

Foot and Ankle Characteristics in Patients with Chronic Gout: a case controlled study

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Attestation of Authorship

“I, *David G. Survepalli* hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgement), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.”

Signed

Date

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Dedicated

To the loving memory of my father



20 May 2009

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Dear Prof Rome

Predictors of foot function in patients with gout: a three-dimensional CT study.

Investigators: Prof Keith Rome, Nicola Dalbeth, Fiona McQueen, David Survepalli, Jane McDonald.

Ethics ref: NTY/08/04/039

List of approved amendments

- Approval is given to recruit and evaluate 24 subjects without gout.
- Information Sheet and Consent Form version 2 dated April 2009.

Thank you for submitting the above amendment, which was considered by the Deputy Chairperson of the Northern Y Regional Ethics Committee under delegated authority and approved.

Please quote the above ethics committee reference number in all correspondence.

Yours sincerely

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ABSTRACT

Introduction: Gout affects approximately 15% of Maori and Pacific men, these men being at risk of early onset, severe disease with formation of gouty tophi and joint damage. Gout most frequently affects the foot, particularly the big toe and midfoot. This disease initially presents as self-limiting attacks of severe joint inflammation, and in the presence of persistent hyperuricaemia, tophaceous disease may also develop. Tophi are collections of monosodium urate crystals surrounded by chronic inflammatory cells and connective tissue. Tophi typically occur in both subcutaneous tissues and within affected joints, and may cause pain, cosmetic problems, mechanical obstruction of joint movement, and joint destruction. Despite the predilection of gout to the foot, the impact of gout on foot function is currently unknown and only case studies relating to hallux pain, tibial sesamoid pain and longitudinal tears in peroneal tendons have been reported in the literature. The aim of this study is to assess the intra-tester reliability of certain biomechanical tests to evaluate foot structure and function (plantar pressure measurements, gait parameters, range of motion at the ankle and first MTPJ and the foot posture index) in individuals with gout and to assess the differences between disability, impairment, foot structure and function between individuals with gout and non-gout controls.

Subjects: A total of 25 patients with chronic gout with a mean age of 61.2 (11.7) years old were recruited from a rheumatology clinic within the Auckland District Health Board. A further 25 age- and sex-matched controls with a mean age of 57.3 (12.2) years old were recruited from AUT University.

Methods: Disability, impairment, foot structure and foot function were assessed for the gout and the control group. Disability and impairment was assessed using the Health Assessment Questionnaire, Foot Function Index, Leeds Foot Impact Scale and Lower Limb Task Questionnaire. Foot structure was investigated using the Foot Posture Index, first metatarsophalangeal joint (MTPJ) dorsiflexion, ankle dorsiflexion movement, subtalar joint and midtarsal joint motion, Foot Problem Score, tophi count and muscle strength of extrinsic and intrinsic foot muscles. Foot function was investigated using an in-shoe pressure system

measuring mean peak plantar pressures and pressure-time integrals. Temporal-spatial gait parameters were evaluated, as well as peripheral sensation and vibration perception threshold. Plantar pressures were assessed using the Tekscan pressure insole system, gait parameters were measured using the Gaitmat walkway system, peripheral sensation and vibration threshold were assessed using 10gm monofilament and biothesiometer respectively.

Intra-tester reliability was investigated using ICC, Standard Error of Measurement and Smallest Real Difference in the gout group for key measures (Foot Posture Index, first MTPJ dorsiflexion, ankle dorsiflexion movement, peak plantar pressures, pressure-time integrals and gait parameters). To investigate the significant difference between the groups, the left and right foot in gout were compared with the left foot of the control group using ANOVA with post-hoc comparisons. Non-parametric tests were used for muscle strength, peripheral sensation and Foot Problem Score and motion at the subtalar and midtarsal joints for comparison between the groups. Walking velocity, cadence and disability and impairment scores between the groups were assessed using an independent t-test with 95% confidence intervals. Significance for all these measures was set to 0.05 except for Chi square where a significance of 0.02 was set.

Results: The ICC for the intra-tester reliability was excellent with low measurement error for the measured outcomes. The gout group recorded significantly higher disability and impairment scores than controls ($p < 0.01$). Significant differences between the two groups were recorded for vibration pressure threshold, muscle strength, Foot Problem Score, first MTPJ dorsiflexion, foot motion and gait parameters ($p < 0.05$). Significant differences were demonstrated under the toes for mean plantar pressures and under the lateral heel, midfoot and hallux regions for pressure-time integrals in the gout cases ($p < 0.05$).

Conclusions: Individuals with gout have reduced quality of life due to greater disability and impairment. The gouty foot is slightly supinated with reduced dorsiflexion at the first MTPJ. Rearfoot and forefoot motions are limited with a high incidence of digital deformities and

dermatological lesions. The foot function in gout is characterized by reduced walking velocity, cadence, step and stride length. The plantar pressures are reduced under the toes with increased duration of loading under the hallux, lateral heel and midfoot regions. Further research using three-dimensional gait analysis is recommended to quantify motion at the foot and ankle joints and also to ascertain the role of proximal joints. Future work could be undertaken to evaluate the impact of acute gout on objective measures of foot function, and to determine predictors of poor foot function in patients with this disease. This will allow further work to investigate or formulate a podiatric management plan in conjunction with pharmacological therapy to improve impairment, disability and function in chronic gout.

*Screw up the vice as tightly as possible – you have
rheumatism; give it another turn, and that is gout.*

Anonymous

CHAPTER 1: INTRODUCTION

Gout is an inflammatory condition resulting from increased uric acid levels and their accumulation in tissues and joint spaces in the form of monosodium urate crystals (Klemp, 1997 and Roddy et al., 2007). Uric acid, the end product of purine metabolism, is excreted through the kidneys while maintaining its normal concentration (6.8 mg/dL) in the blood stream (Teng et al., 2006). A condition called ‘hyperurecemia’ occurs if the uric acid level exceeds 7mg/dL (Klemp, 1997 & Roddy et al., 2007). Hyperurecemia occurs due to either reduced ability of the kidneys to excrete uric acid (nephrolithiasis) or increased purine influx (diet) overloading the kidneys (Teng et al., 2007). The excess uric acid diffuses from the blood stream and deposits within the joint capsule and around the synovium as monosodium urate crystals provoking an intense inflammatory response which is termed as ‘gout flare’ (Klemp, 1997 & Roddy et al., 2007). Repeated flares and long standing hyperurecemia results in the formation of ‘tophus’. A tophus is a deposit of monosodium urate crystals surrounded by connective tissue and inflammatory cells and can be found in both the subcutaneous tissue and intra-articular spaces of the joints (Klemp, 1997 & Roddy et al., 2007).

Gout is of particular significance to New Zealand, which has the highest prevalence of gout worldwide (Klemp, 1997 & Roddy et al., 2007). The incidence of gout has increased three-fold in the last two decades (Teng et al., 2006). Gout affects approximately 15% of men with Maori and Pacific descent. These men are at risk of early onset and high severity with formation of gouty tophi and joint damage. Grahame and Scott (1970) reported that gout is monoarticular in distribution with high incidence for the first metatarsophalangeal joint (25%), ankle (10%) and elbow and wrist (10%). Recent statistics in New Zealand report an increasing incidence of gout among males of Maori and Pacific Island descent (Dalbeth,

2007). The incidence is found to be high for Pacific Island men, 14.9% (with an incidence ratio of 1:7), 9.3% (incidence ratio of 1:10) for Maori and 4.1% for European men (Dalbeth, 2007). In contrast, only 2% of female incidence has been reported (Dalbeth, 2007). Furthermore, 46% of people receiving treatment for gout in the gout clinics under the New Zealand District Health Board (DHB) are Pacific Islanders while 25.6% are Maori (Dalbeth, 2007).

“The architecture of the foot can be disrupted by repeated inflammation of synovial joints and surrounding soft tissues of the foot and ankle” (Turner et al., 2003). This statement was put forward by Turner in an attempt to explain foot pathology in rheumatoid arthritis. Gout flares also affect the synovium within the foot and ankle joints (Roddy et al., 2007; Grahame & Scott, 1970) and one would attempt to extend the above statement to a gout affected foot. However, unlike a rheumatoid foot, to the author’s current knowledge there is limited evidence pertaining to foot and ankle characteristics in gout. The foot allows smooth transition of the body over itself during gait which involves a complex interaction of the osseous and soft tissue structures in the foot and ankle. Hence, structural changes in the foot could bring about functional changes altering the normal biomechanics and causing pain, disability and reduced mobility. Since the incidence of gout in New Zealand is on the increase, the impact of the condition on the foot and ankle is of particular importance and warrants investigation.

Gouty arthritis is the most common inflammatory arthritis in men of over 40 years (Teng et al., 2006). In postmenopausal women the incidence of gout increases to 85% while the prevalence before menopause was reported to be 15% (Kim et al., 2003). In the United States the annual incidence is 1-3/1000 in men compared to 1/1000 in women (Masseoud et al., 2005). In China gout affects 25.8% of men and 15% women, while in Taiwan the incidence is 26% in men and 16% women (Wortman, 2002). Gout is also reported to have a seasonal occurrence, in the northern hemisphere gout flares occur often in spring, while in Israel gout flares are reported to occur in summer and spring seasons and in Australia, flares are reported

to be high in autumn (Schlesinger et al., 1998; Gallerani et al., 1999; Alter, 1994 & Wortman, 2002).

Hyperurecemia can result from increased uric acid production or decreased uric acid excretion by the kidneys (Teng et al., 2006; Maseoud et al., 2005; Falasca, 2006; Schlesinger et al., 1998 & Kim et al., 2003). Schlesinger (2004) states reduced renal clearance of uric acid as the main factor for increased uric acid concentration in the majority of cases. Factors that contribute to reduced uric acid excretion and increased uric acid production are listed in Tables 1.1 and 1.2.

Table 1.1: Factors responsible for reduced uric acid excretion.

Genetic causes or primary causes
Polycystic kidney
Down's syndrome
Acquired causes or secondary causes
Hypertension
Chronic renal failure
Chronic alcoholism
Drugs like cyclosporine, ethambutol, pyrazinamide, diuretics (thiazide, frusemide, loop diuretics, levadopa, nicotinic acid)
Metabolic and endocrine abnormalities: lactic acidosis, ketosis, hypothyroidism and hyperparathyroidism
Dehydration or starvation
Lead intoxication
Sarcoidosis.

Table 1.2: Factors responsible for increased uric acid production.

Genetic causes or primary causes
Enzymatic defects: Hypoxanthine-guanine phosphoribosyl transferase deficiency, Phosphoribosylpyrophosphate synthase overactivity, glucose-6-phosphate aldolase deficiency and fructose-6-phosphate deficiency.
Acquired causes or secondary causes
High purine intake (sea-food, spinach, red meat)
Obesity
Excessive alcohol consumption
Hypertriglyceridemia
Chemotherapy
Psoriasis.

However, the secondary factors associated with increased uric acid production or reduced uric acid excretion can also exist as a co-morbidity for gout. Medical conditions including hypertriglyceridemia, hypertension, cardiovascular diseases, renal failure and obesity have been found to be associated with gout (Choi et al., 2005; Abbott et al., 1998; Ford et al., 2002; Masuo et al., 2003; Sundstorm et al., 2005; Taniguchi et al., 2001; Kang et al., 2002). Hence, the management of gout include not only treating the cause of hyperurecemia but also managing the co-morbidities.

1.1 Classification of gout:

Wortmann and Kelley (2005) classified gout into four stages based on clinical symptoms and features.

Asymptomatic hyperuricemia

This is the primary stage without inflammation or arthritic pain with a serum urate level of greater than 7 mg/dl. As the uric acid level in the blood increases, the risk of supersaturation and crystal formation also increases. The solubility of urate within the joint is dependent on the temperature, pH of the intraarticular fluid and the amount of insoluble collagen and chondroitin sulphate (Bieber & Terkeltaub, 2004; Choi et al., 2005). Hyperuricemia is triggered by certain factors, some being nutritional (high purine diet, alcohol consumption), medication (diuretics, cytotoxic drugs, vitamin B12), metabolic factors (dehydration, lactic acidosis, hypothyroidism, hyper parathyroidism, obesity), renal disease and either genetic or drug-induced reduced renal clearance (Masseoud et al., 2005).

Acute gouty arthritis

This follows the primary stage and is characterised by an intense inflammatory response to the monosodium urate crystal deposits within the joint space or soft tissue (Grahame & Scott, 1970; Kim et al., 2002; Wortmann and Kelley, 2005, p. 1402). The symptoms of acute gout include sudden onset of severe pain, inflammation, limited range of motion and warmth at the affected joints (Kim et al., 2003).

Intercritical gout

This is a pain free period between two gout attacks, and may range from less than one year to ten years (Cassetta and Gorevic, 2004).

Chronic tophaceous gout

Acute gout flares, frequent and recurrent over a period of ten to twenty years would result in the formation of nodules of monosodium urate crystals. Such nodules are called tophi and can occur in cartilage, bone and tendons (Eggebeen, 2007; Cassetta & Gorevic, 2004; Teng et al., 2006). Chronic tophaceous gout is characterised by the presence of visible tophi, destructive arthritis of the involved joints and bony erosions which are polyarticular in distribution (Teng et al., 2006; Sunkureddi et al., 2006). The most common sites for tophi are the olecranon bursa of the elbow, Achilles tendon and the extensor surfaces of hands, feet and knees (Masseoud et al., 2005; Teng et al., 2006; Eggebeen, 2007; Cassetta and Gorevic, 2004; Kim et al., 2002).

The American College of Rheumatology has put forward criteria to diagnose gout (Wallace et al., 1977). Appendix 3 describes the American College of Rheumatology: Preliminary Criteria for the diagnosis of Gout. Although presence of monosodium urate crystals in the synovial fluid is a positive confirmation for gout, synovial fluid analysis is feasible all the time (Eggebeen, 2007) and hyperuricemia is an inconclusive finding as serum uric acid levels drop to normal range during flares in some cases (Campion et al., 1987; Zhang et al., 2006; McCarthy, 1994).

1.2 Tophi formation:

Tophi are a collection of monosodium urate crystals surrounded by inflammatory cells and connective tissue and occur both in subcutaneous tissue and intra-articular spaces in the joints (Grahame & Scott, 1970). Formation of tophi is associated with restricted joint range of motion, joint destruction, pain and cosmetic problems (Grahame and Scott, 1970). Although gout initially presents itself as self-limiting attacks of severe joint inflammation, and in the presence of persistent hyperuricemia tophaceous gout may also develop. However, a review of the literature suggests other sites. Table 1.3 describes the different sites in the body that are affected in gout.

Table 1.3: Body sites frequently affected in gout (in decreasing order).

Site	Structures prone to gouty attack and tophus formation	
	Osseous structures	Soft tissue structures
Foot	Medial aspect of 1 st MTPJ, tibial sesamoid, Midfoot (navicular and calcaneonavicular joint), metatarsal shafts, metatarsal shafts and metatarsocuneiform joints, navicular, cuboid and anterior calcaneus.	peroneal tendons (tendons of peroneus longus and brevis)
Ankle	Talar dome, distal tibiofibular articulation	Achilles tendon and anterior talofibular ligament
Knee	Knee joint (isolated case)	Prepatellar bursa
Elbow	Elbow joint (humero-ulnar joint, humero-radial and proximal radio-ulnar joint)	Olecranon bursa
Hand	Distal interphalangeal joints, proximal interphalangeal joints, metacarpophalangeal joints, carpals and thumb base	Flexor and extensor tendons.
<i>Hip, Sacroiliac, spine, sternoclavicular and the shoulder joints are very rarely affected in gout.</i>		

1.3 Pathophysiology of gout:

Uric acid is reported to stimulate and enhance immune responses by acting as an adjuvant (Shi et al., 2003). An adjuvant assists 'Toll-like Receptors' in recognising the uric acid released from the damaged cells during cell trauma or viral infections and act as a "danger signal" to illicit an immune response (Pillinger et al., 2007). The 'immune activation' function of uric acid is found to be only in its crystalline form which is at concentrations greater than 7 mg/dL, the hyperurecemic levels (Shi et al., 2003). Hu et al. (2004) using a mouse model studied the immune response with uric acid to tumour rejection. They observed that lowering uric acid concentration led to reduced tumour rejection while increasing uric acid concentration enhanced it. These results demonstrate that Toll-like Receptors ability to identify uric acid only in its crystalline form could be a possible reason as to why certain individuals with hyperurecemia continue to be asymptomatic.

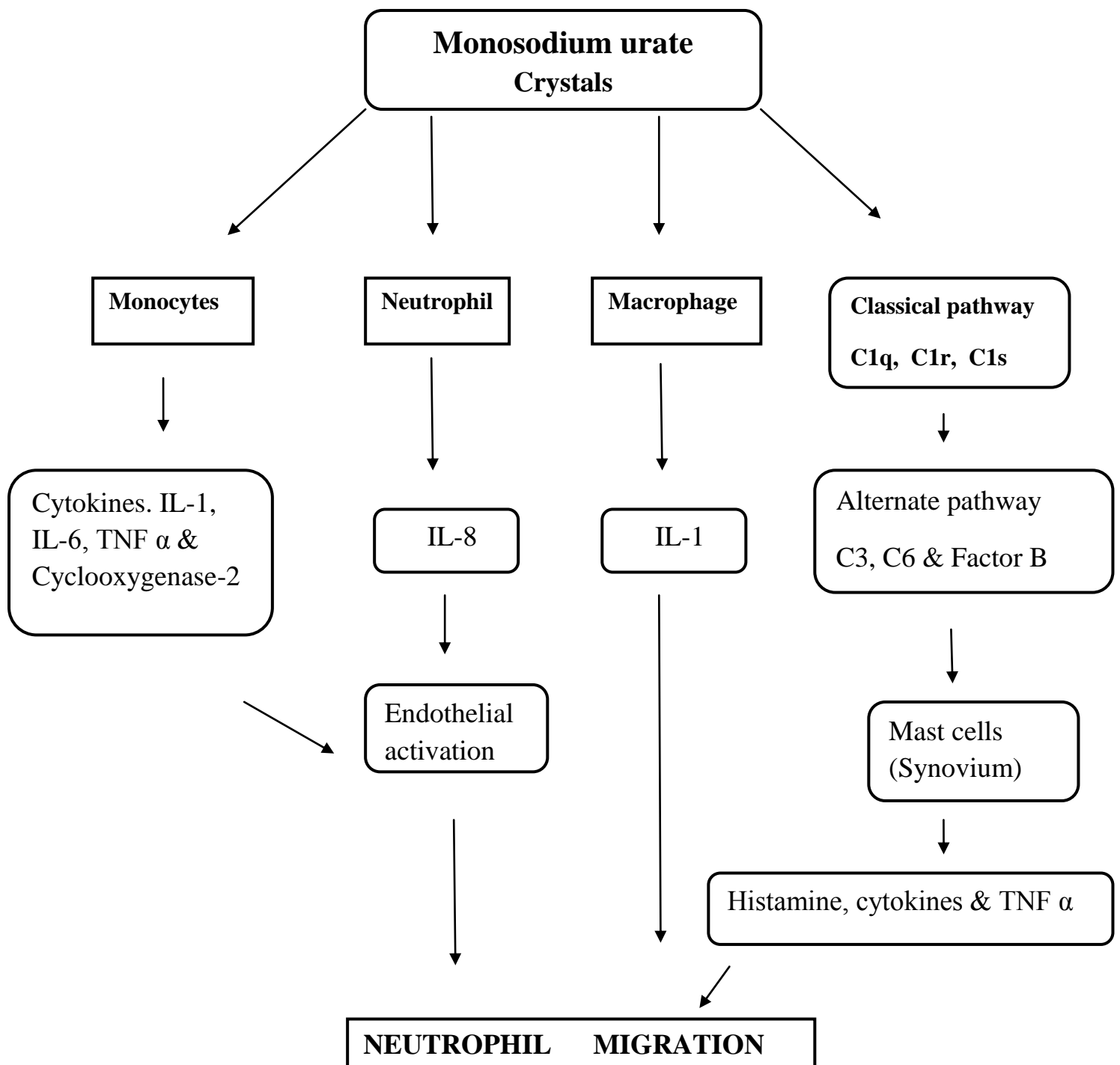
The inflammatory reaction in gout is due to the interaction between MSU crystals and the local tissues (Dalbeth & Haskard, 2005). Formation of MSU crystals in a tissue depends on the temperature and pH of the tissue (Choi et al., 2005). Around the joint, the MSU crystals are periarticular in distribution surrounded by mono and multinucleated leucocytes, macrophages, fibroblasts and lymphocytes (Choi, 2008). An acute attack of gout can be initiated by trauma, high purine diet, alcohol, stress/anxiety which increase the serum urate levels, disrupting the equilibrium between the leucocytes and the MSU crystals and result in the migration of crystals into the joint space triggering inflammation (Dalbeth & Haskard, 2005; Choi et al., 2005; Choi, 2008).

The MSU crystals trigger both the cellular and humoral components with their respective inflammatory mediators (Choi et al., 2005). Initially, as the uric acid begins to crystallize as MSU crystals in the tissues, the classical pathway for the complement system is activated (Figure 1.1). C1q, C1r, C1s attach to the crystal surface undergoing conformational changes to form C3, C6 and factor B of the alternate pathway (Fields et al., 1983; Doherty et al., 1983). The alternate pathway mediators that are bound to MSU crystals activate the mast

cells on the synovium which respond by releasing histamine, cytokines and the Tumour Necrosis Factor- α (Doherty et al., 1983; Dalbeth & Haskard, 2005). Histamine causes vasodilation and increased vascular permeability resulting in neutrophil migration through the endothelium (Yagnik et al., 2004; Dalbeth and Haskard, 2005). The neutrophil-endothelial cell adhesion is mediated by an enzyme E-Selectin in the process activating the neutrophils (Yagnik et al., 2004; Dalbeth and Haskard, 2005). The activated neutrophils release proinflammatory proteins, S100A8 and S100A9 (Ryckman et al., 2004) which further increase neutrophil migration thereby increasing the intensity of inflammation (Ryckman et al., 2003). Endothelial-neutrophil adhesion activates endothelial cells to produce endothelin-1 which further enhances endothelial-neutrophil adhesion and neutrophil migration (Getting et al., 2004). Hence neutrophil migration is considered the hallmark of inflammation as it accompanies the swelling and erythema and further leads to the recruitment of other inflammatory mediators amplifying the response (Dalbeth & Haskard, 2005). Since 90% of the leucocytes in the synovial fluid analysis during a gout flare are neutrophils they are considered to be the initiator of inflammation in gout (Pascual et al., 1999).

The MSU crystals interact directly with the protein component on the phagocyte membrane (neutrophils) activating signal transduction pathways like the Toll-Like Receptor- 2 and 4 (TLR-2 & 4) and Myeloid Differentiation Factor 88 (MyD-88) which are critical for the expression of interleukin-8 (Figure 1.1); (Choi et al., 2005; Liu-Bryan et al., 2005). Furthermore, MSU crystals interact with macrophages in the synovium and are mediated by inflammasomes (NALP) to produce interleukin- 1 (IL-1) (Ogura et al., 2006, Martinon et al., 2006 and Pillinger et al., 2007). Interleukin-8 and 1 play a key role in neutrophil accumulation and inflammation (Tetkeltaub et al., 1998). The MSU crystals are also phagocytised by monocytes which in turn produce interleukin-1, 6 and 8, TNF-alpha, and cyclooxygenase-2, resulting in further activation of endothelial cells (Choi et al., 2005). Interleukin-8 and 1 are of particular importance in neutrophil accumulation once they migrate in to the synovial tissue as neutrophils follow IL-8 (Tetkeltaub et al., 1998; Martinon et al., 2006; Pillinger et al., 2007). IL-8 action is dependent on the complement mediator C6 (Tramontini et al., 2004). Hence, it can be said that the inflammatory reaction during acute

gout is multiphasic, with neutrophils, monocytes and interleukin-8 & 1 being the predominant leucocytes responsible for gouty inflammation.



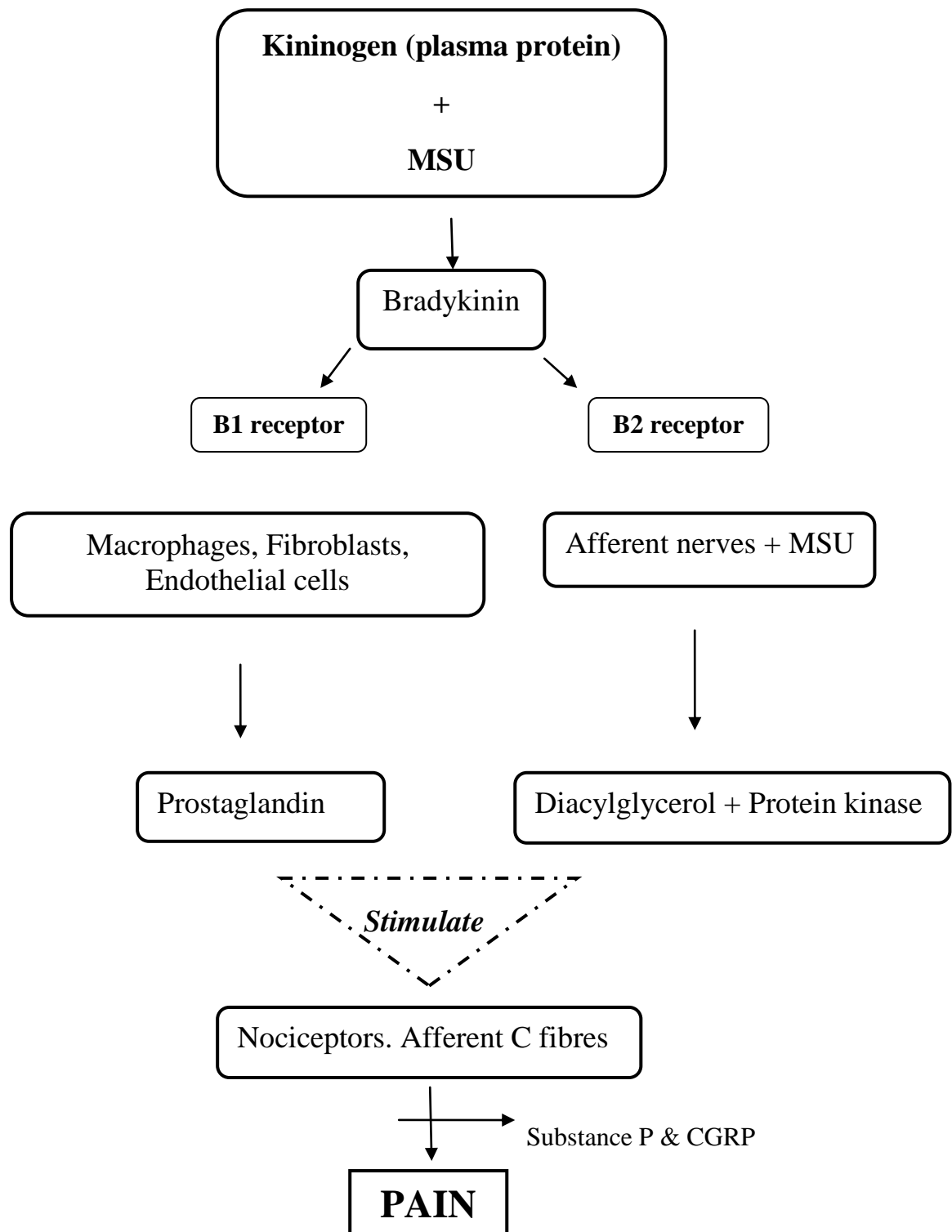
IL-1,6 & 8 – Interleukin (cytokinin), TNF – Tumour Necrosis Factor, S100A8 & S100A9 – Intracellular proteins producing neutrophil migration, C1q, C1r & C1s - Protein receptors of classical pathway, C3, C6 & factor-8 – protein receptors of alternate pathway.

Figure 1.1: Flow diagram for the pathogenesis of inflammation in gout.

1.4 Pain during gout flare:

Inflammation in gout is accompanied by severe joint pain brought about by prostaglandins, bradykinin and substance-P causing sensitization of nociceptors. The diagrammatic representation of this mechanism is shown in Figure 1.2. Following vasodilation, kininogen (a plasma protein) interacts with MSU crystals to activate bradykinin which has a dual action, both as an inflammatory mediator (vasodilation, endothelial activation and neutrophil recruitment) and as an initiator of pain by stimulating nociceptors (Kaplan, 2002; Couture et al., 2001). Bradykinin is expressed as B1 and B2 receptors, the former expressing on the cell surface of macrophages, fibroblasts and endothelial cells and stimulating the release of prostaglandins which stimulate nociceptors producing pain; the latter expressing on the sensory nerves stimulating the production of diacylglycerol and protein kinase C, activating nociceptors causing pain and hyperalgesia (Couture et al., 2001).

Stimulation of unmyelinated nerve fibres releases substance P, resulting in vasodilation, plasma extravasation, leucocyte recruitment and release of prostaglandins and cytokinins (Davies et al., 1984). Following injection of sodium urate into the ankle joints of chickens, Lunam and Gentle (2004) reported depletion of substance P from the nerves around the synovium and the joint capsule, using fluorescence immunohistochemistry. In support of this, the synovial fluid analysis of patients with acute gout shows high concentrations of substance P and Calcitonin Gene Related Polypeptide (CGRP); (Hernanz et al., 1993). The sensory afferent C fibres (nociceptor fibres) in the synovium are rich in CGRP and substance P (Payan, 1989) and the depletion of substance-P and CGRP indicates that C fibres are activated.



MSU – Monosodium urate crystals, B1 and B2 – Bradykinin receptors, CGRP – Calcitonin Gene Related Polypeptide.

Figure 1.2: Flow chart representing pain mechanism in gout.

1.5 Pain during joint movement:

Pain experienced during normal motion of a joint during acute gout is reported to be due to increased activation of C-fibres and also their increased sensitisation (Gentle, 1997; Lunam & Gentle, 2004). In these studies the C-fibres in the presence of MSU crystals exhibited a decreased “response threshold” indicating increased sensitivity or spontaneous activity of these fibres to stimulus. The response threshold of a nerve is defined as the lowest electric potential required to activate that nerve (Gentle, 1997). The increased sensitivity is being attributed to the increased level of activity in these fibres and also to the increased number of C fibre units that are activated in the presence of MSU crystals. This increased sensitisation is thought to be a reason for hyperalgesia reported during a gout flare. Lunam & Gentle (2004) observed that during normal joint movement the number of activated C fibre units increased in joints injected with MSU crystals when compared with normal joints which explains the pain associated with joint movement

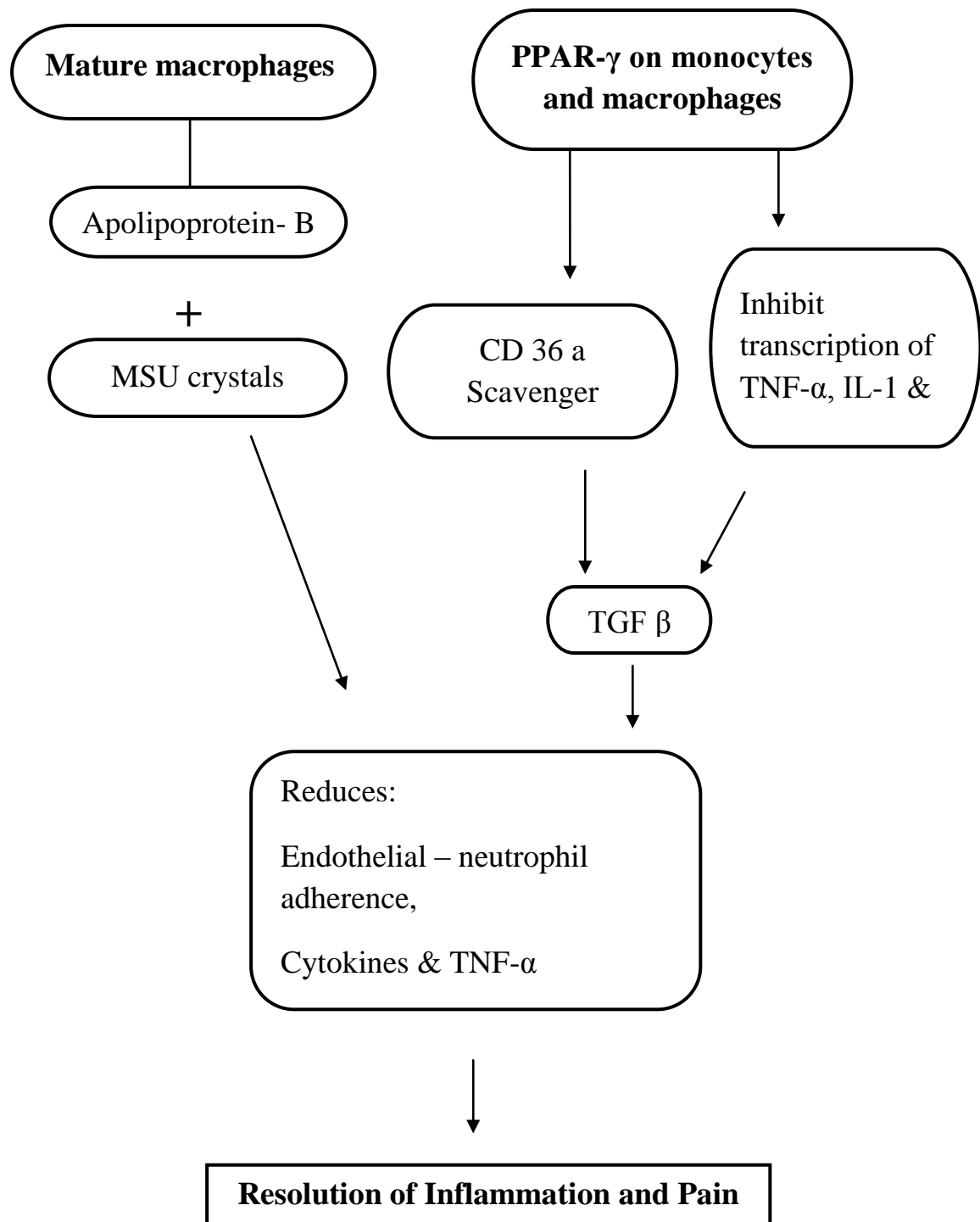
It is also reported that in MSU-injected chicken ankle joints, C fibre sensitivity and the number of activated afferent C fibre units increased with “noxious” movement, a term used to define movement of a joint other than its primary movement (Lunam & Gentle, 2004). A possible explanation for this could be that there are more numbers of C fibres on the sides of the joint that restrict noxious movements, hence releasing greater quantities of substance P (Lunam and Gentle, 2004). However, pain intensities with different movement of the joints are not studied in human subjects. Nevertheless, movement in any plane can induce pain in joints with MSU crystal deposition.

The inflammation in acute gout is self limiting and would resolve in seven to ten days without any treatment (Choi et al., 2005; Bieber & Terkeltaub, 2004). The diagrammatic representation of the mechanism involved in self-resolution of pain and inflammation in gout is shown in Figure 1.3. It is a well established fact that MSU crystals are present in the synovial fluid even during this phase (Pascual & Jovani, 1995; McGill, 2000; Maseoud et al., 2005; Choi et al., 2005), which suggests that an equilibrium exists between the factors

that mediate inflammation and those that resolve inflammation in the presence of MSU crystals (Dalbeth & Haskard, 2005). Synovial fluid analysis during the resolution phase identified macrophages as the predominant cells with MSU crystals and minimal numbers of neutrophils indicating the ability of the macrophage to engulf MSU crystals without inducing inflammatory response (Pascual & Jovani, 1995). It was reported that only mature macrophages, formed after three to five days of differentiation from monocytes (normal range is one to three days) did not secrete inflammatory mediators (TNF, IL-1, IL-6) when exposed to MSU crystals in both animal and human models (Yagnik et al., 2000 & Landis et al., 2002). This suggests that the anti-inflammatory effect of a macrophage is dependent on its stage of differentiation (Figure 1.3).

Spontaneous resolution of gout may also be due to the induction of intracellular anti-inflammatory pathways like the Peroxisome Proliferator-activated Receptor γ , a member of the nuclear hormone receptor superfamily (PPAR- γ); (Dalbeth & Haskard, 2005). PPAR- γ is expressed on monocytes and macrophages which inhibit transcription of inflammatory genes regulating the release of TNF, IL-1 and IL-8, as reported in a mouse air pouch model (Akahoshi et al., 2002). Furthermore, PPAR- γ stimulates expression of CD36, a scavenger receptor on monocytes and macrophages, which upregulates the transforming growth factor (TGF) from macrophages upon phagocytosis of MSU-laden neutrophils (Akahoshi et al., 2002). TGF minimises neutrophil-endothelial adherence and also inhibits interleukin production (Akahoshi et al., 2002). Such macrophages with engulfed neutrophils, called Reiter cells, are isolated from synovial fluid analysis during a gout flare (Selvin et al., 2000).

Changes in the protein that coats MSU crystals can influence its interaction with inflammatory mediators (Dalbeth & Haskard, 2005). An apolipoprotein-B produced from macrophages coats MSU crystals, decreasing neutrophil-MSU interaction and thereby reducing the release of inflammatory materials (Terkeltaub et al., 1984). Similar results of the presence of apolipoprotein- B on MSU crystals was observed in the rat subcutaneous air pouch model during the resolution phase (Ortiz-Bravo et al., 1993). Hence, protein coating on MSU crystals can also bring about an anti-inflammatory affect.



PPAR - Peroxisome Proliferator-activated Receptor γ , TGF – Transforming growth factor, CD 36- scavenger receptor protein, TNF – Tumour necrosis factor, IL – interleukin.

Figure 1.3: Flow chart representing resolution of pain and inflammation in gout.

1.6 Mechanism of tissue injury:

Chronic hyperurecemia is accompanied by chronic inflammation leading to synovitis, cartilage loss and bone erosion (Choi et al., 2007). The mechanism of tissue injury in gout is diagrammatically shown in Figure 1.4 and 1.5. From the pathological perspective, the intra-articular accumulation of monosodium urate crystals attracts neutrophils and a cascade of cellular and humoral inflammatory mediators (tumour necrosis factor, interleukins 1, 6 & 8 and intracellular adhesion molecules), amplifying the inflammatory responses. In vivo, Cooper et al. (1992) and Lubberts et al. (2001) observed synovial inflammation and joint destruction when interleukin-1 and tumour necrosis factor- α were injected into the joints of mice. Pascual et al. (1999) noticed low grade synovitis during the remission period with ongoing intra-articular phagocytosis of MSU crystals indicating that chronic inflammation plays a vital role in tissue injury as infiltration of leucocytes continues. Production of metalloproteinase and nitric oxide has also been identified in the literature to bring about cartilage loss and bone erosion in gout (Chen et al., 2003).

The interaction of MSU crystals with the chondrocytes induces the release of nitric oxide and metalloproteinase (Liu et al., 2001). Chondrocytes release metalloproteinase-3 (MMP-3) in a P38 dependent manner (Liu et al., 2001). Macrophages are reported to release another metalloproteinase, metalloproteinase-9 (MMP-9), as reported in rheumatoid arthritis (Saren et al., 1996). MSU crystals induce MMP-9 release from macrophages by stimulating MMP-9 gene expression (Hsieh et al., 2003). Liu et al. (2001) experiment also reported the release of nitric oxide by chondrocyte-MSU interaction by inducing the expression of inducible nitric oxide synthase enzyme (*i*NOS). Similarly, MSU crystals induce nitric oxide production in macrophages by stimulating the expression of *i*NOS (Jaramillo et al., 2003). The *i*NOS stimulation by MSU crystals is by upregulating the *i*NOS expression on mRNA (Chen et al., 2004). Furthermore, interaction of interleukin-1 (IL-1) with chondrocytes, produced nitric oxide (Taskiran et al., 1994) an inflammatory mediator produced by MSU crystals.

Metalloproteinases (MMP-3 and MMP-9) induce production of collagenase 1, 2 and 3 which destroy collagen-II and proteoglycans (Goldring, 2000). The collagen network comprising mostly collagen- II provide tensile strength, while the proteoglycan aggrecan provide compressive stiffness to the articular cartilage (Ratcliff et al., 1988). Nitric oxide causes cartilage destruction by suppressing the synthesis of the cartilage matrix in response to IL-1 (Taskiran et al., 1994). The MSU crystals cause further joint destruction by altering osteoblast expression to reduce bone formation and amplify osteoblast-mediated bone reabsorption by reducing the activity of osteocalcin and alkaline phosphatase (Bouchard et al., 2002). In addition to nitric oxide and metalloproteinases, prostaglandin E2, an important modulator of pain and inflammation, is capable of causing bone and cartilage destruction by inhibiting collagen synthesis and inducing MMP production by macrophages (Dalbeth & Haskard, 2005). Hence, tissue injury in gout is the result of inflammatory mediators which influence gene expression to cause bone and cartilage destruction.

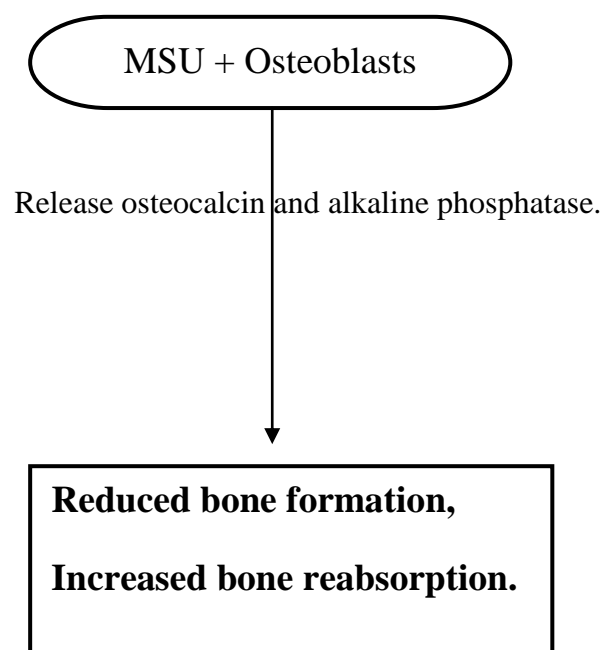
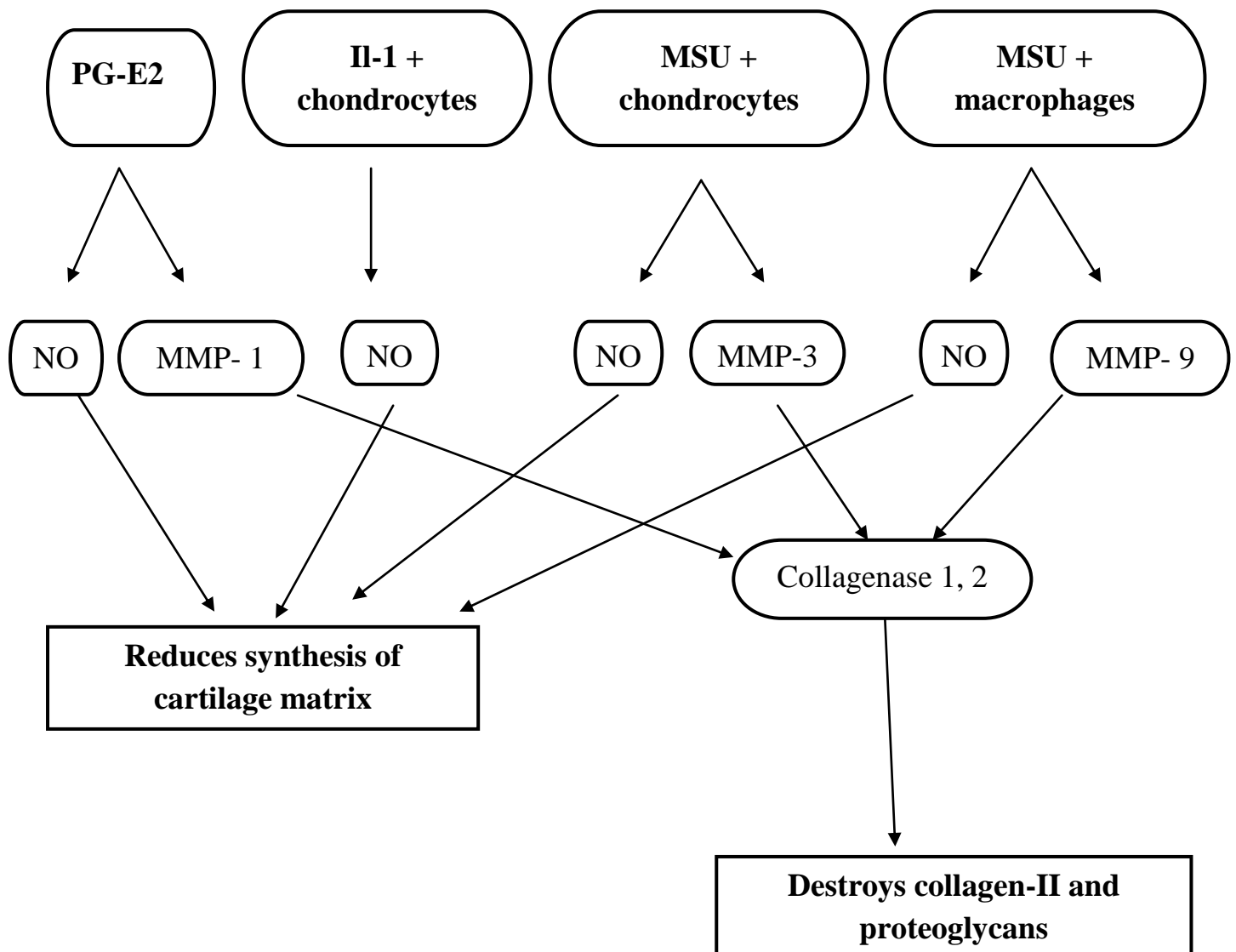


Figure 1.4: Flow diagram representing mechanism of bony destruction in gout.



PG – Prostaglandin E2, NO – Nitric oxide, MMP – Metalloproteinase

Figure 1.5: Flow diagram representing mechanism of cartilage destruction in gout.

The chronic inability of the body to eliminate urate causes this to accumulate in cartilage, tendon, soft tissues, synovial membrane and other parts of the body giving a characteristic nodular appearance called tophus (Cassetta & Gorevic, 2004). It is postulated that the lower temperature of the cartilage, tendons and subcutaneous tissues (approximately 30° C) decreases urate saturation to 4mg/dl, resulting in urate super saturation and accumulation of urate crystals (Lyburn et al., 2002).

Summary: Gout is an inflammatory condition caused by the accumulation of monosodium urate crystals within a joint or soft tissue. The MSU crystal induced inflammation is neutrophil mediated and is reported to breakdown bone and cartilage thereby altering joint structure and function. Since gout predominantly affects the foot, it is imperative to review the normal structure and function of the foot and ankle, to allow us to understand the impact of gout on these structures. The following chapter will briefly discuss structural and functional anatomy of the foot and ankle with an overview on the mechanics of gait cycle.

CHAPTER 2: STRUCTURAL AND FUNCTIONAL ANATOMY OF FOOT AND ANKLE

2.1 Introduction

This chapter presents a brief explanation of the anatomy of foot and ankle. In order to understand the role of these joints and their associated soft tissue structures during gait, this section will explore the type of motion that occurs in these joints during weight-bearing and non-weight-bearing activities. Preference is given to the role played by foot and ankle joints and soft tissue structures during weight bearing, as the chain of events in gait occur in weight bearing, described as a closed kinetic chain. Finally, the different phases in a gait cycle will be discussed, as foot pain and disability are best reflected in the ability to produce smooth locomotion.

The foot is divided basically into rearfoot, the midfoot and the forefoot, which function as a single unit during gait for the smooth progression of the body over the foot. The foot articulates with the proximal lower limb through the ankle joint (Sizer et al., 2003). Since the entire lower limb is interconnected to the foot joints (rearfoot, midfoot and the forefoot) through the ankle, muscles and connective tissues, any alteration in the mechanics of the foot and ankle would influence the function of the lower limb as a whole (Donatalli, 1990).

2.2 The ankle joint complex

The ankle joint is comprised of the talar dome resting within the mortise formed by the lateral and medial malleoli (Sizer et al., 2003). The superior aspect of the talus, called the trochlea, articulates with the inferior lateral aspect of the tibia on the medial side and with the inferior medial aspect of the fibula on the lateral side (Sizer et al., 2003). The ranges of motion for the ankle joint are plantarflexion/dorsiflexion along the sagittal plane, abduction/adduction in the transverse plane and inversion/eversion along the frontal plane (Draves, 1986, Sizer et al., 2003).

The stability of the ankle is maintained by the integrity of the articulating surfaces (talar dome inside the ankle mortise) and the lateral and medial ligaments which resist talar rotation within the mortise (Sizer, 2003 & Draves, 1986). The lateral ankle ligaments (anterior talofibular and posterior talofibular ligaments and calcaneofibular ligament) stabilise the lateral aspect of the ankle during inversion movements while the medial or the deltoid ligament stabilise the medial aspect of the ankle during eversion movements (Seizer et al., 2003 and Draves, 1986). As the ankle is held tightly on the medial and lateral sides by the ligamentous attachments, predominant movement occurs in the sagittal plane, dorsiflexion and plantarflexion (Donatalli, 1990). The ankle dorsiflexion is influenced by the tibialis anterior muscle and the extensor digitorum and hallucis longus muscles (Draves, 1986). Plantarflexion is influenced by the gastroc-soleus complex and tibialis posterior muscle (Draves, 1986). The joint kinematics differ between open kinetic (nonweight-bearing) and closed kinetic chains (weight-bearing). For example ankle dorsiflexion during open kinetic chain movements is associated with talar adduction and external rotation inside the mortise (Sizer et al., 2003). However, in a closed kinetic chain movement (where the movement in one joint produces movement in the other joints and vice versa), ankle dorsiflexion is accompanied by talar adduction and the mortise externally rotates on the talus (Sizer et al., 2003). Since functional anatomy is defined as joint kinetics during dynamic motion (Root et al., 1976) closed kinetic chain motion will be discussed.

During the closed kinetic chain (weight-bearing) inversion and eversion movements of the ankle are restrained by ground reaction forces, and are therefore substituted by the internal and external rotation of the leg on the foot during the dorsiflexion and plantarflexion movements of the ankle (Close, 1956; Donatalli, 1990; Sizer et al., 2003). The resultant torque produced by the rotating leg is transmitted through the talus to midfoot and forefoot influencing their movements (Hertel, 2002; Donatalli, 1990). Root et al. (1976) and Donatalli (1990) describe the ankle joint function to be dependent on the subtalar and midtarsal joint as subtalar joint pronation adducts the talus dorsiflexing the ankle and further internally rotating the leg on the foot. However, Nester (1997) described the excursion of the tibia over the foot during midstance to be independent and uninfluenced by the subtalar joint and midtarsal joint. As the ankle joint motion is both dependent and independent of the subtalar and

midtarsal joints, it could be considered a separate joint and not a part of the “rear foot complex”, described later in this section in more detail.

2.3 The rearfoot

The rearfoot consists of the talus and the calcaneus which articulate to form the subtalar joint (Draves, 1986). However, the talonavicular joint is also considered as a part of the subtalar joint (Sizer et al., 2003 & Hertel, 2002). The subtalar joint is an intricate structure with two joint cavities. The anterior subtalar joint, also called the talocalcaneonavicular joint, is formed by the articulation of the anterior facets of the talus head and the calcaneus and the proximal surface of the navicular (Sizer et al., 2003 & Hertel, 2002). This is a ball and socket joint with the talar head being the ball, and the calcaneus and the navicular forming the socket (Hertel, 2002 & Draves, 1986). The posterior subtalar joint inturn is a gliding joint formed by the articulations between the posterior facets of the talus and calcaneus (Hertel, 2002; Seizer et al., 2003; Draves, 1986). The anterior and posterior subtalar joints are separated by the sinus tarsi (Draves, 1986).

Apart from the articulating surfaces the subtalar joint is stabilised by ligaments. The cervical ligament which lies within the sinus tarsi is responsible for the stability and coordination of both the anterior and posterior subtalar joints while the interosseus ligament stabilises the posterior subtalar joint by resisting inversion (Sizer et al., 2003 & Hertel, 2002). The posterior subtalar joint is further reinforced by the lateral, medial and posterior talocalcaneal ligaments (Seizer et al., 2003; Draves, 1986). The anterior subtalar joint is supported by the talonavicular ligament, the calcaneonavicular ligament, the spring ligament and the bifurcate ligament (Seizer et al., 2003; Draves, 1986).

The axis of the subtalar joint is triplanar with movement in all the three planes (sagittal, frontal and transverse). The predominant movement being in the frontal plane (supination and pronation) (Draves, 1986). Supination at the subtalar joint causes the calcaneus to invert and

the talus to abduct and dorsiflex along the same axis (Seizer et al., 2003 & Draves, 1986). Pronation at the subtalar joint causes the calcaneus to evert and the talus to adduct and plantarflex (Seizer et al., 2003 & Draves, 1986). During gait the weight of the body is dispersed by the talus inferiorly to the calcaneus, through the posterior subtalar joint and distally into the midfoot by the anterior subtalar joint (Viladot, 1992). This dissipated force generates movement in the foot and ankle joints best described as a ‘closed kinetic chain’ where the movement in one joint produces movement in the other joints and vice versa (Lundberg and Svensson, 1993, Nester, 1998 and Donatalli, 1990). The pronation/supination movement of the subtalar joint generates similar movement in the midtarsal joint (talonavicular and calcaneocuboid joint) distally while it produces internal/external rotation of the ankle mortise superiorly (Seizer et al, 2003; Donatalli, 1990; Lundberg & Svensson, 1993; Nester, 1997). Nester (1997) describes the closed kinetic chain of the ankle, subtalar joint and the midtarsal joint as the ‘rearfoot complex’, which includes motion of the talus relative to tibia, calcaneus relative to talus, navicular and cuboid relative to talus and calcaneus. However, Lundberg and Svensson (1993) argue that the talonavicular joint is better understood as part of the midtarsal joint as it differs remarkably to the talocalcaneal joint in the orientation of joint axis and in the amount of rotation about the axes. In support of this, Huson (2000) describes that in a ‘closed kinetic chain’, the motion in a particular joint is influenced by the other joints and vice versa. However, these joints do undergo certain movements which are independent of other joints in the kinetic chain (Huson, 2000). Hence the ‘closed kinetic chain’ is better described as a ‘tarsal mechanism’ consisting of the subtalar joint (rearfoot), the talocrural (ankle), the calcaneocuboid and the talonavicular joints (midtarsal joint) as individual joints (Huson, 2000). Nevertheless, the motion in the talonavicular joint is generated from the talus which makes it an integral part of the closed kinetic chain (Nester, 1998) and its greater motion is attributed to the joint nature (ball and socket joint), an adaptive mechanism of the foot to adapt to uneven terrain (Root et al., 1976). Henceforth, the subtalar joint will be referred to as a rearfoot joint with the exception of the talonavicular joint which will be discussed as a part of the midfoot joint.

2.4 Midfoot

The midfoot comprises the talus, calcaneus, navicular, cuboid and the cuneiforms (medial, lateral and the intermediate); (Donatalli, 1990). The midfoot transmits the forces generated in the rearfoot to the forefoot (Donatalli, 1990). The osseous structures of the midfoot articulate to form the midtarsal joint (Donatalli, 1990). The midtarsal joint (MTJ) consists of the navicular and the anterior medial portion of the calcaneus articulating with the talus (talocalcaneonavicular joint) to form the medial superior aspect; the cuboid articulates with the anteriolateral portion of the calcaneus (calcaneocuboid joint) at the inferior lateral aspect; and finally, the medial, intermediate and lateral cuneiforms articulate with the cuboid and navicular, forming the distal anterior portion (Donatalli, 1990, Sizer et al., 2003 and Draves, 1986). The talocalcaneonavicular joint is a ball and socket joint allowing motion in any direction (Draves, 1986). This joint is compared to the hip joint, with articulation of the calcaneus and navicular similar to the acetabulum, and the head of the talus similar to the head of femur (Donatalli, 1990). The calcaneocuboid joint is a saddle joint, with articulation of concave anterior calcaneus with the convex cuboid (Donatalli, 1990). The pivotal movement of this joint allows the forefoot to dorsiflex on the rearfoot during the conversion of the foot into a rigid lever during propulsion (Donatalli, 1990; Root et al., 1976).

Describing MTJ as a single unit, Manter (1941) described two axes of rotation, the oblique and the longitudinal, to explain plantarflexion/inversion, dorsiflexion/eversion and plantarflexion/adduction and dorsiflexion/abduction movements respectively. Nester et al. (2001) states that the motion in a joint determines its axis and not vice versa and described a single axis for the MTJ which has the ability to vary in time and orientation producing motion in all the three cardinal planes. Nester et al. (2001) argues that the triplanar motion of the MTJ allows movement in any direction and therefore does not need two axes. Reporting forefoot motion as an indicator of MTJ motion, Nester et al. (2002) observed coupled motion consisting of eversion, abduction and dorsiflexion with STJ pronation and inversion, adduction and plantarflexion of the forefoot on the rearfoot with STJ supination. The motion between the rearfoot and the midfoot is described as a “screw like” with talus and calcaneus rotating clockwise with pronation while the MTJ rotates anticlockwise (Manter, 1941). The

navicular moves distally and displaces dorsally, abducting the forefoot, a movement which accentuates in pes planovalgus deformity (Manter, 1941). This rotational movement further stabilises the cuboid into a fulcrum for the peroneus longus muscle to plantarflex the first ray in the early stages of propulsion during gait (Donatalli, 1990). The first ray is the articulation of first metatarsal and medial cuneiform (Root et al., 1976).

Clinically the supination/pronation movement of the MTJ is observed by the rise and fall of the medial longitudinal arch (MLA); (Donatalli, 1990). The calcaneus, talus, navicular, the cuneiforms, and the first three metatarsals, comprise the MLA (Draves, 1986). The plantar fascia maintains the integrity and stability of the arch as it connects the proximal aspect (calcaneus) with the distal end of the arch (all metatarsal heads, the sesamoid bones under the first metatarsal head and base of proximal phalanx); (Huang et al., 1993; Donatalli, 1990; Draves, 1986). The plantar fascia is assisted by the long plantar ligament, the short plantar ligament (calcaneocuboid ligament) and the spring ligament (calcaneonavicular ligament) in maintaining the stability of the arch (Draves, 1986; Huang et al., 1993; Borton & Terence, 1997). The stability of the arch is further enhanced by the action of posterior tibial and peroneus longus muscles (Draves, 1986; Donatalli, 1990). The former raises the arch by exerting a superior and medially directed force at its insertion (navicular, cuneiforms and the second, third and fourth metatarsal bases) while the latter raises the arch by plantar flexing the first ray during the 'windlass mechanism' (Draves, 1986; Donatalli, 1990).

The windlass mechanism is first described by Hicks (1954) and later demonstrated by Fuller (2000). It is the tightening of the plantar fascia and the associated rising of the medial longitudinal arch with the extension of the hallux (Hicks, 1954). The ground reaction force dorsiflexes the hallux after heel lift, the plantar fascia tightens around the sesamoid bones under the first metatarsal head like a windlass pulling the calcaneus and first metatarsal closer in the process, and raising the MLA (Fuller, 2000). The windlass mechanism enables the foot to be converted into a rigid lever over which the body propels itself forward (Root et al., 1974).

2.5 Forefoot

The forefoot consists of the medial, intermediate and lateral cuneiforms, cuboid, metatarsals (1-5) and the phalanges which are distal to the metatarsal heads (Draves, 1986). The first, second and third metatarsals articulate with the medial, intermediate and lateral cuneiforms, while the fourth and fifth metatarsals articulate with the cuboid (Draves, 1986). The articulation of the first metatarsal with the medial cuneiform is described as the first ray and the fifth metatarsal with the cuboid described as the fifth ray. The phalanges are the toes; there are two for the first metatarsal and three phalanges each of each for the remaining four metatarsals (Donatalli, 1990). The three cuneiforms and the cuboid form the transverse arch which runs from the lateral to medial aspect of the foot, allowing dorsiflexion of the forefoot on the rearfoot, a mechanism reported to be essential for effective propulsion (Donatalli, 1990; Root et al., 1976).

The metatarsals are aligned parallel to one another by the Lisfranc's ligament, the transverse metatarsal ligament, the interosseous muscle, and the peroneus longus and posterior tibial tendons (Draves, 1986). The first ray and the fifth ray (fifth metatarsal and cuboid) have triplanar motion while the middle three metatarsals have a two-plane motion along the sagittal and transverse planes (Donatalli, 1990). The frontal plane motion (pronation/supination) of the first and fifth rays allows the forefoot to adapt to uneven terrain, and supination converts the forefoot in to a rigid lever via the MTJ for effective propulsion (Donatalli, 1990).

The triplanar motion of the first and fifth rays allows the forefoot to supinate and pronate with respect to the rearfoot (Root et al., 1976). The metatarsals are described as support beams for the longitudinal and transverse arches (Donatalli, 1990). The plantar fascia fans out to insert into the metatarsal heads, preventing splaying of the metatarsals (Donatalli, 1990). The heads of the metatarsals takes up most of the load during stance phase with the first metatarsal taking the highest (Bevan, 1992). The sesamoid bones under the first metatarsal

head, embedded within the tendon of flexor hallucis brevis, absorb the vertical forces generated during propulsion (Donatalli, 1990).

The toes help to stabilise the longitudinal arch by maintaining ground contact during the stance phase of gait. The toes exhibit a two-planar motion at the metatarsophalangeal joints; dorsiflexion/plantarflexion in the sagittal plane and abduction/adduction along the transverse plane (Donatalli, 1990). Extension of the toes at the metatarsophalangeal joints increases the tension in the plantar fascia which converts the foot to a rigid lever over which the body propels itself. Of importance is the 65° to 75° of extension at the first metatarsophalangeal joint required to trigger the windlass mechanism (Fuller, 2000). During the late propulsion phase the interossei and the lumbricals (the intrinsic foot muscles) stabilise the toes on the ground; a weakness of these is reported to be the cause of claw toes and hammer toes (Root et al., 1976).

2.6 Gait cycle

Gait is defined as the method of locomotion involving alternative and repetitive use of the two limbs for the forward movement of the body while maintaining stability (Whittle, 2007; Perry, 1992). The initial contact of the foot with the ground marks the beginning of the gait (Perry, 1992). A gait cycle is the time taken from the heel contact of one leg to the heel contact of the same leg (Whittle, 2004). The distance between the heel contact of one leg to the heel contact of the opposite leg is the step length, two step lengths makes a stride and the total number of steps in a minute gives the cadence (Perry, 1992). The time for each gait cycle is influenced by the velocity and cadence (Whittle, 2007).

Gait cycle is divided in to two phases, the stance and swing phases (Whittle, 2007). The stance phase is that when the foot is in contact with the ground, and is divided into contact, midstance and propulsion phases (Whittle 2007; Kirtley, 2006; Perry, 1992). The swing

phase is when the other foot is in the air passing over the stance foot until it strikes the ground.

2.6.1 Stance phase: contact period

This phase begins with heel contact of one foot and terminates with forefoot loading of the same foot (Whittle, 2007). The heel strikes the ground in an inverted position by the action of the tibialis posterior (Whittle, 2007). Following heel contact, the STJ pronates until the heel aligns itself perpendicular to the ground; the leg internally rotates, further pronating the STJ until forefoot contact (Perry, 1992 & Whittle, 2007). STJ pronation enables the foot to absorb shock and transmit the loading forces to the distal and proximal aspects of the lower limb (Perry, 1992).

2.6.2 Stance phase: midstance period

This phase begins with forefoot contact and ends with heel lift (Donatalli, 1990). The forefoot slightly abducts and dorsiflexes on the rearfoot to adapt to uneven terrain (Bevan, 1992). As the leg begins to move over the foot, gastrocnemius muscle externally rotates the leg causing the STJ to supinate (Perry, 1992). The tibialis posterior also assists to resupinate the foot at the STJ by raising the medial longitudinal arch, the midfoot supinates locking the MTJ in the process converting the foot from a mobile adaptor to a rigid lever (Whittle, 2007; Perry, 1992).

2.6.3 Stance phase: propulsion period

This phase begins with heel lift and ends with toe off (Donatalli, 1990). Action of the soleus muscle lifts the heel as the ground reaction forces cause extension at the metatarsophalangeal joints, tightening the plantar fascia (Whittle, 2007 & Root et al., 1976). The first MTPJ extension, together with the plantarflexion of the first ray by the peroneus longus, triggers the windlass mechanism (Fuller, 2000). The intrinsic foot muscles stabilise the toes against the

ground as the body weight transfers from lateral to medial foot, onto the first MTPJ, as the contralateral foot prepares to contact the ground (Bevan, 1992).

2.6.4 Swing phase

During this phase the anterior tibial, the extensor hallucis longus, and the extensor digitorum longus muscles, act to dorsiflex and invert the foot to allow ground clearance (Root et al., 1976). The subtalar and the midtarsal joints remain in a supinated position during early swing and progress to a pronated position during mid swing (Perry, 1992). As the swing leg passes the stance leg on to late swing, the ankle dorsiflexors maintain the foot in a supinated position preparing the foot for heel strike (Perry, 1992). The speed at which the swing leg passes over the stance leg determines gait velocity (Bevan, 1992).

The gait pattern of every individual is dependent on joint range of motion, muscle activity and medical condition (Helliwell et al., 2007); in particular, gait velocity is considered one of the predictors of functional status, either of an individual or of a condition (Whittle, 2007; Perry, 1992). For example, rheumatoid gait is reported to be slow, a mechanism to reduce pain and a compensation for altered muscle strength and joint range of motion (Helliwell et al., 2007).

2.7 Summary

The ankle and the foot are the main structures of the lower limb to bear body weight and convert the resultant ground reaction forces to allow respective motion of individual joints in the foot and ankle. The entire lower limb behaves like a kinetic chain during weight-bearing activities where motions in the individual joints are interdependent. However, independent movements do occur in the ankle and midtarsal joints during gait. Hence, the joint mechanics of these joints are explained and discussed individually but not as part of the rearfoot complex. Gait, a passive movement, is the result of the systematic and coordinated movements of all the joints in the kinetic chain and is the measure of an individual's

functional status. The following chapter will review the literature on the incidence of gout in foot and ankle.

CHAPTER 3: LITERATURE REVIEW OF THE FOOT PROBLEMS IN GOUT

3.1 Introduction

This section will explore the literature around the incidence of gout in foot and ankle. First, the search history to identify gout studies is discussed. This includes the various databases searched and all the possible key words used in the search of relevant articles on gout relating to foot and ankle. In order to relate to the present study, the articles obtained from the search are evaluated to identify the structures in the foot and ankle affected by gout, the methods used to identify gout, and any measurement of foot and ankle characteristics in these studies. This allows for a comparison in the structures reported to be affected in gout to the results obtained from the present study and also opens a discussion on the method of diagnosis.

Literature searches of AMED (1985 to May, 2008), Medline (1950 to May, 2008), CINAHL (1982 to May, 2008), Academic Research Library (1971-May, 2008), Dissertations & Theses (1950-May, 2008), Nursing & Allied Health Source, Proquest Proquest Health & Medical Complete, Biomedical Reference Collections: Basic, Clinical reference Systems, Health Source: Nursing/Academic Edition, Psychology & Behavioural Sciences Collection, SportsDiscus with Full Text, SCOPUS (1960 to May, 2008), and the Cochrane database. In addition, hand searches and references from journal articles, were undertaken between March and May, 2008. The language was restricted to English and the following terms were used in the search strategy: ‘comfort’, ‘uncomfortable’, ‘discomfort’, ‘shoe’, ‘footwear’, ‘torsional stiffness’, ‘foot-shape’, ‘foot alignment’, ‘foot land-marking’, ‘foot modelling’, ‘foot outline’, ‘skeletal alignment’, ‘cushioning’, ‘high heels’, ‘orthotics’, ‘insole’, ‘innersole’, ‘instep’, ‘insert’, ‘inlay’, ‘sole’, ‘arch support’, ‘heel cup’, ‘metatarsal pad’, ‘kinematic’, ‘material properties’, ‘impact force’, ‘EVA’, ‘customisation’, ‘finite element analysis’, ‘gout’, ‘pathophysiology’, ‘pathology’, ‘rheumatoid arthritis’, ‘joint structure’, ‘joint range of motion’, ‘gait’, ‘gout and foot’, ‘gout and ankle’, ‘walking velocity’, ‘pressure analysis’, ‘functional status’, ‘muscle strength’.

Fifteen articles reporting gout in the foot and ankle region between the years 1972 to 2007 were extracted from the databases. Thirteen were reported as case studies, one a case controlled study, and the other as a cross-sectional survey. Five cases affected the first MTPJ (medial aspect of the joint and tibial sesamoid) with two of these developing into ulcers (Table 3.1). Five cases have reported tophus in the region of the midtarsal joint affecting various structures (peroneal tendons, navicular and base of the metatarsal shaft, cuboid and cunienavicular articulation (Table 3.1). Finally two cases reported tophus in the Achilles tendon, and one of tophus in the talar dome, distal tibiofibular articulation and midfoot joints. The disease duration among the reported studies is 10 ± 2 years.

The case controlled study conducted by Roddy et al. (2007) reported a high prevalence of gout in the first MTPJ (60 - 66%) followed by midfoot (13 – 20%) and ankle (12 – 15 %) between left and right foot respectively, in 264 individuals with gout. Similarly, Grahame and Scott (1970) reported similar figures, 76% prevalence in the first MTPJ and 50% prevalence in the ankle and foot in a cross-sectional survey of 354 gout patients. As in any other study, limitations in these two studies restrict generalisability of the results.

Roddy et al. (2007) also reported joint restriction in the first MTPJ, midfoot and ankle joint range of motions in their study subjects. However, the authors did not describe the method used to assess the joint range of motion. Furthermore, the Roddy et al. (2007) study found a significant co-prevalence of osteoarthritis and gout incidence in midfoot and first MTPJ ($p = 0.006$ and 0.003 respectively; $p < 0.05$). Therefore, the restriction of ROM in the foot and ankle joints cannot be conclusively attributed to gout because osteoarthritic changes can also cause joint restriction (Menz & Moris, 2005).

The Roddy et al. (2007) study used self-reported measures to assess the extent of joint involvement in gout patients. Positive MSU crystals in synovial fluid aspiration from a joint reported in the subject's medical records was considered a positive confirmation of that particular joint involvement in the Roddy et al. (2007) study. However, this method was not

consistently followed in all the subjects as only 4% of the subjects were reported to have had a positive MSU crystal identification in their synovial fluids. Furthermore, it is not clarified if all the affected foot joints had a positive MSU crystal identification. In an epidemiological survey by Schlesinger et al. (2004), 2% of patients self-diagnosed and reported to have gout in one or more joints. Considering the limitations in Roddy et al. (2004) one can only conclude that the self-reported measures were the only methods used to assess joint involvement. Therefore, the results of this study have to be interpreted carefully.

Grahame and Scott (1970), in their cross-sectional survey, used elevated serum urate levels to diagnose gout, and radiographs (view not reported) to assess joint damage. Joint ranges of motion were not reported in this study. In their assessments, the authors did not differentiate joint destruction due to gouty arthritis from other forms of arthritis like osteoarthritis. Roddy et al. (2007) found co-existence of osteoarthritis with gouty arthritis in the first MTPJ and midfoot joints. Definite characteristics specific for gouty arthritis for example Martel's sign and cystic lesions (Christman, 2003), should be identified and reported in the radiographs to eliminate other forms of arthritic changes and to avoid misreporting. Hence, these two studies are limited in their generalisability due to the absence of reliable measures (Menz et al., 2003).

Among the case reports, gouty tophus was identified using various methods: Predominantly, *after surgical excision of the mass and later positive laboratory confirmation for the presence of MSU crystals* (Lagoutaris et al., 2005; Lemont and Sabo, 2001; DeYoe et al., 1999; Thomas et al., 1998; Reber et al., 1997; Surprenant et al., 1996; Mair et al., 1995), *culture of the exudates from the tophus* (Kitting & Fulp, 1972; Fore, 2005), *radiographs* (Kerman et al., 1993), *MRI* (Lagoutaris et al, 2005; Nirenberg & Carroll, 2007) *and CT imaging* (Surprenant et al., 1996; Gester et al., 1996; Gester et al., 1998). Kerman et al., (1993) reported presence of cystic lesions to the first MTPJ which are suggestive of chronic gout (Christman, 2003) prior to surgical excision of a gouty tophus from the joint area in a 73 year old patient. Kerman et al., (1993) reported that the dorsal aspect of the first MTPJ where the tophus was localised appeared as an area of increased density on the radiograph and thus non-specific to

the identification of a gouty tophus. Lagoutaris et al. (2005) using MRI to assess the integrity of the peroneal tendons, observed longitudinal tears with gouty tophus. Gouty tophus as reported by Lagoutaris et al. (2005) is identified as a diffuse hyperintense image in a contrast MRI (T1 image). Similarly Nirenberg and Carroll (2007) identified gouty tophus using MRI prior to surgical excision. The role of MRI in the identification of gouty tophus is scrutinised by Chen et al. (1999) as pseudo gout and rheumatoid nodules appear as low to intermediate intensity on a T1-weighted image. Surprenant et al. (1996), Gester et al. (1996) and Gester et al. (1998), using CT imaging identified tophus prior to surgical excision in their respective case reports. Tophus as reported by these authors is identified at 160 Hounsfield units on CT; Hounsfield is the unit of CT.

No attempt was made in any of these case reports to assess foot and ankle characteristics such as range of motion in ankle and foot joints, muscle strength, plantar pressure distribution, gait parameters and sensation. Lagoutaris et al. (2005) and Surprenant et al. (1996) reported a cavus foot type associated with tophus presence in the ankle and midfoot respectively. However, this conclusion was purely observational as no biomechanical tests were conducted using objective measures. The significance of these biomechanical tests and the evaluation of spatial-temporal parameters of gait have however been extensively researched and well documented in the rheumatoid foot (Turner et al., 2003 and Van Der Leeden et al., 2005).

Since the incidence of gout which predominantly affects foot and ankle is increasing in New Zealand, therefore a sound knowledge of foot and ankle characteristics (temporal spatial parameters, plantar pressures, kinematics of foot and ankle, foot posture, neurological status and muscle strength) is required to achieve a better understanding of the implications of gout on the foot and ankle.

Table 3.1 Case studies of gouty arthritis/tophus reported in the foot region.

Author	Research design	Site	Age and Gender	Foot assessment
Roody et al., 2007	Postal questionnaire	First MTPJ, Midfoot, Ankle, Knee and Hip	N = 164, M: 133 Fm: 31. Age: 63.4 ± 11 With 10 year duration of onset of gout.	None.
Grahame and Scott, 1970	Cross-sectional study.	76% - First MTPJ 50% - ankle and midfoot	N=354, M=321 Fm=33. Age: 50 ± 30 , with 10 yrs duration of gout onset.	None
Nirenberg and Carroll (2007)	Case report.	Lesion on medial talar dome, Subchondral cyst in: Distal tibiofibular articulation, Anterior calcaneus	41 year old male Age not reported.	ROM of the foot and ankle joints is not reported. However, pain was reproduced on palpation of the dorsum of the ankle and midfoot and plantar heel.

		II tarsometatarsal joint II cuneinavicular articulation Cuboid		
Lagoutaris et al. (2005)	Case report.	Gouty tophus in the tendons of peroneus longus and brevis with longitudinal tear	35 year old male.	Cavus foot with inverted rear foot. Subluxation of the peroneal tendons was observed with resisted dorsiflexion and eversion of the foot.
Fore (2005)	Case report.	A ruptured gouty tophus in the area of medial aspect of the first metatarsophalangeal joint caused the ulceration.	Gender and age is not reported.	Pain was reported with manipulation of the first MTPJ. ROM of other joints of the foot and ankle are not reported.
Lemont and Sabo (2001)	Case report.	Tibial sesamoid.	Male. Age not reported.	No foot assessment is reported. Preoperative radiographs reveal 'C' shaped erosion of tibial sesamoid with plantar cortical destruction.
De Yoe et al. (1999)	Case report.	Gouty tophus in the anterior talofibular ligament and tendon of	30 year old male	ROM of foot and ankle joints not reported, Normal vascular and

		peroneus brevis		neurological status reported for the foot.
Thomas et al. (1998)	Case report.	Gouty tophus in the navicular bone	24 year old female.	Foot and ankle assessments not reported.
Reber et al. (1997)	Case report.	Gouty tophus in between tripartite hallucal sesamoid or a suspected stress fracture of the sesamoid secondary to weakening due to the gouty tophus.	41 year old male	Pain under the first MTPJ reported. No foot and ankle assessment were reported.
Surprenant et al. (1996)	Case report.	Gouty tophus at the base of the medullary cavity of the III metatarsal shaft.	49 year old male.	Cavus foot type. No obvious musculoskeletal deformities were observed. No ROM assessments of the foot and ankle were reported.
Gester et al. (1998).	Case report.	Achilles tendon.	42 year old male with 15 year history of gout.	Foot and ankle assessment is not reported.
Gester et al. (1996)	Case report.	Palpable nodules in the posterior Achilles tendon.	70 year old male with 10 year history of gout.	Foot and ankle assessment is not reported.

Mair et al. (1995)	Case report.	Gouty tophus in between bipartite hallucal sesamoid or a suspected stress fracture of the sesamoid secondary to weakening of the sesamoid due to the gouty tophus.	18 year old male	No foot and ankle assessments were reported.
Kerman et al. (1993)	Case report.	Gouty tophus isolated from the shafts of I and IV metatarsals.	73 year old female.	No neuromuscular deformities observed. Biomechanical assessment of foot and ankle joints is not reported.
Kitting and Fulp (1972)	Case report.	Gouty tophus with secondary bacterial infection around the first metatarsophalangeal joints bilaterally.	70 year old male.	Biomechanical assessment of foot and ankle joints is not reported.

3.2 Summary

Gout predominantly affects the foot and ankle. The literature review reports that within the foot and ankle the first metatarsophalangeal joint has a greater incidence, followed by ankle and midfoot regions. Gouty tophus is also reported within soft tissue structures such as the peroneals and the Achilles tendon. The following chapter will discuss the aims of this current study on the characteristics of foot and ankle in individuals with gout.

CHAPTER 4: AIMS AND HYPOTHESES

4.1 AIMS

The aims of the current study are two fold:

1. To determine within and between session intra-tester reliability of dorsiflexion motion of the first MTPJ and ankle, Foot Posture Index, plantar pressure and gait parameters in gout cases.
2. To evaluate any significant differences in disability, impairment, foot structure and foot function between gout and age-matched controls.

4.2 Hypothesis

4.2.1. Null hypothesis 1

There will be no significant relationship in ‘within and between intra-tester reliability’ for dorsiflexion motion of the first MTPJ and ankle, Foot Posture Index, plantar pressure and gait parameters in the gout group.

4.2.2. Alternate hypothesis 1

There will be significant relationship in ‘within and between intra-tester reliability’ for dorsiflexion motion of the first MTPJ and ankle, Foot Posture Index, plantar pressure and gait parameters in the gout group.

4.2.3. Null hypothesis 2

There will be no significant differences in measures of disability, impairment, foot structure and foot function in gout affected and normal healthy individuals.

4.2.4. Alternate hypothesis 2

There will be significant differences in measures of disability, impairment, foot structure and foot function in gout affected and normal healthy individuals.

All the tests will be conducted at a 5% level of significance.

CHAPTER 5: LITERATURE REVIEW OF METHODS

5.1 Introduction

This chapter focusses on the literature relating to the battery of tests used in the current study. The clinical tests are classified on their ability to measure impairment, disability and foot function. A general description of each tool, together with a discussion on the validity and reliability of each of the tests, is described. Table 5.1 categorises the tests to the outcome measures of the present study.

Table 5.1 Classification of the tests based on outcome measures.

Outcome Measure	Test
Disability and impairment scales	Foot Function Index Leeds Foot Impact Scale Lower Limb Task Questionnaire Health Assessment Questionnaire
Foot structure	Evaluation of foot type Range of motion at ankle and first metatarsophalangeal joint. Motion at subtalar and midtarsal joints. Muscle strength (extrinsic and intrinsic) Foot Problem Score Tophi count.

Foot function	Peripheral sensation Vibration Perception Threshold, Plantar pressures Gait parameters
Clinical outcomes	Serum urate levels Blood tests (CRP & creatinine)

5.2 Disability and Impairment

5.2.1 Introduction

This section will review the evidence on the ability of the selected tools to measure disability and impairment as a measure of quality of life. Four measurement tools were selected for these outcome measures. The Foot Function Index (Budiman-Mak et al., 1991) and the Leeds Foot Impact Scale (Helliwell et al., 2005) measure pain, disability and functional status specifically relating to the influence of a disease or condition on the foot, while the Lower Limb Task Questionnaire (McNair et al., 2007) measures pain, disability and functional status of an individual, relating to the entire lower limb. The Health Assessment Questionnaire has a more holistic perspective in its measurement of pain, disability and functional status (Fries et al., 1982). Scoring for the respective questionnaires will be discussed individually. All the questionnaires except the Leeds Foot Impact Scale explore different activities pertaining to daily-living and recreation, and, using an analogue scale, rate the subject's abilities in performing those activities. Questions are directed to investigate pain experienced during these activities of daily-living and recreation and scored on the analogue. The Leeds Foot Impact Scale is the only tool which uses yes/no answers to measure pain, disability and functional status.

Patient-reported outcomes are of particular importance in evaluating the impact of pathology on physical disability, health related quality of life and work disability (Taylor et al., 2007). Instruments like the health assessment questionnaire and functional status questionnaire are widely used to measure pain and disability (Budiman-Mak et al., 1991; Saag et al., 1994; Fries, 1982; Soohoo et al, 2006). The above mentioned tools are validated to measure the effect of pain, disability and quality of life caused by all the affected joints in the body and do not isolate the affect of pathology on foot function alone (Budiman-Mak et al., 1991; Soohoo et al., 2006).

5.2.2 Foot Function Index (FFI)

The FFI is a tool which measures the impact of pathology in the foot alone (Budiman-Mak et al., 1991). The FFI consists of 17 items precisely selected to reflect the impact of foot pathology on pain, disability and function in individuals with Rheumatoid arthritis (Budiman-Mak et al., 1991). The 17 items are divided into three sub-scales, pain subscale, disability subscale and activity limitation subscale (Appendix 4); (Budiman-Mak et al., 1991). The extent of impairment is dependent not only on the intensity of pain, disability and activity limitation but also on the number of situations in which pain, disability and activity limitation hinder daily life activities (Budiman-Mak et al., 1991). The subscales measures pain severity, difficulty in performing various activities and limitation of activity due to foot problems (Budiman-Mak et al., 1991). FFI items are scored using a visual analogue scale rated from zero to ten, with zero being no pain/disability/activity limitation and ten being the worst imaginable pain/disability/activity limitation (Budiman-Mak et al., 1991).

The FFI is designed to measure the past and current status of each item by describing the ability to perform a given task during the previous week, which makes FFI an effective tool for evaluating function and disability (Budiman-Mak et al., 1991). The total score and the individual subscales of FFI are reported to measure the particular function they represent (pain, disability and activity limitation) suggesting excellent consistency for the total FFI

using Cronbach's alpha ($\alpha = 0.95$) and within FFI, pain ($\alpha = 0.94$), disability ($\alpha = 0.92$) and activity limitation ($\alpha = 0.73$).

Comparing the FFI total score and individual sub-scale scores to previously validated measures such as the total number of painful joints, and walking time, Budiman-Mak et al., (1991) reported that pain subscale significantly correlates to painful foot joint counts ($p = 0.0001$), disability ($p = 0.0001$) and activity limitation ($p = 0.0006$). Furthermore, the walking time significantly correlates to disability and activity limitation ($p = 0.0001$ and 0.001 respectively). Similarly Soohoo et al. (2000) reported high to moderate significant correlation of FFI sub-scales to Medical Outcome Study Short Form-36 (SF-36) in terms of the Pearson coefficient ($r = -0.23$ to -0.69) for disability, ($r = -0.28$ to -0.64) for activity limitation and ($r = -0.10$ to -0.61) for pain, thus establishing FFI validity in a wide range of chronic orthopaedic foot and ankle disorders resulting in pain, disability and activity limitation. The negative values of the correlation coefficient are because the higher scores of FFI represent worse health and higher scores of the SF-36 represent improved health (Soohoo et al., 2000).

Budiman-Mak et al. (1991) reported good test retest agreement for the total FFI score (ICC = 0.87) and good to fair for the sub-scales activity limitation (ICC = 0.81), disability (ICC = 0.84) and an ICC of 0.7 for pain sub-scale. Similarly Saag et al. (1994) reported good test retest reliability for FFI in 30 rheumatoid patients (ICC = 0.8). Agel et al. (2005) also reported moderate test retest reliability for FFI in 54 individuals. In this study Agel et al. (2005) reported that 23.5% of the individuals' response during the FFI retest differed by one point to the initial value while 45.3% provided the same response as on the first occasion. This suggests that 68.8% of the time, the retest values for FFI will differ by only a single point, thus establishing its test retest reliability. The FFI has been widely used in rheumatoid arthritic research as it is a valid and reliable tool to study the impact of, footwear (Williams et al., 2007), foot orthoses in alleviating pain and disability (Conrad et al., 1996, Woodburn et al., 2002) and evaluate foot pain and disability in rheumatoid subjects (VanDerLeeden et al., 2006). Although FFI has never been used in gout patients, because of its proven validity and reliability it is now used in this current study to measure pain, disability and functional status.

5.2.3 Leeds Foot Impact Scale (LFIS)

The LFIS is a foot specific scale designed by Helliwell et al. (2005) to measure disability and impairment in individuals with rheumatoid arthritis (Appendix 5). Previously established tools (HAQ, FFI and SF-36) measure pain and disability that occur as a consequence of a disease state; however these tools do not address the psychological impact of the disease on an individual (Bennett et al., 1998, Rowan. 2001) whereas LFIS does.

The LFIS is a foot specific questionnaire that measures pain and disability caused from a disease state, using a holistic approach by including both the disease and non-disease items. The non-disease items of the questionnaire investigate how an individual feels about their general appearance and /or disability caused by the affect of the disease on the foot and ankle. LFIS comprises 51 items divided into two sub-scales, each item to be scored as either yes or no (Appendix E); (Helliwell et al., 2005). The subscales include the impairment/footwear subscale consisting of 21 items, and that of activity limitation/participation restriction which includes 30 items (Helliwell et al., 2005). The total score is obtained from the sum of all the 'yes' answers recorded, and the higher the score greater the impairment/limitation/disability according to the subscale (Hellewell et al., 2005).

Applying the Rasch model for the two sub-scales to evaluate validity and reliability in 188 subjects, Helliwell et al. (2005) reported that all the items of LFIS fit the Rasch model. The degree of freedom for the impairment/shoes sub-scale ($\chi^2 = 45.07$; $p = 0.35$) and activity limitation/participation subscale ($\chi^2=64.4$; $p= 0.18$) indicate that all items are easy to understand and score for all the participants and that the answers are without any bias (Hellewell et al., 2005). The person separation index is reported to be 0.8 and 0.9 for the impairment/shoes subscale and activity limitation/participation subscale respectively, which proves that LFIS has the ability to differentiate patients with varying disease states and disease severity (Hellewell et al., 2005). Turner et al. (2008) using regression analysis on 74 rheumatoid and 54 controls,, reported that foot pain and walking speed are strongly correlated to the impairment/shoes subscale ($p<0.0005$ and 0.001) and activity limitation/participation

($p < 0.0005$ and 0.001) subscales of LFIS, both of which are proven to be predictors of disease severity.

Good to excellent test retest reliability has been reported ($ICC = 0.84$ and 0.96) for the impairment/shoes and activity limitation/participation subscales respectively (Hellewell et al., 2005). The LFIS has frequently been used in rheumatoid studies to evaluate impact of the disease (Hellewell et al., 2005, Turner et al., 2006; Turner & Woodburn, 2008; Turner et al., 2008).

Due to its proven validity and reliability the LFIS is used in the current study to implement a holistic approach to measuring the impact of gout on the foot and ankle.

5.2.4 Health assessment questionnaire (HAQ)

The HAQ was established by Fries (1982) to understand patient health with regard to functional status, treatment preferences, symptoms, satisfaction and quality of life through patient-reported outcomes in the rheumatoid population (Appendix 6); (Fries, 1982; Bruce & Fries, 2005). The HAQ is designed to capture the long term implication of chronic illness on daily living (Bruce & Fries, 2005). The original HAQ has 20 items to determine patients' degree of difficulty, modelled after the American Rheumatism Association/American College of Rheumatology functional classes and each item is scored within a scale of 0 – 3 according to order of increasing disability.

The criterion validity for the original HAQ had been established as it correlated well with interview scores and the ability to perform tasks tested by the HAQ ($r = 0.71$ and 0.95 respectively); (Bruce & Fries, 2005). Furthermore, the HAQ is reported to be significantly correlated with the Western Ontario McMasters Universities Osteoarthritis Index (WOMAC) ($r = 0.67$, $p < 0.0001$); (Bruce & Fries, 2004). Pincus et al. (1983) established the modified HAQ with eight items in an attempt to make it shorter and faster in assessing disability. However, Ziebland et al. (1992) reported significant correlation between modified HAQ (MHAQ) and standard rheumatological tests like the Ritchie Index, grip strength, morning

stiffness, ESR ($p < 0.001$). Furthermore, MHAQ was found to have a high correlation to the global transition item ($p < 0.001$) in the rheumatoid patients, which proves its sensitivity. The global transition item is the general question put to patients on how they describe pain/activity compared with the previous time. In a comparison of HAQ with MHAQ, Uhlig et al. (2006) reported MHAQ and HAQ scores have good correlation ($r = 0.88$) in 182 rheumatoid patients. However, Uhlig et al. (2006) noticed that MHAQ has a 23% “ceiling effect” (inefficiency of a tool to detect changes) compared with that of HAQ (12%). Serrano et al. (1996) point out that the additional complementary questions in the original HAQ examine each item several times which MHAQ does not do, and thus HAQ scores higher than MHAQ. Uhlig et al. (2006) argue that MHAQ is a valid tool of physical assessment in a population with low prevalence of physical disability to shield the ceiling effect. Therefore, in the current study, as the physical functional status in gout is unknown, the MHAQ is used to assess physical function.

5.2.5 The Lower Limb Task Questionnaire (LLTQ)

The LLTQ will be used to assess the physical tasks related to lower limb function to specific activities of daily living and activities more often associated with recreation (Appendix 7); (McNair et al., 2007). The ability to do each of these tasks in the previous 24 hours is rated using an analogue scale of 0 – 4, where 0 means being unable to do an activity and 4 to having no difficulty in doing it. The previous 24 hour testing time allows a comprehensive picture of an individual’s lower limb physical ability at that particular state to be presented. This will be of particular interest in understanding an acute phase of a disease state, for example, in this case a gout flare.

The LLTQ also examines the importance of each task in the individual’s daily life by rating the importance of a given task on a scale of 1 to 4, 1 being not important and 4 being very important. This feature of LLTQ allows the examiner to understand the relevance of a stated task in their life. Furthermore, this feature will ascertain the validity of the questionnaire depending on the individual’s requirement. For example, an individual who reports severe

difficulty with recreational activities but rates these activities as unimportant may not be affected. However, the same individual reporting severe difficulty in the activities of daily living and also rating these activities as very important would suggest that the disease state has severely limited daily life and thus can affect the psychological wellbeing of the individual.

The LLTQ has also been reported to possess good factor structure and composition, relates well with other measures of function, differentiates patients with regard to certain characteristics or processes known to occur after injury, and shows high levels of test retest reliability and responsiveness (McNair et al., 2007).

5.2.6 Summary

Four self-administered questionnaires will be used to measure the impact of pain and disability. None of these questionnaires have been used previously for gout but have been used for the rheumatoid foot, except for the Lower Limb Task Questionnaire. All the questionnaires investigate the influence of a disease on activities involving daily living and recreation. However, each questionnaire differs in the activities used to measure disability and pain. The FFI and LFIS measure the limitations in the activities specifically due to foot pain or foot involvement from a disease. The LFIS investigates the influence of other factors like choice of foot wear and the psychological aspect (patient's general impression of their feet) and its influence on their daily lives, and participation in recreational activities. The LLTQ takes a broader perspective as it takes into account the influence of a disease on the ability to perform activities involving the entire lower limb. The FFI measures pain and disability during the past week while LLTQ investigates disability in the past 24 hours. In contrast the HAQ is not time specific, similar to LFIS. HAQ captures the impact of the disease on an individual in a more holistic approach. Pain, defined as an experience of unpleasant feeling of a noxious stimulus has been investigated in this study both qualitatively using the questionnaires and quantitatively as part of the visual analogue scale. Disability can also occur due to structural changes that manifest in the bone and soft tissues during the

course of the disease involving synovitis, as evident in rheumatoid arthritis. Pain and disability can limit functional capabilities in the individual, compromising quality of life. Therefore, the latter part of this study will aim to identify which measure of functional status of the foot and ankle relate to disability and/or pain in subjects affected with gout.

These questionnaires thus help to measure quality of life (pain, disability and functional status) at different times and during various activities, both daily living and recreational. Table 5.2 highlights general characteristics of the questionnaires.

Table 5.2 Brief overview of the questionnaires

Questionnaire	Measures	Time	Body part investigated	Brief description of the questionnaire
LLTQ	Disability and functional status	Last 24 hours	Entire lower limb	<i>Pain and disability at the present state. Captures both acute, chronic and temporary disease changes</i>
FFI	Pain, disability and functional status	During the last week	Foot and ankle	
LFIS	Pain, disability, psychological impact of the disease and the individual's perception on the affect of the disease.	Indefinite; overall perception of the individual.	Foot and ankle	<i>Considers the overall affect of the condition. Captures chronic or permanent disease changes and complications.</i>
HAQ	Disability and quality of life.	Indefinite; overall perception of the individual.	The whole body	

LLTQ: Lower Limb Task Questionnaire, FFI: Foot Function Index, LFIS: Leeds Foot Impact Scale, HAQ: Health Assessment Questionnaire

5.3 Foot structure and function

5.3.1 Introduction

Identification and understanding of normal structure and function is important to appreciate how deviations from these norms may contribute to the development of pathology (Valmassy, 2001). This section will review the literature on the methods used to evaluate foot structure and function. The foot structure is assessed using foot type, muscle strength, range of motion at the first metatarsophalangeal joint, ankle, subtalar and midtarsal joints, foot problem score and tophi count in the foot and ankle region. Foot function is assessed using neurological status, peak plantar pressures, pressure-time integrals and gait parameters. Firstly, a general description of the individual parameters is given, followed by a literature review on the validity for the technique used to measure the parameter. This is followed by a review on the reliability of the technique chosen to measure the parameter for this study.

5.3.2 Foot type

Abnormal foot posture has been implicated as a factor in lower limb injuries (Williams et al., 2001). Various methods have been developed to evaluate foot posture. Some of these include Navicular drop (Mueller et al., 1993), Valgus index, Calcaneal inversion/eversion (Smith-Oricchio and Harris, 1990), Kirby's subtalar joint axis (Kirby, 2001) and the Foot Posture Index (Redmond et al., 2006). The Foot Posture Index is well established in the literature for its proven validity and reliability and is therefore the method of choice in the current study to assess foot type.

5.3.2.1 Foot Posture Index (FPI)

Foot type was chosen as one of the outcome measures for the present study based on the notion that excessive foot pronation (low arch) or supination (high arch) has long been reported as a major cause of foot pathology (Easley and Trnka, 2007 and Yates and White, 2004).

The Foot Posture Index (FPI-6) was developed by Redmond et al. (2006). The FPI allows multiple plane evaluation that provides information on rearfoot, midfoot and forefoot segments. Clinicians use a score-based system to rate the degree of pronation or supination of the foot. Originally, the tool consisted of eight criteria (FPI-8) but these were reduced to six after a series of reliability and validity tests. FPI-8 was proved to have a moderate to excellent intra-tester and inter-tester reliability ($ICC = 0.61 - 0.92, 0.58 - 0.91$ respectively) across a wide range of the population (Burns & Crosbie, 2005; Evans et al., 2003, Menz & Munteanu, 2005; Noakes & Payne, 2003). Scharfbillig et al. (2004) found it not sensitive enough to detect small changes when tested against standard radiographs. Four FPI criteria (medial longitudinal arch, talonavicular head palpation, abduction and adduction of the forefoot, and congruence of the lateral border) showed poor correlation with radiographic measurements (Spearman's $\rho = -0.28$ to 0.42).

A Rasch analysis conducted by Keenan et al. (2007) between FPI - 8 and FPI- 6, proved FPI- 6 to be a valid measure of foot assessment. The authors applied a Rasch analysis model to the data obtained from 143 participants (age range 8-65 years) using FPI-6 and FPI-8. Rasch analysis is described by the authors as “a probabilistic mathematical modelling technique used to assess properties of outcome measures including uni-dimensionality (the extent to which items measure a single construct), item difficulty (the relative difficulty of the items when compared to one another), and person separation (the extent to which items distinguish between distinct levels of functioning)”. This sophisticated analytic model indicated that data collected from FPI-8 did not fit the Rasch model as well as FPI-6, X^2_{16} test = 27.63 ($P = 0.03$) *versus* X^2_{12} test = 11.49, ($P = 0.49$), thus proving FPI-6 a better version of the FPI.

Due to it being quick and easy to perform nature, FPI-6 has been used more frequently in clinical settings and in studies of risk factors for injuries in athletes (Burns et al., 2005; Cain et al., 2006), orthotic intervention studies (Burns et al., 2006; Munteanu & Bassed, 2006; Payne et al., 2003; Rome & Brown, 2004), fall risk study in the elderly (Menz et al., 2006), pressure analysis study (Menz & Morris, 2006), plantar heel pain study (Radford, 2006), and

the study of differences in the ankle dorsiflexion ROM between different foot types (Burns and Crosbie, 2005).

High inter-tester and intra-tester reliability was reported for FPI-6 in a wide range of people, children, adolescents and adults (ICC: 0.8, CI: 0.73 - 0.89); (Evans et al., 2003) and studies involving orthotic intervention (ICC – 0.95 and 0.95 respectively, IC = 0.90 – 0.98); (Munteanu & Bassed, 2006). Hence, the FPI is a valid and a reliable tool and gives an estimate of the foot's weight bearing position (pronated, neutral or supinated) in the current study.

5.3.3 Range of motion (ROM)

Adequate range of motion is required at the ankle and the first metatarsophalangeal joint during gait to allow smooth progression of the body over the stance foot and for effective propulsion.

5.3.3.1 Ankle joint range of motion

A minimum of 10° of ankle dorsiflexion is needed for the forward progression of the body over the foot during the midstance phase of gait (Dannenberg, 2004). Tightness of triceps surae muscles decreases the ankle joint range of motion causing Achilles tendonitis, plantar fasciitis (Redford et al., 2006, Bolgia & Malone, 2004, Pribut, 2007; Pfeiffer et al. (1999) and reduced balance (Menz et al., 2005).

Conflicting evidence exists in the choice of the procedure and the tool used to measure ankle joint dorsiflexion. Weight-bearing measures, especially the Lunge Test, received great attention as they appear to represent the midstance phase of the gait cycle during functional tasks (Bennell et al., 1998). The Lunge test has been used in the rheumatoid and osteoarthritic population and healthy individuals between the ages of 65 to 90 years in an attempt to

establish predictors for foot pain and incidence of falls in these age groups (Menz & Morris, 2005, Menz et al., 2006; Scott et al., 2007). Bennell et al. (1998) reported excellent inter-rater and intra-rater reliability (ICC of 0.96 and 0.98 respectively) for the Lunge test.

The non weight-bearing technique was also researched extensively (Bohannon et al., 1989, Baggett & Young, 1993; Rome, 1996; Siezet et al., 2003). However, this technique is subject to scrutiny owing to the fact that ankle range of motion is excessive in a nonweight-bearing setting when compared to weight-bearing (Bohannon et al., 1989; Baggett & Young, 1993; Siezet et al., 2003). The increased motion in the nonweight-bearing ankle range of motion technique is due to coupled motion of the subtalar joint, the calcaneocuboid and the talonavicular joints (Draves, 1976; Lundberg et al., 1989; Siezet et al., 2003). Root et al. (1976) recommends that the subtalar joint neutral position should be maintained during nonweight-bearing measurement of ankle dorsiflexion to minimise coupling of other joint motions.

Nevertheless, the nonweight-bearing method has been used in the past to measure the passive ankle dorsiflexion range in patients with plantar fascioses who had difficulty doing the lunge (Riddle et al., 2003), patients with cerebral palsy who experience difficulty balancing (Kilgour et al., 2003, Evans & Scutter; 2006 & Allington et al., 2002) and in patients with ankle injuries (Tabrizi et al., 2000). Bohannon et al. (1989) reported three methods to measure ankle dorsiflexion during nonweightbearing with the patient lying in a supine position:

- 1) Dorsiflexing the ankle passively by the examiner till tension is felt in the plantar muscles,
- 2) Passive ankle dorsiflexion by the examiner with maximal force until resistance is felt,
- 3) Ankle dorsiflexion actively assisted by the subject.

Bohannon et al. (1989) found significant difference between these three nonweight-bearing methods for the ankle dorsiflexion ($p < 0.001$). However, the passive ankle dorsiflexion with maximal force has been used and documented to be a valid and reliable method (Arlington et al., 2002; Kilgour et al., 2002; Riddle et al., 2003). Allington et al. (2002) compared the

nonweightbearing passive ankle dorsiflexion measurement with visual measurement from a video recording of the gait in 24 cerebral palsy children and reported a high correlation between these two methods. The passive nonweight-bearing method is reported to have a good to excellent inter and intra-rater reliability in children (ICC- 0.7, 0.95 and 0.75, 0.75 respectively); (Kilgour et al., 2003; Allington et al., 2002) and in adults (ICC – 0.88 and 0.99); (Riddle et al., 2003).

In this present study the passive nonweight-bearing method is used to measure ankle joint dorsiflexion to minimise any inconvenience to the participants associated with the Lunge test. Readers are directed to Section 6.5.2 for a detailed description of the technique. As gout is documented to frequently affect the foot it was decided a nonweight-bearing method will be appropriate to assess the motion of the ankle. Furthermore, as the incidence of falls or problems with balance is unknown in gout patients it is presumed safe to conduct a non-weight bearing measurement for ankle dorsiflexion.

Choosing a measurement tool is as important as choosing the right testing procedure. Various tools (weight-bearing radiographs, standard goniometers, electrogoniometers, and digital inclinometer) were used in the past to measure ankle joint dorsiflexion (Menz et al., 2003; Rome, 1996; Burns & Crosbie, 2005). Only one study (Rome, 1996) looked at the consistency between these measuring tools (electrogoniometer, fluid goniometer and universal goniometer) and found significant difference between the universal goniometer when compared to electro and fluid goniometer ($p < 0.05$). The study demonstrated poor inter-device reliability (electrogoniometer, fluid goniometer and universal goniometer) both within and among observers so the results need to be interpreted with caution. Rome (1996) states the universal goniometer to be a reliable tool if consistency in marking the surface landmarks (head of the fibula, centre of lateral malleolus and the lateral column of the foot for ankle measurement) is maintained. Past studies reported good to excellent reliability (intra and inter respectively) in measuring ankle dorsiflexion using universal goniometer, ICC = 0.98, 0.78 (Kilgour et al., 2003), ICC = 0.87 (Menz et al., 2003), ICC = 0.96 & 0.98 (Bennell et al., 1998).

For the reasons mentioned above, the current study will employ the nonweight-bearing test and a universal goniometer to measure and record ankle joint dorsiflexion, as it is a cheap and efficient measurement tool.

5.3.3.2 First metatarsophalangeal joint (MTPJ) dorsiflexion

In healthy individuals, the normal passive range of first MTPJ motion is approximately 30° in plantarflexion and 90° in dorsiflexion; slightly less is required during normal ambulation (Glasoe et al., 1999). In order to achieve an effective propulsion at the first MTPJ, 45 to 75 degrees of hallux dorsiflexion is necessary (Root et.al, 1977, Dananberg, 1993; Fuller, 2000; Payne and Dananberg, 1997; Munteanu & Bassed, 2006 and Paton, 2006). The dorsiflexion of the hallux at the first MTPJ triggers the onset of the windlass mechanism.

The weight-bearing measurement for the first MTPJ received greater attention as it seems to closely represent the dynamic phase of the gait cycle (Buell et al., 1988; Nawoczenski et al., 1999; Hopson et al., 1999; Hogan & Kidd, 2002). The nonweight-bearing passive dorsiflexion of the first MTPJ has also been used as it is reported to initiate and identify the efficiency of the windlass mechanism (Kappel-Bargas et al., 1998) and also in the prescription of foot orthosis in rheumatoid arthritis patients (Shrader & Siegel, 2003). Following the discussion in the previous section, the current study employs a nonweight-bearing technique to reproduce the first MTPJ dorsiflexion and a universal goniometer is used to record first MTPJ dorsiflexion value.

Several techniques for the nonweight-bearing method have been described in the literature. Payne et al. (2002) describes the nonweight-bearing manual dorsiflexion test to evaluate hallux limitus, which involves dorsiflexing the first ray by loading the first metatarsal head plantarly with one hand while the other hand dorsiflexes the hallux. Laroche et al. (2005) and Shrader and Seigel (2003) describe a nonweight-bearing active dorsiflexion test, the patient

lying supine and actively dorsiflexing the hallux at the first MTPJ, and the angle measured. Finally Kappel-Bargas et al. (1998) describe the passive nonweight-bearing test, with the patient supine and the examiner passively dorsiflexing the hallux. The latter two tests (active and passive) were used in rheumatoid patients specifically to assess joint mobility.

Similar to the evaluation of ankle joint dorsiflexion the nonweight-bearing passive hallux dorsiflexion test will be used in the current study to measure first MTPJ dorsiflexion. Readers are directed to Section 6.5.3 for a detailed description of the technique. The passive hallux dorsiflexion technique also enables the examiner to observe how well the windlass mechanism functions (tightening of plantar fascia) upon hallux dorsiflexion (Kappel-Bargas et al., 1998). However subjective this observation maybe, Kappel-Bargas et al. (1998) reported good correlation between passive dorsiflexion values and windlass activation during gait ($p < 0.05$) – the less the value of hallux dorsiflexion with passive extension the greater the delay in the onset of the windlass mechanism. Nawoczenski et al. (1999) used an electromagnetic tracking device to assess static and dynamic function of the first MTPJ. The motion in the first MTPJ during the nonweight-bearing passive hallux dorsiflexion test correlated well with hallux dorsiflexion during dynamic motion ($r = 0.7$; $p < 0.001$). Shrader and Siegel (2003) argue that the passive hallux dorsiflexion test enables the examiner to primarily assess the mobility in the first MTPJ, especially in chronic rheumatoid arthritis where restriction of the first MTPJ is reported secondary to excessive pronation.

Test retest reliability for the passive hallux dorsiflexion test is reported to be excellent (ICC = 0.99 and 0.97); (Nawoczenski et al., 1999; Allen & Gross, 2003 respectively). The nonweight-bearing passive hallux dorsiflexion test is used in this current study to measure the range of hallux dorsiflexion. The reliability of goniometric measurement of the first MTPJ dorsiflexion is reported to be good to excellent. Hopson et al. (1995) reported excellent intra-tester reliability (ICC = 0.98) for the measurement of first MTPJ dorsiflexion with a universal goniometer using the single heel rise test. Using the same measurement technique and tool as Hopson et al. (1995), Hogan and Kidd (2001) reported good to excellent intra-tester reliability (ICC = 0.87 and 0.98) for left and right foot respectively. Test and retest

measurements taken two weeks apart show only 3° of variance. Such high reliability with low standard error fully justified the use of goniometry in the current study.

5.3.4 Muscle strength

Muscle weakness has long been regarded as an outcome measure for functional disability in osteoarthritis and rheumatoid arthritis (McAlindon et al., 1993; Steultjens et al., 2001; Hakkinen et al., 2001; Stuki et al., 1998; Hakkinen et al., 2006). In the above mentioned studies, strength of trunk, hip and knee muscles were assessed using a strain gauge or dynamometer. None of the studies attempted to compare strength of extrinsic and intrinsic muscles of the foot to functional disability. Vlieland et al. (1996) observed reduced hand muscle strength (wrist and fingers) and range of motion in the metacarpophalangeal joints to be associated with impaired hand function in 50 rheumatoid arthritic patients and therefore regarded these as predictors of reduced hand function in rheumatoid patients. For the first time, Van-Schie et al. (2004), using a semi-quantitative grading system (Table 5.4) assessed the strength of the extrinsic foot muscles in a diabetic population with neuropathy. Muscle strength according to Van-Schie et al. (2004) is the ability of the muscle to produce active movements against the examiners resistance (Van-Schie et al., 2004). Muscle strength is assessed by the examiner by resisting the movement of the muscle being tested in its respective plane of action. The resistance of the muscle action as perceived by the examiner is graded in a scale of 0 to 3, 0 being normal strength and 3 being total loss of strength.

Using nerve conduction velocity (peroneal and tibial nerves) of less than 40m/sec as a threshold for decreased nerve conduction (neuropathy), Van-Schie et al. (2004) observed that the muscle strength using the semi quantitative grading method corresponded closely with the nerve conduction velocity of the respective nerves ($p < 0.0001$ and $p < 0.001$ for peroneal and tibial nerve respectively). Thus, the validity of the semi-quantitative grading method has been established.

5.3.4.1 Assessment of muscle strength for extensor, flexor and the peroneal groups

Muscle strength for the extensor, flexor and peroneal muscle groups of the leg (flexor hallucis longus, flexor digitorum longus, tibialis anterior, peroneus longus and peroneus brevis, extensor hallucis longus and extensor digitorum longus) are assessed and graded using the semi-quantitative grading system established by Van-Schie et al. (2004); (Table 5.3).

Table: 5.3 – Grading of muscle strength. (Van-Schie et al., 2004)

Grade	Description
0	Complete loss of strength
1	Moderate weakness
2	Mild weakness
3	Normal strength

5.3.4.2 Posterior tibial strength

Dysfunction or weakness of the muscle causes flattening of the medial longitudinal arch rendering the foot unstable for propulsion (Squires & Jeng, 2006; Weinraub & Saraiya, 2002; Kohls-Gatzoulis et al., 2004). The strength of the posterior tibial tendon is assessed by a double or single heel raise test. Failure or decreased calcaneal inversion is a sign of posterior tibial weakness or dysfunction (Squires & Jeng, 2006). The validity of this single heel raise test has not been proved.

Hintermann and Gachter (1996) introduced “The first metatarsal rise sign” as a test for posterior tibial dysfunction (Figure 5.1).

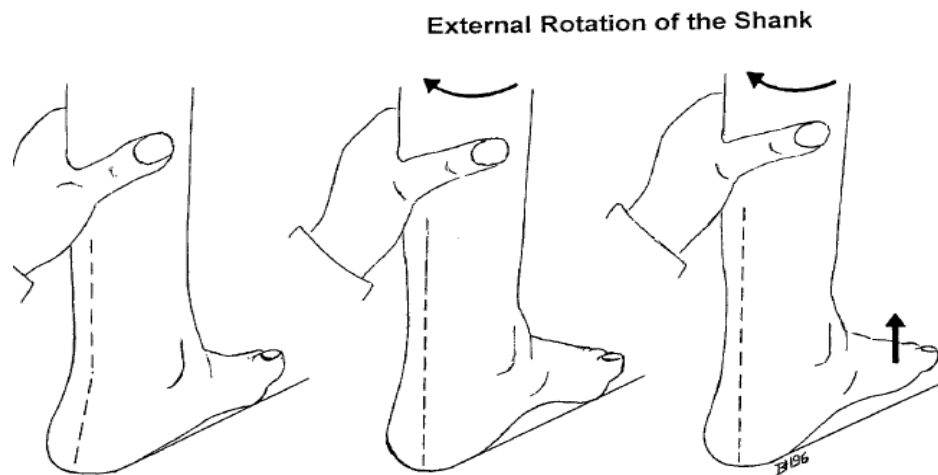


Figure 5.1: First metatarsal rise test from Hintermann & Gachter. (1996).

The first metatarsal rise test proved to be reliable when the objective measurement is compared to operative findings. The test involves externally rotating the shank of the affected limb so that the heel is brought into varus position. The head of the first metatarsal remained on the ground in normal tibialis posterior function but lifted in dysfunction (Hintermann, 1997 & Trnka, 2004). However, between the two above mentioned tests the first metatarsal rise sign test gained validity when compared to the heel rises. For the purpose of this study The first metatarsal rise sign test is used as a measure of posterior tibial weakness.

5.3.4.3 Intrinsic muscle strength

Described in the earlier sections, the intrinsic muscles play the role of anchoring the phalanges to the ground during the propulsion phase of the gait cycle. In this study intrinsic muscle strength is assessed using the “paper grip test” developed by Thevuvnet and Roche (Win et al., 2002). The test is performed with the patient sitting straight with the hips, knees and ankles flexed to 90°. With the patient’s heel resting on the floor a paper slip is placed under the toes distal to the metatarsophalangeal joints. The paper is pulled away in a horizontal direction while the patient resists by gripping the paper with the toes. The strength of the intrinsic muscles is assessed by the ease (or otherwise) with which the paper can be retrieved from beneath the toes (Win et al., 2002).

The validity of the paper grip test is conducted by paralysing the intrinsic muscles by injecting 5 cc of 1% bupivacaine, local anaesthetic agent in to the tarsal tunnel to block the posterior tibial nerve conduction and conducting the paper grip test before and after the nerve block (Win et al., 2002). The paper grip test was reported to be weak after the posterior tibial nerve block, suggesting the paper grip test to be a valid tool to measure intrinsic muscle strength (Win et al., 2002). Due to the approved validity of the paper grip test, it is used in the current study to assess intrinsic muscle strength.

5.3.5 Foot Problem Score

A modified foot problem scoring system will be used to provide an overall measure of an individual's foot problems (Menz et al., 2001). This involves observing and documenting the presence of bony prominences, hallux valgus (bunion), lesser toe deformities (hammer toes, claw toe and mallet toes) and hyperkeratotic lesions on both the feet. Each abnormal observation on each foot will be scored one point. Hammer toes, claw toes and hallux valgus are reported to be characteristic of the rheumatoid foot (Helliwell et al., 2007) and are the result of imbalance in both extrinsic and intrinsic foot muscles (Root et al., 1974). Hallux valgus and lesser toe deformities are reported to affect balance due to lateral excursion of centre-of-pressure and reduced somatosensory input from the toes. Similarly Menz and Lord (2001) reported the FPS as a best predictor of stability during the stance phase of gait ($p < 0.01$). The FPS was therefore chosen as the predictor of disability. Menz and Lord (2001) and Menz et al. (2003) recorded an excellent intertester reliability (ICC - 0.98) and (ICC - 0.92) respectively in determining the presence and absence of these conditions.

5.3.5.1 Manchester Scale

Incorporated within the Foot Problem Score, hallux valgus deformity was assessed using the Manchester Scale, was first developed by Garrow et al. (2001). The instrument consists of 4

standardised photographs (Figure 5.2) representing the four grades of HAV – none, mild, moderate and severe. The Manchester Scale strongly correlated with radiographic measures, the hallux abductus angle (HAA), ($p = 0.73$, $P < 0.01$) and moderately associated with intermetatarsal angle (IM) angle ($p = 0.49$, $P < 0.01$) (Menz & Munteanu, 2005). Using kappa-statistics, Manchester Scale was reported to have 80 – 86% agreement for inter-rater reliability (Menz & Lord, 2001; Garrow et al., 2001) while the intra-tester reliability was reported to have an 84% agreement (Menz et al., 2003). Hence, as the Manchester Scale is reported to be a valid and reliable tool to rate the degree of hallux valgus deformity, it is used in this study as part of the foot problem score.

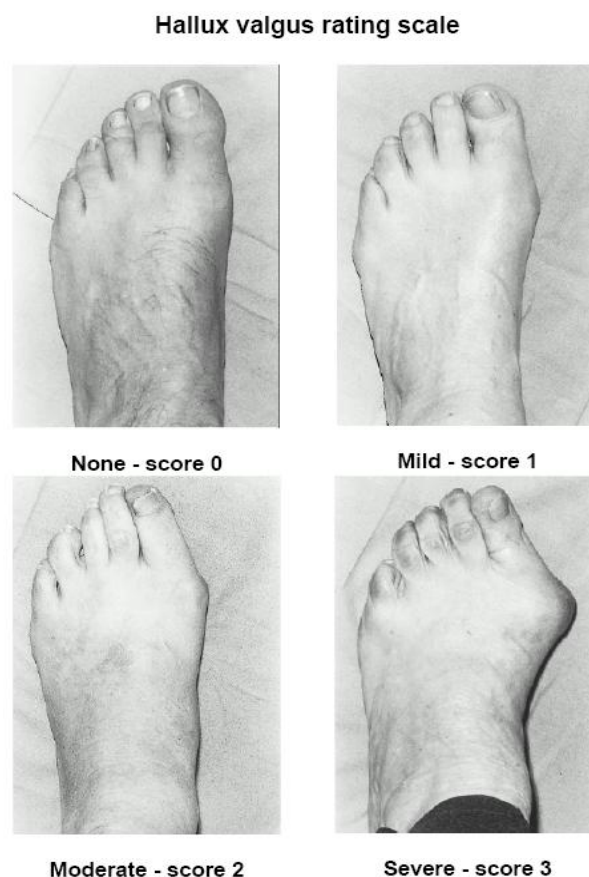


Figure 5.2. The Manchester Scale from Garrow et al. (2001).

5.3.6 Measurement of tophi and tophi count

The assessment of tophus size has been reported as an outcome measure in *Outcome Measure in the Rheumatology Clinical Trial VIII* (Schumacher et al., 2007). The

accumulation of monosodium urate crystals around the joint or the presence of gouty tophus over the joint can lead to structural changes of the joint (Buckley, 1996). Furthermore, assessment of tophus size is considered an important outcome measure as an indication of disease severity (Schumacher et al., 2007). Dalbeth et al. (2007) reported tophaceous gout as a major predictor of loss of hand function in patients with gout.

Tophi measurement can be conducted using physical measurement tools like tape and callipers (Schumacher et al., 2005; Perez-Ruiz et al., 2002; Dalbeth et al., 2007), ultrasound (Perez-Ruiz et al., 2005), MRI (Schumacher et al., 2006) and CT (Gester et al., 2002). The imaging modalities are reliable but also time consuming and expensive. Physical measurement of the tophus is an equally valid and reliable measurement (Dalbeth et al., 2007 and Schumacher et al., 2005). Schumacher et al. (2005) reported good intra-rater and inter-rater reliability for tophus measurement using tape in 52 tophi from 13 individuals. Dalbeth et al. (2007), using 150 mm digital vernier callipers measured 47 tophi in 20 patients with gout and reported excellent inter and intra-tester reliability ($ICC = 0.99$ and 0.99). Furthermore, the author also reported that the physical measurement by the digital callipers correlated well with CT measurement ($P > 0.0001$). Callipers were used once before to measure tophus size as a measure to evaluate the efficacy of urate lowering therapy (Perez-Ruiz et al., 2002). Unfortunately Perez-Ruiz et al. (2002) did not report reliability measures. Due to the high correlation of the digital callipers with more valid CT and MRI, they are used in this study to measure the size of the tophus in the foot and ankle region.

In a hand function study, Dalbeth et al. (2006) reported that tophi size and count are the best predictors of decreased hand function in 20 patients. The authors reported that the number of tophi in the hand is the best single predictor of the Sollerman score, a valid tool to evaluate hand function in tetraplegics. Furthermore, the hand tophi number correlated well with serum urate concentration ($P = 0.016$), number of gout flares in the previous six months ($P = 0.003$), pain level ($P < 0.001$) and radiographic damage ($P < 0.001$). Previously Perez-Ruiz et al. (2002) used the number of tophi in the whole body to evaluate the effectiveness of urate-

lowering therapy and reported that the tophi count correlated well with the disease severity ($P < 0.05$).

This study will measure and count the number of tophi present in the foot and ankle region to determine the best predictors of foot function in gout. The total number of tophi in the whole body will also be included to allow the author to correlate the total tophi count in the foot to foot function.

5.3.7 Neurological status

Diminished peripheral sensation, and vibration threshold are associated with peripheral neuropathy in diabetic patients (ONeill et al., 2006; MayField & Sugarman, 2000). Since the neurological status in gout has not been reported in the past, peripheral sensation and vibration threshold is used here to assess neurological status in gout subjects.

5.3.7.1 Peripheral Sensory Perception

Chronic inflammation is reported to alter overlying skin sensation due to the altered central processing of somatosensory functions leading to decreased sensory functions (Leffler et al., 2002). Rosenbaum (2001) states that arteriolar vasculitis associated with chronic inflammation causes ischemia of nerve fibres with consequent nerve fibre degeneration. Decreased plantar sensations are observed in 25 subjects with rheumatoid arthritis which is an inflammatory condition (Rosenbaum et al., 2005).

Pressure perception of the plantar aspect of the foot (tip of the toes, under the metatarsal heads, heel and the arch) will be determined using a series of research grade monofilaments (6g, 8g and 10g). Monofilaments specifically activate alpha-fibres which are responsible for tactile sensation (Schwartz & Kandel, 1985). These filaments are used extensively in people with diabetes (Thomson, 2006) and for the first time in rheumatoid arthritis (Rosenbaum et

al., 2005) to assess plantar sensitivity. The typical sites assessed are the plantar aspect of the first third and fifth metatarsal heads, under the arch and the heel region (Thomson, 2006). Since these monofilaments have not previously been used in people with gout, it is intended to use these same sites. Mayfield and Sugarman (2000), in a systematic review of six studies, concluded that Semmes-Weinstein monofilament is an effective screening tool for peripheral sensation. Because of its proven validity to detect plantar tactile sensation, Semmes-Weinstein monofilament is used in this study to assess plantar sensation in subjects with gout.

5.3.7.2 Vibration perception

A neurothesiometer is used to determine the vibration perception threshold (VPT); (Bloom et al., 1984). A neurothesiometer delivers vibrations of increasing strength enabling the examiner to determine the threshold values of vibration felt by the subject (Faris, 1991). The vibration threshold is reported to increase with age and 25 hertz is reported to be the mean threshold in 519 subjects (Bloom et al., 1984). A vibration perception threshold (VPT) of >25 Hz is reported to be an effective predictor for foot ulceration in a diabetic population (Young et al., 1994, Kastenbauer et al., 2001; Crawford et al., 2007). In rheumatoid patients the neurothesiometer has scarcely been used; in one instance it was used to determine the integrity of the large afferent nerve fibres (Bekkelund et al., 1996). Bekkelund et al. (1996) reported an increase in VPT (hallux) with disease duration in 56 subjects with rheumatoid arthritis ($p<0.0001$).

Gout is a chronic inflammatory condition, yet the integrity of the large afferent nerve fibres has not been studied in the affected population. Isolated case studies by Kitting and Fulp, (1972) and Fore, (2005) reported ulcerations secondary to gouty tophus. Therefore, this study will measure VPT using a neurothesiometer to assess the integrity of large afferent nerve fibres, allowing us to envisage the possible risk of ulcerations in patients with gout.

5.3.8 Plantar pressure measurements

Excessive loading of human tissues either by trauma or overuse can be harmful (Nicolopoulos et al., 2000). Plantar pressures can be assessed using pressure platforms (EMED, Optical Pedobarograph and Musgrave foot print) or in-shoe pressure devices (PEDAR, micro EMED and FScan); (Cavanagh and Ulbrecht, 1994). Plantar pressures are derived from the force generated between the foot and the ground using a force-sensitive sensor (Cavanagh & Ulbrecht, 1994). The alignment of these sensors and their number, determine the sensitivity and resolution of the pressure device (Orlin & McPoil, 2000). The pressure platform has a greater number of sensors and hence greater resolution; furthermore, the sensors are positioned parallel to the supporting surface and therefore provide a true vertical force measurement (Orlin & McPoil, 2000). The pressure in-shoe devices have lower resolution than pressure platforms as the number of sensors that can be incorporated into an insole are less compared to pressure platform (Orlin & McPoil, 2000). The position of the insole sensor relative to the supporting surface allows the measurement of 'normal' force but not 'true' force as in a force platform (Orlin & McPoil, 2000). It is reported that subjects consciously altered their gait in an attempt to strike the platform, which was a limitation of these devices (McPoil et al., 1999). The in-shoe devices have solved the problem of striking as they capture pressure data when the patient is walking normally (Orlin & McPoil, 2000). The device is especially useful for capturing in-shoe pressure data which could be used to design a particular shoe or orthotic to modify the pressures acting under the foot (Orlin & McPoil, 2000).

In this study the plantar pressures will be assessed using the F-Scan® of TekScan mobile in-shoe system, Version 6X. Peak pressures (kPa) and pressure-time integral (duration of the pressure at a point) under the foot will be measured using a sensor insole. In diabetic patients, increased plantar pressures are considered to be a contributing factor to plantar foot ulcerations (Mueller et al., 2004), callus formations, necrosis and muscle atrophy (Mueller & Maluf, 2002). In rheumatoid arthritis TekScan is used extensively to measure plantar pressure (Otter et al., 2004) as a predictor for the effectiveness of orthotic therapy (Hodge et al., 1999; Jackson et al., 2004), description of an rheumatoid foot (Turner et al., 2008) and forefoot

joint damage (VanderLeeden et al., 2005). Pressure-time integrals have been of particular importance in the rheumatoid foot with intact plantar sensation and normal values of vibration threshold, as the incidence of ulcers has been attributed to increased pressure-time integrals (Woodburn et al., 2007; Helliwell et al., 2007).

Mueller and Strube (1996) compared the measurements from the F-Scan to those from a force platform, reporting excellent correlation between these two measurement tools in ten individuals. In their study, the authors compared the mean plantar pressure value of the F-Scan to the mean value from the force platform using the “three step method” and reported that the output on the F-Scan is linear to that of the output of the force platform, establishing the validity of the tool. Similarly, Chen and Bates (2000) compared the F-Scan to a strain gauge force plate finding no statistical difference between the two systems ($p > 0.05$) in 30 individuals.

The reliability of the F-Scan was reported to be fair to good. Ahroni et al. (1998) reported good reliability under the metatarsal heads (ICC = 0.75) and fair to good reliability under the mid-foot and heel region (ICC = 0.5 and 0.8) in 51 diabetic individuals. Similarly, Randolph et al. (2000) evaluated the reliability of F-Scan in ten healthy subjects. Three recordings of peak pressure were recorded, the intra-subject variance reported to be 1.4 kPa, 2 and 2.7 Kpa for rearfoot, forefoot and midfoot respectively. In contrast Mueller and Strube (1996) reported an index of dependability (representing the ability of a measure to reproduce the same scores on two separate occasions) value of 0.6 which suggests poor reliability; this was attributed to the fact that sensors were not placed inside the shoe prior to the calibration to stabilise the temperature and environment (Hsiao et al., 2002). To maintain accuracy and precision of F-Scan measurement; 1. Calibration should be in the range of the estimated applied pressure; 2. Temperature for the sensor should be maintained by wearing the sensor in-sole in the shoes for ten to fifteen minutes prior to calibration and measurement (Hsiao et al., 2002; Maluf et al., 2001). Due to the validity and reliability of the F-Scan system, it has been used in the present study to assess plantar pressures in people with gout.

5.3.9 Gait parameters

Walking speed is used as a measure of patient status and treatment efficacy in clinical care and research studies (Selby-Silverstein & Besser, 1999; Cultip et al., 2000). Table 5.4 illustrates walking velocity values. Walking speed can be measured visually using a stop clock (Perry, 1992). Recent advances in gait parameters revealed gait variability as measured by step and stride length to be of greater importance in predicting patient status (Beauchet et al., 2006). Electronic walkway systems like GAITRite®, SMTEC® and GAITMAT II™, both user friendly and portable, measure temporal and spatial parameters (Beauchet et al., 2008).

Table 5.4: Description of walking velocities Rodgers. (1995).

Rate	Velocity (m/Sec)
Very slow	<0.40
Slow	0.41-0.70
Slow to moderate	0.71-1.00
Moderate	1.01-1.30
Moderate to fast	1.31-1.60
Fast	1.61-1.90
Very fast	>1.90

In the current study the walking speed will be assessed using the GAITMAT™ II walkway system. The concurrent validity of GaitMat II was determined by comparing the results of GaitMat II with the gold standard Vicon motion analysis system (Barker et al., 2006). Excellent agreement was found in the results between GaitMat II and the Vicon motion analysis system, thus establishing the concurrent validity of GaitMat II. Furthermore, Barker et al. (2006) reported excellent test retest reliability (ICC = 0.99) for the GaitMat II.

5.4 Summary of foot outcomes

The extent of disability experienced by an individual can be related to their functional status. The literature reports the use of foot type and the range of motion in the joints of foot and ankle in the evaluation of functional status and disability. Variation in the neuromuscular status such as reduced muscle strength of the foot and ankle, and reduced plantar sensation and increased vibration threshold, are associated with increased plantar pressures, resulting in gait abnormalities. This association is observed in certain disease conditions like diabetes and rheumatoid arthritis but has not previously been investigated in gout.

5.5 Clinical outcomes

5.5.1 Measurement of serum urate levels

The normal serum urate level in men is 7 mg/dL; for women it is 6 mg/dL (Teng et al., 2006). An increased serum urate level above normal values, hyperurecemia, is reported as the strongest risk factor for gout (Teng et al., 2006). It is included as one of the criteria in the diagnosis for gout by the *American Classification of Rheumatology Criteria for the Diagnosis for Gout* (Wallace et al., 1977). In a cohort of 2,046 subjects, Campion et al., (1987) reported a 4.9% incidence of gout with serum uric acid levels greater than 9 mg/dL and a 0.5% incidence for a uric acid level of 7 to 8.9 mg/dL. A five year follow up of the cohort group revealed increasing incidence of gout with uric acid levels higher than normal. Table 5.5 describes the measured urate levels and the observed incidence.

Table 5.5 Incidence of gout with increased urate levels.

Serum urate levels	5-Year incidence
7 - 7.9	2
8 – 8.9	4.1
9 – 9.9	19.8
≥ 10	30.5

Campion et al. (1987) indicate elevated serum urate levels to be associated with increasing gout incidence. Grahame and Scott (1977) surveyed 354 gout patients revealing a positive association between joint damage and elevated urate levels ($p < 0.05$). Serum urate level is the best predictor of gout when other risk factors like age, hypertension, cholesterol level and alcohol intake are controlled (Campion et al., 1987). However, serum urate levels in some individuals are in the normal range during an acute flare while others with elevated serum urate levels continue to be asymptomatic (Falasca, 2006; Kim et al., 2003; Wortmann, 2002; Schlesinger, 2004; Eggebeen, 2007). Genetic predisposition in asymptomatic individuals is widely accepted (Bleyer & Hart, 2006). Furthermore, normal urate levels during acute flares are possibly due to the effect of pro-inflammatory cytokines (McGill, 2000). The major risk factors for gout, those of genetic predisposition (enzyme action), renal insufficiency, hormonal imbalance (hypothyroidism and hyperparathyroidism) and increased purine intake, influence gout incidence by elevating urate levels. Hence, the role of elevated urate levels in the pathogenesis of gout cannot be overlooked.

5.6 Summary

The functional status of the foot and ankle as reported from previous studies is dependent on foot posture, range of motion in the joints of foot and ankle, muscle strength, plantar pressures and spatial-temporal parameters of gait. The aim of this study is to investigate the reliability of these measures in the feet of individuals with gout and how these measures relate between individuals with and without gout. The following chapter will discuss the methodology and the method of assessing disability, impairment and foot structure and function in the current study.

CHAPTER 6: METHODOLOGY

6.1 Introduction

This chapter describes the selection of potential subjects for the study, followed by the range of clinical and diagnostic tests performed to evaluate foot and ankle characteristics in patients with gout. The chapter also includes a full description of the method used to conduct the clinical and podiatric biomechanical tests, followed by a battery of questionnaires to measure pain and disability. The tests conducted in this study were to evaluate pain, disability and function in subjects with gout. The Foot Function Index (FFI), Leeds Foot Impact Scale (LFIS), Lower Limb Task Questionnaire (LLTQ) and Health Assessment Questionnaire (HAQ) measure pain and disability while the Foot Problem Score measure disability only. The Foot Posture Index (FPI), range of motion (ankle and first MTPJ), muscle strength, peripheral sensation, vibration perception threshold, temporal and spatial parameters, and generic and specific tophi count were conducted to measure function in subjects with gout.

6.2 Study Design

The study is divided into two parts:

Part 1 investigates within and between intra-tester reliability of foot posture, dorsiflexion of the first MTPJ and ankle joints, plantar pressure measurements and gait parameters of gout cases only.

Part 2 is a case-control design to evaluate differences in disability, impairment and foot function between 25 gout cases and 25 age-matched controls.

6.3 Subjects

The Northern Y Region Ethics and the AUT University Ethics Committee approved the study and informed consent was obtained from all potential participants prior to their participation

in the study. Baseline measures were recorded including the patient's duration of gout, number of flares during the previous 6 months, medications, height, weight, gender and ethnicity. A total of 25 participants from the rheumatology clinic at Greenlane Clinical Centre were recruited, the rheumatology nurse selecting the cases with the assistance of a consultant rheumatologist. The selected subjects were contacted by two independent researchers by telephone and recruited for the study after they had given an informed consent. Gout cases were selected where a diagnosis had been made of gout based on the American College of Rheumatology diagnostic criteria for gout (Appendix 3); (Wallace et al., 1977); gout cases with diabetes mellitus were excluded. Since diabetes is known to cause limited joint mobility, exclusion of this disease group will allow the minimising of confounding variables.

6.4 Measurement of disability and impairment

Each participant (case and control) was given the self-administered questionnaires and asked to complete them at the time of data collection.

6.4.1 Foot Function Index

This self-administered questionnaire consists of 17 items divided into three domains of pain (5 items), disability (9 items) and activity limitation (3 items); (Budiman-Mak et al., 1991). Every item in the domain is scored using a visual analog scale of 1 to 10, 1 being the least pain or difficulty and 10 being the worst imaginable pain or difficulty (Budiman-Mak et al., 1991). The total score is the sum of the individual item score for that particular domain. The total FFI score is the sum of the individual domain scores. The final Foot Function Index score is calculated by dividing the total Foot Function Index score by the maximum score.

$$\text{Final FFI score} = \text{Total score} / 170 \times 100$$

The final score is multiplied by 100 to eliminate decimals.

The higher the score the greater the impact of gout on foot function.

6.4.2 Leeds Foot Impact Scale

The questionnaire consists of 51 items distributed into two domains, impairment/footwear (21 items) and activity limitation/participation restriction (30 items); (Helliwell et al., 2005). Each answered item 'yes' or 'no'. Each 'yes' is awarded one point while a 'no' is awarded zero. The highest score for the Leeds Foot Impact Scale is 51, with individual domain scores of 21 and 30 for impairment/footwear and activity limitation/participation restriction respectively. Hence, the higher the score the greater the impact of gout on foot function.

6.4.3 Health Assessment Questionnaire

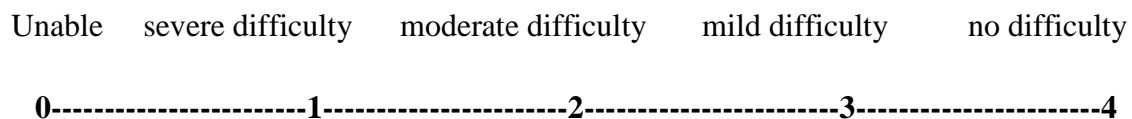
The modified Health Assessment Questionnaire, consisting of ten items, measures how gout affected the subject's ability to function in the activities of daily living in the previous week (Pincus et al., 1983). Each item is scored on a scale of 0 -3, 0 being without any difficulty and 3 being unable to perform that activity (Pincus et al., 1983).

Without any difficulty	some difficulty	much difficulty	Unable
0-----	1-----	2-----	3-----

The total score is obtained from the sum of the scores for the individual items. The final score is calculated by dividing the total score recorded by the total number of items. Final score = Total score / 10.

6.4.4 Lower Limb Task Questionnaire

The Lower Limb Task Questionnaire consists of 20 items equally divided between two domains, 'Activities of Daily Living' and 'Recreational Activities' (McNair et al., 2007). Each item is scored between 0 - 4, 0 being unable to perform a specified activity and 4 being able to perform it without any difficulty (McNair et al., 2007).



Each of the domains is scored individually, the total score being obtained from the sum of the individual scores of the respective domains (McNair et al., 2007). The final score is calculated by dividing the total score of a domain by the maximum score of the particular domain (McNair et al., 2007). Final score of a domain = Total domain score / 40.

6.5 Measurement of foot structure and function

6.5.1 Foot Posture Index

The Foot Posture Index is an observational tool that determines whether the foot is in a pronated position or supination or neutral position, based upon six parameters that examine the foot in the frontal and sagittal planes (Redmond et al., 2005). Please refer to appendix 8 for the individual items of FPI. The sum of the individual items gives the final score for FPI (Redmond et al., 2005). The reference values that categorise the foot into supinated or neutral or pronated are:

- ☐ Highly supinated: -5 to -12
- ☐ Supinated: -1 to -4;
- ☐ Neutral/Rectus: 0 to 5,
- ☐ Pronated: +6 to +9;
- ☐ Highly pronated: +10 to +12.

Each participant was asked to stand unassisted and the examiner observed and records each of the six items of the FPI on a scale of -2 to +2. The participant was instructed by the researcher (D.S) to march at the same spot before recording individual item scores. This was

conducted to prevent the participant from shifting their weight onto one leg which usually occurs during static stance (Redmond, 1998).

6.5.2 Ankle joint range of motion

Ankle joint dorsiflexion was measured using a small plastic goniometer. A non weight-bearing technique is used to measure the range of dorsiflexion at the ankle. Prior to measuring the ankle dorsiflexion range, surface landmarks were identified and bisection lines drawn for the purpose of reference using the technique described by Rome (1996). The surface landmarks and the bisection lines were located and drawn for both right and left feet.

With the subject lying supine on the plinth the researcher (D.S.) marked the midpoint of the lateral malleolus. The fibula shaft was bisected and connected to the midpoint of the lateral malleolus. The shaft of the fifth metatarsal was bisected to represent the lateral column. Using the midpoint of the lateral malleolus as the axis, the stationary arm of the goniometer was placed against the fibular bisection while the movement arm was placed in line with the fifth metatarsal bisection. With the subject completely relaxed, the STJ neutral was palpated and the ankle dorsiflexed by pushing against the lateral column to the point where the subject experiences pain at the end range of dorsiflexion. The angle made by the movement arm to the stationary arm of the goniometer was recorded to give the ankle dorsiflexion value. Three repetitions and a mean reading are recorded. The ankle dorsiflexion measurement was repeated using the same technique, to establish test retest reliability.

6.5.3 First metatarsophalangeal joint dorsiflexion range

The first MTPJ dorsiflexion range is measured using a small plastic goniometer. The non weight-bearing technique described by Allen and Gross (2003) is used to ascertain the available motion within the first MTPJ. Prior to the measurement, the researcher (D.S.) identifies the surface landmarks for the first MTPJ (midpoint of the first metatarsal, bisection of the proximal phalanx and the first metatarsal shaft as described by Hopson et al. (1995).

The landmarks and the bisection lines are drawn for both right and left foot. The same procedure is repeated for all the participants.

With the subject lying supine, the midpoint of the first MTPJ is located and marked on the medial side of the joint. The shaft of the first metatarsal and the proximal phalynx is bisected. Using the midpoint of the first MTPJ as the axis, the stationary arm of the goniometer is placed in line with the bisection line of the first metatarsal shaft while the movement arm is placed in line with the bisection line of the proximal phalynx of the first metatarsal. The hallux is dorsiflexed by applying a proximally directed force onto the plantar aspect of the proximal phalynx until the maximum resistance is felt. In this particular study since gout affects the first MTPJ, during dorsiflexion of the hallux the point where the subject experienced pain is considered the end range of dorsiflexion. The angle made by the movement arm relative to the stationary arm is recorded as the hallux dorsiflexion value. Three repetitions and a mean reading are recorded.

6.5.4 Subtalar and midtarsal joint range of motion

Manual mobilisation of the subtalar and midtarsal joints were undertaken. Each joint was assessed under the categories of average range of motion, limited motion or restricted motion. Three repetitions were undertaken to obtain a mean. Both right and left feet were assessed.

To assess the subtalar joint, with the subject lying supine on the plinth, the examiner holds the heel of the subject's foot with one hand. The index finger and the thumb of the other hand are used to palpate the talar head on either side of the navicular. Inverting and everting the heel the head of the talus is palpated on either side of the navicular. The point during the inversion/eversion of the heel where the talar head cannot be palpated on either side of the navicular is described as the subtalar joint neutral. Using the subtalar joint neutral as the reference point, the amount of inversion movement available and the amount of eversion movement available are noted. The normal range of motion for the subtalar joint is 2:1,

inversion to eversion movement. The subtalar joint motion is considered 'limited' in either inversion or eversion if there is only small movement in either diversion from the subtalar joint neutral position. The subtalar joint is described as 'restricted' if the examiner cannot produce either inversion or eversion in the joint.

To assess the midtarsal joint, with the subject lying supine on the plinth the examiner holds the subject's heel with one hand, and the subtalar joint neutral position is palpated using the other. Holding the foot in that position, traction is applied on the heel in the anterior-posterior direction towards the examiner. This retraction is to minimise subtalar and talocrural joint influence on the motion of the midtarsal joint. With the other hand the examiner clasps the midfoot and an inversion/eversion movement is exerted. Normal midtarsal joint motion is the ability of the examiner to move the midfoot into inversion/eversion with ease; any difficulty in moving the midfoot being recorded as 'limited' and complete loss of movement as 'restricted'.

6.5.5 Muscle strength

The extrinsic foot muscle strength is assessed manually and scored using a semi quantitative grading scale as described by VanSchie et al. (2004). The strength of a muscle is its ability to produce active movements against the examiner's resistance. Depending on the resistance felt against the examiner's hand muscle strength is scored between 0 and 3, 0 being complete inability of the muscle to produce active movement and 3 being strong. Table 6.1 describes manual muscle testing for the extrinsic foot muscles (Valmassy, 1996). Three repetitions and a mean reading are recorded. The procedure is repeated after an hour to establish test-retest reliability.

Table 6.1: The procedure for manual muscle testing for extrinsic foot muscles

Muscle	Subject position	Position of foot	Force applied by the subject	Force applied by the examiner
Flexor hallucis longus	Supine	STJ in neutral, and metatarsal heads stabilised	Plantarflexion of hallux at interphalangeal joint (IPJ).	Dorsiflexion force against the distal phalynx of hallux.
Flexor digitorum longus	Supine	STJ in neutral and metatarsal heads stabilised	Plantarflexion of the digits (2 to 5) at the distal IPJ.	Dorsiflexion force against the distal phalanges of the digits 2 to 5.
Extensor hallucis longus	Supine	Foot and ankle in slight plantarflexion.	Dorsiflexion of hallux at IPJ and at MTPJ	Plantarflexion force to the dorsum of the hallux.
Extensor digitorum longus	Supine	Foot and ankle in slight plantarflexion.	Dorsiflexion of the digits 2 to 5 at all the IPJs and MTPJ	Plantarflexion force to the dorsum of the digits 2 to 5.
Tibialis anterior	Supine	Knee bent, hallux and lesser digits flexed.	Dorsiflexion and inversion at the ankle, avoiding hallux dorsiflexion.	Plantarflexion and eversion force applied to the ankle.
Peroneus longus	Supine	Distal leg supported	Plantarflexion and eversion of the foot	Dorsiflexion and inversion force applied to the foot.
Peroneus brevis	Supine	Distal leg	Abduction of foot	Adduction force applied

		supported		to the foot
Gastrocnemius	Supine	Knee maintained in extension, STJ in neutral	Plantarflexion at the ankle	Dorsiflexion force to the ankle
Soleus	Supine	Knee maintained in flexion, STJ in neutral	Plantarflexion at the ankle	Dorsiflexion force to the ankle

6.5.5.1 Posterior tibial dysfunction

The first metatarsal rise sign test is used to ascertain the integrity of the posterior tibial tendon (Hintermann & Gachter, 1996). The first metatarsal rise sign test is conducted using the method described in Hintermann (1997) and Trinkka (2004). The participant is asked to stand in the angle and base of gait. The tibialis posterior tendon integrity is tested by externally rotating the shank of either leg so that the heel is brought into a varus position. During this manoeuvre the head of the first metatarsal is observed. The head of the first metatarsal remains on the ground during the varus rotation of the heel in normal functioning of the tibialis posterior tendon; however, the first metatarsal rises above the ground in dysfunction. Depending on the excursion of the first metatarsal head from the ground the dysfunction can be rated as 1 or 2; normal is 0 (Table 6.2). The test is completed three times and the average reading documented. The procedure is repeated after one hour to establish test retest reliability.

Table 6.2: Grading of tibialis posterior tendon function using the 1st metatarsal rise test.

Grade	Tibialis posterior tendon integrity as a measure of metatarsal position
0	Normal functioning of the tendon (1 st metatarsal remains on the ground with the varus rotation of the heel)
1	The first metatarsal head rises slightly above the ground with the varus rotation of the heel.
2	1 st metatarsal rise is accentuated with varus rotation of the heel

6.5.5.2 Intrinsic muscle strength

Intrinsic foot muscle strength was assessed using the paper grip test already described in section 5.4.4.3 (Win et al. 2002). The test was performed with the patient sitting straight, with the hips, knees and ankles flexed to 90°. With the subject's heel resting on the floor, a paper slip is placed under the toes distal to the metatarsophalangeal joints. The paper is pulled away in a horizontal direction while the patient resists by gripping it with their toes. The strength of the intrinsic muscles is assessed by the ease with which the paper can be retrieved from beneath the toes (Win et al., 2002). The paper grip test was conducted separately for the hallux and for the lesser digits (2 to 5). Three repetitions were undertaken to obtain a mean score.

6.5.6 Foot Problem Score

The FPS is an observational tool to record foot problems. Presence of digital deformities such as bunions, hammer toes, claw toes and mallet toes are recorded and scored according to the severity. Each individual flexion/extension deformity and each dermatological lesion was scored one point. A lesser toe deformity (for example, hammer toe) was characterised by extension of the MTJ and flexion of the proximal interphalangeal joint. Therefore, FPS was scored as one for the MTPJ extension and one for the proximal interphalangeal joint flexion. Hyperkeratosis lesion (corn and callus), bony prominences (exostosis and tailor's bunion) and

any other soft tissue prominences were recorded and scored. The sum of all these observations gives the final Foot Problem Score.

6.5.6.1 Hallux valgus deformity

Hallux valgus was identified using the Manchester scale (Garrow et al., 2001). The severity of deformity is related to the degree to which the hallux is deviated. Mild hallux valgus is $< 15^\circ$ of lateral deviation, moderate hallux valgus is between 15° to 45° of lateral deviation, and severe hallux valgus is 45° of lateral deviation (Garrow et al., 2001).

Four standardised photographs were presented (Figure 5.2) showing four levels of severity of HAV: none, mild, moderate and severe. Enlarged photographs published in Garrow et al.s study were printed and laminated. Participants stood in the angle and base of gait, eyes looking straight ahead and arms by their sides. The examiner (D.S.) placed the photographs alongside each subject's foot, choosing the one that most resembled the degree of HAV. According to the observation a score was awarded - None: 0, Mild: 1, Moderate: 2, Severe: 3.

6.5.7 Gout tophi

A 150 mm digital vernier calliper (Kennedy Tools™, England) was used to measure the diameter of the tophus. The presence of gouty tophi was physically identified as, and later confirmed by the rheumatology nurse, and marked. A gouty tophus appears like a soft or firm movable nodule, often painful (Wortmann & Kelley, 2005). Each identified tophus was awarded one point by the researcher and added to the Foot Problem Score. The size of the tophus was measured by the researcher using the longest diameter rule developed by Schumacher et al. (2005). According to this rule the borders of the tophus are marked by a pen (Dalbeth et al., 2007) and the farthest end points of the tophus are measured using a vernier calliper as the size of the tophus (Schumacher et al., 2005).

6.5.8 Peripheral sensation

Plantar sensation is assessed using 10g monofilament. The pressure applied to the handle of the monofilament is sufficient to gently bow the filament (MayField & Sugarman, 2000). Eight sites on the foot are selected for testing. The subject was positioned supine with eyes closed to prevent visual feedback (MayField & Sugarman, 2000). The sites include tips of the toes (hallux, second and fifth toe), metatarsal heads (first, third and fifth), midfoot and under the heel. The monofilament was placed on the site to be tested. Slight pressure was applied through the monofilament until the filament bends, and is held in this position for up to 1.5 seconds (Kochman et al., 2002). The subject was instructed to say “yes” if the pressure of the monofilament is experienced. A positive response is recorded as 1 and a negative response as 0. Three repetitions and a mean reading are recorded. (In cases of two responses being negative and one response positive, the test on that site is repeated). The procedure was repeated after an hour to establish test retest reliability.

6.5.9 Vibration perception threshold (VPT)

The VPT was assessed using a biothesiometer (Biomedical Instruments, Newbury, Ohio). The instrument consists of a probe that vibrates at 100 Hertz frequency at amplitude that varies between 0 to 50 volts. The tip of the hallux and the medial aspect of the first MTPJ are assessed by the researcher. The biothesiometer was tested on the subject’s hand prior to the testing on the feet to allow the subject to familiarise with the sensation. The tip of the biothesiometer was placed firmly on the site to be tested; care was taken not to apply too much pressure on the skin (Cassella et al., 2000). The intensity of vibration was gradually increased, starting from 0 volts. The patient was instructed to say “yes” when the vibration is felt. The vibratory perception reading was noted. A threshold of ≤ 25 volts was considered normal and scored as 1, and $>25V$ is scored as 0 (Kastenbauer et al., 2001). Three repetitions and a mean reading was recorded for each site.

6.5.10 Pressure analysis

Plantar pressure readings were obtained using a pressure insole system (Tekscan Inc, Boston, USA). Each pressure insole is 0.18 mm thick with approximately 960 pressure cells connected to a cuff that was attached to the ankle using a velcro strap. An electrical cable attaches the sensors and the cuff to a computer interface. Calibration of the sensors was conducted using the step calibration method advised by the system manufacturer. The step calibration was conducted with the subject standing, and wearing the shoe fitted with the pressure insole. To calibrate the right foot the subject instructed is to stand on the left foot by lifting the right foot off the ground to apply all the body weight through one sensor for a span of three seconds before shifting the whole body weight over to the right foot. The same procedure was repeated to calibrate the left foot.

The pressure sensor insoles were trimmed to the size and shape of the subject's shoe insole. The trimmed pressure insole was positioned on top of the shoe insole and attached using an adhesive tape. The use of adhesive tape minimised crinkling of the pressure insole when the subjects attempted to wear the shoes. Furthermore, the subjects were advised to wear socks to prevent the pressure sensors from sticking to their feet. In the case of a subject using an orthotic, the pressure insole was placed over the orthotic and secured using an adhesive tape. The insole was placed back in the shoe and the subject was allowed to put the shoes back on after which were instructed to walk about the room to allow them to familiarise with the insole. The sensors were plugged onto a cuff secured around the ankle using a velcro strap. An interface cable to the computer was plugged into the cuff at the ankle. Following step calibration the subject was instructed to walk along the length of the examination room until the examiner instructed them to stop.

Seven steps were captured and the number of steps converted to stance phases by the FScan software. The first and last steps were excluded to eliminate acceleration and deceleration phases during the walk. The remaining five steps were averaged to obtain mean peak plantar

pressure (KPa) for the region of interest. The plantar foot was masked (Figure 6.2) into six regions, medial and lateral heel, midfoot and forefoot regions, as described by Hodge et al. (1999) and Turner et al. (2003). The medial forefoot comprises the first and second metatarsal heads, and the lateral from the third to fifth metatarsal heads.

The pressure-time integral (PT) for a masked region was also obtained by calculating the area under the graph (Figure 6.1); this is the product of the mean peak pressure (MPP) and the duration of the mean pressure under the particular region (T); (Figure 6.1). The duration of the mean pressure (T) under a particular region of the foot was obtained by subtracting the time at which the plantar pressure was dropped to the minimum or zero (T2) with the time at from the time at which the loading started (T1).

$$PT = MPP \times T$$

$$T = T2 - T1$$

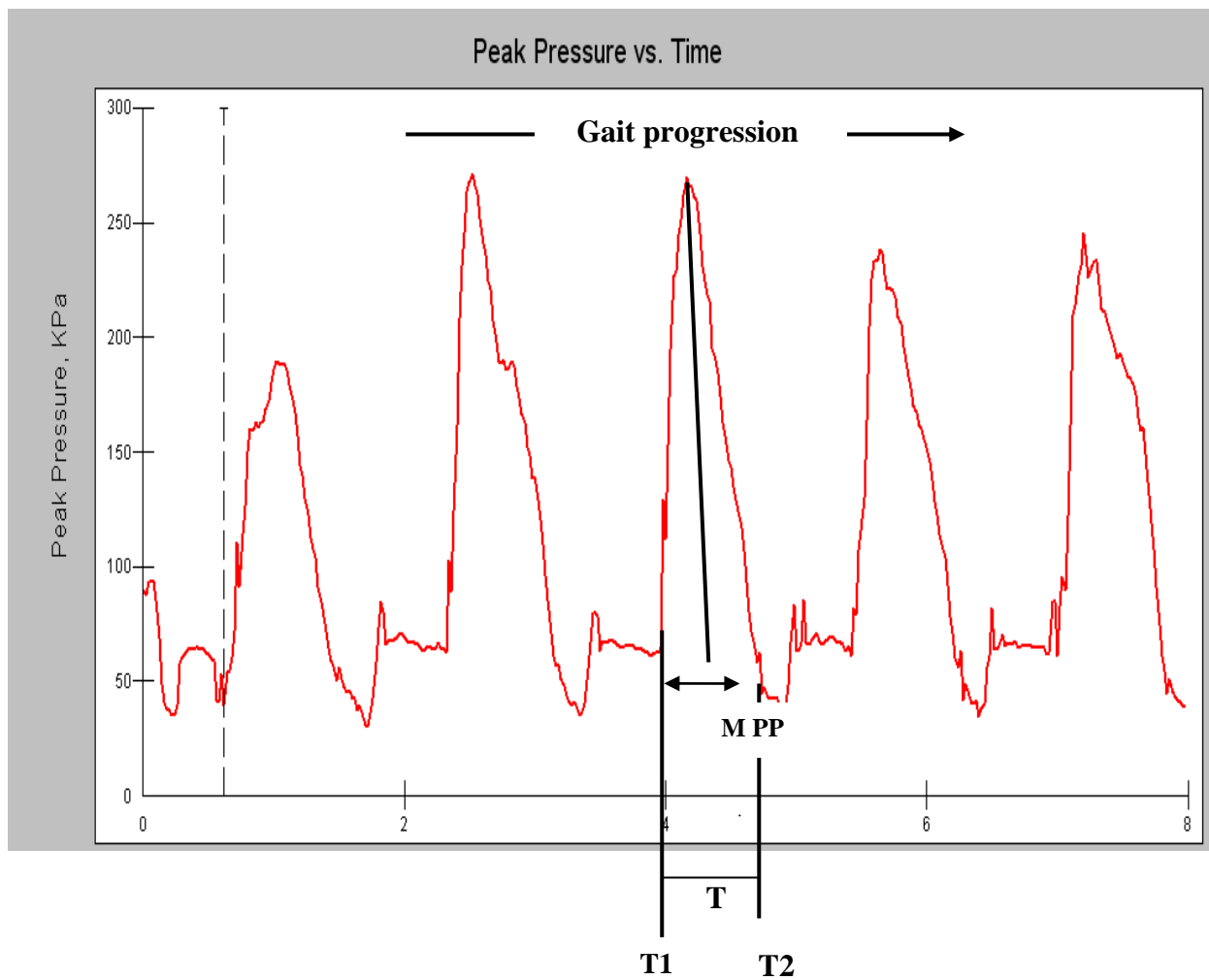


Figure 6.1: Pressure-time graph for the masked regions

MPP – Mean plantar pressure,

T1 – Time initially at loading in seconds,

T2 – Time at end of loading in seconds.

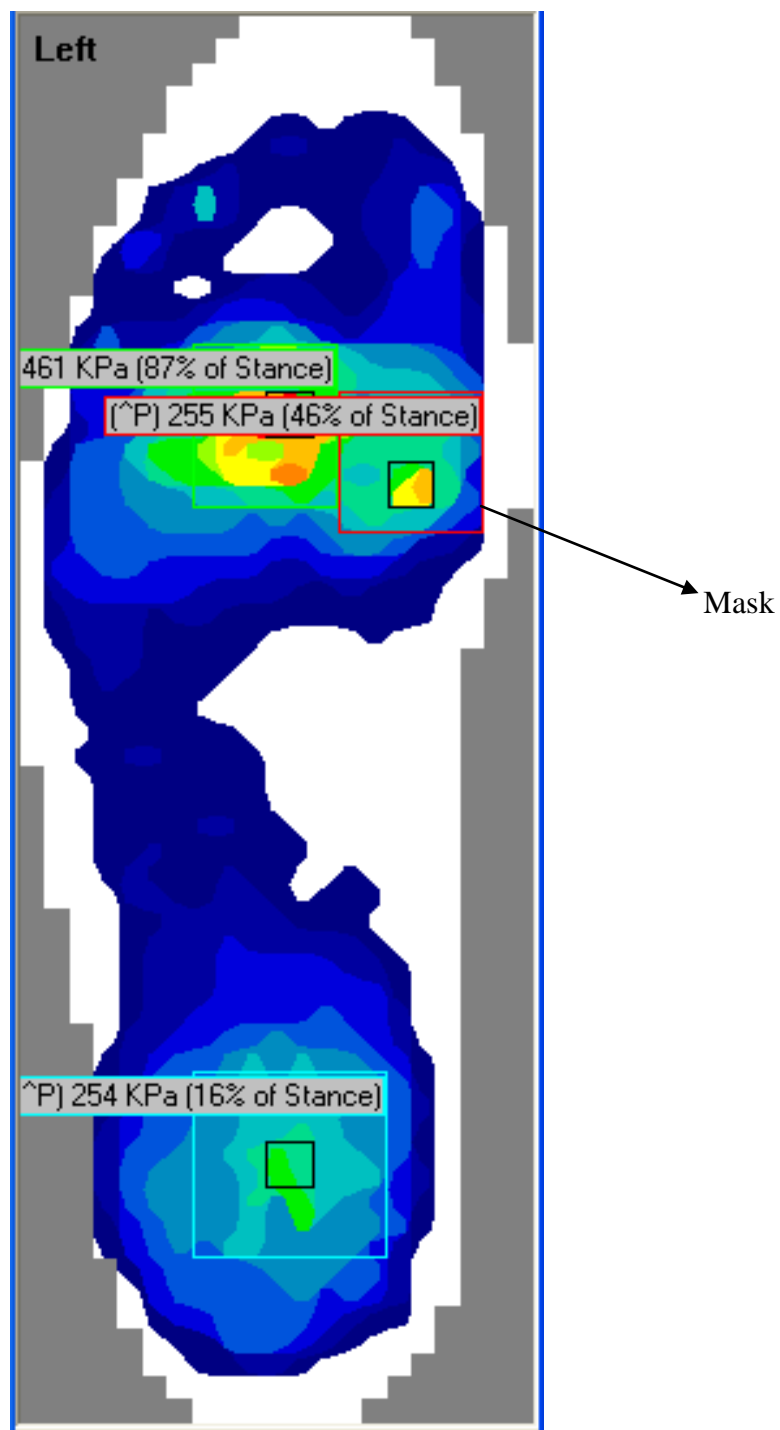


Figure 6.2: Figure showing the masked regions of the foot.

6.5.11 Temporal-spatial parameters of gait

Walking velocity, cadence, stride length and double limb support are measured using Gaitmat™ which consists of a walkway 3.7 meters long and 1 meter wide. The surface of the walkway contains 9728 switches arranged in 38 rows, each row containing 256 switches which are normally open. When a subject traverses the mat, the switches transiently close and then reopen as the subject's feet contact and break contact with the mat. The states of all switches are constantly monitored by the computer. When a switch closes and then reopens, the computer records the closing and opening times, recording temporal and spatial characteristics (stride length, double support time, step length, step time, average velocity, etc) of the patient's gait. The Gaitmat walkway is connected to a computer installed with Gaitmat software (Version 5.2.4).

Each subject was instructed to walk over the Gaitmat at their self selected walking speed and the temporal-spatial parameters were recorded in the computer. To avoid acceleration and deceleration problems in gait the subject was instructed to commence walking one meter prior to the GaitMat and continue walking for one meter after the end of the GaitMat. No encouragement of any type was given to the subjects during the assessment. Three repetitions and a mean reading were recorded. The procedure was repeated after an hour to establish test retest reliability of the measures.

6.6: Clinical measure

All clinical measures such as blood tests were undertaken by rheumatology team based at Greenlane Hospital.

The results for disability, impairment, foot structure and function are analysed using statistical software in the following chapter.

CHAPTER 7: STATISTICAL ANALYSIS

Statistical analysis was conducted using *Statistical Package for Social Sciences* (SPSS) version 16.0. The data was assessed for normality, to justify the appropriateness of the statistical test used. Measures of skewness and kurtosis were checked using the normality test. The data was further assessed using the histogram graph with the normality curve to determine the distribution. The data was found to be normally distributed for the following outcome measures: first MTPJ dorsiflexion, ankle dorsiflexion, FPI, muscle strength, VPT, peripheral sensation, disability and impairment scales, peak plantar pressures, pressure-time integrals and gait parameters. However, the data for the Foot Problem Score subtalar joint and midtarsal joint range of motion was skewed.

7.1 Descriptive information

All the parameters except the Foot Problem Score were normally distributed and are described using mean and standard deviation. Peripheral sensation and muscle strength which had normal distribution are described as a percentage value. The Foot Problem Score data being skewed, will be described using median and interquartile ranges.

7.2 Within and between session intra-tester reliability

Intraclass Correlation Coefficients (ICC) was calculated to determine consistency in the measurement between the sessions. ICCs were calculated for first MTPJ dorsiflexion, ankle dorsiflexion, FPI, peak plantar pressures, pressure-time integrals and gait parameters. The level of reliability for ICC is classified using the values reported in Menz et al. (2004). The characterisations were, slight if ICC ranged from 0.00 to 0.20, fair if ICC ranged from 0.21 to 0.40, moderate if ICC ranged from 0.41 to 0.60, good if ICC ranged from 0.61 to 0.80, and excellent if ICC ranged from 0.81 to 1.00.

Although ICC is an accepted measure of reliability, it is dependent on the variability within the groups being measured (McPoil et al., 2009). Atkinson and Nevill (1998) agree, adding that ICC should never be used in isolation as a measure of reliability. Hence, Standard Error of Measurement (SEM) or typical error, was also used as a measure of reliability. SEM is defined as within subject standard deviation (Hopkins, 2000), which is to say SEM represents the error in the measurement between two or more occasions (McPoil et al., 2009). SEM has the same units as the original measurement and was calculated using the formula $SEM = SD (\sqrt{1 - ICC})$, where SD is the standard deviation (Stratford & Goldsmith, 1997). The standard deviation value used in this study was derived from the average of the standard deviation of the two occasions. In this study, SEM has been converted to a percentage to allow the reader to have a better appreciation of the error. The percentage value for SEM was calculated using the formula $SEM\% = SEM / \text{Mean} \times 100$. The mean score for the measurement was calculated by averaging the mean scores for the measurement from the two occasions.

In addition to SEM, the Smallest Real Difference (or Minimal Detectable Change) was calculated for all reliability measurements. The smallest real difference (SRD) was derived from SEM using the formula $SRD = SEM \times 1.645 \times \sqrt{2}$, where 1.645 is the 90% confidence interval (Beckerman et al., 2001). SRD identifies whether or not the measurement error is clinically significant to be a true variance (Beckerman et al., 2001). For the change in the scores to be considered significant the change score should exceed SRD (McPoil et al., 2009). In this study the change in the scores is the difference in the mean values between the two occasions as reported in Ota et al. (2006).

7.3 Case control trial

Paired t-tests with 95% CI were conducted to investigate significant differences between left and right feet for all measurements except for disability and impairment scales, walking velocity and cadence. One of the feet from the control group was arbitrarily selected and compared to the left and right foot of the gout group. Hence, three groups are investigated to identify differences between gout and control.

Analysis of Variance (ANOVA) was conducted to investigate differences between the gout and control groups for the first MTPJ and ankle dorsiflexion, FPI, muscle strength, VPT, plantar pressure, pressure-time integrals and gait parameters, except walking velocity and cadence. Dunnett's post-hoc test was conducted later to identify which foot differed among the groups. An alpha level of 0.05 was established for this test.

Chi squared test was conducted to investigate any significant differences between the groups for muscle strength, peripheral sensation, subtalar and midtarsal joint range of motion. Since the Chi square cannot identify differences between groups, Bonferroni correction has been used to avoid possible type I error (Hopkins, 2000). Applying Bonferroni correction the previously established alpha of 0.05 was divided by the total number of groups (3) and an alpha level of 0.02 was established.

A Wilcoxon signed t-test was conducted to investigate the difference between the groups for Foot Problem Score. An alpha level of 0.05 was established for this test.

Disability and impairment scales, walking velocity and cadence between the groups was investigated using an independent t-test, with an alpha level of 0.05.

CHAPTER 8: RESULTS

8.1 Introduction

This chapter details the results in two sections. The first section will present within and between intra-tester reliability measures for gait and pressure parameters in gout cases only. The second will present the descriptive statistics and the significant differences between the gout group and the control group for all outcome measures. The data for all the parameters showed normal distribution except for Foot Problem Score.

8.2 Demographics

A total of 50 participants were included in the study. The gout group consisted of 25 participants (19 males and 6 females) who were age and gender matched with the control group, 25 healthy participants without gout (19 males and 6 females). In the gout group we failed to conduct the peak plantar pressure readings and gait parameters for one participant. The demographics include age (years), height (m), weight (kg) and body mass index (kg/m^2) of all subjects (Table 8.1). The gout group consisted of patients with a mean of 12 years of disease duration. None of the participants in the gout group experienced an acute flare during the study. The inflammatory marker CRP (C - reactive protein) 4.4 (6) g/L was within the normal value of < 5 . The serum creatinine and serum urate levels were 105 (29) $\mu\text{mol/L}$ and 0.36 (0.1) mmol/L respectively. The results demonstrated no significant difference between the two groups for age ($p = 0.25$) and BMI ($p = 0.30$). However, significant difference was observed in height ($p = 0.04$) and weight ($p < 0.001$) between the groups.

The reliability tests were conducted for only the gout group. The outcome measures that were repeated in the gout group included the first MTPJ dorsiflexion, ankle dorsiflexion and foot posture index, peak plantar pressures, pressure-time integrals and temporal-spatial parameters of gait.

	Age (years) Mean (SD)	Height (meters)* Mean (SD)	Weight (kilograms)* Mean (SD)	BMI (kg/m²) Mean (SD)
Gout	61.2 (11.7)	1.7 (0.1)	95.3 (15.7)	32.1 (5.6)
Controls	57.3 (12.2)	1.6 (0.2)	80.2 (10.9)	30.3 (6.4)

* p<0.05

Table 8.1: Demographics information for gout and control group.

8.3 Within and Between Intra-tester Reliability Results

This section will present the within and between intra-tester reliability measures relating to the gout group only. Peak plantar pressures, pressure-time integrals, gait parameters, first MTPJ and ankle dorsiflexion motion and Foot Posture Index were assessed. Intraclass Correlation Coefficient (ICC) (1,1) was used to assess the reliability of the repeated measures. The error in measurement for these repeated measures was assessed using standard error of measurement (SEM). The SEM was interpreted as a measure of percentage error. To investigate if the error in the measurement was a true error or not the smallest real difference (SRD) was used.

8.4 Foot structure

Table 8.2 displays descriptive information for the parameters that measure foot structure. These outcome measures were measured on two separate occasions. An excellent reliability with ICC ranging from 0.93 – 0.98 was measured for all the above parameters on both the left and right feet. The confidence intervals were also high (ranging from 0.83 – 0.99) indicating

that the ICC would fall between the confidence interval values 95% of the time. Table 8.3 describes the ICC, SEM and SRD for foot and ankle characteristics.

The SEM values are described in Table 8.3. The percentage change of error is less for the first MTPJ dorsiflexion movement, moderate error for the ankle dorsiflexion movement and a very high error for the FPI (Table 8.3). The SRD values are displayed in Table 8.3 along with the difference in the mean values between the occasions for the above parameters. The difference in the mean values between the two occasions is less than the SRD values and thus the difference or the error is too small to be considered.

Table 8.2 Descriptive information for first MTPJ, ankle and FPI for occasions 1 and 2 in the gout group

	Left Foot Occasion 1 Mean (SD)	Right foot Occasion 1 Mean (SD)	Left foot Occasion 2 Mean (SD)	Right Foot Occasion 2 Mean (SD)
First MTPJ dorsiflexion movement (Degrees)	58 (27)	58 (29)	60 (26)	59 (28)
Ankle dorsiflexion movement (degrees)	13 (6)	15 (6)	14 (7)	15 (6)
Foot Posture Index (FPI)	1 (5)	1 (5)	1 (5)	1 (5)

Table 8.3 ICC, SEM and SRD values for first metatarsophalangeal joint (MTPJ) and ankle dorsiflexion movement and Foot Posture Index (FPI).**SEM and SRD units for first MTPJ and ankle dorsiflexion in degrees**

Variable	ICC (95% I)		Standard Error of Measurement (SEM)		% error of SEM		Smallest real difference (SRD)		Mean difference	
	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot
First MTPJ Dorsiflexion	0.97 (0.95 – 0.99)	0.98 (0.96 – .99)	4.6	4.1	6.5	5.7	12.7	11.1	2	1
Ankle Dorsiflexion	0.95 (0.90 – 0.98)	0.93 (0.83 – .97)	2.8	3.1	20.0	19.5	7.6	8.6	1	0
FPI	0.98 (0.96 – 0.99)	0.97 (0.93 – .99)	0.6	0.9	42.1	93.1	1.7	2.5	0	0

8.5 Foot function

Peak plantar pressures, pressure-time integrals and gait parameters were repeated on two separate occasions to investigate intra-tester reliability for these measures.

8.5.1 Peak plantar pressures

The peak plantar pressures were measured on two separate occasions under ten regions of the foot. Table 8.4 presents the descriptive information for plantar pressures under different regions of the foot for both occasions. The ICC for peak plantar pressures was found to be excellent on repeated occasions (Table 8.5). The lower confidence interval ranged from 0.81 – 0.93 on the left foot and 0.84 – 0.93 on the right foot.

Table 8.4 Descriptive information for peak plantar pressures in kilopascals on two occasions in gout group.

	Left foot Occasion 1 Mean (SD)	Left foot Occasion 2 Mean (SD)	Right foot Occasion 1 Mean (SD)	Right foot Occasion 2 Mean (SD)
Medial heel	264.9 (98.8)	274.9 (84.5)	253 (103.2)	262.1 (97.7)
Lateral heel	249.8 (88.2)	260 (81.9)	240.4 (88.7)	244.1 (83.6)
Midfoot	120.9 (59.3)	129 (58.7)	156.4 (74.6)	154.4 (90.5)
First metatarsal region	252.9 (113.9)	252.7 (91.7)	213.1 (113.5)	231.2 (134.7)
Second metatarsal region	309.7 (141.6)	350.5 (147.5)	297.5 (121.2)	315.7 (124.5)
Third metatarsal region	333.3 (173.5)	350.8 (150.5)	313.7 (138.8)	340.2 (149.8)
Fourth metatarsal region	248.8 (127.1)	245.9 (109.9)	249.7 (103.8)	244.3 (91.9)
Fifth metatarsal region	153.1 (10.7)	160.5 (68.9)	206.9 (136.4)	198.7 (120.8)
Under 1st toe	143.8 (96.9)	142.5 (103)	153.4 (100.1)	152.8 (101.8)
Under 2nd-5th toes	124.2 (85.9)	130.9 (75.7)	133.4 (70.3)	130.5 (72.5)

The measurement error between the two occasions, a measure of standard error of measurement (SEM), was low for the left and right foot (Table 8.5). The SEM for the left foot ranged from 13 KPa to 35.4 KPa and 17.2 KPa to 34.1 KPa on the right foot. Reporting SEM as measure of percentage error, the left foot recorded (0.8% – 13.7%) across all the foot regions (Table 8.5) and the error for the right foot ranged from 6.2% – 20% (Table 8.5). To establish if the recorded measurement error is clinically relevant the Smallest Real difference (SRD) is calculated. Table 8.5 describes the SRD values for the left and right foot. The difference in the mean values for the left and the right foot for both occasions is compared to the SRD value to ascertain the real difference.

Table 8.5: ICC, SEM and SRD values of the plantar pressure readings for gout group

Foot region	ICC (95% CI)	ICC (95% CI)	Standard Error of Measurement (SEM) (Kpa)		% error of SEM		Smallest real difference (SRD) in Kpa		Difference in mean values in Kpa	
	Left foot	Right foot	Left foot	Right Foot	left foot	Right foot	Left foot	Right foot	Left foot	Right foot
Medial eel	0.95 (0.88 – 0.98)	0.97 (0.93 – 0.99)	20.5	17.4	7.6	6.7	47.8	40.5	10	9
Lateral heel	0.93 (0.83 – 0.97)	0.96 (0.91 – 0.98)	22.5	17.2	8.4	6.9	52.4	40.1	10	4
Midfoot	0.95 (0.89 – 0.98)	0.93 (0.84 – 0.97)	13.2	20.2	11.3	14.4	30.8	47.1	9	2
First metatarsal region	0.94 (0.86 – 0.97)	0.94 (0.85 – 0.97)	25.2	30.4	10.8	14.8	58.7	70.6	0	18
Second metatarsal region	0.94 (0.86 – 0.97)	0.93 (0.85 – 0.97)	35.4	32.5	10.9	10.6	82.5	75.7	41	18
Third metatarsal region	0.97 (0.94 – 0.99)	0.95 (0.88 – 0.98)	28.1	32.3	8.3	6.3	65.5	75.3	17	27
Fourth metatarsal region	0.95 (0.88 – 0.98)	0.95 (0.89 – 0.98)	26.5	21.8	12.2	9.1	61.7	50.8	3	5
Fifth metatarsal region	0.92 (0.81 – 0.96)	0.93 (0.85 – 0.97)	19.7	34.1	13.7	20.1	45.9	79.4	7	8
Under 1 st toe	0.97 (0.93 – 0.99)	0.97 (0.93 – 0.99)	17.3	17.5	13.1	13.2	40.3	40.8	1	1
Under 2 nd -5 th toes	0.97 (0.93 – 0.99)	0.94 (0.86 – 0.97)	13.9	17.5	12.1	13.7	32.4	40.8	6	3

8.5.2: Pressure-time integrals

The pressure-time integrals were calculated for the two occasions under ten regions of the foot. Table 8.6 presents the descriptive information for pressure-time integrals on repeated occasions.

Table 8.6: Descriptive information for Pressure-time integrals in Kilopascals.sec on two occasions in gout.

Foot region	Left foot Occasion 1 Mean (SD)	Left foot Occasion 2 Mean (SD)	Right foot Occasion 1 Mean (SD)	Right foot Occasion 2 Mean (SD)
Medial heel	53.8 (23.8)	50.8 (19.7)	46.9 (16.9)	44.1 (14.8)
Lateral heel	50.8 (19.1)	50.1 (19.1)	47.6 (15.5)	43.8 (16.7)
Midfoot	30.0 (10.3)	27.4 (10.1)	39.1 (22.1)	34.4 (15.2)
First metatarsal region	44.8 (19.1)	40.4 (17.1)	39.9 (22.1)	39.4 (20.8)
Second metatarsal region	56.9 (22.2)	56.9 (22.2)	51.1 (21.2)	51.7 (23.7)
Third metatarsal region	65.2 (36.9)	68.6 (32.6)	59.2 (29.1)	59.1 (27.6)
Fourth metatarsal region	53.8 (25.2)	56.9 (24.1)	59.5 (27.2)	57.6 (26.1)
Fifth metatarsal region	41.1 (22.8)	40.9 (17.9)	60.1 (46.7)	53.9 (37.4)
Under 1st toe	17.6 (13.0)	15.8 (12.9)	19.7 (17.1)	16.9 (9.7)
Under 2nd-5th toes	17.5 (13.6)	16.5 (11.5)	23.8 (16.4)	21.2 (10.9)

The reliability for the pressure-time integrals ranged from good to excellent (ICC: 0.87 – 0.94) on the left foot and fair to excellent (ICC: 0.61 to 0.93) on the right foot (Table 8.7). However, the reader is cautioned to consider the low lower confidence intervals for all the regions under the right foot except for the medial heel, second and fifth metatarsal regions and for the first metatarsal region on the left foot (Table 8.7).

The error in measurement (SEM) for pressure-time integrals was small for all the regions under the foot (Table 8.7). Interpreting SEM in percentage, a 29.4% error was calculated under the hallux on the left foot (Table 8.7) while the first metatarsal and the toes under the right foot showed an error of 28% and 39.7% respectively (Table 8.7).

Finally to investigate if the error measured is true,; the smallest real difference (SRD) is compared to the difference in the mean of the pressure-time integral value from the two occasions (Table 8.7).

Table 8.7: ICC, SEM and SRD of pressure-time integrals for gout group (KPa.sec)

Foot region	ICC (95% CI)		Standard Error of Measurement (KPa. Sec)		% error of SEM		Smallest real difference (SRD) (Kpa. Sec)		Difference in mean value in KPa.sec	
	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot
Medial heel	0.94 (0.87 – 0.97)	0.89 (0.87 – 0.97)	5.3	5.3	10.4	11.8	12.4	12.3	3	3
Lateral heel	0.92 (0.81 – 0.96)	0.79 (0.52 – 0.91)	2.6	7.4	5.2	16.1	6.1	17.2	1	4
Midfoot	0.92 (0.82 – 0.97)	0.71 (0.34 – 0.88)	2.9	8.5	10.4	23.1	6.7	19.8	3	5
First metatarsal region	0.86 (0.67 – 0.94)	0.75 (0.51 – 0.91)	6.8	10.8	16.2	28.1	15.8	25.1	5	1
Second metatarsal region	0.88 (0.72 – 0.95)	0.8 (0.72 – 0.95)	7.7	10.1	13.8	20.1	17.9	23.5	1	1
Third metatarsal region	0.94 (0.85 – 0.97)	0.76 (0.50 – 0.90)	8.5	13.9	12.7	23.5	19.8	32.4	4	1
Fourth metatarsal region	0.93 (0.84 – 0.97)	0.78 (0.50 – 0.91)	6.9	12.5	12.8	21.5	16.1	29.1	4	3
Fifth metatarsal region	0.92 (0.80 – 0.96)	0.93 (0.83 – 0.97)	5.8	11.1	14.5	20.1	13.5	25.1	2	8
Under 1 st toe	0.87 (0.71 – 0.95)	0.72 (0.36 – 0.88)	4.7	7.1	29.4	39.4	10.9	16.5	3	4
Under 2 nd -5 th toes	0.90 (0.76 – 0.96)	0.61 (0.11 – 0.83)	3.9	8.6	23.1	39.1	9.1	20.1	2	3

8.5.3: Gait parameters

The gait parameters were measured on two occasions. The descriptive information for the individual parameters on both these occasions is presented in Table 8.8.

Table 8.8: Descriptive information for gait parameters for the two occasions in gout

	Left foot Occasion 1 Mean (SD)	Right foot Occasion 1 Mean (SD)	Left foot Occasion 2 Mean (SD)	Right foot Occasion 2 Mean (SD)
Step length (m)	0.56 (0.14)	0.56 (0.12)	0.55 (0.13)	0.56 (0.13)
Stride length (m)	1.1 (0.24)	1.1 (0.25)	1.1 (0.26)	1.12 (0.26)
Swing phase (s)	0.5 (0.33)	0.41 (0.04)	0.47 (0.33)	0.4 (0.04)
Single leg support (s)	0.4 (0.04)	0.57 (0.79)	0.41 (0.04)	0.56 (0.79)
Double leg support (s)	0.27 (0.41)	0.25 (0.24)	0.28 (0.41)	0.24 (0.25)
Stance phase (s)	0.99 (0.77)	1.1 (1.2)	0.96 (0.76)	1.04 (1.18)
Velocity (m/s)	0.90 (0.28)		0.92 (0.30)	
Cadence (steps/min)	93.7 (16.9)		96.5 (16.9)	

The reliability of the gait parameters was excellent (ICC: 0.89 – 0.99) for the left foot and (ICC: 0.91 – 1) for the right foot in the gout group (Table 8.9). The confidence intervals were large for all the gait parameters ranging from 0.77 to 1 on the left foot to 0.78 to 1 on the right foot. SEM for all the gait parameters ranged from 0 – 0.08 seconds. The SEM for velocity and cadence were 0.07 m/s and 3.37 steps/min respectively (Table 8.9). The SRD is used to test the sensitiveness of Gaitmat to detect clinically relevant changes. The SRD values are displayed in Table 8.9. The differences in the mean values for the gait parameters for the left and right foot on the two occasions are also listed in Table 8.9.

Table 8.9: ICC, SEM and SRD for gait parameters

Variable	ICC (95% CI)		Standard Error of Measurement (SEM)		% error of SEM		Smallest Real Difference (SRD)		Mean difference	
	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot	Left Foot	Right foot
Step length (m)	0.91 (0.8 – 0.96)	0.95(0.88 – 0.98)	0.04	0.03	6.9	5	0.11	0.08	0	0.01
Stride length (m)	0.94 (0.86 – 0.97)	0.95 (0.88 – 0.98)	0.06	0.06	5	5.3	0.17	0.17	0	0.04
Swing phase (s)	0.99 (0.99 – 0.99)	0.91 (0.78 – 0.96)	0.03	0.01	7.5	2.5	0.08	0.03	0	0
Stance phase (s)	0.99 (0.98 – 0.99)	0.99 (0.99 – 0.99)	0.08	0.12	9.7	14.6	0.22	0.33	0	0
Single leg support (s)	0.89 (0.77 – 0.96)	0.99 (0.99 – 1)	0.01	0	2.5	0	0.03	0	0	0
Double leg support (s)	0.99 (0.99 – 1)	0.99 (0.98 – 0.99)	0.04	0.02	21	10.5	0.11	0.05	0	0
Velocity (m/s)	0.94 (0.87 – 0.97)		0.07		7.8		0.19		0.02	
Cadence (steps/min)	0.96 (0.9 – 0.98)		3.4		3.5		9.3		2.4	

8.6 Case-Control Trial

Analysis of Variance (ANOVA) was conducted for the first MTPJ and ankle dorsiflexion movement, Foot Posture Index and vibration perception threshold, peak plantar pressures, pressure-time integrals, and all the gait parameters except those of velocity and cadence. Muscle strength, peripheral sensation, subtalar joint and midtarsal joint range of motion were investigated using a chi square test. The Foot Problem Score between the groups was investigated using the Wilcoxon signed t-test. For ANOVA the left foot of the control group was arbitrarily selected and individually compared with the left and right feet of the gout group. If a significant difference was observed with ANOVA, Dunnett's test was conducted to identify between which groups the significance existed. Differences in disability and impairment scales, walking velocity and cadence were investigated using independent t-tests with 95% confidence intervals. Descriptive information for all the parameters is presented in this Section.

8.7 Foot structure

The foot and ankle characteristics that are used to investigate foot structure include measurement of dorsiflexion in the first metatarsophalangeal joint (MTPJ) and the ankle joint, Foot Posture Index (FPI), Foot Problem Score (FPS), subtalar (STJ) and midtarsal joint (MTJ) range of motion and muscle strength of the extrinsic and intrinsic muscles of the foot.

8.7.1 Range of motion

The mean dorsiflexion movement of the first MTPJ and the ankle joints is presented in Table 8.10 which also describes the motion at STJ and MTJ between the gout and control groups. The results demonstrated significant differences for first MTPJ dorsiflexion movement ($p = 0.009$). Post-hoc analysis using the Dunnett's test demonstrated a significant reduction in first MTPJ dorsiflexion movement of both feet in the gout group when compared to the control group. Significant differences were also demonstrated for the range of motion at the subtalar joint ($p < 0.0001$) and midtarsal joint ($p < 0.0001$).

8.7.2 Foot Posture Index

The descriptive information for the Foot Posture Index is presented in Table 8.10. ANOVA for FPI demonstrated that foot posture was non-significant between the groups (Table 8.10).

8.7.3 Foot Problem Score

The Foot Problem Scores skewed distribution is described using median and interquartile ranges, in Table 8.10. The Wilcoxon signed t-test for the Foot Problem Score was significantly different ($p = 0.03$) on the left foot only in the gout group, compared to the controls.

Table 8.10 Descriptive information for the first MTPJ, Ankle, FPI and FPS

Variable	Gout group		Control group	
	Left Foot Mean (SD)	Right foot Mean (SD)	Left Foot Mean (SD)	Right foot Mean (SD)
(a)First MTPJ dorsiflexion movement (Degrees)*	58 (27)	58 (29)	77 (10)	79 (10)
(a) Ankle dorsiflexion movement (degrees)	13 (6)	15 (6)	15 (4)	14 (4)
(a) Foot Posture Index (FPI)	1 (5)	1 (5)	3 (2)	3 (2)
(b)Foot Problem Score (FPS)*	1 (0 -8)	1 (0 – 5)	0 (0 – 1)	0 (0 – 1)
(b) Subtalar joint range of motion ***	1(1- 1)		0 (0-0)	0 (0-0)
(b) Midtarsal joint range of motion ***	1(1- 1)		0 (0-0)	0 (0-0)

(a): ANOVA *($p < 0.05$), (b): Wilcoxon signed t-test **($p < 0.05$), (b) median (Interquartile ranges), (b): chi square ***

($p < 0.02$)

8.7.4 Muscle strength

Descriptive information for muscle strength is displayed in Tables 8.11 and 8.12. Results demonstrate that there are significant differences in muscle strength for all muscle groups, between the gout and the control group. The muscle strength between the gout and control groups was measured using a Chi Square. The results demonstrate that all the muscles in the gout group are weaker with the exception of the long extensor muscles, the extensor digitorum longus and extensor hallucis longus. The percentage value indicate response rate of the muscle against resistance. For example in gout group grade 2 muscle strength was demonstrated in 60% of patients for gastrocnemius and soleus muscles.

Table 8.11: Muscle strength in percentage values in Gout group.

	Grade 0		Grade 1		Grade2		Grade 3	
	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot
Gastrocnemius			36	36	60	60	12	12
Soleus			36	36	60	60	12	12
Tibialis posterior	28	28	56	56	16	16		
Extensor hallucis longus	8	8	64	64	28	28		
Extensor digitorum longus	8	8	60	60	32	32		
Flexor hallucis longus	8	8	64	64	28	28		
Flexor digitorum longus	8	8	60	60	32	32		
Tibialis anterior			44	44	56	56		
Peroneus longus	8	8	56	56	32	32	4	4
Peroneus brevis	8	8	68	68	24	24		
Intrinsic muscles of hallux	32	32	68	68				
Intrinsic muscles of the digits	32	32	68	68				

Muscle strength grading: 0 = Complete weakness, 1= Moderate weakness, 2= Mild weakness, 3= Strong

Intrinsic muscles: 0 = no resistance, 1 = good resistance,

Tibialis posterior: 0 = Good strength, 1 = Slight weakness, 3 = Complete weakness)

Table 8.12: Muscle strength in percentage values in control group.

	Grade 0		Grade 1		Grade2		Grade 3	
	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot	Left foot	Right foot
Gastrocnemius *					100	100		
Soleus *					100	100		
Tibialis posterior *	12	12	88	88				
Extensor Hallucis longus **			92	92	8	8		
Extensor Digitorum Longus **			92	92	8	8		
Flexor Hallucis Longus *			4	4	96	96		
Flexor Digitorum longus *			4	4	96	96		
Tibialis Anterior *					100	100		
Peroneus Longus *					100	100		
Peroneus Brevis *					100	100		
Intrinsic muscles of Hallux *			100	100				
Intrinsic muscles of the Digits *			100	100				

(Muscle strength grading: 0 = Complete weakness, 1= Moderate weakness, 2= Mild weakness, 3= Strong)

Intrinsic muscles: 0 = no resistance, 1 = good resistance,

Tibialis posterior: 0 = Good strength, 1 = Slight weakness, 3 = Complete weakness)

*Chi square $p < 0.02$ (Significantly stronger in controls than gout group,

**Chi square $p < 0.02$ (significantly stronger in gout than in controls)

NB: The percentage value indicate response rate of the muscle against resistance. For example in control group grade 2 muscle strength was demonstrated in all patients (100%) for gastrocnemius and soleus muscles)

8.8 Foot Function

Peripheral sensation, vibration perception threshold, plantar pressures, pressure-time integrals and gait parameters were used to assess foot function in both groups.

8.8.1: Peripheral sensation:

The descriptive information for peripheral sensation is illustrated in Table 8.13 in percentage values. Using a Chi square, it was seen that the results demonstrated no significant differences in peripheral sensation between gout and healthy controls ($p < 0.02$).

Table 8.13: Peripheral sensation in percentage values for gout and controls

Foot region	Gout (%)		Control (%)	
	Left foot	Right foot	Left foot	Right foot
Under first metatarsal head	92	92	96	96
Under third metatarsal head	92	92	96	96
Under fifth metatarsal head	92	92	96	96
Under hallux tip	88	88	96	96
Under third toe tip	88	88	96	96
Under fifth toe tip	88	88	96	96
Plantar heel	72	76	96	96

Peripheral sensation % indicates the number of participants in the group who responded with a positive response for the touch of monofilament for that particular region under the foot.

8.8.2: Vibration Perception Threshold

The descriptive information for the Vibration Perception Threshold is displayed in Table 8.14. Results using ANOVA demonstrate a significant difference in the vibration perception threshold on both sites, the tip of the hallux ($p = 0.001$) and medial aspect of the first MTPJ ($p < 0.0001$) between the groups. Dunnett's post-hoc test demonstrate significant difference in the VPT for the medial aspect of the first MTPJ ($p < 0.001$ & < 0.001) on both left and right feet in gout; however the VPT for the hallux tip was significantly higher only on the right foot ($p = 0.003$) in the gout group.

Table 8.14: Descriptive information for vibration perception threshold in volts

Site	Gout		Control	
	Left foot Mean (SD)	Right foot Mean (SD)	Left foot Mean (SD)	Right foot Mean (SD)
Hallux tip (V) *	24 (13)	35 (28)	13 (4)	13 (4)
Medial aspect of 1st MTPJ(V) *	24 (13)	26 (12)	13 (6)	13 (6)

ANOVA *($p < 0.05$)

8.8.3 Plantar pressure measurement

Peak plantar pressures and pressure-time integrals are reported from ten regions under the foot (medial and lateral heel, midfoot, the five metatarsal heads, under the hallux and under the second to the fifth lesser toes). Table 8.15 presents descriptive information for peak plantar pressures in Kilopascals for the ten regions in gout and controls. Table 8.16 presents descriptive information of the pressure-time integrals in Kilopascals.sec for the ten regions in the gout and control group.

8.8.3.1 Peak plantar pressure

The results demonstrated no significant differences in the peak plantar pressures under the medial and lateral heel, midfoot and under the five metatarsal regions (Table 8.15). A significant difference was, however demonstrated under the hallux ($p = 0.001$) and 2nd to 5th toes ($p = 0.005$) (Table 8.15). Dunnett's post-hoc test revealed reduced peak plantar pressures under the hallux ($p = 0.001$ and 0.005) and under 2nd to 5th toes ($p = 0.002$ and 0.01) for both feet in the gout group compared to controls.

Table 8.15: Descriptive information for peak plantar pressures kilopascals (Kpa) for gout and control groups

	Gout group		Control group	
	Left foot Mean (SD)	Right foot Mean (SD)	Left foot Mean (SD)	Right foot Mean (SD)
Medial heel	264.9 (98.8)	253 (103.2)	297.6 (87.2)	268.2 (87.5)
Lateral heel	249.8 (88.2)	240.4 (88.7)	272.9 (92.8)	277.6 (105.9)
Midfoot	120.9 (59.30)	156.4 (74.6)	119.8 (128.1)	144.2 (131.2)
First metatarsal region	252.9 (113.9)	213.1 (113.5)	249.6 (140.1)	243.6 (175.6)
Second metatarsal region	309.7 (141.6)	297.5 (121.2)	281.2 (140.5)	262.6 (134.1)
Third metatarsal region	333.3 (173.5)	313.7 (138.8)	299.5 (83.7)	274.5 (81.2)
Fourth metatarsal region	248.8 (127.1)	249.7 (103.8)	246.1 (84.5)	259.1 (86.5)
Fifth metatarsal region	153.1 (10.7)	206.9 (136.4)	237.8 (112.1)	255.6 (94.2)
Under 1 st toe*	143.8 (96.9)	153.4 (100.1)	263.8 (123.9)	248.1 (118.1)
Under 2 nd -5 th toes*	124.2 (85.9)	133.4 (70.3)	213.6 (129.1)	182.6 (112.7)

*ANOVA $p < 0.05$

8.8.3.2 Pressure-time integrals

The results demonstrate a significant difference in the pressure-time integrals under the lateral heel ($p = 0.03$), midfoot ($p = 0.002$), and under the hallux ($p = 0.003$) between gout and controls (Table 8.16). Dunnett's post-hoc test demonstrates an increased pressure-time integral under the lateral heel ($p = 0.02$) of the left foot and midfoot area ($p = 0.002$) of the right foot in the gout group when compared to controls. However, pressure-time integrals under the hallux were significantly reduced in the gout group for both left ($p = 0.004$) and right foot ($p = 0.01$) compared to controls (Table 8.16).

Table 8.16: Descriptive information for Pressure-time integrals Kilopascals.sec (Kpa.s) for gout and controls

Foot region	Gout		Control	
	Left foot Mean (SD)	Right foot Mean (SD)	Left foot Mean (SD)	Right foot Mean (SD)
Medial heel	53.8 (23.8)	46.9 (16.9)	42.2 (13.6)	40.4 (14.3)
Lateral heel*	50.8 (19.1)	47.6 (15.5)	39.2 (13.4)	44.9 (12.4)
Midfoot*	30 (10.3)	39.1 (22.1)	23.1 (9.5)	28.9 (10.9)
First metatarsal region	44.8 (19.1)	39.9 (22.1)	44.2 (22.2)	37.1 (17.3)
Second metatarsal region	56.9 (22.2)	51.1 (21.2)	56.4 (22.4)	47.7 (18.7)
Third metatarsal region	65.2 (36.9)	59.2 (29.1)	59.5 (18.9)	46.6 (22.4)
Fourth metatarsal region	53.8 (25.2)	59.5 (27.2)	48.9 (19.1)	52.2 (16.2)
Fifth metatarsal region	41.1 (22.8)	60.1 (46.7)	42.8 (20.6)	50.3 (23.5)
Under 1 st toe*	17.6 (13.0)	19.7 (17.1)	33.1 (19.4)	32.3 (19.2)
Under 2 nd -5 th toes	17.5 (13.6)	23.8 (16.4)	22.3 (9.6)	28.6 (16.9)

*ANOVA $p < 0.05$

8.8.4 Gait parameters

The gait parameters included step length, stride length, swing time, single support time, double support time, velocity, cadence and stance time. The descriptive information is displayed in Table 8.17.

Independent t-test demonstrated significant difference between the two groups for walking velocity ($P = 0.02$) and cadence ($p = 0.02$). ANOVA demonstrated significant difference in step length ($p = 0.01$) and stride length ($p = 0.004$) between the two groups. Post-hoc analysis demonstrate significant differences between the gout and control groups for step length ($p = 0.02$ and 0.01) and stride length ($p = 0.01$ and 0.005) on both left and right feet when compared to controls. No other significant differences were observed with the other gait parameters

Table 8.17: Descriptive information for gait parameters in gout and controls

Variable	Gout		Controls	
	Left foot	Right foot	Left foot	Right foot
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Step length (m)*	0.56 (0.14)	0.56 (0.12)	0.66 (0.09)	0.66 (0.09)
Stride length (m)*	1.1 (0.24)	1.1 (0.25)	1.3 (0.17)	1.3 (0.17)
Swing phase (s)	0.5 (0.33)	0.41 (0.04)	0.41 (0.03)	0.41 (0.04)
Single leg support (s)	0.4 (0.04)	0.57 (0.79)	0.42 (0.04)	0.42 (0.03)
Double leg support (s)	0.27 (0.41)	0.25 (0.24)	0.27 (0.41)	0.16 (0.02)
Stance phase (s)	0.99 (0.77)	1.1 (1.2)	0.75 (0.07)	0.74 (0.08)
Velocity (m/s)**	0.90 (0.28)		1.1 (0.26)	
Cadence (steps/min)**	93.7 (16.9)		113.5 (36.9)	

8.9 Disability and impairment scores

Four self administered scales were used to investigate disability and impairment and included the Health Assessment Questionnaire (HAQ), Lower Limb Task Questionnaire (LLTQ), Foot Function Index (FFI) and Leeds Foot Impact Scale (LFIS). The descriptive information is illustrated in Table 8.18. The results demonstrate significant differences between the two groups across all disability and impairment scales ($p < 0.001$).

Table 8.18: Descriptive for disability and impairment scales

Disability and Impairment scales	Gout Mean (SD)	Control Mean (SD)
Health Assessment Questionnaire *	0.47(0.53)	0.01(0.17)
Lower Limb Task Questionnaire (activities of daily living) *	28 (21)	37 (17)
Lower Limb Task Questionnaire (recreational activities) *	19 (14)	34 (9)
Foot Function Index (total) *	23 (23)	1 (2)
Foot Function Index (pain) *	13 (13)	2 (4)
Foot Function Index (disability) *	23 (25)	1 (3)
Foot Function Index (activity limitation)*	2 (3)	0 (2)
Leeds Foot Impact Scale (total)*	24 (16)	1 (3)
Leeds Foot Impact Scale(shoes/impairment)*	10 (6)	1 (2)
Leeds Foot Impact Scale (activity/Participation)*	15 (10)	0 (1)

*Independent t-test $p < 0.05$

8.10: Summary of the results

The reliability of the goniometer in measuring the dorsiflexion range in the first metatarsophalangeal joint and ankle joint is high in patients with gout. The Foot Posture Index is also a reliable tool for measuring foot posture in individuals with gout. Excellent reliability was also found for plantar pressure and gait measurements.

Patients with gout experience more pain, disability and limitation in activities of daily living and recreation than age and gender-matched controls. The gout group had significantly reduced peak plantar pressures under the toes. The pressure-time integrals or the duration of loading was significantly higher under the lateral heel and midfoot area and reduced under the hallux for the gout group. Furthermore the gout group demonstrated a significant reduction in walking speed and cadence in comparison to the control group. The gout group reported a significant increase in pain and reduction in activity levels over the controls. Pain could be one of the causative factors for the reduced walking speed and increased stance phase in gait.

The gout group demonstrated significantly limited motion in the subtalar and midtarsal joints. The first MTPJ dorsiflexion motion was also significantly reduced. However, the ankle joint was not restricted in its dorsiflexion motion compared to healthy controls. Reduced muscle strength of the foot and ankle musculature except for the long extensor group, were stronger in the gout group. The gout group also demonstrated significantly higher incidence of foot deformities than controls, on the right foot only. The peripheral sensation was intact under the foot and the VPT for the gout group was significantly greater than the controls. The VPT value for gout on both the feet was greater than 25V which is a threshold for peripheral neuropathy.

Chapter 9: Discussion

9.1 Introduction

The aims of this study were, to investigate within and between session intra-tester reliability of a battery of podiatric biomechanical tests in a group of individuals with gout. The second aim was to identify foot and ankle characteristics in a group of individuals with gout and to investigate the differences in foot and ankle characteristics between individuals with gout and healthy non-gout controls.

For the current study a total of 25 participants were selected for the gout group, the control group being matched with the gout group for age and gender. Both the gout and control group contained 19 males and 6 females, a male to female ratio of 3:1, in accordance with a previous study in gout which also recruited a similar 3:1 male to female ratio (Thiele & Schlesinger, 2007). Among the 25 participants in the gout group, 60% (15/25) were European, 20% (5/25) were of Maori descent, 12% (3/25) were of Pacific Island descent and 8% (2/25) were of Indian descent. The control group were all European descent. Since the New Zealand incidence of gout is found to be high for Pacific Island men (14.9%) followed by 9.3% for Maori and 4.1% for European men (Dalbeth, 2007), the convenient sample in the current study may not be a true representation of gout in New Zealand. However, it may reflect the gout patient population in the Greenlane Rheumatology Clinic, Auckland District Health Board. Of note is that previous gout studies in New Zealand recruited participants from both Auckland District Health Board and Counties Manukau District Health Board, which could have better represented New Zealand gout incidence (Dalbeth et al., 2007).

9.2 Within and between session intra-tester reliability

The intra-tester reliability for all the outcome measures, except for pressure-time integrals, was excellent, with an ICC of greater than 0.9 for both the left and right foot (Tables 8.3, 8.5 and 8.9). The ICC (0.61 to 0.79) for pressure-time integrals demonstrates moderate intra-tester reliability for the right foot only while the ICC (>0.9) on the left foot demonstrates excellent intra-tester reliability (Table 8.7). The moderate to excellent reliability could be due to the period of time between the two measurement sessions. In the current study, measurements were repeated on the same day with an hour between the two sessions, thereby controlling factors like fatigue, tiredness and change in mood which are reported to influence the reliability of a measure (Polit & Beck, 2006). None of the participants had a gout flare during the period of measurement which suggesting that their disease state was unchanged during the measurement sessions, this could also have contributed to the excellent reliability recorded.

The moderate reliability recorded for the pressure-time integral on the right foot indicates increased measurement error (Table 8.7). The difference in the reliability of pressure-time integrals between the feet could be the result of a change in foot function due to tophi formation. In the gout group, tophi were observed only in the left foot over the first MTPJ, fifth MTPJ and midfoot regions. It is hypothesised that the right foot in the gout group, in an attempt to offload the left foot, adopts different compensatory strategies or more stable loading patterns. This fluctuation in the loading pattern could have been reflected as a measurement error in the right foot for the pressure-time integral.

A high ICC value does not necessarily mean that the test is reliable (Menz et al., 2004). This is because ICC is independent of the variability between the scores (Hopkins, 2000). To account for this problem, the SEM and SRD have been used in this study to identify the measurement error. SEM gives the variability in the measurement of a subject on two different occasions (Hopkins, 2000). The percentage error (SEM) for the reliability

measures was low (Tables 8.3, 8.5, 8.7 and 8.9) except for the Foot Posture Index which recorded a 93% error on the right foot and a 42% error on the left foot (Table 8.3). The pressure-time integrals also recorded a 40% error under the toes. Fosang et al. (2003) states that SEM reflects participants' true scores only 68% of the time and furthermore that SEM only identifies the error, not specifying it is of importance. The smallest real difference (SRD) which is derived from SEM identifies the minimum error value above which the measurement error would become clinically significant (Backerman et al., 2001). A clinically significant change is said to exist if the mean difference exceeds SRD (Ota et al., 2006 and Wilson et al., 1998). In the current study the value of mean difference for all the reliability measures was less than the calculated SRD (Tables 8.3, 8.5, 8.7 and 8.9), indicating that the error measured between the two occasions is not significant. Therefore excellent ICCs with non significant measurement error indicate these measurements are reliable if undertaken in individuals with gout on a particular day. Between-day reliability for this measure would be highly desirable as this is reported to ascertain the clinical value of an instrument (Gurney et al., 2008).

9.3 Case control trial

This section of the current study describes foot and ankle characteristics in individuals with gout and further discusses the differences in these characteristics between the gout group and a healthy control group. The outcome measures of this study will be discussed under the subsections of disability and impairment scores, foot structure and foot function.

9.3.1 Disability and impairment scores

In this study the Health Assessment Questionnaire (HAQ), Lower Limb Task Questionnaire (LLTQ), Foot Function Index (FFI) and Leeds Foot Impact Scale (LFIS) were used to assess pain, disability and impairment in individuals with gout and those in

the control group. The gout group recorded significantly higher scores for pain, disability and impairment than the controls (Table 8.18). The emphasis was on assessing the impact of chronic gout on foot pain, disability and impairment, in addition to the assessment of global disability and impairment.

9.3.1.1 Foot pain

The gout group experienced significantly greater foot pain during both barefoot and shoe walking as recorded by the pain subscale of the Foot Function Index (FFI) (Table 8.18). Higher pain values were reported for other rheumatological conditions like rheumatoid arthritis using FFI (Woodburn et al., 2002 and VanDerLeeden et al., 2005).

Pain in the gout group maybe due to inflammation secondary to monosodium urate crystal deposition (Dalbeth et al., 2007). The gout group were all non-symptomatic with C - reactive protein (the inflammatory marker) within normal limits (2-3) mg/L. The serum urate (0.35) mmol/L and creatinine levels (103) μ mol/L were also within normal limits indicating that the gout group were non-symptomatic during the study. Since individuals with active flares were excluded, it is thought that factors other than inflammation could have been the cause of foot pain in the gout group. Their high pain scores may have been associated with restriction in joint motion secondary to tophi formation or increased pressure-time integrals or elevated peak plantar pressures. The first MTP joint dorsiflexion motion and the subtalar joint and midtarsal joints motion were significantly reduced in the gout group compared to the controls. Restriction of motion in these joints has been reported to cause foot pain due to changes in foot function. For example, blockage of the windlass mechanism associated with reduced first MTPJ dorsiflexion during the late midstance phase of the gait cycle can result in increased tissue stress due to altered plantar pressures under the foot (Dananberg, 1993). The altered plantar pressures and pressure-time integrals in addition to reduced motion at

the first MTPJ, midtarsal and subtalar joints were reported to be the cause of foot pain in Pescavus foot (Burns et al., 2004) and in rheumatoid arthritis (Turner et al., 2008).

Another possible reason for foot pain in the gout group could be due to nerve impingement from overlying tophi (Fessel, 1971). In the current study, tophi were observed over the first and fifth metatarsal heads and dorsum of the foot over the midtarsal and subtalar joints. Since tophi can occur during the relapse phase or non-inflammatory phase of gout foot pain secondary to nerve impingement, they are thought to be one of the potential reasons for foot pain in the gout group.

9.3.1.2 Disability and Impairment

Disability and impairment was assessed as the measure of difficulty in performing certain activities, in other words the level of impairment experienced in performing activities required in daily life and also in activities required for recreation. Disability measured by the disability subscale of FFI; impairment/shoes and activity/limitation subscales of LFIS; and activities of daily living and recreational activities subsections of LLTQ, recorded higher scores for the gout group, indicating greater disability and impairment when compared to the control group (Table 8.18).

Performing activities like standing, walking, getting up from a chair and walking up and down the stairs are indicative of activities of daily living, 76% (19/25) of the gout group experienced some limitation in these activities for the FFI (disability subscale). The LLTQ (activities of daily living subscale, ADL) recorded a 72% (18/25) limitation for ADL in the gout group. In comparison to gout group the control group recorded 16% (6/25) and 28% (7/25) limitation in ADL for FFI and LLTQ respectively. The disability and impairment in the gout group was reported to be due to foot pain and footwear as recorded by the shoes/impairment subscale of the LFIS. The reader is directed to

questions 1 to 12 of the shoes/impairment subscale of the LFIS in Appendix D. The gout group reported limitations in their choice of footwear and that their inability to find shoes of their choice, in addition to the disability, has resulted in psychological distress as recorded from the shoes/impairment subscale of the LFIS. A similar level of psychological distress, was reported in individuals with rheumatoid arthritis using LFIS (Turner et al., 2006; Turner and Woodburn, 2008). In activities involving recreation such as playing sports, the gout group recorded greater difficulty, with 88% (21/25) of the gout group and 32% (8/25) in the control group reporting some kind of limitation in sporting activities.

Foot pain was reported to be the cause of disability and impairment in 72% of gout individuals compared to none in the control group as reported in the activity limitation subscale of FFI (Appendix D). In addition, 80% of the gout group reported that their disability and impairment was the result of some foot related problem as reported in the activity/participation subscale of LFIS (Appendix E). Some of the foot related problems included foot pain, instability and fear of falls, and walking style. The psychological distress and frustration associated with foot related disability and impairment was reported to be higher in the gout group. The Health Assessment Questionnaire, which is a global measure of disability, also recorded significantly higher scores for the gout group than the controls (Table 8.18) which is in agreement with the Lee et al. (2009) study which reported reduced health-related quality of life in individuals with gout using the Short Form-36 (SF-36) questionnaire which measures disease impact.

It has been documented that foot pain is a strong predictor of disability in other rheumatological conditions such as rheumatoid arthritis (Helliwell et al., 2005; Soka et al., 2000; Rupp et al., 2006). Disability can also be influenced by the presence of foot problems like hallux valgus, digital deformities (hammer toes and claw toes) and dermatological lesion like corns and calluses (Menz & Lord, 1999; Menz & Lord, 2001).

In the current study, the group recorded significantly greater foot problem scores than controls. Incidence of hallux valgus and hammer toes was high in the gout group. These foot problems included the presence of hallux valgus, lesser toe deformities and dermatological lesions. Of the gout subjects 60% presented with hallux valgus, hammer toes and calluses, thirty two percent (32%) had only hammer toes on third or fourth toes and 8% had a callus under the third metatarsal head.

A possible reason for the reduction in the activity levels in the gout group could be due to reduced muscle strength; in the current study the extrinsic and intrinsic muscles of the foot and ankle were significantly weaker than in controls. Reduced strength of the foot and ankle musculature is reported to be a reason for reduced activity levels in healthy individuals (Menz & Lord, 2001), individuals with osteoarthritis (Steultjens et al., 2001), rheumatoid arthritis (Hakkinen et al., 2006) and individuals with diabetes (Van Schie et al., 2004). Reduced activity levels in addition to limited footwear choice and the cosmetic appearance of their foot could have contributed to the psychological distress reported in the gout group as demonstrated by the high LFIS scores. Footwear which meets patient's personal satisfaction is as important as its therapeutic benefits and was reported to reduce pain and disability, and increase activity levels, and psychological wellbeing in patients with rheumatoid arthritis (Williams et al., 2007).

Another reason for the reduced activity levels could be kinesiophobia which is an excessive, irrational and debilitating fear of movement and activity from a feeling of vulnerability to severe pain (Burwinkle et al., 2005). The fear of pain is associated with reduced physical activity and withdrawal from work or recreational activity resulting in disability and reduced activity levels (Susan et al., 2002). Psychological distress was high in the gout group from the LFIS scores. The role of kinesiophobia in chronic gout is unknown and requires further investigation.

9.3.2 Foot Structure

In the current study the foot structure in the gout and the control group was investigated using the following podiatric biomechanical tests; joint motion at the first MTPJ, ankle, subtalar joint (STJ) and midtarsal joint (MTJ), Foot Problem Score, Foot Posture Index and muscle strength.

9.3.2.1 Joint motion

The gout group demonstrated significantly reduced dorsiflexion movement at the first MTPJ over the control group. Gout is reported to predominantly affect the first MTPJ (Roddy et al., 2006). In the current study ten participants out of 25 in the gout group had superficial tophi over the first and fifth MTPJ, over the mid foot and over the Achilles tendon. All the ten participants had tophi over the first MTPJ. It is postulated that mechanical obstruction in the joint due to monosodium urate crystal accumulation within the joint space could be a reason for reduced dorsiflexion at the first MTPJ.

The ankle dorsiflexion movement was non-significant between the groups. The ankle dorsiflexion range between them ranged from 13° to 15°, which is more than the required dorsiflexion of 10° for effective gait (Dananberg, 2000). The ankle dorsiflexion value recorded in this study is in agreement with the results of Locke et al. (1983) who reported 11° of ankle dorsiflexion value using a passive nonweight-bearing method. Further study investigating the dynamic motion of the ankle during gait using three-dimensional gait analysis, would be of a great interest as ankle dorsiflexion is demonstrated to influence propulsion (Cornwall & McPoil, 1999).

The STJ and MTJ in the gout group were significantly limited than in control group. A possible explanation for the limited motion at the STJ and MTJ could be mechanical

obstruction from an overlying tophus. The tophi were observed over the midfoot in the gout group; however it was not possible to locate the exact position of the tophi through naked eye observation. A recent study reported limitation in the joint range of motion with overlying tophi in hand joints (Dalbeth et al., 2007). Superficial tophi were observed over the midfoot in ten participants in the gout group. It was not possible with observation to isolate the exact position of the tophus. Another possible explanation for limited STJ and MTJ motion could be muscle imbalance. The tibialis posterior muscle which maintains the medial longitudinal arch by inverting the foot was stronger in the gout group than its antagonist the peroneus brevis muscle, which everts the foot (Table 8.12). Muscle imbalance between the tibialis posterior and the peroneus brevis has been stated as a potential reason for limitation in the STJ and MTJs (Valmassy, 2000).

9.3.2.2 Foot Problem Score

The gout group had significantly higher number of digital deformities and dermatological lesions than the control group (Table 8.10). Hammer toes and claw toes are reported to occur as a result of the long extensors (extensor hallucis longus and extensor digitorum longus) and long flexors (flexor hallucis longus and flexor digitorum longus) compensating for a weak tibialis anterior, described as a “extensor substitution and flexor stabilisation mechanism” (Myerson & Sheriff, 1989). However, a different mechanism may be operating in gout subjects as the tibialis anterior muscle was stronger than the long extensors in individuals with gout (Table 8.11). It is postulated that in an attempt to offload the first MTPJ and fifth MTPJ which had the incidence of tophi, the forefoot is dorsiflexed over the rearfoot in an attempt to redistribute the pressure to the midfoot and rearfoot by activating the tibialis anterior muscle. The dorsiflexed position of the forefoot is thought to continue throughout the gait cycle, thereby activating the long extensors and flexors to assist the tibialis anterior muscle resulting in the extension at the metatarsophalangeal joint. With the toes off the ground the flexor hallucis and flexor digitorum longus muscles activate resulting in flexion at interphalangeal joints. This hypothesis was based on the reason that FPS was higher in the left foot (tophi) and than

the right foot (without tophi); (Table 8.10). Intrinsic muscle weakness can also lead to digital deformities. The intrinsic foot muscles in the gout group were significantly weaker than in controls. Intrinsic foot muscles function by anchoring the toes to the supporting surface and increasing the surface area of contact (Hughes et al., 1990). Weakness of these muscles will be compensated by the long flexors and extensors, thereby developing flexion contractures or digital deformities.

Callus formations in the gout group were observed under the second and third metatarsal heads, and on the plantar and posterior aspects of the heel. The presence of callus in the gout group could have been due to increased peak plantar pressures and/or pressure-time integrals under these foot regions. Higher plantar pressures and pressure-time integrals are reported to increase the turnover rate of keratinocyte cells of the stratum corneum layer of the skin as a protective mechanism forming a callus (Menz et al., 2007).

9.3.2.3 Muscle strength

The muscle groups of the foot and ankle were weaker in the gout group than in controls except for the extensor hallucis and extensor digitorum longus muscles (Tables 8.11 and 8.12). This weakness could be explained by three mechanisms: reflex inhibition, supraspinal influences and disuse atrophy.

Reflex inhibition as a reason for muscle weakness in the gout group could be related to the inflammatory process within the affected joints. Inflammation within a joint would diminish the ability of a muscle to contract even though it is not damaged (Hopkins and Ingersoll, 2000). At the knee joint, inflammation and swelling has been shown to stimulate receptors within the capsule of the joint, which subsequently transmit signals to the central nervous system (Rice et al., 2009). These signals activate various spinal reflex pathways, which act on inhibitory interneurons and in turn inhibit the alpha

motorneurons supplying the quadriceps muscle, ultimately leading to a reduction in activation and hence the force generated by the muscles (Rice et al., 2009). It is possible that reflex responses to inflammation in the joints of the foot and ankle could act via similar pathways and induce weakness to foot and ankle joint muscles. In the current study, tophi were observed over the first and fifth MTPJs and the midfoot regions, and it seems likely that these joints would also have effusions. At this time, little research has investigated this mechanism at these joints.

Another related mechanism for the reduced muscle strength in the gout group could be reduced voluntary activation of the muscles (Hurley et al., 1997). This mechanism is more related to supra spinal pathways and may include a psychological element. Muscle strength relies on the motivation of the individual generating the force (Bearne et al., 2002). It has been suggested by Stucki et al. (1999) that reductions in strength may be partly due to a subconscious reduction in voluntary effort, perhaps related to fear of further pain and damage at the injured joint. There is also evidence of changes in brainstem regulation of spinal motorneurons leading to reduced activation of muscles. These latter changes are thought to be related to articular damage at the affected joints as seen in osteoarthritis and rheumatoid arthritis (Stucki et al., 2002).

A final reason for reduced muscle strength in the gout group could be disuse (Bearne et al., 2002). In chronic inflammatory disease conditions, the pain and inflammation associated with the affected joints impede joint mobility and thus function. A consequence is that the muscles crossing the joint become atrophied (Bearne et al., 2002). The mechanism behind this atrophy is thought to be a decrease in protein synthesis and an increase in protein degradation (Jackman & Kandarian, 2004).

9.3.2.4 Foot Posture

The foot posture for both the gout and control group suggests a normal foot type. However, the foot posture in the gout group during static standing suggests a tendency

towards a supinated foot type (FPI = 1). The higher mean peak plantar pressures and pressure-time integrals under the second, third and fourth metatarsals demonstrate pressure distribution pattern from the central to the lateral aspect of the foot, a tendency observed in a supinated foot type (Burns et al., 2004). It is postulated that in an attempt to offload the first and the fifth MTPJs which recorded the highest incidence of tophi, individuals with gout assumed a slightly supinated foot position.

9.3.3 Foot Function

In the current study the foot function in the gout and control groups was assessed by investigating neurological status using peripheral sensation and vibration perception threshold (VPT), peak plantar pressures, pressure-time integrals and gait parameters.

9.3.3.1 Neurological status

Tactile sensation was intact in both the gout and control groups. However, Vibration Perception Threshold (VPT) for the gout group was greater than 25V on the right foot and 24V on the left foot on both sites (hallux tip and medial aspect of first MTPJ) when compared to controls (Table 8.14). VPT greater than 25 volts is documented to be a predictor of peripheral neuropathy in individuals with diabetes (Crawford et al., 2007; Garrow & Boulton, 2006; Kastenbauer et al., 2001) and rheumatoid arthritis (Pallis et al., 1965). VPT was measured around the first MTPJ, which had the highest prevalence of tophus in the current study. One of the reasons for increased VPT could be due to neurolysis of the peripheral sensory nerve secondary to chronic inflammation at the site of tophus formation (Fessel, 1971). It is stated that peripheral neuropathy may exist in gout individuals if the tophus is in close contact with the peripheral nerve (Fessel, 1971). Fessel (1971) also stated that chronic alcoholism as observed in their study participants could have been one of the aetiology for peripheral neuropathy observed in their study. Since the alcohol consumption of the gout participants was not assessed in this study the affect of alcohol on VPT values cannot be ruled out. This maybe also one of the reasons for the high VPT on the right foot which did not have any superficial tophi.

9.3.3.2 Plantar pressure

During the stance phase the pressure pattern in the control group exhibited a gradual progression of pressure from the heel to the forefoot (Figure 9.1). In the forefoot, plantar pressure increased from first to third MTPJs, followed by a gradual reduction in the plantar pressure over the lateral column and finally loading on the hallux (Figure 9.1, B). This pattern is identical to the normal biomechanical function of the foot during the facilitation of the windlass mechanism (Hicks, 1954).

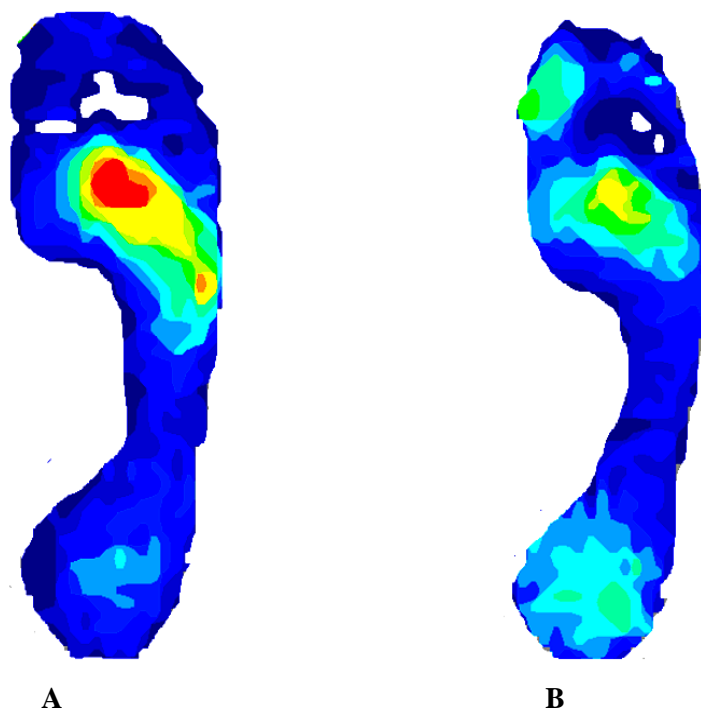


Figure 9.1: Pressure pattern, A – Gout group, B - Control group

Compared to the control group, the gout feet exhibited significantly reduced plantar pressure only under the toes (Figure 9.2). No other regions under the foot showed any significant difference from the control group. The mean peak plantar pressures were higher under the midfoot and the second and third metatarsal regions, while the first metatarsal and the fourth metatarsal regions recorded higher mean peak plantar pressures only under the left foot in the gout group (Figure 9.1 and 9.2). Both the lateral and medial aspects of the heel in the gout group recorded lower peak plantar pressures (Figure 9.2).

In comparison to other musculoskeletal conditions that impact the foot the rheumatoid foot has been shown to exhibit similar patterns with reduced plantar pressure under the heels and higher mean peak plantar pressures under the midfoot and all the metatarsal heads (Turner et al., 2003; Woodburn & Helliwell, 1996). The mean difference in the peak plantar pressures between the groups in the current study under the midfoot, second and third metatarsal areas, ranged from 10 KPa to 40 KPa which was similar to pressure differences observed in the rheumatoid foot (Turner et al., 2003). The pressure pattern in the gout foot is more centrally located, from midfoot to the second and third metatarsal heads (Figure 9.1). Ten participants out of 25 in the gout group had superficial tophi over the foot and ankle. All ten had tophi over the first metatarsophalangeal joint and six had tophi over the fifth metatarsophalangeal joint. Therefore, in an attempt to reduce load at the first and the fifth MTPJ, the pressure pattern in a chronic gout patient was more centrally placed. Eight participants presented with tophi over the anterior ankle region, and hence the reduced plantar pressures may be a strategy that gout patients use to reduce pain during the loading phase of gait in the peritalar region.

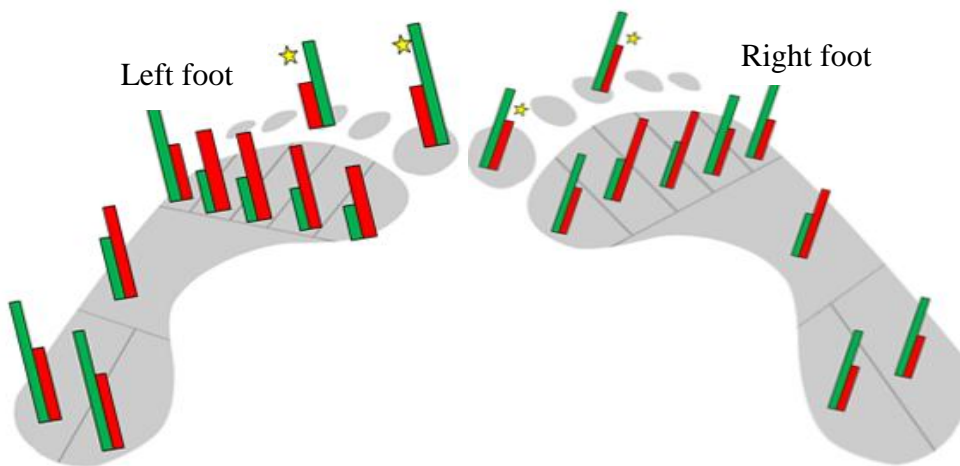


Figure 9.2: Graphical representation of peak plantar pressures.

Red: Gout group

Green: Control group

$P < 0.05$ ★

The pressure-time integral provides the duration for which loading occurs on the particular region of the foot. The mean pressure-time integrals for the gout group were higher on all foot regions except the toes (Figure 9.3). Increased pressure-time integrals in the gout group are thought to be either the result of increased duration of foot contact which is thought to be the result of an antalgic gait pattern or due to reduced lower limb muscle strength. Burns et al. (2008) reported that reduced lower limb strength can increase the duration of foot contact during gait. Even though the mean pressure-time integrals in the gout group were higher than in controls, statistical significance was observed only under the hallux, lateral heel and midfoot regions (Figure 9.3). The gout group recorded significantly high pressure-time integrals under the left heel only and right midfoot (Figure 9.3).

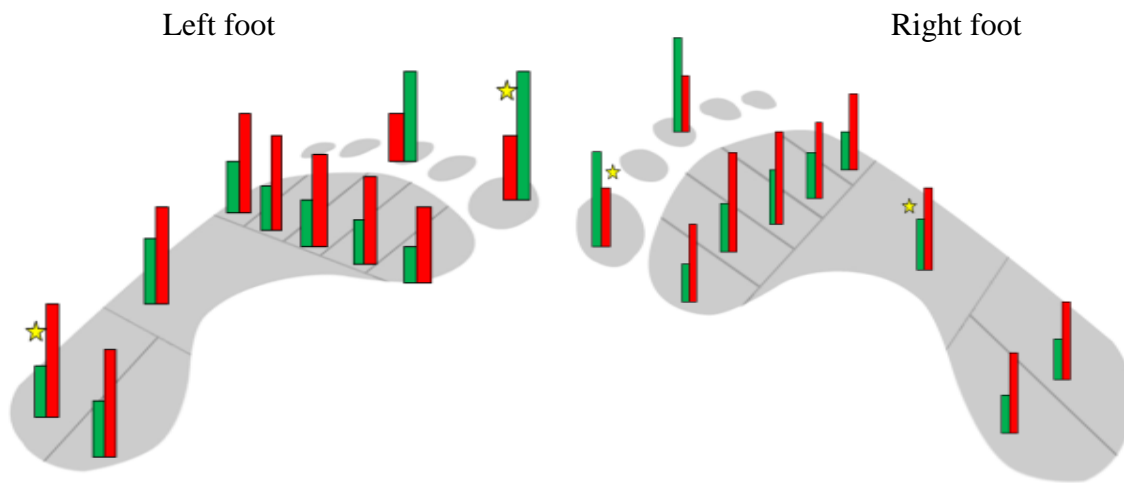


Figure 9.3: Graphical representation of pressure-time integrals.

Red: Gout group

Green: Control group

$P < 0.05$ ★

This asymmetry is thought to be the result of the compensatory load reduction mechanism. Tophi in the gout group were observed only on the left foot over the first and fifth MTPJs and the anterior ankle. It is hypothesised that limitation in the midtarsal joint coupled with the slightly supinated foot type could have increased the duration of loading under the lateral heel on the left foot as a means of a compensation strategy. Furthermore, it is thought that the increased duration of loading under the midfoot region of the right foot is to gain stability and also to reduce load on the left foot. It has been reported that motion at the midtarsal joint is closely related to plantar pressure patterns under the heel and midfoot (Morag & Cavanagh, 1999).

A number of variables can influence peak plantar pressure distribution. Taylor et al. (2004) stated that walking speed can influence plantar pressure distribution under the heel and toes. Taylor et al. (2004) stated increased walking speed can generate greater forces at heel strike and under the toes (greater force generated during propulsion). High plantar pressures were recorded under the heel and toes in the control group when compared to the gout group. Taylor et al. (2004) also suggest that only fast walking can cause a significant rise in the plantar pressures under the foot. The control group in the current study walked significantly faster than the gout group. Therefore walking speed could have been a reason for the high plantar pressures in the control group when compared to the gout group.

Plantar pressure under the first MTPJ and hallux is reported to be influenced by dorsiflexion motion at the first MTPJ (Menz & Morris, 2006). Plantar pressures were reported to be reduced under the first MTPJ and increased under the hallux in hallux limitus (a condition in which the dorsiflexion motion at the first MTPJ is less than 65°) than individuals with normal dorsiflexion (65°) at the first MTPJ (Bryant et al., 2000; Zammit et al., 2008). The results of the current study are not in accordance with the results of Bryant et al. (2000) and Zammit et al. (2008). The first MTPJ dorsiflexion was

significantly reduced in the gout group with no significant difference in the plantar pressures under the first MTPJ between the groups (Table 8.10). Furthermore, the plantar pressures under the hallux were significantly reduced in the gout group when compared to the control group (Table 8.15). At this stage we can only speculate as to the reason due to lack of evidence on the mechanics of gait in gout. It is reported that a minimum of 65° dorsiflexion movement is required at the first MTPJ, for the smooth progression of body over the foot during propulsion (Dananberg, 2000). It may be that in an attempt to reduce load on the first MTPJ which has reduced dorsiflexion due to mechanical obstruction from tophi, the gout subject slightly supinates the foot to allow the body weight to progress over the second and third metatarsals during the propulsion phase of the gait cycle. In support of this statement the mean peak plantar pressure was found to be higher (253 Kpa) under the left foot (high incidence of tophus in the sample) than the right foot (213 Kpa). It is reported that changes in the bony architecture of the foot observed in other rheumatological conditions such as rheumatoid arthritis are reported to cause abnormal variations in the ankle, subtalar joint and midtarsal joints motion, and these changes in the joint motion are reported to influence plantar pressures in this disease group (Woodburn et al., 2002; Turner et al., 2003). A further study using 3-D gait analysis of the foot in a chronic gout patient will be of great interest in evaluating the amplitude of joint motions at the foot and ankle joints.

The peak plantar pressures under the hallux were significantly reduced in the gout group, which is contrary to the findings of Zammit et al. (2008), Mueller et al. (2003) and Bryant et al. (2000), who reported higher peak plantar pressures under the hallux in individuals with hallux limitus. This could be due to the weakness of the intrinsic and extrinsic foot muscles destabilising the toes, and as a result reducing the contact area and duration of contact during the propulsive phase of gait, hence the reduced plantar pressures (Hughes et al., 1990).

9.3.3.3 Gait parameters

Gait parameters, especially walking velocity are widely used as an indicator of pathology or a measure of health status, for example in the assessment of motor function (Eppeland et al., 2008; Turner et al., 2003). In the current study walking velocity for the control group (1.1 m/sec) was higher than that of the gout group (Table 8.17). The average walking velocity in the control group is similar to that reported in other studies investigating gait parameters in healthy older adults. Menz et al. (2004) reported an average walking velocity of 1.16 m/sec in older individuals (76 to 87 years) in a study which investigated differences in the gait parameters between young and older individuals. In the current study, the gout group walked slowly with a reduced cadence and stride length. Individuals with rheumatoid arthritis have been shown to exhibit similar gait characteristics compared to controls but in addition to reduced walking velocity, cadence and stride length, the double support time was also increased (Helliwell et al., 2006; Locke et al., 1986). There was no significant difference in the double support time between the gout and control group in this study. Turner et al. (2003) state that pain associated with any joint in the lower extremity can reduce walking speed and shorten stride length. The gout individuals in this study recorded high levels of pain as measured on the pain subscale of FFI and hence the reduced walking speed and stride length could be attributed to that. A future study investigating foot structure and function during acute gout flare would be of interest to understand how foot structure and function differ between acute and chronic gout stages.

9.4 Possible explanation for crystal accumulation on the medial aspect of the first MTPJ

Tophus most frequently affects the foot, in particular the big toe joint and the midfoot region (Klemp, 1997; Roddy, 2007). In the big toe, the medial aspect is affected and inflammation at this site is one of the criteria for the diagnosis of gout under the ACR classification (Klemp, 1997). Why the medial aspect of the first MTPJ is affected remains

unclear. It is believed that since the first MTPJ is the farthest joint from the heart, the resulting cooler environment leads to reduced uric acid solubility and accumulation of crystals.

Another possibility could be biomechanical, due to increased thickness of the articular cartilage on the medial aspect of the first MTPJ, a possibility of uric acid accumulation at this site and further occurrence of crystallisation. Kiviranti et al. (1988) reported an increase in the articular cartilage thickness in regions which are exposed to the highest load. Kiviranti et al. (1988) measured increased articular cartilage thickness and glycosaminoglycan (GAG) content in dog knees after they were allowed to run on a treadmill at an inclination of fifteen degrees for fifteen weeks. They postulated that increased loading, as detected by the cilia of the connective tissue, allowed for the increase in cartilage thickness and GAG content. The first MTPJ is an important joint as it provides the pivot point and act as a “rocker” for the body to propel itself forward (Grady et al., 2002). Mays (2005) states that the medial aspect of the first MTPJ is exposed to chronic pressure during the propulsion phase as evidenced from the tibial sesamoid being more prone to stress injuries (Kurtz, 2003). It is assumed that an increase in the cartilage thickness can be a cause of accumulation of MSU crystals over the medial aspect of the joint.

Another possibility is the anatomy of the medial aspect of the first MTPJ. The abductor hallucis tendon crosses the medial aspect of the first MTPJ along with the tendon for the medial slip of the flexor hallucis brevis (Peter, 1995). These tendons cross the medial aspect of the first MTPJ, passing underneath the transverse metatarsal ligament, thus closer to the osseous structures. However, no tendons pass the lateral aspect of the joint. As mentioned earlier, crystal deposition is favoured in the tendons due to low temperature; tophi can be thought to predominate the medial aspect because of the presence of the abductor hallucis and flexor hallucis brevis tendons at that site. The

absence of tendons crossing the lateral aspect of the joint could possibly be the reason for the lateral aspect of the first MTPJ not being affected.

9.4 Limitations

Certain limitations that should be considered when viewing the results of this study will be discussed in this Section.

In the current study the mean values for the peak plantar pressure and pressure-time integrals were high under the forefoot region in the gout group; however they failed to reach statistical significance. The effect size for the peak plantar pressures and pressure-time integrals as calculated by effect size calculator (Becker, 1999) were 0.1 which is very small. Therefore the sample size of 25 could have been too small to detect significant changes in the peak plantar pressure and pressure-time integrals between gout and control groups. Menz. (2004) reported that raising the statistical power by increasing the sample size is a solution if type I error is suspected.

The majority of participants in the gout group were of European descent, a point to be considered when viewing the intra-tester reliability and foot and ankle characteristics of this study. These cannot be extended to other ethnic groups like Pacific Island and Maori as it is reported that reliability measures differ between different ethnic groups (Gurney et al., 2008).

CHAPTER 10: CONCLUSION

Gout is an accumulation of uric acid in the form of monosodium urate crystals in and around joints, tendons and subcutaneous spaces initiating an intense inflammatory response called a flare. Frequent flares over a period of ten or more years result in tophaceous gout where MSU crystals accumulate into nodules called tophi. The foot and ankle are more susceptible to gout with a high incidence in the first MTPJ followed by ankle and midfoot. Worldwide, and specifically in New Zealand, gout is of importance due to its high prevalence in the Pacific Island community and Maori community and its link to diabetes and osteoarthritis. Although gout predominantly affects the foot there is very limited evidence in the literature relating to changes in foot structure and function in chronic gout. Previous literature is presented as case studies describing pharmacological and surgical intervention of the tophus in the foot and ankle region. A sound knowledge of foot structure and function in gout would enable us to have a better understanding of any changes that may be occurring during the disease process.

The current study had two aims. The first was to investigate intra-tester reliability of some key outcome measures used to assess foot structure (FPI, first MTPJ and ankle dorsiflexion movement) and foot function (plantar pressures and gait parameters) in a group of individuals with gout. These outcome measures were repeated on two separate occasions to assess intra-tester reliability. Quantifiable measures like intraclass correlation coefficient (ICC), standard error of measurement (SEM) and smallest real difference (SRD) were used to determine the intra-tester reliability of these measures. The reliability results from the current study indicate that intra-tester reliability for these outcome measures of foot structure and function was excellent. The error in the measurement (SEM) recorded for this outcome measure was found to be small.

The second aim was to conduct a case controlled study comparing quality of life, foot structure and function between individuals with gout, with age-and gender-matched non-

gout individuals. The results demonstrated that individuals with gout experience a significantly reduced quality of life brought about by foot pain, and they are limited in their ability to perform activities required in daily life and also as a part of recreation; for example going for a walk or playing a sport, in comparison to healthy non-gout individuals. The foot structure and function in gout individuals was significantly different for the majority of key characteristics, compared to controls. The gout group demonstrated a high-arch foot profile with limited dorsiflexion movement at the first MTPJ and reduced strength of the extrinsic and intrinsic muscles of the foot and ankle. In addition to reduced muscle strength, the gout group also had higher incidence of toe deformities and dermatological lesion, as evidenced by their high Foot Problem Score.

The foot function in the gout group demonstrated significant reduction in plantar pressures and pressure-time integrals under all the toes compared to the control group. The somatosensory evaluation demonstrated that while the gout group had good peripheral sensation on the plantar surface of the foot they recorded a high vibration threshold. However, a significant increase in the duration of loading (pressure-time integral) was recorded under the lateral heel and midfoot regions for left and right feet respectively. The gait parameters demonstrated that the gout group walked slowly, with a shorted step and stride length.

10.1 Future work

Based upon the current findings there are a number of future areas of exploration to better understand the functional impact of gout on the foot. It is hoped that this study have opened further research in to the problem.

Numerous studies have investigated the impact of inflammatory arthropathies such as rheumatoid arthritis on functional outcomes (Turner et al., 2008; Van der Leeden et al,

2006; Conrad et al., 1996; Helliwell et al., 2005). The presence of persistent active inflammatory disease, as indicated by pain, joint tenderness and swelling, raised inflammatory markers and radiographic damage, predicts functional impairment in rheumatoid arthritis. By contrast the impact of gout on the foot and predictors of poor functional outcome in gout are not well recognised and this research study is an attempt towards greater recognition of the problem. Future work could be undertaken to evaluate the impact of gout on objective measures of foot function, and to determine predictors of poor foot function in patients with this disease. This will allow further work to be investigated to formulate a podiatric management plan in conjunction with pharmacological therapy to improve impairment, disability and function in chronic gout.

Imaging is a helpful tool for clinicians to evaluate diseases that induce chronic joint inflammation. Chronic gout is associated with changes in joint structures that may be evaluated with diverse imaging techniques. Computed tomography may best evaluate bone changes. Evaluation of the presence and extent of crystal deposition, and structural changes that may impair function or functional outcomes in the foot, and also monitoring of the response to urate-lowering therapy, may be considered for future work.

It has long been assumed that foot function and morphology differ between ethnicities (Gurney et al., 2008). However, quantitative research proving or disproving this relationship is sparse. The results from the current study suggest that differences between ethnic groups may occur. This may be relevant in future work that needs to take into consideration footwear design issues, where allowances need to be made during the design process for anatomical differences between ethnicities. However, these observations cannot be generalised over whole ethnic populations and further research is required on non-athletes to build on the current research findings.

In-shoe pressure redistribution to provide relief of forefoot pain in rheumatoid arthritis has been reported and is based on assumed links between pressure and pain (Kavlak et al., 2003; Hodge et al., 1999). However, little is known about the size of the pressure change required to reduce pain or the capacity of other plantar regions to bear increased pressure in chronic gout. A future direction could evaluate the quantification of plantar pressure pain threshold in chronic gout and compare it to age and gender-matched control participants.

Altered plantar pressure distribution is reported to be closely related to disease severity and 3-D gait analysis has been used to identify such changes as observed in rheumatoid arthritis (Turner et al., 2008). The kinetics and kinematics of joint motion observed from 3-D gait analysis could be useful to formulate a better treatment plan and also to observe the effectiveness of an intervention (Turner et al., 2003 and Woodburn et al., 2002). A future study could evaluate the three-dimensional gait analysis and kinematics of the foot and ankle to investigate functional and structural deficits during walking in chronic gout individuals. Furthermore, a comparison in the foot structure and function between acute and chronic gout would be of interest.

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HAQ. *Ann Rheum Dis*, 51, 1202-1205.

Appendix 1

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26 May 2008

Participant Consent Form

Understanding the impact of gout on foot function

English	I wish to have an Interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakoha korero.	Ae	Kao
Samoaan	Ou te mana'o ia I ai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i total tangata uri reo.	Ae	Kare
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai

I have read the study information sheet (Version June 2008) for volunteers taking part in the study to understand the impact of gout on foot function

YES/NO

The study has been explained to me by: Prof/Dr/Mr/Mrs/Ms _____

I have been given the opportunity to ask questions and discuss this study with the investigator and my whanau/family, and I have received satisfactory answers to all my questions.

YES/NO

I have received enough information about the study and have had enough time to think about it.

YES/NO

I understand that taking part in this study is voluntary (my choice) and that I am free to withdraw from the study at any time, without having to give a reason for withdrawing and without affecting my future medical care.

YES/NO

I know who to contact if I have any questions about the study.

YES/NO

I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.

YES/NO

I consent to the researchers storing a specimen of my blood for its later use as part of this study. You may wish to discuss this process with your whanau before agreeing

YES/NO

I consent to my blood sample being stored for future research into gout (subject to approval being given by an accredited ethics committee)

YES/NO

I understand that my blood sample will be destroyed at the end of the 10-year storage period

YES/NO

the approval of the research ethics committee (which approves all aspects of how the research study is organised). The blood collections will be kept for 10 years and then destroyed, according to the usual medical regulations.

We are happy to give you information about the progress of the project and about future projects at your request at any time. We will keep you informed of the results of the study. Please note that there may be a delay between your study visit and when the results are made public.

We will provide you with vouchers to cover your travel expenses for the study visit. No payments are being made to any doctors or researchers for including patients in this study. We plan to publish results from this study in scientific journals so that the information is freely available to other doctors, scientists and the public. Patients will not be identified in any report or publication and indeed all information about your identity will be kept strictly confidential. If you agree, we will tell your GP and rheumatologist that you are involved in the study, and provide them with the results of your tests.

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions or medical problems during this study, you should call the study doctor Professor Keith Rome who is in charge of this research or one of the study staff. The study doctor or study staff will also answer any questions you have about this research study or your participation in the study. You have the right to ask questions about this study at any time.

Study Doctor: Professor Keith Rome
Telephone Number: 921 9999 extension 7688

If you have any queries or concerns regarding your rights as a participant in this study you may wish to contact an independent Health and Disability Advocate

Telephone: 0800 555 050

Free Fax: 0800 2787 7678 (0800 2 SUPPORT)

Email: advocacy@hdc.org.nz

For Auckland District Health Board Maori health support, please contact Mata Forbes, RGON; Coordinator / Advisor, Maori Health Services, Auckland Hospital, Grafton, Mobile 021 348432, Tel: (09) 307 4949 extension 7292.

If you choose to help us with our research we ask you to sign a consent form to show that you agree to the above. Thank you for reading this.

This study has received ethical approval from the Northern Y Ethics Committee.

Appendix 2

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26 May 2008

Participant Information Sheet

Understanding the impact of gout on foot function

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve.

Your participation is entirely voluntary (your choice). You do not have to take part in this research study, and if you decide not to take part, this will not affect your normal medical care in any way.

We are interested in finding out how gout affects your life. There has been a lot of work done studying how other types of arthritis affect the lives of patients. However, there have been very few research studies examining how gout influences people's ability to manage with day to day activities (such as walking, dressing, eating and washing). This study may also help us understand how gout can result in damage to your joints and whether 3D scans (CT scanning) can be used to accurately measure the size of gouty lumps (which are a symptom of gout) for future research.

We would like to ask you to consider taking part in our research study. This will involve a visit to the Department of Rheumatology at Greenlane Clinical Centre. During this visit, we will do a number of tests with you:

1. We will ask questions about your gout and your general health.
2. We will examine the joints in your foot.
3. We will ask you to fill in forms to understand how gout affects your life.
4. A podiatrist will measure how well your foot moves.
5. We will take photographs of your feet.
6. We will arrange X-rays and a 3D scan (CT scan) of your feet.
7. We will take 10mls (2 teaspoons) of blood.

All of these tests will be done on the same day. The entire visit will take up to three hours.

All these tests will be done to help us better understand the amount of damage that is happening in the joints of your feet, and especially how joint damage occurs in gout. The risks of exposure to radiation (from X-rays) at the time of these tests is considered to be very small, and should not cause any risk to your health.

We ask that you agree (consent) to having a blood test taken as part of the research study. We will collect and study some parts of your blood (cells) that may cause joint damage and separate these parts from the collection (sample) so they can be used for experiments. We may freeze small amounts of these blood parts and keep them stored for up to ten years. You may wish to discuss this process with your whanau before agreeing to take part in this research study.

After this research study is completed, any leftover blood collections may be kept and used in future research studies about the causes of gout. This is to make sure that all blood collections are only used to benefit medical research and are not wasted. Future research studies will only be done if they have

I wish to receive a copy of the results YES/NO

I agree to my GP and rheumatologist being informed of my participation in this study YES/NO

I agree to take part in this study. YES/NO

Signed.....Date.....

(NAME IN BLOCK CAPITALS).....

Investigator's signature.....Date:

(NAME AND ROLE IN BLOCK CAPITALS).....

Whanau/family member signature.....Date.....

(NAME IN BLOCK CAPITALS).....


Appendix 3

American College of Rheumatology: Preliminary Criteria for Gout
(Wallace et al., 1977).

American College of Rheumatology: Preliminary Criteria for Gout
Gout may be diagnosed if one of the following criteria is present:
<p>Monosodium urate crystals in synovial fluid</p> <p>Tophi confirmed with crystal examination</p>
<i>At least six of the following findings:</i>
<p>Asymmetric swelling within a joint on a radiograph</p> <p>First metatarsophalangeal joint is tender or swollen (i.e., podagra)</p> <p>Hyperuricemia</p> <p>Maximal inflammation developed within one day</p> <p>Monoarthritis attack</p> <p>More than one acute arthritis attack</p> <p>Redness observed over joints</p> <p>Subcortical cysts without erosions on a radiograph</p> <p>Suspected tophi</p> <p>Synovial fluid culture negative for organisms during an acute attack</p> <p>Unilateral first metatarsophalangeal joint attack</p> <p>Unilateral tarsal joint attack</p>

Appendix 4

Foot Function Index



Section 1: To be completed by patient Name: _____ Age: _____ Date: _____
 Occupation: _____ Number of days of foot pain: _____ (this episode)

Section 2: To be completed by patient
 This questionnaire has been designed to give your therapist information as to how your foot pain has affected your ability to manage in every day life. For the following questions, we would like you to score each question on a scale from 0 (no pain) to 10 (worst pain imaginable) that best describes your foot over the past WEEK. Please read each question and place a number from 0-10 in the corresponding box.

No Pain	0	1	2	3	4	5	6	7	8	9	10	Worst Pain Imaginable
1.												
2.												
3.												
4.												
5.												

Answer all of the following questions related to your pain and activities over the past WEEK, how much difficulty did you have? *Disability Scale*

No Difficulty	0	1	2	3	4	5	6	7	8	9	10	So Difficult unable to do
6.												
7.												
8.												
9.												
10.												
11.												
12.												
13.												
14.												

Answer all the following questions related to your pain and activities over the past WEEK. How much of the time did you: *Disability Scale:*

None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
15.												
16.												
17.												

Section 3: To be completed by physical therapist/provider SCORE: _____ /170 x100= _____% (SEM 5, MDC 7)
 SCORE: Initial _____ Subsequent _____ Subsequent _____ Discharge _____
 Number of treatment sessions: _____
 Diagnosis/ICD-9 Code: _____

¹ Adapted from Budiman-Mak E, Conrad KJ, Roach K. The foot function index: A measure of foot pain and disability. J Clin Epidemiology. 4(6): 561-70, 91.

Appendix 5

Leeds Foot Impact Scale for Rheumatoid Arthritis, © 2005,
The University of Leeds; All rights reserved

Please choose the response that applies best to you at the moment.

	TRUE	NOT TRUE
1. My feet get painful when I'm standing.....	<input type="checkbox"/>	<input type="checkbox"/>
2. My feet hurt me.....	<input type="checkbox"/>	<input type="checkbox"/>
3. I find the pain in my feet frustrating.....	<input type="checkbox"/>	<input type="checkbox"/>
4. The pain is worse when I've been on my feet all day.....	<input type="checkbox"/>	<input type="checkbox"/>
5. At the end of the day there is pain and tension in my feet.....	<input type="checkbox"/>	<input type="checkbox"/>
6. I never get rid of the stiffness in the background.....	<input type="checkbox"/>	<input type="checkbox"/>

Please remember to read each statement thinking about your feet.
Please choose the response that applies best to you at the moment.

	TRUE	NOT TRUE
7. My feet throb at night.....	<input type="checkbox"/>	<input type="checkbox"/>
8. My feet wake me up at night.....	<input type="checkbox"/>	<input type="checkbox"/>
9. I feel as though I've got pebbles in my shoes.....	<input type="checkbox"/>	<input type="checkbox"/>
10. I get pain every time I put my foot down.....	<input type="checkbox"/>	<input type="checkbox"/>
11. I get a burning sensation all the time.....	<input type="checkbox"/>	<input type="checkbox"/>
12. I cry with pain.....	<input type="checkbox"/>	<input type="checkbox"/>

Please check you have ticked a box for every statement on this page

Leeds Foot Impact Scale for Rheumatoid Arthritis, © 2005,
The University of Leeds; All rights reserved

Please remember to read each statement thinking about your feet.
Please choose the response that applies best to you at the moment.

	TRUE	NOT TRUE
13. I can only walk in certain shoes.....	<input type="checkbox"/>	<input type="checkbox"/>
14. I need shoes with plenty of room in them.....	<input type="checkbox"/>	<input type="checkbox"/>
15. I am limited in my choice of shoes.....	<input type="checkbox"/>	<input type="checkbox"/>
16. I need a wider fit of shoes.....	<input type="checkbox"/>	<input type="checkbox"/>
17. I feel I need a lot of padding under my feet.....	<input type="checkbox"/>	<input type="checkbox"/>
18. My footwear always feels heavy.....	<input type="checkbox"/>	<input type="checkbox"/>
19. I have to keep swapping and changing my shoes.....	<input type="checkbox"/>	<input type="checkbox"/>
20. I can't get any shoes on.....	<input type="checkbox"/>	<input type="checkbox"/>
21. I walk bare foot all the time.....	<input type="checkbox"/>	<input type="checkbox"/>

Please remember to read each statement thinking about your feet.
Please choose the response that applies best to you at the moment.

	TRUE	NOT TRUE
22. I feel unsafe on my feet.....	<input type="checkbox"/>	<input type="checkbox"/>
23. I have to walk for a bit and sit for a bit.....	<input type="checkbox"/>	<input type="checkbox"/>
24. I can't run.....	<input type="checkbox"/>	<input type="checkbox"/>
25. I find I shuffle around.....	<input type="checkbox"/>	<input type="checkbox"/>
26. I am limping about all the time.....	<input type="checkbox"/>	<input type="checkbox"/>
27. I have to use a walking stick or walking frame.....	<input type="checkbox"/>	<input type="checkbox"/>

Please check you have ticked a box for every statement on this page

Leeds Foot Impact Scale for Rheumatoid Arthritis, © 2005,
The University of Leeds; All rights reserved

**Please remember to read each statement thinking about your feet.
Please choose the response that applies best to you at the moment.**

	TRUE	NOT TRUE
28. It takes me all my time to climb the stairs.....	<input type="checkbox"/>	<input type="checkbox"/>
29. I need help to climb stairs.....	<input type="checkbox"/>	<input type="checkbox"/>
30. I can't walk on cobbles.....	<input type="checkbox"/>	<input type="checkbox"/>
31. I am unsteady on uneven surfaces.....	<input type="checkbox"/>	<input type="checkbox"/>
32. I can't walk as far as I would like to.....	<input type="checkbox"/>	<input type="checkbox"/>
33. It takes me longer to do things.....	<input type="checkbox"/>	<input type="checkbox"/>
34. My whole life has been adapted.....	<input type="checkbox"/>	<input type="checkbox"/>

**Please remember to read each statement thinking about your feet.
Please choose the response that applies best to you at the moment.**

	TRUE	NOT TRUE
35. My feet restrict my movement.....	<input type="checkbox"/>	<input type="checkbox"/>
36. I get annoyed because I'm slower.....	<input type="checkbox"/>	<input type="checkbox"/>
37. I get frustrated because I can't do things so quickly....	<input type="checkbox"/>	<input type="checkbox"/>
38. My whole life has slowed down.....	<input type="checkbox"/>	<input type="checkbox"/>
39. It's reduced the range of things I can do.....	<input type="checkbox"/>	<input type="checkbox"/>
40. I have to plan everything out.....	<input type="checkbox"/>	<input type="checkbox"/>
41. I can't keep up like I used to.....	<input type="checkbox"/>	<input type="checkbox"/>
42. Socially its affected me a lot.....	<input type="checkbox"/>	<input type="checkbox"/>
43. I am ashamed of how I walk.....	<input type="checkbox"/>	<input type="checkbox"/>
44. I'm nervous of missing a curb edge.....	<input type="checkbox"/>	<input type="checkbox"/>

Please check you have ticked a box for every statement on this page

Leeds Foot Impact Scale for Rheumatoid Arthritis, © 2005,
The University of Leeds; All rights reserved

Please remember to read each statement thinking about your feet.
Please choose the response that applies best to you at the moment.

	TRUE	NOT TRUE
45. I feel isolated because I can't go very far.....	<input type="checkbox"/>	<input type="checkbox"/>
46. I feel I slow other people down.....	<input type="checkbox"/>	<input type="checkbox"/>
47. I can't do some of the things I take for granted.....	<input type="checkbox"/>	<input type="checkbox"/>
48. I can't go for walks with the people close to me.....	<input type="checkbox"/>	<input type="checkbox"/>
49. I'm finding it difficult to be independent.....	<input type="checkbox"/>	<input type="checkbox"/>
50. I dread finishing up in a wheelchair.....	<input type="checkbox"/>	<input type="checkbox"/>
51. I get frustrated because I can't do things for myself..	<input type="checkbox"/>	<input type="checkbox"/>

Please check you have ticked a box for every statement on this page

Appendix 6

HAQ-II questionnaire

We are interested in learning how your illness affects your ability to function in daily life.

Place an x in the box which best describes your usual abilities over the past week.

Are you able to:	Without any difficulty	With some difficulty	With much difficulty	Unable
Get on and off the toilet?				
Open car doors?				
Stand up from a straight chair?				
Walk outdoors on flat ground?				
Wait in a line for 15 minutes?				
Reach and get down a 5-pound object (such as a bag of sugar) from just above your head?				
Go up 2 or more flights of stairs?				
Do outside work (such as yard work)?				
Lift heavy objects?				
Move heavy objects?				

Appendix 7

Lower Limb Task Questionnaire

ACTIVITIES OF DAILY LIVING SECTION

Patient: _____

Date: _____

INSTRUCTIONS

Please rate your ability to do the following activities in the **past 24 hours** by circling the number below the appropriate response.If you did not have the opportunity to perform an activity in the **past 24 hours**, please make your *best estimate* on which response would be the most accurate.

Please also rate how important each task is to you in your daily life according to the following scale:

1. = Not important
2. = Mildly important
3. = Moderately important
4. = Very important

Please answer all questions.

		NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE	IMPORTANCE OF TASK			
1.	Walk for 10 minutes	4	3	2	1	0	1	2	3	4
2.	Walk up or down 10 steps (1 flight)	4	3	2	1	0	1	2	3	4
3.	Stand for 10 minutes	4	3	2	1	0	1	2	3	4
4.	Stand for a typical work day	4	3	2	1	0	1	2	3	4
5.	Get on and off a bus	4	3	2	1	0	1	2	3	4
6.	Get up from a lounge chair	4	3	2	1	0	1	2	3	4
7.	Push or pull a heavy trolley	4	3	2	1	0	1	2	3	4
8.	Get in and out of a car	4	3	2	1	0	1	2	3	4
9.	Get out of bed in the morning	4	3	2	1	0	1	2	3	4
10.	Walk across a slope	4	3	2	1	0	1	2	3	4
TOTAL (/40) : _____										

RECREATIONAL ACTIVITIES SECTION

Patient: _____

Date: _____

INSTRUCTIONS

Please rate your ability to do the following activities in the **past 24 hours** by circling the number below the appropriate response.If you did not have the opportunity to perform an activity in the **past 24 hours**, please make your *best estimate* on which response would be the most accurate.

Please also rate how important each task is to you in your daily life according to the following scale:

1. = Not important
2. = Mildly important
3. = Moderately important
4. = Very important

Please answer all questions.

		NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE	IMPORTANCE OF TASK			
1.	Jog for 10 minutes	4	3	2	1	0	1	2	3	4
2.	Pivot or twist quickly while walking	4	3	2	1	0	1	2	3	4
3.	Jump for distance	4	3	2	1	0	1	2	3	4
4.	Run fast/sprint	4	3	2	1	0	1	2	3	4
5.	Stop and start moving quickly	4	3	2	1	0	1	2	3	4
6.	Jump upwards and land	4	3	2	1	0	1	2	3	4
7.	Kick a ball hard	4	3	2	1	0	1	2	3	4
8.	Pivot or twist quickly while running	4	3	2	1	0	1	2	3	4
9.	Kneel on both knees for 5 minutes	4	3	2	1	0	1	2	3	4
10.	Squat to the ground/floor	4	3	2	1	0	1	2	3	4
TOTAL (/40) : _____										

Appendix 8

Foot Posture Index Scores

Table 1: Scoring of ‘talar head’ for the foot posture index.

Score	-2	-1	0	1	2
Talar head location	Talar head Palpable only On the lateral side	Talar head Palpable on the Lateral and Slightly on the Medial side	Talar head Equally Palpable on the Lateral and Medial side.	Talar head Palpable on the Medial side, Slightly Palpable on the Lateral side	Talar head not Palpable on the Lateral side, Palpable on medial side.

Table 2: Scoring of 'supra and infra malleolar curvature' for the foot posture index.

Score	-2	-1	0	1	2
Supra and infra Malleolar curvature	Curve below Malleolus Either straight Or convex	Curve is is concave flatter More shallow then the curve above the malleolus	The infra and Supra malleolar Curves are same	The curve below Is more concave Then the curve Above	The curve below The malleolus Is more concave Then the curve Above.

Table 3: Scoring of 'calcaneal position' for the foot posture index.

Score	-2	-1	0	1	2
Calcaneal position	More then 5 Degree of varus	Between vertical and 5 degree varus	Heel is vertical	Between Vertical and Valgus	More then 5 degree of valgus

Table 4: Scoring of ‘bulging of the talonavicular joint’ for the foot posture index.

Score	-2	-1	0	1	2
Bulging of The TNJ	The TNJ is Concave	The area of TNJ slightly Concave	The TNJ is Flat	Slight bulging Of the TNJ	Prominent Bulging of TNJ

Table 5: Scoring of ‘height and congruency of medial longitudinal arch’ for the foot posture index.

Score	-2	-1	0	1	2
Height and Congruency of MLA	High MLA With an acute Angle posteriorl	Moderate MLA height And slightly Acute Posteriorly	MLA normal	MLA lowered With flattening In the central Portion	MLA very low With severe Flattening in The central Portion.

Table 6: Scoring of ‘Abduction and adduction of the forefoot’ for the foot posture index.

Score	-2	-1	0	1	2
Abduction and Adduction Of the forefoot	Toes visible On the medial Side, no toes Visible on the Lateral side	Toes visible More clearly On the medial Aspect then Lateral	Toes visible Equally on both Lateral and Medial side	Toes are Visible on the Lateral side More clearly Then on Medial side	Toes are Visible only On lateral side With no toes Visible on Medial side.