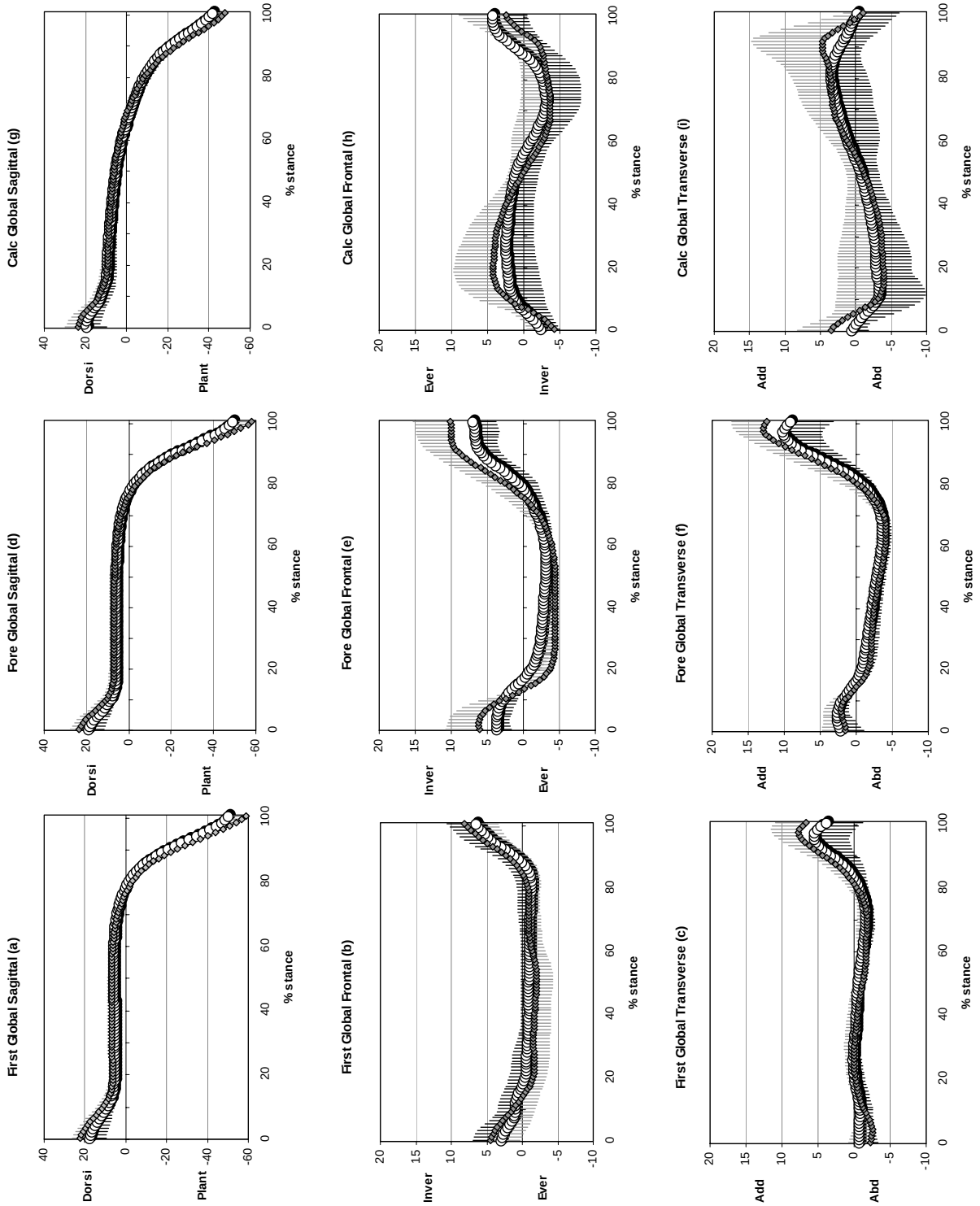


Figure 4.2: Ensemble averaged kinematics of the first ray, forefoot and calcaneus relative to the GCS. Circles represent subjects with DM, Diamonds represent Ctrl subjects; Error bars represent ±SD



CHAPTER V:

RELATIONSHIPS BETWEEN SEGMENTAL FOOT MOBILITY AND LOADING IN INDIVIDUALS WITH AND WITHOUT DIABETES AND NEUROPATHY

Introduction:

With over 7% of the population (20 million people) in the United States affected by diabetes mellitus (DM), DM has emerged as a significant health problem (National Institute of Diabetes and Digestive and Kidney Diseases 2005). Regular physical activity, such as walking, offers significant health benefits to individuals with DM (Gregg, Gerzoff et al. 2003). However, they are at high risk for ulcer formation on the sole of their foot (Gordois, Scuffham et al. 2003). Ulcer formation, in this population, has been strongly linked with mechanical stress under the ball of the foot (Brand 1981). Factors contributing to high loads on the sole of the foot are therefore of considerable interest.

During normal walking, body weight is transferred from the heel to the forefoot. Factors that affect this weight transfer may affect the timing and the magnitude of the loading experienced by the forefoot. Clinical studies have reported that changes in foot mobility may adversely affect plantar loading (Mueller, Diamond et al. 1989). Limited joint mobility and increased stiffness of the small joints of the foot have been hypothesized to limit excursion and lessen the ability of the foot to attenuate shock (Glasoe, Allen et al. 2004). These factors may contribute to the development of foot ulcers by causing abnormal pressures at susceptible sites (Delbridge, Perry et al. 1988; Fernando, Masson et al. 1991; Glasoe, Allen et al. 2004).

Previous reports have documented that subjects with DM have reduced passive subtalar joint mobility (Mueller, Diamond et al. 1989; Fernando, Masson et al. 1991), as a result of which, they may be expected to demonstrate reduced eversion range of motion.

Hindfoot eversion allows the foot to attenuate shock (Root, Orien et al. 1977; Hunt and McPoil 1995) and loss of hindfoot motion may serve as an important functional marker of loss of foot flexibility.

Reduced first ray mobility (Birke, Franks et al. 1995; Glasoe, Allen et al. 2004), attributed, in part to increased plantar fascia thickness in subjects with DM (D'Ambrogi, Giurato et al. 2003; Bolton, Smith et al. 2005; Giacomozzi, D'Ambrogi et al. 2005) has been reported in subjects with DM. Increased plantar fascia thickness and reduced first ray mobility may be expected to manifest during gait as reduced sagittal plane first ray motion.

Evidence confirming the functional consequences of limited joint mobility and increased stiffness in the foot is limited, partly due to the lack of biomechanical models that afford the opportunity to track segmental motion of the foot in 3D during gait. In the absence of multi-segment foot models, regression based statistical models have been implemented to determine predictors of loading (Cavanagh, Sims et al. 1991; Morag and Cavanagh 1999; Payne, Turner et al. 2002; Mueller, Hastings et al. 2003). These models provide valuable insights and help identify etiological factors on the basis of how much variance they explain in the dependent variable. However, they do not shed light on the mechanisms of action.

Results from studies that have used multisegment models (Leardini, Benedetti et al. 1999; Nawoczenski, Baumhauer et al. 1999; Carson, Harrington et al. 2001; Hunt, Smith et al. 2001; Allen, Cuddeford et al. 2004) have not addressed the relationship between foot mobility and plantar loading during gait. Further, these studies were conducted on non-DM subjects with intact sensation, their extrapolation to subjects with DM who have different impairments in terms of foot structure and mobility may not be valid.

Thus, while segmental foot mobility has been identified as an important potential contributor to foot function and loading especially in individuals with DM (Fernando,

Masson et al. 1991; Birke, Franks et al. 1995; Arkkila, Kantola et al. 1997; D'Ambrogi, Giurato et al. 2003; Zimny, Schatz et al. 2004), the nature, extent and mechanisms underlying changes in segmental foot mobility and its relationship with loading are not well understood. The purpose of our study is to examine dynamic foot function as it relates to plantar loading in individuals with DM. This information is important because it may help elucidate underlying mechanisms, add to our understanding of the DM disease process and its effects, and thus may help develop effective intervention strategies.

Methods:

Subjects:

All procedures were approved by the Institutional Review Board at the University of Iowa Hospitals and Clinics. 15 subjects with DM and neuropathy and 15 non-diabetic control subjects participated in this study. Inclusion criteria for subjects with DM were: diagnosis of DM (ADA criteria (2006)), no current foot ulcer, great toe or transmetatarsal amputation, absence of ipsilateral or contralateral Charcot neuroarthropathy. Presence of neuropathy was documented using 5.07 Semmes-Weinstein monofilaments (Mueller 1996) and VPT (Pham, Armstrong et al. 2000). Subjects in the control group were screened for diabetes and matched in age and gender to subjects with DM. Subject characteristics are summarized in Table 4.1.

Data acquisition:

Kinematic and kinetic data were acquired as subjects walked along a 10 m walkway at 0.89 m/s (2 mph). Kinematic data were collected at 120 Hz using an active marker system (Optotrak, NDI, Waterloo, Canada). Three infra-red markers were placed in a non collinear arrangement to define technical co-ordinate systems for each of the following segments: first ray, forefoot, calcaneus and leg. Kinetic data were collected at

360 Hz using a forceplate embedded in the walkway (Kistler Inc, NY) and at 50 Hz using a pedobarograph (EMed, Novel Inc).

Kinematic and kinetic data were low-pass filtered using a fourth order butterworth filter with cut-off frequencies of 6 and 8 Hz respectively and processed using Visual3D motion (C-motion Inc., NIH, MD). A threshold of 10 N was used to determine heelstrike and toe off from the force plate data. Plantar pressure data were processed using Novel Win software (Novel Inc, MN). The following sub-areas of interest were defined as a percentage of foot length: Heel (0-28%), Midfoot (28-55%), Forefoot (55-80%). Each sub area was divided into medial and lateral (50% foot width). Peak loading and timing of peak loading was computed within each sub area. 5 successful trials were collected for each subject. A trial was considered successful if the subject made clean forceplate or pedobarograph contact on the tested side, without targeting.

Multisegment kinematic model of the foot:

A multi-segment kinematic model of the foot based on Wilken et al (Wilken, Saltzman et al. 2004) was used to examine segmental mobility of the foot. Anatomical landmarks were identified as virtual points with respect to the relevant technical co-ordinate system. Anatomically based local coordinate systems were established using the criteria defined in Appendices A and B (Chapter 4).

Motion of the distal segment was expressed relative to the proximal segment and was calculated using Euler angles with the following sequence of rotations: sagittal, frontal and transverse. Processed data were time normalized to 100 percent stance. For kinematic data, stance phase mean was subtracted from pattern to correct for systematic offsets (Hunt, Smith et al. 2001).

MRI:

Sagittal T1 scans were acquired using a 3T Trio scanner (Siemens, PA). The imaging parameters used were repetition time (TR) 742-822 ms, echo time (TE) 8-9.2

ms, with isotropic resolution of 1.743-1.91 pixels/mm in all directions, depending on the field of view (approximately 20 cm x 15 cm). Posterior aspect of the heel and the distal end of the first metatarsal were used to define the field of view. Each individual acquisition was kept to within 8 minutes for subject comfort and to minimize the potential for motion artifacts. Plantar fascia thickness was measured at the proximal end, at one fifth of its total length, using ImageJ (Rasband 2006).

Passive ankle stiffness and ROM:

Ankle stiffness and ROM were measured with the knee extended using the methods described in Chapters 2 and 3.

Statistical Analysis:

A two sample t test was used to assess differences between the two groups (α=0.05). Pearson product moment correlation (r) was used to assess the relationship between variables of interest. Statistical significance (H_o: ρ=0) and equality of correlations (H_o: $\rho_1=\rho_2$) were assessed using approximate tests based on Fisher's Z transformation (α=0.05).

Results:

Subjects in both groups walked with similar speed (0.89±0.13 and 0.93±0.11 m/s, DM and Ctrl respectively, p=0.169) and stride length (1.08±0.15 and 1.12±0.10 m, DM and Ctrl respectively, p=0.166).

Kinematics:

Subjects with DM showed decreased excursion of the first metatarsal relative to the calcaneus in the frontal plane as well as transverse plane. Trends towards reduced frontal plane excursion of the forefoot relative to the calcaneus were noted in subjects with DM. Subjects with DM showed reduced sagittal and frontal plane excursion of the calcaneus relative to the tibia. These results are summarized in Table 5.2.

Kinetics:

Although subjects with DM showed less plantarflexor torque (1.27±0.17 and 1.40±0.17 Nm/kg, DM and Ctrl respectively, p= 0.03) and less plantarflexor power generation at push off (1.52±0.60 and 2.51±0.49 Nm/kg*s, DM and Ctrl respectively, p<0.01), they sustained significantly higher plantar loads under the forefoot (Table 5.3). Heel rise occurred later in subjects with DM (66.3±12.4 and 57.0±10.3 % stance, DM and Ctrl respectively, p= 0.016), and subjects with DM showed significantly longer forefoot contact time (Table 5.4). There were no differences in the timing of peak pressure at the heel (16.9±7.7 and 15.1 ±6.4 % stance, DM and Ctrl respectively, p= 0.243) or the forefoot (72.7±17.3 and 78.3±4.6 % stance, DM and Ctrl respectively, p= 0.112) between the groups.

Associations between kinematics and loading:

In subjects with DM, first metatarsal sagittal plane excursion during gait was negatively associated with peak pressure sustained under the medial forefoot (r = -0.42 and -0.06, DM and Ctrl respectively, p= 0.02). Similarly, lateral forefoot sagittal plane excursion during gait was negatively associated with peak pressure sustained under the forefoot (r = -0.56 and -0.11, DM and Ctrl respectively, p= 0.02). Frontal plane excursion of the calcaneus was negatively associated with medial (r= -0.57 and 0.12, DM and Ctrl respectively, p< 0.01) and lateral (r= -0.51 and 0.13, DM and Ctrl respectively, p< 0.01) heel and medial forefoot (r= -0.56 and -0.02, DM and Ctrl respectively, p< 0.01) pressure.

Associations between plantar fascia thickness, ankle measures and kinematics:

Subjects with DM showed increased plantar fascia thickness (2.78±0.64 and 1.51±0.33 mm, DM and Ctrl respectively, p<0.01), decreased ankle dorsiflexion (14.4±4.7 and 21±3.5 degrees, DM and Ctrl respectively, p<0.01) and increased ankle stiffness (1.236±0.186 and 1.016±0.153 Nm/degree, DM and Ctrl respectively, p<0.01).

No significant correlations were found between plantar fascia thickness and first ray motion. No relationships were found between ankle characteristics and the timing or magnitude of calcaneal motion.

Discussion:

We applied a novel multi-segment kinematic model to examine mechanisms contributing to plantar loading sustained during gait. Our results revealed significant differences in patterns of segmental mobility and loading between individuals with DM and neuropathy compared to non-diabetic control subjects. Decreases in frontal plane calcaneal motion were accompanied by reduced midfoot mobility and increased forefoot loading. In subjects with DM, sagittal motion of the first metatarsal and forefoot, and frontal motion of the calcaneus were negatively associated with the magnitude of plantar loading under the respective segment. These findings highlight the importance of segmental foot mobility in individuals with DM and suggest possible mechanisms underlying the evolution of increased loading under susceptible sites.

Heel contact, which marks the beginning of foot floor interaction in the stance phase, was followed by rapid calcaneal eversion and loading of the stance limb, in both groups, consistent with previous reports (Leardini, Benedetti et al. 1999; Carson, Harrington et al. 2001; Hunt, Smith et al. 2001; MacWilliams, Cowley et al. 2003). Our data concur with previous reports documenting that peak plantar loading at the heel occurs in early stance (Bryant, Tinley et al. 2000; Warren, Maher et al. 2004). In subjects with DM, we found decreased frontal plane mobility of the calcaneus. Several factors, including increased subtalar joint stiffness (Delbridge, Perry et al. 1988; Mueller, Diamond et al. 1989), loss of heel pad compliance (Kao, Davis et al. 1999) and neuropathy (Giacomozzi, Caselli et al. 2002) may contribute to the reduction in calcaneal mobility noted in subjects with DM.

Decreases in frontal plane calcaneal mobility were associated with increases in heel loading in subjects with DM but not in the control group. These findings support the theory that calcaneal mobility plays a key role in mediating shock absorption in early stance (Root, Orien et al. 1977) especially in subjects with DM. The importance of the relationship between frontal plane calcaneal mobility and heel loading may be magnified in DM because the ability of the foot to deform and adapt may be compromised (Chapter 4) due to stiffness and neuropathy.

Gradual arch deformation followed calcaneal pronation in both groups, in agreement with previous reports (Leardini, Benedetti et al. 1999; Carson, Harrington et al. 2001; Hunt, Smith et al. 2001; MacWilliams, Cowley et al. 2003). Unexpectedly, peak arch deformation did not differ between the two groups, indicating that relative sagittal plane motion between the first metatarsal and calcaneus did not differ during midstance. However subjects with DM sustained higher loads for longer durations on the forefoot. Further, sagittal plane arch mobility and forefoot loading were inversely related in subjects with DM. Both groups had similar standard deviations and dispersion, however only subjects with DM showed increases in loading associated with decreases in mobility. These findings underscore the vital relationship of segmental mobility and loading in subjects with DM.

In terminal stance, subjects with DM showed decreased calcaneal plantarflexion, first metatarsal and forefoot supination. Decreased calcaneal plantarflexion may result from reduced plantarflexor contraction at push off ((Maluf, Mueller et al. 2004), Chapter 3). These decreases accentuate the finding that it takes less supination in the foot with DM to create a stable, rigid lever at push off. In subjects with DM, midfoot stability may be derived from soft tissue such as the plantar fascia (Giacomozzi, D'Ambrogi et al. 2005).

The plantar fascia has been identified as an important contributor to midfoot stability and arch support (Hicks 1954; Wright and Rennels 1964; Thordarson, Schmotzer

et al. 1995). Increased plantar fascia thickness, attributed to qualitative and quantitative changes in collagen fibers of the plantar fascia, has been reported in subjects with DM (Duffin, Lam et al. 2002; D'Ambrogi, Giurato et al. 2003; Bolton, Smith et al. 2005; D'Ambrogi, Giacomozzi et al. 2005; Giacomozzi, D'Ambrogi et al. 2005). Due to its attachments on the calcaneus and on the ball of the foot (Bojsen-Moller and Flagstad 1976), plantar fascia strain is closely related to segmental foot mobility (Nawoczenski, Flanigan et al. 2005). (In subjects with DM, in response to decreased calcaneal eversion in early stance the plantar fascia may be expected to undergo less stretch. Subsequent to decreased calcaneal plantarflexion and forefoot inversion in terminal stance, the plantar fascia may be expected to undergo less shortening in terminal stance. Thus,) Reductions in segmental foot mobility noted in subjects with DM may result in decreased plantar fascia strain.

The plantar fascia also has significant load transfer functions during stance phase of gait. The arch lowering moment, created by ground reaction forces acting at the forefoot and heel, is resisted by tension in the plantar fascia (Hicks 1954). Based on the truss model (Wright and Rennels 1964; Gefen 2003), the plantar fascia in subjects with DM may be expected to develop higher tension and sustain it over a longer duration. At terminal stance, Achilles tendon forces (Erdemir, Hamel et al. 2004) add to preexisting factors and promote further tension development in the plantar fascia. This combination of increased tension and reduced strain supports the hypothesis of increased plantar fascia stiffness in subjects with DM.

Increased plantar fascia stiffness and forefoot loading may signal that increased bending moments are sustained at the apex of the arch (Trepman, Nihal et al. 2005). The combination of increased loading and reduced frontal and transverse plane segmental mobility introduce the possibility of increased torsional moments about the midfoot. Increases in plantar loading thus have implications for not only tissue breakdown and

potential ulcer development but also the evolution of Charcot changes at the midfoot, due to both, bending as well as torsional stresses.

The key findings of our study were that reductions in segmental foot mobility were accompanied by increases in local loading in subjects with DM. The combination of increased tension and reduced strain emphasizes the possibility of increased plantar fascia stiffness in subjects with DM. The reductions in segmental foot mobility and concurrent increase in loading may imply that the foot in DM sustains higher bending as well as torsional stresses. These results support the view that limitations in segmental mobility have significant consequences in terms of both, potential ulcer development as well as the evolution of Charcot changes in the foot with DM.

	DM	*Control*
N	15	15
Age	58±11	56±12
Gender F:M	5:15	5:15
Height (m)	1.77±0.11	1.75±0.10
Mass (kg)	90.6±13.8	74.6±13.3
VPT	48±5	13±6
HbA1C	8.1±1.1	
Type 2	12 (80%)	
Duration (yrs)	19±6	

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Segment	*Plane*		*DM*	*Ctrl*	*P value*
First Ray	Sagittal	Dorsi	6.5±3.8	5.6±1.9	*0.147*
		Range	13.0±2.5	14.7±3.3	*0.270*
	Frontal	Inver	6.0±3.5	11.8±5.3	*0.001*
		Ever	-6.3±3.6	-8.6±4.6	*0.073*
		Range	9.9±3.7	12.3±3.2	*0.029*
	Transverse	Add	3.2±1.2	6.0±3.3	*0.003*
		Abd	-3.9±2.7	-5.0±3.5	*0.197*
		Range	7.1±3.1	9.6±3.6	*0.026*
Forefoot	Sagittal	Dorsi	6.4±2.6	5.9±2.5	*0.302*
		Range	13.8±3.3	15.3±4.0	*0.139*
	Frontal	Inver	7.4±4.7	10.6±6.7	*0.075*
		Ever	-8.5±6.3	-11.4±6.5	*0.119*
		Range	13.6±5.3	16.7±5.2	*0.062*
	Transverse	Add	7.4±2.0	9.7±4.6	*0.056*
		Abd	-4.9±2.4	-5.1±2.1	*0.396*
		Range	12.3±3.2	14.7±6.0	*0.102*
Calcaneus	Sagittal	Dorsi	5.9±2.1	6.7±2.2	*0.015*
		Plant	-7.7±3.2	-13.0±3.9	*0.000*
		Range	12.7±4.3	19.6±4.4	*0.000*
	Frontal	Ever	4.5±2.0	6.5±2.4	*0.010*
		Inver	-4.9±3.0	-8.7±3.5	*0.002*
		Range	9.5±4.3	15.0±3.9	*0.000*
	Transverse	Add	7.7±5.8	10.6±5.2	*0.084*
		Abd	-6.9±4.8	-8.8±5.2	*0.164*
		Range	15.6±11.9	19.1±9.8	*0.191*

Table 5.2: Summary of segmental kinematics (Mean±SD)

	DM	*Ctrl*	*P value*
Pressure (N/cm^2)			
Medial Heel	40.1±15.9	37.6±4.5	*0.277*
Lateral Heel	39.6±16.8	40.1±7.4	*0.455*
Medial Forefoot	82.4±29.0	49.8±10.7	*0.000*
Lateral Forefoot	57.7±29.8	44.0±13.5	*0.054*
Pressure (Normalized to Body Weight)			
Medial Heel	0.047±0.022	0.053±0.011	*0.168*
Lateral Heel	0.047±0.024	0.056±0.013	*0.081*
Medial Forefoot	0.095±0.039	0.071±0.023	*0.021*
Lateral Forefoot	0.067±0.036	0.060±0.013	*0.244*
Pressure Time Integral ([N/cm^2]*s			
Medial Heel	20.1±11.1	10.3±4.0	*0.001*
Lateral Heel	16.8±10.0	10.8±4.2	*0.019*
Medial Forefoot	36.2±13.5	21.1±9.2	*0.001*
Lateral Forefoot	26.9±6.8	19.5±6.9	*0.003*
Pressure Time Integral (Normalized to Body Weight)			
Medial Heel	0.221±0.106	0.138±0.048	*0.004*
Lateral Heel	0.185±0.099	0.144±0.047	*0.072*
Medial Forefoot	0.410±0.171	0.289±0.126	*0.017*
Lateral Forefoot	0.301±0.076	0.257±0.060	*0.040*

Table 5.3: Peak plantar loading sustained during gait

	DM	*Ctrl*	*P value*
Contact Time			
Heel	701.3±322.4 (59.8)	583.8±220.6 (60.8)	*0.102*
Forefoot	1046.7±424.0 (89.2)	797.5±124.8 (83.1)	*0.005*
Hallux	681.3±311.4 (58.1)	602.5±194.0 (62.8)	*0.201*
Total	1173.3±409.2	1060.0±345.8	*0.073*

Table 5.4: Contact duration in ms (% stance time) of loading under each region of the foot

CHAPTER VI:

SUMMARY AND CONCLUSIONS:

The goal of this work was to examine determinants of dynamic foot function and plantar loading in individuals with DM. By integrating kinematic modeling and kinetic measures, we sought to apply an innovative approach to obtain insights into mechanisms underlying plantar loading.

One key finding of our investigation (Chapter 2) demonstrated that subjects with DM have both, significantly lower peak dorsiflexion range of motion and higher passive ankle stiffness than non-diabetic individuals. In subjects with DM, we found a positive association between the extent of the pathology and the magnitude of changes in the mechanical characteristics of the plantarflexors. In both, the DM and Ctrl groups, knee flexion was accompanied by an increase in peak dorsiflexion ROM but not in ankle stiffness highlighting the gastrocnemius as the predominant factor responsible for ankle stiffness in 0-20 degree range of knee flexion in both groups.

To examine the functional consequences of these impairments, a second investigation (Chapter 3) was undertaken. Specifically, we sought to address three questions: i. Does peak passive DF ROM predict ankle DF ROM used during gait? ii. Does passive ankle stiffness predict ankle stiffness used during gait? iii. Are any of the passive or gait ankle measures associated with plantar loading? We found that in spite of differences in passive ankle DF ROM and stiffness, subjects with DM demonstrated ankle motion, stiffness and plantar pressures, similar to control subjects, while walking at the identical speed, 0.89 m/s (2 mph). Based on these data, we concluded that clinical measures of heel cord tightness and stiffness do not represent ankle motion or stiffness utilized during functional activities of daily living such as gait. Further, despite utilizing strategies such as reduced push-off (Mueller, Minor et al. 1994) and shortened stride

length (Chapter 3), subjects with DM sustained plantar loads similar to control subjects suggesting the concomitant existence of other factors, possibly intrinsic to the foot, which may render individuals with DM vulnerable to increased plantar loading.

In Chapter 4, we sought to examine the role of intrinsic factors such as segmental foot mobility, which have been identified in clinical studies (Fernando, Masson et al. 1991; Birke, Franks et al. 1995; Arkkila, Kantola et al. 1997; D'Ambrogi, Giurato et al. 2003; Zimny, Schatz et al. 2004), as key contributors to dynamic foot function and plantar loading. Our results revealed significant differences in patterns of segmental mobility between the two groups, with DM subjects showing lower magnitudes of motion. The reductions in motion were not generalized – they were particularly dramatic in the calcaneus (20%) compared to the forefoot and first metatarsal. Decreases in frontal plane calcaneal motion (30%) were accompanied by reduced midfoot mobility, discerned as reduced first metatarsal and forefoot motion, allowing us to conclude that subjects with DM demonstrate dramatic differences in foot function in early stance in shock absorption and in propulsion in terminal stance.

Our final investigation (Chapter 5) represents an attempt to examine the relationships between segmental kinematics and loading in individuals with DM. Our data revealed that sagittal motion of the first metatarsal and forefoot, and frontal motion of the calcaneus, in subjects with DM, was negatively associated with the magnitude of plantar loading under the respective segment (Chapter 5). These findings highlight the importance of segmental foot mobility in individuals with DM and provide new insights into possible mechanisms underlying the evolution of increased loading under susceptible sites. The reductions in segmental foot mobility and concurrent increase in loading may signal that the foot in DM sustains higher bending as well as torsional stresses. These results allow us to conclude that limitations in segmental mobility have significant consequences and may play a role in potential ulcer development as well as the evolution of Charcot changes in the foot with DM.

The apparent discrepancy in terms of results related to loading in Chapters 3 and 5 may be explained as a combination of two main factors: One key difference between the two studies is that subjects wore their customary footwear in the former and were barefoot during gait testing in the latter. Footwear not only affords a more even distribution of loads on the sole of the foot (Cavanagh, Ulbrecht et al. 2001) but may also facilitate forward transfer of body weight (van Schie, Ulbrecht et al. 2000). A second difference relates to methodology. The in-shoe measuring device used in Chapter 3 has a spatial resolution of about 1 sensor per square centimeter whereas the pedobarograph used in Chapter 5 has a spatial resolution of 4 sensors per square centimeter. While the advantage of the in-shoe device was that it allowed us to measure plantar loading in the shod condition, the trade-off was that the larger sensor size may 'filter' higher pressures (Davis, Cothren et al. 1996). Both sets of results reflect underlying biomechanics in individuals with DM. and neuropathy. Chapter 3 is representative of what happens when walking at 2 mph in customary footwear; while Chapter 5 relates to the barefoot condition and highlights the role of the plantar fascia in transmitting loads to the forefoot.

In conclusion, our investigations elucidate the mechanisms by which intrinsic and extrinsic factors contribute to plantar loading in individuals with and without DM and neuropathy. These findings are clinically significant because they provide new insights about the functional consequences of frequently observed impairments in this patient population.

CHAPTER VII:

LIMITATIONS AND FUTURE DIRECTIONS:

1. Peak pressure and pressure time integral were used as the main indicators of plantar loading based on previous reports that have showed an association between elevated pressures and the development of foot ulcers (Veves, Murray et al. 1992). The development of more sophisticated kinetic models to characterize tension in the plantar fascia, torsional and stresses at the midfoot as well as measures of cumulative plantar loading, in combination with segmental foot kinematics may provide additional insights into mechanisms underlying foot loading.
2. We acknowledge the tremendous variability intrinsic to this patient population. While an attempt was made to develop screening criteria to identify an appropriate sample, no attempt was made to control for factors such as physical activity or foot type. There is limited evidence clarifying the role of these factors in segmental foot kinematics and plantar loading in individuals with DM and neuropathy and additional research is warranted in this area.

APPENDIX A. DEFINITION OF LOCAL CO-ORDINATE SYSTEMS (WILKEN, SALTZMAN ET AL. 2004)

Segment	Axis	Definition
First Ray	X	Aligned with long axis of first metatarsal
	Y	Orthogonal to X and Z axes
	Z	Parallel to floor and orthogonal to X axis
Forefoot	X	Aligned with long axis of second metatarsal
	Y	Orthogonal to X and Z axes
	Z	Orthogonal to long axis of 2nd MT and parallel to the floor
Calcaneus	X	Posterior heel to midpoint of foot at the level of the 5th MT flair
	Y	Calcaneal bisector
	Z	Orthogonal to X and Y axes
Leg	X	Orthogonal to Y and Z axes
	Y	Passing through midpoint of femoral condyles and malleoli
	Z	Aligned with malleoli and passing through mid malleolar point (orthogonal to Y)

APPENDIX B. MARKER PLACEMENT (WILKEN, SALTZMAN ET AL. 2004)

Segment	Marker	Location
First Ray	1	Mounted on triad on dorsal medial surface of first metatarsal
	2	Mounted on triad on dorsal medial surface of first metatarsal
	3	Mounted on triad on dorsal medial surface of first metatarsal
Forefoot	4	Proximal end of 2nd metatarsal
	5	Distal end of 2nd metatarsal
	6	Distal end of 5th metatarsal
Calcaneus	7	Posterior surface of calcaneus
	8	Lateral aspect of calcaneus superior to calcaneal fat pad
	9	Lateral aspect of calcaneus superior to calcaneal fat pad
Leg	10	Medial surface of tibia
	11	Medial surface of tibia
	12	Medial surface of tibia

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