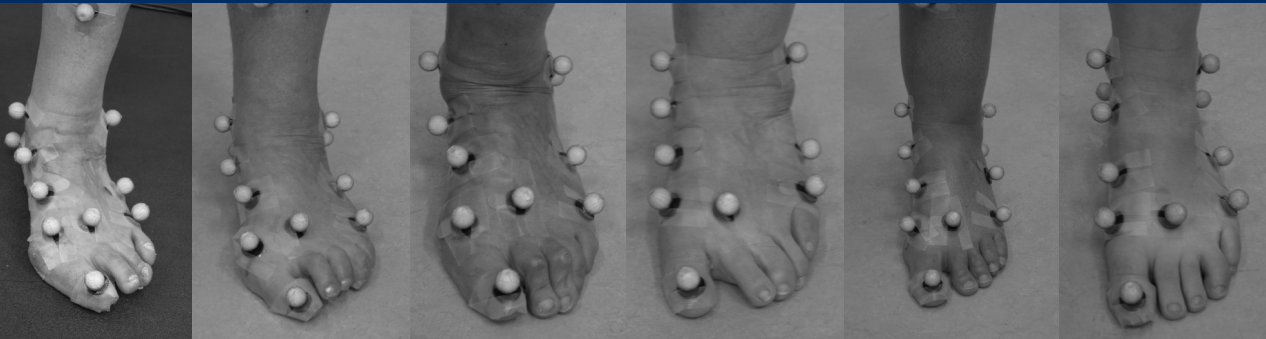


Towards a better understanding of foot and ankle kinematics in rheumatoid arthritis

The effects of walking speed and structural impairments



Rosemary Dubbeldam

TOWARDS A BETTER UNDERSTANDING OF FOOT AND ANKLE
KINEMATICS IN RHEUMATOID ARTHRITIS

THE EFFECTS OF WALKING SPEED AND STRUCTURAL IMPAIRMENTS

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1

General introduction

Background

Rheumatoid arthritis (RA) is a systemic disease with a prevalence of 0.5-1%. It is an autoimmune disease, which manifests itself with chronic inflammation in multiple joints and may occur at any age. At the onset of the disease, 60% of the patients suffer from walking impairments, while this percentage is 40% later on in the disease [Van der Leeden 2008]. These walking impairments have been related to the effects of the disease on foot and ankle structures. Metatarsal pain, global foot pain, disease activity, the number of swollen foot joints and hind foot deformity all affect and impair walking at some point during the disease process [Baan 2011, O'Connell 1998, Platto 1991, Turner 2008]. Walking impairments of patients with RA have also been related to temporal-spatial gait characteristics such as reduced walking speed and reduced stride length [O'Connell 1998, Platto 1991, Schmiegel 2008, Van der Leeden 2006]. In healthy subjects and RA patients, the temporal-spatial gait characteristics are directly influenced by dynamic foot and ankle function such as muscle activation and joint kinematics [Chiu 2007, Eppeland 2009, Ivanenko 2004, Laroche 2007, Lelas 2002, Murray 1994, Neptune 2008, Rosenbaum 1994]. A good understanding of the factors influencing walking impairment of patients with RA may contribute to the development and understanding of conservative or surgical foot and ankle treatment.

In the past, mostly combined scores were reported to qualify and quantify the onset and progression of damage and inflammations of the foot and ankle in patients with RA [Drossaers-Bakker 2000, Hulsman 2000]: In these combined scores, such as the Sharp Van der Heijde score (SHS), the sub-scores of the feet and hands were added together [Van der Heijde 1996]. While several studies have described the occurrence and prevalence of specific foot and ankle pathological changes [Wiener-Ogilvie 1999], the foot still received limited study considerations in terms of foot function, daily activity and participation limitations or treatments, in comparison to the hand or larger limb joints. Only recently, the effects of the disease on the progression of pathological changes to individual foot and ankle structures and especially the leg tendons have received more attention [Baan 2011, Bal 2006, Bouyset 2003, Giacomozzi 2009, Helliwell 2007, Liu 2007, Van der Leeden 2008 & 2010]. Improvements in imaging technologies such as magnetic resonance imaging and ultrasound enable such detailed clinical observations of pathological changes. Concurrently, initiatives have started to classify foot pathologies and investigate the possibilities and effects of conservative and surgical foot and ankle interventions [Doorn 2011, Hennessy 2011, Rosenbaum 2011, Van der Heijde 2010, Van der Leeden 2011, Walmsley 2010, Woodburn 2003].

Gait analysis has become valid and effective clinical decision and evaluation tool for treatment of individuals with cerebral palsy or cerebral vascular accident [Benedetti 2011, Engbers 2009, Lofterød 2008, Nene 2005, Wren 2011]. Hence, also for RA patients gait analysis may provide insight into the relationship between foot and ankle pathologies and function and may contribute to the clinical decision and treatment process. The effects of the disease on gait characteristics of patients with RA have been recorded and studied: since the early nineties gait analysis studies report temporal-spatial characteristics of RA gait, such as reduced walking speed and stride length [Isacson 1988, Keenan 1991, O'Connell 1998, Platto 1991]. The last decade, improvements in optical recording techniques and the development of computer models have enabled foot and ankle gait analysis [Carson 2001, De Mits 2012, Leardini 1999 and 2007, Simon 2006, Wright 2011]. By now, several studies have demonstrated the differences in segment motions of the foot and ankle of patients with RA compared to healthy subjects [Isacson 1988, O'Connell 1998, Khazzam 2007, Turner 2008, Woodburn 2004]. However, still little is known about how pathological changes of the foot and ankle relate to observed kinematic changes during gait of RA patients.

Improvements in the pharmacological treatment, especially the introduction of biologicals and treatment to the target of remission, changed the course of RA. However, walking impairments continue to be an issue for RA patients during flares and in those patients where the activity of the disease in general or during exacerbations cannot be controlled yet: pharmacological treatment was not able to effectively avoid the onset or progression of structural damage in the feet of RA patients [Aletaha 2011, Bowen 2010, Van der Leeden 2010]. Hence, improving our understanding of the influence of pathological changes to foot and ankle structures on corresponding dynamic function during walking continues to be necessary for the RA population. This thesis focuses on foot and ankle gait kinematics of patients with RA and healthy subjects. The general aim of this study is to improve our understanding of the factors influencing foot and ankle kinematics of patients with RA.

Gait analysis in RA

Therapists recognise the typical gait pattern, also known as the “Rheumatoid shuffle”, of patients with RA. This pattern can be described by temporal-spatial characteristics and lower extremity kinematics. The temporal-spatial characteristics are easily measured by means of time and distance recordings. Assessment of lower extremity segment kinematics

requires more advanced optical recording technologies and for the calculation of foot segment motions detailed foot and ankle computer models have been developed. The temporal-spatial and kinematic parameters of gait are influenced and controlled by the interaction of external forces on and internal forces within the body. External forces are measured by means of ground reaction forces and plantar pressures. Internal forces are, among others, influenced by muscle activation, which can be assessed by means of electromyography. A variety of studies have recorded gait of patients with RA and assessed one or more of the above mentioned gait parameters. This thesis provides an overview of all gait studies related to the lower extremity of patients with RA (CHAPTER 2). The quality of the gait studies is assessed and an overview of the reported RA gait parameters is given.

Assessment of foot and ankle segment kinematics

For usage in clinical practice, the kinematic measures need to be repeatable and reliable. The repeatability and reliability of the measure depend on the research question asked and the sample measured [de Vet 2006]. Both are calculated by means of variability values of the assessed kinematic measure. The variability may be influenced by several factors [Long 2010]: Firstly, a measurement error is made due to the accuracy of the measurement system and assessment method, the so-called residual error. In most gait studies, this value is not assessed for foot and ankle kinematics. Secondly, the variability in walking pattern of the subject himself will result in a so-called within-subject variability. The latter is a natural process, but the quantity of the variability may increase or decrease in subjects with certain pathologies [Roetenberg 2003, Woodburn 2003]. Thirdly, each person has his own typical walking pattern, which results in individual kinematic differences, the so-called between-subject variability. And fourthly, each time a subject is measured again, marker placement or other session specific properties will influence the assessed measure and result in so-called between-session variability.

In conclusion, the assessment of foot and ankle kinematics from gait analysis is not trivial. In healthy feet, the between-subject variation is the largest contributor to variation of kinematic measures within the population [Long 2010]. Furthermore, when regarding individual kinematic assessment of healthy feet, the between-session variability is higher than the within-session variability [Simon 2006, Wright 2011]. Hence, measuring individuals on different days or pre- and post interventions may result in unreliable assessment of kinematic measures. An issue one should be aware of and kept as small as possible.

Repeatability issues of marker placement influence the between-session variability. Some calculated foot and ankle segment angles are very sensitive to marker placement. However, most of that sensitivity is caused due to an initial offset angle [Simon 2006, Wright 2011, Hyslop 2010]. Hence, using the assessed range of motion instead of the absolute angle values or correct the assessed absolute value with a reference value may solve most marker placement issues in healthy subjects. The feet of patients with RA, however, often include swellings, deformations or both, which challenges repeatable marker placement and thus may affect repeatability of the measurements even more. Hyslop demonstrated that foot and ankle swellings are able to influence the repeatability of the measurements for patients with psoriatic arthritis [Hyslop, 2010]. In this thesis, effects of repeated marker placement on assessed foot and ankle kinematics of patients with RA is presented (CHAPTER 3).

Effect of walking speed on foot and ankle kinematics

Several studies have pointed out numerous differences in foot and ankle kinematics of patients with RA compared to healthy subjects during various phases of stance [Khazzam 2007, Turner 2008, Woodburn 2004]. However, also walking speed and stride length are lower for the RA patients, and these temporal-spatial factors influence foot and ankle kinematics as well. Hence, healthy subjects walking at similar speeds as RA patients might display similar foot and ankle kinematics, as Isacson demonstrated for hip and knee kinematics [Isacson 1988]. Therefore, it is unclear if all differences in foot and ankle kinematics between RA patients and healthy subjects are pathological and require medical attention, or if all or some can be explained by reduced walking speed alone. In case of the latter, the foot and ankle kinematics in RA might be different from those of healthy subjects walking at comfortable speed, but the RA foot and ankle kinematics would still represent normal foot and ankle function.

At the time of this study, only the effects of walking speed on the ankle kinematics in the sagittal plane and the first metatarso-phalangeal joint are reported in literature [Laroche 2007, Rosenbaum 1994]. Therefore, as a first step, the effects of walking speed on hallux, forefoot, midfoot, hindfoot and ankle kinematics of healthy subjects are studied (CHAPTER 4). In a second step, the influence of the disease and walking speeds on foot and ankle kinematics are studied as two independent factors (CHAPTER 5).

Role of pathological structural changes on foot and ankle kinematics

Pathological changes to foot and ankle structures affect foot and ankle kinematics during gait [Canseco 2008, Khazzam 2006, Laroche 2007, Ness 2008, Rattanaprasert 1999, Wu 2000]. These kinematic effects are not only localised to the sight of the pathology, but are also observed elsewhere in the foot and ankle. This may be explained by the fact that several active and passive structures cross one or multiple joints and are attached to the bony segments of the foot and ankle. These active and passive structures are thus able to restrain, influence or control the motion of the foot and ankle bony segments with respect to each other. The guiding mechanisms result in coupling of adjacent and non-adjacent bony segments. A better understanding of such coupling mechanisms in healthy subjects may provide additional insight in foot and ankle dynamic function during gait and in the full effects of localised structural pathologies [Ferber 2011, Fowler 2009]. The attained knowledge may enable identification of primary and secondary issues and focus treatment of patients with foot and ankle impairments.

Coupling motions between adjacent foot and ankle segments of healthy subjects have been studied [Chang 2008, Eslami 2007, Ferber 2011, Fowler 2009, Pohl 2007]. However, several active and passive foot and ankle structures such as the leg tendons and plantar fascia cross multiple joints and attach non-adjacent segments. As a result coupling between the leg and midfoot motion and between hindfoot and forefoot motion is expected. Therefore, coupling between adjacent and non-adjacent foot and ankle segments of healthy subjects is studied in this thesis (CHAPTER 6).

Only a limited number of studies have reported on the effects of pathological changes to foot and ankle structures on foot and ankle kinematics of patients with RA. These studies looked into the effects of pathological changes to the first metatarso-phalangeal joint [Laroche 2006 and 2007], regional damage to the forefoot and hindfoot [Turner 2008] and misaligned hindfoot posture [Keenan 1991]. Many other foot and ankle structural pathologies, such as ankle joint arthrosis or tibialis posterior tendon dysfunction are prevalent in RA patients. How these structural pathological changes affect foot and ankle kinematics has been studied, but not in a RA population [Khazzam 2006, Ness 2008, Rattanaprasert 1999]. This thesis provides a cross-sectional explorative study to analyse effects of joint swelling and erosion and tendon pathologies on foot and ankle kinematics of patients with RA (CHAPTER 7).

Aim and outline of the thesis

The aim of this thesis is to improve our understanding of the causes of the alterations in foot and ankle kinematics of patients with RA compared to healthy subjects. Specific aims are to (1) determine the main effects of the disease on foot and ankle kinematics, independent of walking speed, (2) evaluate coupling mechanisms of these main kinematic measures within the feet of healthy subjects, (3) relate the main kinematic measures to foot and ankle structural inflammations and damage. The findings of this study may provide new insights in the relationships between foot and ankle structural pathologies and joint kinematics and hence, contribute to improved treatment of foot and ankle and walking impairments.

In chapter 2, a systematic review of available gait studies on rheumatoid arthritis patients is performed. An overview of the temporal-spatial parameters, foot and ankle kinematics and the different available computational foot models is given.

Repeatability studies have addressed the effect of marker-placement on foot and ankle kinematics of healthy subjects. The rheumatoid foot however, with swelling and structural deformities, may give rise to increased variation of marker-placement. Effects of marker-placement variation on deformed and swollen feet on foot and ankle kinematics are presented in chapter 3. The findings will be used to define measurement method limitations and assist the choice of kinematic parameters for following studies.

A lower walking speeds results in kinematic changes of the hip, knee and ankle joint in healthy subjects. In chapter 4, the effects of walking speed on foot and ankle kinematics of healthy subjects is assessed.

In chapter 5 we aim to study if the observed reduced walking speed of patients with RA is able to explain the differences in foot and ankle kinematics compared to healthy subjects. By means of a linear mixed model, the contribution of the disease and walking speed is evaluated as independent factors in a population of healthy subjects and RA patients. The main kinematic parameters influenced by the disease will be defined.

Local pathologies do not only affect local kinematics but also affect kinematics elsewhere in the foot and ankle. This might be explained by a coupling of foot and ankle segment motions. In chapter 6, kinematic coupling between adjacent and non-adjacent foot and ankle segment motions is assessed.

In chapter 7, local inflammations and damage of foot and ankle structures of patients with rheumatoid arthritis are related to the previously assessed main foot and ankle joint kinematics. Finally, an overall discussion of the main findings of this thesis is presented in chapter 8.

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2

Gait analysis of the lower limb in patients with rheumatoid arthritis, a systematic review

Baan H, Dubbeldam R, Nene AV, van de Laar MAFJ. Gait analysis of the lower limb in patients with rheumatoid Arthritis, a systematic review. *Seminars Arthritis Rheumatism* 2012; 33 (3): 390-395

Abstract

Introduction. In rheumatoid arthritis (RA), signs and symptoms of feet and ankle are common. In order to evaluate the dynamic function of feet and ankles, namely walking, a variety of gait studies have been published. In this systematic review, we provide a systematic overview of the available gait studies in RA, give a clinimetric assignment and review the general conclusions regarding gait in RA.

Methods. A systematic literature search within the databases Pubmed, CINAHL, sportdiscus, Embase and Scopus was described and performed, and delivered 78 original gait studies that were included for further data extraction.

Results. The clinimetric quality of the 78 included RA gait studies measured according a tailored QUADAS item list and proposed clinimetric criteria by Terwee et al. is moderate. General conclusions regarding the walking abnormalities of RA patients point to: a slower walk, longer double support time and avoidance of extreme positions. Frequently found static features in RA are: hallux valgus, pes planovalgus and hind foot abnormalities.

Conclusions. Gait studies in RA patients show moderate clinimetric properties, but are a challenging way of expressing walking disability. Future gait research should focus on more uniformity in methodology. When this need is satisfied, more clinical applicable conclusions can be drawn.

Introduction

In rheumatic conditions, especially rheumatoid arthritis (RA), signs and symptoms of the feet are prevalent. The majority of the RA patients present with arthritis of the feet and 20% of them have radiographic damage at the time of diagnosis ¹. Prevalence of radiographic damage of the feet increases over time up to 80% at a disease duration of 5 years ². Obviously, other involvement of the lower limb such as involvement of the ankle can additionally result in substantial disability ³.

When measuring disease activity, damage or function of the foot, the applied instruments like X-ray, MRI, laboratory tests and questionnaires are static. The obtained information is used for decisions on intervention, follow-up and outcome evaluation. These methods fail however by definition to give information on dynamic function. With the development of clinical gait analysis (esp. 3D kinetics and kinematics), a dynamic instrument is within reach, and it is possible to describe normal walking patterns and distinguish them from pathological patterns. Advancing computer technology and software facilitate the investigator in gathering, adapting and interpreting the gait data, and have since lead to an increasing interest for gait analysis as a tool for measuring joint function in RA, in particular of the foot and ankle ⁴⁻¹⁶.

A variety of gait studies have been published. These studies are heterogeneous. The lack of uniformity in methodology and gait models often prevents comparison. A systematic review on foot and ankle instruments has been published earlier ¹⁵, but this review included other functional outcome measures than gait alone, like self reported questionnaires and a variety of pain and function related scoring systems. Moreover, it was mainly focused on the clinimetric properties of the studies, and did not include the knee and hip. Another review by Rankine et al describes multisegmental foot models, but this was not a systematic review, and focuses solely on kinematic foot models ¹⁶.

In the present study, we systematically reviewed all gait studies involving adult RA patients. All studies reporting kinetic, kinematic, plantar pressure data, muscle mechanics and electromyographic data were investigated.

Kinematic variables address motion, independent of the forces that cause the movement. Linear and angular displacements and velocities of the joint as well as of whole body mass are measured. For example, the foot models used in gait analysis of RA patients are based on the protocol of Carson or a variation, like the protocol developed by the Heidelberg group

^{17,18}. Reflective markers are attached to the skin in a standardized manner and patients are asked to walk several times a certain distance up and down at a self-selected speed. Several cameras record the course of the markers (raw data) and afterwards inter-segment and joint angles are calculated using special software. Then post processing is performed for averaging, normalisation of the data to the gait cycle, graphical representation and temporospatial calculations.

Kinetics is the term that describes the forces that cause the movement. Force is that which can cause an object with mass to change its acceleration and consequently its position. Forces can be internal (from muscles, ligaments) or external (gravity). Kinetic variables are important in gait analysis, because they give information on what causes the movement of the joint or the limb, movement strategies and neural compensation.

Muscle mechanics describes the variation in mechanical properties and characteristics of the muscles. How they can vary in length and tension with every action, and how neural recruitment affects this.

EMG (electromyography) is the registration of the primary signal to describe the input to the muscular system. EMG shows a non-linear relationship with muscle tension. Sometimes there is significant neural activation, without a single muscle movement. Therefore, EMG covers more than the resulting movement of the muscle. This has especially been useful in the assessment and treatment of cerebral palsy and has led to new operation techniques and better planning of surgical procedures.

In the present study, we aim to give a systematic overview of gait analysis in rheumatoid arthritis. The first goal of this study is to provide a complete overview of gait studies in rheumatoid arthritis patients and to review the clinimetric properties of them. The second goal is to outline the main results and conclusions regarding the aberrant walking pattern of RA patients.

Methods

All studies included in this systematic review were original articles addressing gait in rheumatoid arthritis patients. The selected studies used kinematic, kinetic, muscle mechanics and EMG data as outcome measure. We searched the electronic databases

PubMed, CINAHL, Embase, Scopus and Sportdiscus. Pertinent narrative review articles and reference lists of key articles were searched for further relevant publications. Two authors (HB and RD) independently screened articles for inclusion in the full text review by an initial screen of all titles and abstracts retrieved from the search strategy. Articles were included if they reported data from an original study in which RA patients or at least a subcohort, were subjected to gait analysis. Any articles identified from the first screen by either reviewer as possibly relevant to the study question were brought forward to the full text review. Full text review was undertaken as the next step. Articles were included in the systematic review if they reported original data on 1) RA patients > 17 years 2) the language was English, Dutch or German. 3) foot/ankle, knee or hip gait analysis. Moreover, abstracts, books, theses, and conference proceedings were not included. Finally, all articles references were searched manually for additional eligible studies. A description of the aim and methodology was extracted from the selected articles, including used measures, study population, aim and, when applicable, intervention. For the purpose of clinimetric assignment, we used a tailored QUADAS item list, as proposed by the QUADAS study group. Only the items that applied to this type of research were used. (i.e. the items regarding the comparison of a new instrument compared with the reference standard were left out). The following QUADAS items were used as criteria and each QUADAS item were scored yes, no or unclear:

- QUADAS 1: *Was the spectrum of patients representative of the patients who will receive the test in practice?*
Addresses the generalizability.
- QUADAS 2 *Were selection criteria clearly described?*
Concerns all relevant information regarding how participants were selected for inclusion in the study.
- QUADAS 8 *Was the execution of the index test described in sufficient detail to permit replication of the test?*
Addresses whether a study reports a sufficient detailed description of the execution of test method to permit replication of the test.
- QUADAS 10 *Were the index test results interpreted without knowledge of the results of the reference standard?*
Checks if the study clearly states that the test results were interpreted blind to the results of the other tests.

QUADAS 12 *Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?*

Addresses the availability of clinical data during interpretation of test results that may affect estimates of test performance.

QUADAS 13 *Were uninterpretable/ intermediate test results reported?*

A diagnostic test can produce an uninterpretable / indeterminate / intermediate result with varying frequency depending on the test. These problems are often not reported in diagnostic accuracy studies with the uninterpretable results simply removed from the analysis. This may lead to the biased assessment of the test.

QUADAS 14 *Were withdrawals from the study explained?*

If patients lost to follow-up differ systematically from those who remain, for whatever reason, then estimates of test performance may be biased.

Moreover, according to the proposed quality criteria on clinimetric properties by Terwee¹⁷ internal consistency, agreement, reliability, construct validity, responsiveness, interpretability were assessed. The definition and scoring of these seven items is given in the following:

1. *Internal consistency*: The extent to which items in a (sub-)scale are inter-correlated, thus measuring the same construct

- + factor analyses performed on adequate sample size (7 x no of items) AND Cronbach's alpha(s) calculated per dimension in a sample size of at least 50 patients AND Cronbach's alpha(s) > 0.70
- ? no factor analysis OR doubtful design or method OR sample size too small
- Cronbach's alpha(s) < 0.70, despite adequate design and method
- 0 no information found on internal consistency

2. *Agreement*: The extent to which the scores on repeated measures are close to each other (absolute measurement error)

- + (minimal important change (MIC) OR 0.5 x standard deviation (SD)) > smallest detectable change (SDC) OR (MIC OR 0.5 SD) outside the limits of agreement (LOA) AND SDC and MIC both determined in a sample size of at least 50 patients
- ? doubtful design or method or sample size < 50
- (MIC OR 0.5 x SD) < SDC OR (MIC OR 0.5 SD) inside LOA, despite adequate design
- 0 no information found on agreement.

3. *Reliability*: The extent to which patients can be distinguished from each other, despite measurement errors

- + intraclass correlation coefficient (ICC) or kappa >0.70 with the lower limit of the confidence interval >0.60 or a sample size of at least 50 patients.
- ? doubtful design or method (e.g. time interval not mentioned, Pearson correlation) OR ICC or kappa >0.70 with the lower limit of the confidence interval 0.60 or sample size <50 .
- CC or kappa <0.70 , despite adequate design and method.
- 0 no information found on reliability

4. *Construct validity*: The extent to which scores on a particular instrument relate to other measures in a manner that is consistent with theoretically derived hypotheses concerning the concepts that are being measured

- + specific hypotheses were formulated AND at least 75% of the results are in accordance with these hypotheses in a sample of at least 50 patients.
- ? doubtful design or method OR sample size <50 .
- less than 75% of the hypotheses were confirmed despite adequate design and methods.
- 0 no information found on construct validity

5. *Responsiveness*: The instruments ability to detect important change over time in the concept being measured

- + specific hypotheses were formulated AND at least 75% of the results are in accordance with these hypotheses in a sample of at least 50 patients.
- ? doubtful design or method OR sample size <50 .
- less than 75% of the hypotheses were confirmed despite adequate design and methods.
- 0 no information found on responsiveness

6. *Interpretability*: The degree to which one can assign qualitative meaning to quantitative scores

- + mean and SD scores presented of at least 2 relevant subgroups of patients in a sample size of at least 50 patients.
- ? doubtful design or method OR less than 2 subgroups OR sample size < 50
- 0 no information found on interpretability

Results

On Nov the 17th 2010, we conducted the search of PubMed, EMBASE, CINAHL and Scopus according to the methodology described. We searched for publications in English, German or Dutch language on the following search terms: rheumatoid arthritis AND foot OR ankle OR rear foot OR hind foot OR hip OR knee AND gait OR kinematics OR kinetics OR plantar pressure. For the complete search strategy we refer to the Appendix A. We obtained the following number of abstracts from the searches: 565 in Pubmed, 117 in Embase, 172 in CINAHL, and 473 in Scopus. After screening abstracts, 249 studies seemed eligible for full text review. Completing full text reading, 73 studies remained eligible for review and data extraction. After checking the references of the included studies, another 5 articles were added, resulting in 78 full text articles.

The included studies all fulfilled the listed criteria and reported original gait data on RA patients, the language was English, Dutch or German, and foot/ankle, knee or hip gait analysis studies were included.

The selected studies were classified according to their measurement concept and method to the following categories:

- plantar pressure measurement with the EMED system
- plantar pressure measurement using F-scan
- other or not specified plantar pressure measurement methods
- studies reporting temporospatial data
- 3-D gait studies
- EMG-studies
- a mixed group with: studies of range of motion (ROM), kinetic data, nerve conduction and röntgen stereophotogrammetry.

Forty-seven of the 78 publications reported on plantar pressure measurement data; 18 used EMED, 6 F-scan and there was a miscellaneous group. Thirty-five of the 78 studies reported data regarding temporospatial variables. Only 16 studies reported on three-dimensional variables, 2 used EMG, 1 Rontgen stereophotogrammetry, 6 range of motion (ROM), 3 reported on kinetic data, and finally 1 article, in which nerve conduction was studied.

For the results of the description of the studies concerning the methodology, measurement concept, study population, aim and intervention, we refer to Table 1 (Appendix B), in which a complete overview is given.

In Table 2 (Appendix C), we present the results of the scoring of the tailored QUADAS list. The first QUADAS item (Was the spectrum of patients representative of the patients who will receive the test in practice?) was nearly always scores as yes. In three studies, the studied population was not described adequately. The second QUADAS item (Were selection criteria described?) was present in 59 of the 78 studies. QUADAS item 8 (Was sufficient description of the index test reported) was met in 68 of the 78 studies. QUADAS item 10 (Were the test results interpreted without knowledge of the results of the reference standard?), was positive in 24 of the studies, most of them scored NA. QUADAS Item 12 (Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?) was scored as a yes in 74 of the studies. QUADAS item 13 (Were uninterpretable/ intermediate test results reported) was scored in 47 studies, and QUADAS item 14 (Were withdrawals from the study explained?) was only mentioned in 14 of the 78 studies.

The clinimetric properties are shown in Table 3 (Appendix D). None of the studies reported on all items. Only 18 of the 78 (23%) studies fulfilled (positive or indeterminate) more than one of the criteria. The studies that scored positive (+) or indeterminate (?) on one or more items are summarised in table 2. The item internal consistency was in only 2 studies given an indeterminate score. The item agreement was given 13 times indeterminate and once a positive score. Reliability was 21 times scored as indeterminate and 4 times as positive. Construct validity was 35 times scored as indeterminate and 3 times given positive score. Responsiveness was 15 times indeterminate and 2 times positive. Interpretability was the most frequently met criterion; 52 times it was assessed as indeterminate and 15 times as positive.

The second goal of our review was, to summarise the results and the findings of the studies, regarding the gait of RA patients. That what is traditionally known as the “rheumatoid shuffle”, can be more meticulously defined. Some plantar measurement studies revealed that plantar pressures in RA patients are higher, esp. the static plantar pressure^{19,20}. This may not be true for early RA patients²¹. Some investigators found a higher pressures under the first and second ray of the metatarsals^{22,23}, others report that especially on the outer metatarsals, the pressure was higher²⁴. There are however studies that could not confirm a

higher plantar pressure in RA patients^{25,26}. When higher plantar pressure was found in RA patients, it was in most studies, but not in all, associated with clinical variables like pain and erosions. Exact reasons for high pressures in RA are not given, but it has been suggested that antalgic walking patterns, in order to avoid pain under the forefoot while walking, may lead to higher pressures elsewhere. Hallux valgus, lesser toe deformities and severe hindfoot disease also cause higher forefoot pressures²⁷. When corrective measures were applied (i.e. orthoses or corrective surgery), both plantar pressure distribution and clinical signs and symptoms can improve, but are not necessarily correlated²⁸⁻³¹.

With respect to temporospatial parameters, RA patients tend to walk slower, with a longer gait cycle, a shorter step length, a longer double support time and a lower cadence (when compared with similar walking speed in healthy subjects)³²⁻³⁵. Definite conclusions have to be drawn with care, because speed-dependent gait variables are affected when controlling for the effect of speed in subjects with RA³⁶. The reduction in walking speed can be related to an increase in MTP 1 stiffness³⁷. Furthermore it was suggested that reduced speed may be caused by antalgic walking patterns, the need for “pain control”, and muscle weakness³⁸.

Regarding kinematic features, smaller ranges of motion combined with reduced joint moments and power of the hip flexion/extension, the hip abduction/adduction, the knee flexion/extension and the ankle plantar flexion occur in RA, and influence the HAQ (Health Assessment Questionnaire) as a measure of functional disability³⁹. There is an increased internal rotation of the tibia, a delayed heel rise, a decreased plantar flexion at toe-off and an abnormal eversion of the hind foot. Often a reduction of MTP-1 dorsiflexion is observed and an increased abduction of the forefoot. Aforementioned features can cause a considerable loss of normal rocker function^{38, 40-44}.

Static features are hallux valgus, an exaggerated valgus heel posture and collapse of the medial longitudinal arch with decreased navicular height. Although often occurring in combination, abnormalities of the hind foot more than of the forefoot, seem to affect gait in RA. Greater levels of foot-related disability and a greater number of abnormal kinematic features were found in patients if the hindfoot was severely deformed, compared to those with severe forefoot deformity²⁷. Whether static hindfoot or midfoot deviations were caused by insufficiency of the tibialis posterior, or the other way round is still the subject of debate^{38, 45}. Another association with stance abnormalities of the hind foot is increased muscle activity of the gastrocnemius and the soleus⁴⁵, to compensate for increasing valgus.

Discussion

Combining the 78 gait studies in patients with RA, our data show that measurement and clinimetric properties can be improved. However, consistently the studies reveal a slower walk, longer double support time and avoidance of extreme positions during walking of RA patients.

None of the 78 included studies has been tested for all measurement properties. Part of the moderate results regarding the measurement properties of the selected studies, can be explained by the fact that we did not select on clinimetric properties, to avoid selection bias. The limitation of using the QUADAS criteria lies in the fact that the QUADAS is a list that is meant for assessing the quality of diagnostic tests. Most of the used methods or measurement concepts in our selected studies were not compared with a golden standard or a more validated test, simply because there is none. The criteria list proposed by Terwee et al¹⁷ that we used for measurement properties performed equally moderate. The majority of the items could not be scored positive, but only indeterminate, because of the small sample size or non-optimal methodology and analysis. We do acknowledge that this is a very strict set of criteria, but this was predominantly done so, to avoid drawing conclusions from underpowered studies. There is however no standard set of criteria applicable to the elaboration and the rating of gait analysis. It would be very helpful if the professional association or the experts came up with one.

Agreement and reliability can improve by standardly reporting results of between-day, between-trial, between-subject and between-clinician repeatability. Construct validity and interpretability may improve, when gait parameters are compared with clinically meaningful outcome measures (i.e. of function or damage). More practical conclusions and recommendations can make a translation to daily practice easier and might benefit the patient directly.

To facilitate the comparability between studies and centers, it would help if there were a larger uniformity in methodology. Within the group of the 3D studies, 4 up to 11-segmented models are used, based on functional or either anatomical segments. The labour intensive methods of gathering and processing the data vary widely, which makes a proper comparison difficult. Also the lack of normative data for normal as well as pathological subjects is counteracting in the interpretation of the findings. Furthermore, especially in RA, it would be helpful to have more longitudinal data to investigate the natural course of rheumatoid arthritis or to measure the effect of targeted interventions.

Future research should focus on more uniformity of measurement methodology and terminology, for a proper validation of the motion analysis system, and strive for a more thorough clinical translation and interpretation, leading eventually to better understanding and treatment of gait problems in RA. Moreover, longitudinal studies are needed. Despite varying methods of research, there is a deal of consensus on the interpretation of gait abnormalities in RA in these 78 studies. Static features frequently encountered are hallux valgus or lesser toe deformities, more often a pes planovalgus, sometimes associated with severe stance abnormalities of the hind foot. This results among others in the following kinematic features: patients with RA walk slower, with a longer double support time. They tend to avoid extreme positions of the joints. These gait abnormalities are caused whether by structural damage like erosions or stance deviations, or by active inflammation of the joints, both as hallmark of rheumatoid disease. For another part, gait in patients with RA is determined by avoiding pain. They tend therefore to walk slower in order to control the speed of heel strike and toe-off.

In conclusion, gait studies in RA patients show moderate clinimetric properties, but are a challenging way of expressing walking disability. Future gait research should focus first on more uniformity in methodology. Secondly, longitudinal studies are needed to be able to work out more exactly the sequence of inflammatory and destructive events that lead to walking disability in RA. When these needs are satisfied the treatment of walking problems in RA patients can be improved.

Statement

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Appendix A: Search terms

("arthritis, rheumatoid"[MeSH Terms] OR ("arthritis"[All Fields] AND "rheumatoid"[All Fields]) OR "rheumatoid arthritis"[All Fields] OR ("rheumatoid"[All Fields] AND "arthritis"[All Fields])) AND (("biomechanics"[MeSH Terms] OR "biomechanics"[All Fields]) OR ("gait"[MeSH Terms] OR "gait"[All Fields]) OR (pedobarogr*) OR mechanical[All Fields] OR ("biomechanics"[MeSH Terms] OR "biomechanics"[All Fields] OR "kinematics"[All Fields]) OR "kinetics"[MeSH Terms]) OR (plantar[All Fields] AND ("pressure"[MeSH Terms] OR "pressure"[All Fields]))) AND (("foot"[MeSH Terms] OR "foot"[All Fields]) OR ("ankle"[MeSH Terms] OR "ankle"[All Fields] OR "ankle joint"[MeSH Terms] OR ("ankle"[All Fields] AND "joint"[All Fields]) OR "ankle joint"[All Fields]) OR (hind[All Fields] AND ("foot"[MeSH Terms] OR "foot"[All Fields])) OR (rear[All Fields] AND ("foot"[MeSH Terms] OR "foot"[All Fields])) OR ("knee"[MeSH Terms] OR "knee"[All Fields] OR "knee joint"[MeSH Terms] OR ("knee"[All Fields] AND "joint"[All Fields]) OR "knee joint"[All Fields]) OR ("hip"[MeSH Terms] OR "hip"[All Fields]) OR ("lower extremity"[MeSH Terms] OR ("lower"[All Fields] AND "extremity"[All Fields]) OR "lower extremity"[All Fields] OR ("lower"[All Fields] AND "limb"[All Fields]) OR "lower limb"[All Fields]) OR ("lower extremity"[MeSH Terms] OR ("lower"[All Fields] AND "extremity"[All Fields]) OR "lower extremity"[All Fields])) AND (English[la] OR German[la] OR Dutch[la] OR French[la]) NOT ("animals"[MeSH Terms:noexp] OR animals[All Fields])

Appendix B

Table 1: Description of the studies by method and author name (reference number)

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Plantar pressure EMED (1-20)							
Bitzan (1)	1997	RA patients	26 feet in 16 patients after forefoot surgery	16	Plantar pressure	To evaluate resection of all MT heads in RA pts	Forefoot surgery. Resection of metatarsal heads
Davys (3)	2005	RA	RA pts	38	Plantar pressure	To compare forefoot pain, pressure and function before and after normal and sham callus treatment in RA	Prescription of insoles for pts with painful rheumatic foot deformities
Giacomozzi (4)	2009	RA, selection on basis of the HAQ	RA and healthy subjects	112 RA patients; 30 healthy	Pressure, peak force, pressure time integral, force time integral, PPC, and NFC	To detect gait alterations in RA patients using peak pressure curves (PPC) and normalized force curves (NFC) in comparison with the HAQ	None
Hodge (5)	1999	RA	RA with forefoot pain	12	Plantar pressure gait velocity	To investigate the effectiveness of foot orthoses in the management of plantar pressure and pain in subjects with rheumatoid arthritis	Four styles of foot orthosis were compared
Mulcahy (6)	2003	RA pts after forefoot surgery	RA pts after forefoot surgery	100 feet in 61 pts	Area of contact (cm ²), pressure time integral (PTI; Ns/cm ²), and peak pressures (N/cm ²)	To compare the functional, radiographic, and pedobarographic results of different reconstructive methods for severe rheumatoid forefoot deformities.	2 types of reconstructive forefoot surgery were compared:

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Philipson (7)	1994	Inflammatory arthritis	11 RA, 1 SLE, 3 non-specific foot deformities	15	Plantar pressure, peak pressure. PTI. Contact areas	To determine how effective forefoot arthroplasty is at reducing the pressures under the forefoot	Forefoot arthroplasty
Rosenbaum (8)	2006	RA	25 RA patients, 21 healthy controls	46	Dynamic plantar pressure. Plantar sensitivity	to investigate the tactile sensitivity of the plantar surface in rheumatoid feet and its relationship to walking pain and plantar foot loading characteristics	none
Samnegard (9)	1990	RA	10 RA pts, post surgery feet	10 RA pts, 10 healthy controls	Plantar pressures	Examination of ten RA patients with an EMED gait analysis system in a mean four years after foot surgery and compared that with ten normal subjects.	4 years after forefoot surgery. No pre-operative measurement
Schmiegel (10)	2008	RA	RA pts and healthy controls	112	Pedobarography	To evaluate the use of pedobarographic measurements for detecting changes in plantar loading characteristics and their relationship to foot pain in RA	None
Schmiegel (11)	2008	RA	RA pts and healthy controls	16 RA pts, 21 healthy controls	Pedobarography	To compare RA patients' clinical, radiographic and pedographic status in order to investigate the relationship between mechanical damage and plantar pressure distribution under the forefoot	None
Semple (12)	2007	RA	RA pts and healthy controls	74 RA, 53 matched controls	Pedobarography	To undertake a comparison of the regionalized duration and velocity of the centre of pressure between rheumatoid arthritis patients with foot impairments and healthy able-bodied adults	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Tastekin (13)	2009	RA	RA and heel valgus	50 RA pts	Plantar pressure	To document the plantar pressure distribution changes in RA patients with heel valgus and to compare results in those without valgus.	None
Tuna (14)	2005	RA	RA	50 RA pts, 50 healthy controls	Plantar pressure	To assess probable plantar pressure alterations in RA patients compared with normals and the probable relation between pressure and radiologic foot erosion score	None
Turner (15)	2006	RA	RA with foot problems	12 RA pts, 12 controls	Temporospatial data, plantar pressure. Gait analysis	To compare clinical disease activity, impairment, disability, and foot function in normal and early RA	None
Turner (16)	2008	RA	RA	74 RA pts, 54 controls	Temporospatial data, plantar pressure. Gait analysis	To evaluate biomechanical foot function and determine factors associated with localised disease burden in patients with this disease.	None
Turner (17)	2008	RA	RA with forefoot/hindfoot or combined problems	28 RA pts, 50 healthy controls	Temporospatial data, plantar pressure. Gait analysis	To describe the clinical and biomechanical characteristics of patients with severe rearfoot, forefoot or combined deformities and determine localised disease impact	None
Van der Leeden (18)	2004	RA	RA	20 pts with inflammatory disease, 15 RA, 1 SpA, 1 JIA, 2 PsA	Plantar pressure	To compare the reproducibility of measurements among one-step, two-step, and three-step protocols for data collection in patients with arthritis.	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Van der Leeden (19)	2006	RA	RA	62 RA pts with foot complaints	Plantar pressure	To assess the relationship between forefoot joint damage and foot function, pain, and disability in patients with foot complaints secondary to RA	None
Woodburn (20)	2000	RA	RA	8 RA pts with 14 callosities	Plantar pressure	To determine the effect of expert debridement of foot callosities on forefoot pain and plantar pressure distribution in rheumatoid arthritis (RA)	Debridement of callosities
Plantar pressure F-scan (21-26)							
Grondal (21)	2006	RA pts	RA pts	14 plantar pressure, 12 gait data.	Stride data, plantar pressure	To study the effect of the difference between the Mayo resection vs. arthrodesis in RA forefoot reconstruction	Forefoot surgery in RA patients
Jackson (22)	2004	RA	RA pts, 9 female, 1 male	10	Plantar pressure	To determine which design could better manage high forefoot plantar pressures in patients with RA	Two prefab insoles
Li (23)	2000	RA	RA	12 RA pts, 8 healthy controls	Plantar pressure	To compare the foot pressures and loading forces during gait in RA patients and healthy subjects, and evaluate the effects of foot orthoses in RA	Prescription of foot orthoses
Novak (24)	2009	RA pts	RA pts	12	Plantar pressure	To compare foot orthoses and unshaped orthotic material on plantar pressure, pain reduction and walking ability in RA.	Foot orthosis (functional or unshaped)

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Vidmar (25)	2009	RA	RA pts with forefoot complaints	12 RA	Plantar pressure	To assess reliability of the F-Scan plantar pressure measurement system in rheumatoid arthritis patients	None
Woodburn (26)	1996	RA	Ra and healthy controls	104 RA, 42 controls	Plantar pressure	To investigate the relation between the position of the rearfoot and the distribution of forefoot plantar pressures and skin callosities in rheumatoid arthritis.	None
Plantar pressure otherwise or not specified (27-49)							
Andriacchi (27)	1977	Patients with knee disability	Patients with knee disability. 11 OA, 5 RA. 17 healthy normals	16	Temporospatial parameters, plantar pressure	To examine two types of gait parameters (temporal and ground reaction force) obtained from normal subjects and patients with knee joint disabilities.	None
Barrett (28)	1976	RA patients	RA pts with callosities at the MTP's	25	Plantar pressure points	To discuss the role of shoe-wear in the treatment of painful metatarsalgia in RA patients and to evaluate a special sandal developed for this purpose	Treatment of metatarsalgia with special sandal
Beauchamp (29)	1984	RA pts	RA patients who underwent forefoot surgery	37	Plantar pressure	To compare joint fusion MTP 1 with excision of the MTP1	To compare 2 types of forefoot arthroplasty (MTP1 fusion or excision)

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Betts (30)	1988	RA pts	RA PTS PRE- AND POST Kates Kessel	60 feet in 35 RA patients, 18 feet in 10 controls	Plantar pressure	To assess the results of forefoot arthroplasty in both a prospective study group of 60 feet and in a retrospective study group of 18 feet	Forefoot surgery (Kates Kessel)
Carl(2)		RA	20 RA patients with painful foot deformities who were provided with insoles	20	Plantar pressure	To examine the clinical effectiveness of insoles and to establish pedobarography as a means of quality control for orthotic management of the rheumatic foot.	Insoles
Collis (31)	1972	RA	RA patients	10 healthy feet, 10 rheumatoid feet	Plantar pressure	To measure the pressures under the different parts of the foot and describe the pressure pattern for normal feet and some of the changes that occur in rheumatoid arthritis	None
Dereymaeker (32)	1997	RA	RA pts, who underwent forefoot reconstruction	38	Plantar pressure	To evaluate the results after forefoot reconstruction	Forefoot reconstruction
Firth (33)	2007	RA pts	RA	10	Plantar pressure	Validity and reliability of PressureStat in patients with RA	None
Godfrey (34)	1967	RA	RA? And volunteers	?	Plantar pressure	To introduce a new method of pressure measurement during walking	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Hamilton(48)	2001	RA	24 early RA pts	24 early RA	Plantar pressure, stride data	To assess the clinical usefulness of a prototype walkmat system in patients with early RA	None
Harris(49)	1997	RA	RA pts who underwent forefoot surgery	35	Plantar pressure	To present a prospective 10-16 year clinical and pedobarographic evaluation of a modification to the Kates et al forefoot arthroplasty	Kates forefoot arthroplasty
Henessy (35)	2007	RA	RA with forefoot pain	20	Plantar pressures and pressure time integral	To evaluate the effect of running footwear as an alternative to off-the-shelf orthopaedic footwear on plantar pressure	Running shoes vs. orthopaedic footwear
Masson (36)	1989	RA,DM	RA and diabetes pts	37 RA pts, 38 diabetic pts	Plantar pressure, nerve conduction velocity.	To examine the relationship between high foot pressure, neurological abnormalities, and ulceration in RA and DM	None
Minns (37)	1984	RA/normal s	RA patients and healthy controls	124 RA, 67 normal subjects	Plantar pressure	To compare static and dynamic forces in a large cohort	None
Otter (39)	2004	RA	RA pts	25 EARLY RA. 25 controls	Plantar pressure	To investigate the magnitude and duration of peak forefoot plantar pressures in rheumatoid arthritis	None
Rome (40)	2009	RA	Ra pts	19 RA, 21 healthy controls	Gait data, centre of pressure	To evaluate postural stability in rheumatoid arthritis patients	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Sharma (41)	1979	RA	RA pts and controls	27 RA pts, 30 volunteers	Plantar pressure	To quantify the force distribution under the feet of patients and controls of similar age and weight.	None
Siegel (42)	1995	RA	6: 4 RA, 1 excessive pronation, 1 healthy subject	6: 4 RA, 1 excessive pronation, 1 healthy subject	Gait variables, plantar pressure	A technique to measure foot function during the stance phase of gait is described. Advantages of the method include its three-dimensional approach with anatomically based segment coordinate systems..	None
Simkin (43)	1981	RA	RA	18 RA. 20 controls	Stride parameters, vertical + local forces	Measuring the dynamic force distribution under the foot in RA and normals	None
Stauffer (44)	1977	KNEE diseased, OA and RA	OA and RA	65 OA (108knees) and 30 RA (54 knees). 29 healthy volunteers	Stride parameters, vertical forces	Biomechanical parameters of knee joint function for 95 patients (162 knees) with RA and degenerative joint disease were studied and compared with those for 29 normal subjects.	None
Stockley (45)	1989	RA	RA after surgery	35 pts	Pressure under forefoot	The modified Kates et al. metatarsal head resection arthroplasty has been evaluated in RA	A modified Kates procedure
Stockley (46)	1990	RA	RA	47 feet in 28 RA patients	Pressure under forefoot	To assess the relationship between hindfoot deformity and forefoot pressure in 28 RA after forefoot	Forefoot reconstruction Kates. Kessel. Kay (1967)

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Turner 2003 (47)	2003	RA	RA pts with pes planovalgus	23 RA pts 23 age-matched controls	Temporospatial data, Joint angles, plantar pressures	To compare gait and foot function between RA patients with painful pes planovalgus deformity and healthy age- and sex-matched adults.	None
Temporospatial data (4, 5, 14-17, 21, 27, 43, 44, 47, 48, 50-72)							
Giacomozzi (4)	2009	RA, selection on basis of the HAQ	RA and healthy subjects	112 RA patients; 30 healthy	Pressure, peak force, pressure time integral, force time integral, PPC, and NFC	To detect gait alterations in RA patients using peak pressure curves (PPC) and normalized force curves (NFC) in comparison with the HAQ	None
Hamilton(48)	2001	RA	24 early RA pts	24 early RA	Plantar pressure. Stride data	To assess the clinical usefulness of a prototype walkmat system in patients with early RA	None
Hodge (5)	1999	RA	RA with forefoot pain	12	Plantar pressure gait velocity	To investigate the effectiveness of foot orthoses in the management of plantar pressure and pain in RA	Four styles of foot orthosis were compared
Tuna (14)	2005	RA	RA	50 RA pts, 50 healthy controls	Plantar pressure	To assess plantar pressure alterations in RA patients compared with normal and in relation with erosion scores	None
Turner (15)	2006	RA	RA with foot problems	12 RA pts, 12 controls	Temporospatial data, plantar pressure. Gait analysis	To compare clinical disease activity, impairment, disability, and foot function in normal and early RA	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Turner (16)	2008	RA	RA	74 RA pts, 54 controls	Temporospatial data, plantar pressure. Gait analysis	To evaluate biomechanical foot function and determine factors associated with localised disease burden in patients with this disease.	None
Turner (17)	2008	RA	RA with forefoot/hindfoot/combined problems	28 RA pts, 50 healthy controls	Temporospatial data, plantar pressure. Gait analysis	To describe the clinical and biomechanical characteristics of patients with severe rearfoot, forefoot or combined deformities and determine localised disease impact	None
Grondal (21)	2006	RA pts	RA pts	14 plantar pressure, 12 gait data.	Stride data, plantar pressure	To study the effect of the difference between the Mayo resection vs. arthrodesis in RA forefoot reconstruction	Forefoot surgery in RA patients
Andriacchi (27)	1977	Patients with knee disability	Patients with knee disability. 11 OA, 5 RA. 17 healthy normals	16	Temporospatial parameters, plantar pressure	To examine two types of gait parameters (temporal and ground reaction force) obtained from normal subjects and patients with knee joint disabilities.	None
Simkin (43)	1981	RA	RA	18 RA. 20 controls	Stride parameters, vertical + local forces	Measuring the dynamic force distribution under the foot in RA and normals	None
Stauffer (44)	1977	KNEE diseased, OA and RA	OA and RA	65 OA and 30 RA., 29 normals	Stride parameters, vertical forces,	To compare biomechanical parameters of knee joint function for 95 patients (162 knees) with RA and normal subjects.	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Turner 2003 (47)	2003	RA	RA pts with pes planovalgus	23 RA pts 23 age-matched controls	Temporospatial data, Joint angles, plantar pressures	To compare gait and foot function between RA patients with painful pes planovalgus deformity and healthy age- and sex-matched adults.	None
Brinkmann (50)	1985	Pts with arthritis of the knee	RA/OA	72 healthy adults, 69 RA and 20 OA	Gait velocity, range of motion	To determine the relationship between gait velocity and rate and ROM knee, during ambulation, for healthy and arthritic subjects	Total knee replacement
Eastlack (51)	1991	RA pts	RA pts with abnormal gait	3	Videotaped observational gait-analysis (VOGA)	To determine the interrater reliability of videotaped observational gait-analysis (VOGA) assessments	None
Eppeland (52)	2009	RA pts	Asymptomatic RA pts	17	Gait parameters	To investigate the characteristics of gait in RA vs. controls.	None
Fransen (53)	1997	RA pts	RA pts	30	Gait variables	To assess the effectiveness of off-the shelf orthopedic footwear in RA	Prescription of orthopedic footwear
Fransen (54)	1999	RA pts	RA pts	31	Gait variables	To assess the reliability and responsiveness of gait speed, cadence and stride length at two self-selected speeds (SSS) in RA	None
Fransen (55)	1994	RA pts	RA pts and normal subjects	113 RA pts, 104 normal subjects	Gait/stride parameters	Differences in the gait parameters at three different self selected speeds between 113 subjects with rheumatoid arthritis and 104 normal controls	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Gyory (56)	1976	Knee patients	RA, OA and healthy controls	65 OA, 29 healthy, 30 RA pts	Gait variables, motion of the knee	To study functional performance of the knee joints of 29 normal volunteers, 65 OA patients and 30 RA pts	None
Isacson (57)	1988	RA	Female RA pts < 50 years	17	ROM, gait velocity stride parameters	Detecting early aberrations of gait in rheumatoid arthritis 17 women suffering from that disease were examined.	None
Kavlak (58)	2003	RA	RA pts	18	Physiologic cost index (PCI), stride data, VAS pain	To determine the effect of foot orthoses on pain, gait, and energy expenditure in patients with RA.	Different orthotic interventions
Keenan (59)	1991	RA	RA pts	20	Electromyography, gait/stride data, ROM	To investigate the cause of valgus hindfoot in RA and to characterize the effects of the deformity on gait.	None
Kettelkamp (60)	1972	RA	RA pts with knee problem?	27	Stride data, floor reaction force	To correlate various clinical characteristics to gait abnormalities in the rheumatoid knee	None
Khazzam (61)	2007	RA	RA pts,	22 RA pts, 29 feet	Temporospatial parameters.	To examine specific changes in segmental foot motion in patients with RA as compared to normals subjects	None
Laroche (62)	2007	RA with forefoot damage	RA pts	9 RA pts with malalignment of the forefeet, 7 controls	Stride parameters, duration, kinematic data	To investigate the modifications of gait parameters in RA To extract the mechanisms used to compensate for these impairments	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Laroche (63)	2005	RA with forefoot damage	RA pts	9 RA pts with malalignment of the forefeet, 7 controls	Walking frequency, walking velocity, stride length, duration	To evaluate the effects of loss of ROM of the MTP joint on the kinematic parameters of walking in RA	None
Locke (64)	1984	RA with ankle and subtalar	25 RA pts, 20 healthy subjects	25 RA pts, 20 healthy subjects	ROM, stride data	To document ankle and subtalar motion during gait in 20 healthy subjects and in 25 RA patients, to determine stride characteristics with and without the use of an extended orthosis in RA patients.	Use of an extended University of California Biomechanics Laboratory orthosis
Long (65)	2003	RA pts	RA pts before + after surgery	10 RA	Temporospatial, kinematic	A new series of ten RA patients are evaluated before and after surgical intervention	Forefoot surgery, not specified
MacSween (66)	1999	RA pts	RA pts with and without orthoses	8 RA pts	Temporospatial parameters	To study the effect of custom moulded EVA foot orthoses on walking ability in RA.	Use of a custom moulded foot orthosis
Marshall (67)	1980	RA pts	RA pts with subtalar involvement	6 RA pts with subtalar involvement	Temporospatial, kinematic	To describe changes in the orientation of ankle and subtalar axes in RA	None
Mejjad (68)	2004	RA	RA pts with metatarsalgia	16	Spatiotemporal gait variables	To assess the efficacy of foot orthoses in RA patients with pain and if improvement of pain was related to an improvement in gait	Cross over design: orthotics of 10mm semiflexible mat

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Murray (69)	1975	Total hip pts	Total hip pts	30 pts with total Hip, of which 4 RA pts	ROM, muscle strength, CoP, stride parameters. Forces cane/crutch	To measure function before and at six and twenty-four months after 100 McKee-Farrar total hip replacements in eighty-three patients	McKee-Farrar total hip replacement
Platto (70)	1991	RA	RA pts	31	Stride data	We evaluated the relationships among pain, structural deformity of the foot, 4 variables of gait, and an index of function in 31 RA patients.	None
Weiss (71)	2007	RA + ankle surgery	RA	14 RA pts, 14 matched controls	3D gait analysis, kinetic and time distance parameters	To evaluate the effects of ankle/hindfoot arthrodesis in RA on gait pattern of the knee and hip	Ankle joint surgery
Woodburn (72)	2004	RA	RA	11 RA, 5 healthy volunteers	3D kinematics, temporospatial parameters	To test a multisegment foot model for kinematic analysis during walking in RA patients with foot impairments.	None
3D gait (14-17, 38, 42, 47, 51, 57, 65, 67, 71-75)							
Tuna (14)	2005	RA	RA	50 RA pts, 50 healthy controls	Plantar pressure	To assess plantar pressure alterations in RA patients compared with normal and in relation with erosion scores	None
Turner (15)	2006	RA	RA with foot problems	12 RA pts, 12 controls	Temporospatial data, plantar pressure. Gait analysis	To compare clinical disease activity, impairment, disability, and foot function in normal and early RA	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Turner (16)	2008	RA	RA	74 RA pts, 54 controls	Temporospatial data, plantar pressure. Gait analysis	to evaluate biomechanical foot function and determine factors associated with localised disease burden in patients with this disease.	None
Turner (17)	2008	RA	RA with forefoot/hindfoot or combined problems	28 RA pts, 50 healthy controls	Temporospatial data, plantar pressure. Gait analysis	To describe the clinical and biomechanical characteristics of patients with severe rearfoot, forefoot or combined deformities and determine localised disease impact	None
O Connell (38)	1998	RA	10 RA, 7 healthy subjects	17	Plantar pressure, ankle ROM	To evaluate how painful metatarsal arthritis affects foot and ankle mechanics and mobility	None
Siegel (42)	1995	RA	6: 4 RA, 1 excessive pronation, 1 healthy subject	6: 4 RA, 1 excessive pronation, 1 healthy subject	Gait variables, plantar pressure	A technique to measure foot function during the stance phase of gait is described. Advantages of the method include its three-dimensional approach with anatomically based segment coordinate systems..	None
Turner (47)	2003	RA	RA pts with pes planovalgus	23 RA pts 23 age-matched controls	Temporospatial data, Joint angles, plantar pressures	To compare gait and foot function between RA patients with painful pes planovalgus deformity and healthy age- and sex-matched adults.	None
Eastlack (51)	1991	RA pts	RA pts with abnormal gait	3	Videotaped observational gait-analysis (VOGA)	To determine the interrater reliability of videotaped observational gait-analysis (VOGA) assessments	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Isacson (57)	1988	RA	Female RA pts < 50 years	17	ROM, gait velocity stride parameters	Detecting early aberrations of gait in rheumatoid arthritis 17 women suffering from that disease were examined.	None
Long (65)	2003	RA pts	RA pts before + after surgery	10 RA	Temporospatial, kinematic	A new series of ten RA patients are evaluated before and after surgical intervention	Forefoot surgery, not specified
Marshall (67)	1980	RA pts	RA pts with subtalar involvement	6 RA pts with subtalar involvement	Temporospatial, kinematic	To describe changes in the orientation of ankle and subtalar axes in RA	None
Weiss (71)	2007	RA + ankle surgery	RA	14 RA pts, 14 matched controls	3D gait analysis, kinetic and time distance parameters	To evaluate the effects of ankle/hindfoot arthrodesis in RA on gait pattern of the knee and hip	Ankle joint surgery
Woodburn (72)	2004	RA	RA	11 RA, 5 healthy volunteers	3D kinematics, temporospatial parameters	To test a multisegment foot model for kinematic analysis during walking in RA patients with foot impairments.	None
Weiss (73)	2008	RA	RA and controls	50 RA, 37 healthy subjects	3D gait analysis, ground reaction forces	To analyse kinematic and kinetic gait changes in RA in comparison to healthy controls and to examine whether HAQ-scores were associated with gait parameters.	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Woodburn (74)	2002	RA	RA	50RA+orthosis, 48 RA controls and 45 controls	3D kinematics of the AJC	To evaluate the efficacy of custom foot orthoses for the management of painful rearfoot in RA	Prescription of custom foot orthoses
Woodburn (75)	1999	RA	RA and healthy	10 RA, 10 controls	3D kinematics of the AJC	To determine the feasibility of using electromagnetic tracking (EMT) for quantifying 3D kinematics at the ankle joint complex (AJC)	Footwear/orthotic intervention in 10 RA
EMG (59, 76)							
Keenan (59)	1991	RA	RA pts	20	Electromyography, gait/stride data, ROM	To investigate the cause of valgus hindfoot in RA and to characterize the effects of the deformity on gait.	None
Garling (76)	2005	RA with TKA	RA with TKA	7	EMG	To assess the differences in muscle activity (surface EMG) between 2 types of TKA in RA	TKA
Other: Rontgen stereophotogrammetry, ROM, Kinetic data, Nerve conduction							
Rontgen stereophotogrammetry (77)							
Eberhardt (77)	1986	RA pts	RA pts with knee damage	4	Roentgen stereo photogrammetry	To demonstrate the usefulness of röntgen stereophotogammetry, to locate the axis of rotation.	None
ROM (38, 52, 56, 57, 64, 69)							
O Connell (38)	1998	RA	10 RA, 7 healthy subjects	17	Plantar pressure, ankle ROM	To evaluate how painful metatarsal arthritis affects foot and ankle mechanics and mobility	None

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Eppeland (52)	2009	RA pts	Asymptomatic RA pts	17	Gait parameters	To investigate the characteristics of gait in RA vs. controls.	None
Gyori (56)	1976	Knee patients	RA, OA and healthy controls	65 OA, 29 healthy, 30 RA pts	Gait variables, motion of the knee	To study functional performance of the knee joints of 29 normal volunteers, 65 OA patients and 30 RA pts	None
Isacson (57)	1988	RA	Female RA pts < 50 years	17	ROM, gait velocity stride parameters	Detecting early aberrations of gait in rheumatoid arthritis 17 women suffering from that disease were examined.	None
Locke (64)	1984	RA with ankle and subtalar	25 RA pts, 20 healthy subjects	25 RA pts, 20 healthy subjects	ROM, stride data	To document ankle and subtalar motion during gait in 20 healthy subjects and in 25 RA patients, to determine stride characteristics with and without the use of an extended orthosis in RA patients.	Use of an extended University of California Biomechanics Laboratory orthosis
Murray (69)	1975	Total hip pts	Total hip pts	30 pts with total Hip, of which 4 RA pts	ROM, muscle strength, CoP, stride parameters. Forces cane/crutch	To measure function before and at six and twenty-four months after 100 McKee-Farrar total hip replacements in eighty-three patients	McKee-Farrar total hip replacement
Kinetic data (71, 73, 78)							
Weiss (71)	2007	RA + ankle surgery	RA	14 RA pts, 14 matched controls	3D gait analysis, kinetic and time distance parameters	To evaluate the effects of ankle/hindfoot arthrodesis in RA on gait pattern of the knee and hip	Ankle joint surgery

Method/Measurement concept	Year of public.	Target population	Study population	Study number	Measure(s)	Aim	Intervention/treatment
Weiss (73)	2008	RA	RA and controls	50 RA, 37 healthy subjects	3D gait analysis, ground reaction forces	To analyse kinematic and kinetic gait changes in RA in comparison to healthy controls and to examine whether HAQ-scores were associated with gait parameters.	None
Sakauchi (78)	2001	RA	RA patients with knee problems	14 RA pts, 7 healthy subjects	Angular changes were analysed by an EM tracking instrument	To analyse abnormal gait patterns in patients with rheumatoid arthritis involving the knee joint.	None
Nerve conduction (36)							
Masson (36)	1989	RA, DM	RA and diabetes pts	37 RA pts, 38 diabetic pts	Plantar pressure, nerve conduction velocity.	To examine the relationship between high foot pressure, neurological abnormalities, and ulceration in RA and DM	None

Appendix C

Table 2: Results of scoring of selected QUADAS items, by method and author name (reference number)

METHOD	QUADAS 1	QUADAS 2	QUADAS 8	QUADAS 10	QUADAS 12	QUADAS 13	QUADAS 14
Plantar pressure EMED (1-20)							
Bitzan (1)	Yes	Yes	Yes	NA	Yes	No	Yes
Davys (3)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Giacomozzi (4)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Hodge (5)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Mulcahy (6)	Yes	Yes	Yes	NA	Yes	Yes	Yes
Philipson (7)	Yes	Yes	Yes	NA	Yes	Yes	NA
Samnegard (9)	Yes	No	Yes	NA	Yes	No	NA
Schmiegel (10)	Yes	Yes	Yes	NA	Yes	Yes	NA
Schmiegel (11)	Yes	Yes	Yes	NA	Yes	No	NA
Semple (12)	Yes	Yes	Yes	NA	Yes	Yes	NA
Tastekin (13)	Yes	Yes	Yes	NA	Yes	Yes	NA
Tuna (14)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner 2006 (15)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner 2008 (16)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner 2008 (17)	Yes	Yes	Yes	NA	Yes	Yes	NA
Van der Leeden (18)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Van der Leeden (19)	Yes	Yes	Yes	NA	Yes	Yes	NA
Woodburn (20)	Yes	No	Yes	NA	Yes	Yes	Yes

METHOD	QUADAS 1	QUADAS 2	QUADAS 8	QUADAS 10	QUADAS 12	QUADAS 13	QUADAS 14
Plantar pressure F-scan (21-26)							
Grondal (21)	Yes	Yes	Yes	Yes	Yes	No	Yes
Jackson (22)	Yes	Yes	Yes	NA	Yes	No	Yes
Li (23)	Yes	Yes	Yes	NA	Yes	Yes	NA
Novak (24)	Yes	Yes	Yes	NA	NA	No	NA
Vidmar (25)	Yes	No	Yes	Yes	Yes	No	NA
Woodburn (26)	Yes	No	Yes	NA	Yes	Yes	NA
Plantar pressure otherwise or not specified (27-49)							
Andriacchi (27)	Yes	No	Yes	NA	Yes	Yes	No
Barrett (28)	Yes	Yes	Yes	NA	Yes	No	No
Beauchamp (29)	Yes	No	No	NA	Yes	No	No
Betts (30)	Yes	No	Yes , in other study	NA	Yes	Yes	No
Carl(2)	Yes	Yes	Yes	NA	Yes	Yes	No
Collis (31)	Yes	No	Yes	NA	Yes	No	No
Dereymaeker (32)	Yes	No	Yes	No	Yes	Yes	Yes
Firth (33)	Yes	No	Yes	Yes	Yes	Yes	NA
Godfrey (34)	No	No	No	Yes	Yes	No	No
Henessy (35)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Hamilton(48)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Harris(49)	Yes	No	No	NA	Yes	No	Yes
Masson (36)	Yes	Yes	earlier study	NA	Yes	Yes	NA
Minns (37)	Yes	Yes	Yes	MA	Yes	No	NA
Otter (39)	Yes	Yes	Yes	NA	Yes	Yes	Yes

METHOD	QUADAS 1	QUADAS 2	QUADAS 8	QUADAS 10	QUADAS 12	QUADAS 13	QUADAS 14
Rome (40)	Yes	Yes	Yes	NA	Yes	No	NA
Sharma (41)	Yes	No	No	NA	Yes	No	NA
Siegel (42)	Yes	Yes	Yes	NA	Yes	Yes	NA
Simkin (43)	Yes	No	1, in another study	NA	Yes	No	NA
Stauffer (44)	Yes	Yes	Yes	NA	Yes	Yes	NA
Stockley (45)	Yes	No	No	NA	No	No	No
Stockley (46)	Yes	No	No	NA	Yes	No	No
Turner 2003 (47)	Yes	Yes	Yes	NA	Yes	Yes	NA
Temporospatial data (4, 5, 14-17, 21, 27, 43, 44, 47, 48, 50-72)							
Giacomozzi (4)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Hamilton(48)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hodge (5)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Tuna (14)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (15)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (16)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (17)	Yes	Yes	Yes	NA	Yes	Yes	NA
Grondal (21)	Yes	Yes	Yes	Yes	Yes	No	Yes
Andriacchi (27)	Yes	No	Yes	NA	Yes	Yes	No
Simkin (43)	Yes	No	Yes, in another study	NA	Yes	No	NA
Stauffer (44)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (47)	Yes	Yes	Yes	NA	Yes	Yes	NA
Brinkmann (50)	Yes	Yes	Yes	NA	Yes	No	No
Eastlack (51)	Yes	Yes	Yes	Yes	Yes	Yes	NA

METHOD	QUADAS 1	QUADAS 2	QUADAS 8	QUADAS 10	QUADAS 12	QUADAS 13	QUADAS 14
Eppeland (52)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Fransen (53)	Yes	Yes	Yes	No	Yes	Yes	Yes
Fransen (54)	Yes	Yes	Yes	Yes	Yes	No	NA
Fransen (55)	Yes	Yes	Yes	NA	Yes	Yes	NA
Gyory (56)	Yes	Yes	Yes	Yes	Yes	No	NA
Isacson (57)	No	Yes	No	NA	Yes	No	No
Kavlak (58)	Yes	Yes	Yes	Yes	Yes	No	No
Keenan (59)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Kettelkamp (60)	Yes	No	No	Yes	Yes	No	NA
Khazzam (61)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laroche (62)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Laroche (63)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Locke (64)	Yes	Yes	Yes	NA	Yes	Yes	NA
Long (65)	Yes	No	Yes	NA	Yes	No	No
MacSween (66)	Yes	Yes	Yes	NA	Yes	Yes	NA
Marshall (67)	Yes	Yes	No	NA	Yes	No	NA
Mejjad (68)	Yes	Yes	Yes	NA	Yes	No	NA
Murray (69)	Yes	Yes	No	NA	No	No	No
Platto (70)	Yes	Yes	Yes	NA	Yes	Yes	NA
Weiss (71)	Yes	Yes	Yes	NA	Yes	Yes	Yes
Woodburn (72)	Yes	Yes	Yes	NA	Yes	Yes	NA
3D gait (14-17, 38, 42, 47, 51, 57, 65, 67, 71-75)							
Tuna (14)	Yes	Yes	Yes	NA	Yes	Yes	NA

METHOD	QUADAS 1	QUADAS 2	QUADAS 8	QUADAS 10	QUADAS 12	QUADAS 13	QUADAS 14
Turner (15)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (16)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (17)	Yes	Yes	Yes	NA	Yes	Yes	NA
O Connell (38)	Yes	Yes	Yes	NA	NA	No	NA
Siegel (42)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (47)	Yes	Yes	Yes	NA	Yes	Yes	NA
Eastlack (51)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Isacson (57)	No	Yes	No	NA	Yes	No	No
Long (65)	Yes	No	Yes	NA	Yes	No	No
Marshall (67)	Yes	Yes	No	NA	Yes	No	NA
Weiss (71)	Yes	Yes	Yes	NA	Yes	Yes	Yes
Woodburn (72)	Yes	Yes	Yes	NA	Yes	Yes	NA
Weiss (73)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Woodburn (74)	Yes	Yes	Yes	Yes	Yes	Yes	No
Woodburn (75)	Yes	No	Yes	NA	Yes	Yes	NA
EMG (59, 76)							
Keenan (59)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Garling (76)	No	Yes	Yes	NA	Yes	Yes	NA
Other:							
Rontgen stereophotogrammetry (77)							
Eberhardt (77)	Yes	Yes	Yes	Yes	Yes	No	NA
ROM (38, 52, 56, 57, 64, 69)							
O Connell (38)	Yes	Yes	Yes	NA	NA	No	NA

METHOD	QUADAS 1	QUADAS 2	QUADAS 8	QUADAS 10	QUADAS 12	QUADAS 13	QUADAS 14
Eppeland (52)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gyori (56)	Yes	Yes	Yes	Yes	Yes	No	NA
Isacson (57)	No	Yes	No	NA	Yes	No	No
Locke (64)	Yes	Yes	Yes	NA	Yes	Yes	NA
Murray (69)	Yes	Yes	No	NA	No	No	No
Kinetic data (71, 73, 78)							
Weiss (71)	Yes	Yes	Yes	NA	Yes	Yes	Yes
Weiss (73)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Sakauchi (78)	Yes	Yes	Yes	NA	Yes	No	NA
Nerve conduction (36)							
Masson (36)	Yes	Yes	Earlier study	NA	Yes	Yes	NA

Appendix D

Table 3: Summary of the evaluation of the clinimetric measures, by method and author name (reference number)

Method	Internal consistency	Agreement	Reliability	Construct validity	Responsiveness	Interpretability
Plantar pressure EMED						
Semple (12)	0	? CoV 3.5% to 14.3% control 5.7% to 19.3%	0	0	0	+
Tastekin (13)	0	0	0	?	0	+
Tuna (14)	0	0	0	0	0	+
Turner (16)	0	0	0	?	0	+
Van der Leeden (19)	0	0	?, max Pearson's CC 0,352	+	0	+
Plantar pressure F-scan						
Woodburn (26)	0	0	0	+	0	+
Plantar pressure otherwise or not specified						
Hamilton (48)	?	?, CoV < 4 % kinematic parameters, < 7% kinetic parameters	? in another study	? sample size < 50	? sample size < 50	? sample size < 50
Masson (36)	0	0	0	? differences DM/RA (statistic method NS)p <0,01	0	+
Minns (37)	0	0	?	?	0	+
Temporospatial data						
Hamilton (48)	?	?, CoV < 4 % kinematic parameters, < 7% kinetic parameters	? in another study	? sample size < 50	? sample size < 50	? sample size < 50
Tuna (14)	0	0	0	0	0	+
Turner (16)	0	0	0	? sample size < 50	0	? sample size < 50

Method	Internal consistency	Agreement	Reliability	Construct validity	Responsiveness	Interpretability
Fransen (54)	0	? Sample size 31 ICC CI 0,60-0,96	0	? Sample size < 50	0	? Sample size < 50
Fransen (55)	0	0	? MWU, p>0,001 for differences in fast stride data	0	0	+
Gyory (56)	0	0	?, statistical method ?, sign differences between RA and normals	0	0	+
Keenan (59)	0	0	? no differences between the 2 groups	?	0	? sample size < 50
MacSween (66)	0	? ICC 0,91-0,96 in 22 normal controls	? small sample size (8), only sign difference in velocity	0	0	? sample size 8
Woodburn (72)	0	? MC 0.677 to 0.982 in healthy, 0.830 to 0.981 in RA	? sample size 11	0	0	? sample size 11
3D gait						
Tuna (14)	0	0	0	0	0	+
Turner (16)	0	0	0	? sample size < 50	0	? sample size < 50
Woodburn (72)	0	? CoMC 0.677 to 0.982 in healthy, 0.830 to 0.981 in RA	? sample size 11	0	0	? sample size 11
Weiss (73)	0	0	? sign. mean differences with 95% CI	-	0	+
Woodburn (74)	0	CoMC 0.97 to 0.77 in former study	? sample size 45	? sample size 45	? sample size 45	? sample size 45
Woodburn (75)	0	? CoMC 0,81 to0,97	? sample size 20	? sample size 20	? sample size 20	? sample size 20

Method	Internal consistency	Agreement	Reliability	Construct validity	Responsiveness	Interpretability
EMG						
Keenan (59)	0	0	? no differences between the 2 groups	?	0	? sample size < 50
Other: ROM						
Gyory (56)	0	0	?, statistical method ?, sign differences between RA and normals	0	0	+
Kinetic data						
Weiss (73)	0	0	? sign. mean differences with 95% CI	-	0	+
Sakauchi (78)	0	0	? sample size 21	? sample size 21	0	? sample size 21
Nerve conduction						
Masson (36)	0	0	0	? differences DM/RA (statistic method NS) p <0,01	0	+

References to Appendices

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3

The effect of foot marker placement variation on assessed joint kinematics in rheumatoid arthritis: a model simulation

Dubbeldam R, Buurke JH, Nene AV, Baan H, Droassaers-Bakker KW, van de Laar MAFJ, Hermens H. Assessment of foot and ankle kinematics in rheumatoid arthritis: consistency, repeatability and model simulation. *Gait Posture* 2007; 26S O30 pS20

Abstract

Introduction. Gait analysis methods are currently applied to improve the understanding of foot and ankle impairments in rheumatoid arthritis (RA). The aim of this study was to analyse the effect of foot marker placement variations on gait kinematics using a 5-segment foot and ankle model simulation study for RA subjects.

Method. Gait of three RA subjects with moderate to severe foot and ankle impairments was recorded repeatedly in three sessions. The between-day results were evaluated for changes in the joint range of motion for assessed foot and ankle joints. Marker placement variations were simulated in a model simulation study using one of the measured RA subjects as input. Insight, attained from this simulation study, was used to understand the differences in results in the between-day measurements.

Results. In the model simulation and between-day measurements, variations in pattern (up to 5°) and differences in offset (up to 15°) were found in joint range of motion. These variations could be explained by differences in initial marker location, as well as by variations in walking speed and stride length.

Introduction

In rheumatoid arthritis (RA) up to 80% of the patients complain of and suffer from severe foot and ankle problems¹⁻³. With the recent development of multi-segment models of the foot and ankle⁴⁻⁶, detailed kinematics studies can be performed to analyse the motion of these structures. Several studies have analysed and reported foot and ankle kinematics of patients suffering from RA⁷⁻⁹. In these studies, the repeatability of the measurement for healthy subjects is applied to RA patients.

However, the RA foot tends to be, in time, a pes planovalgus with a flattened medial arch and hallux valgus with bunion². Such foot deformations, in combination with technical marker placement requirements, may influence the marker placement. Furthermore, while using detailed multi-segment models, the distance between several markers is small. Hence, a small difference in marker position will significantly influence the assessed joint angle.

During prior gait measurements on patients with RA it was observed that it was difficult to place markers consistently on the bony structure of the navicular and distal metatarsal I bones: swelling and bunions made it difficult to comply with the prescribed marker position. These marker positions are crucial in the multi-segment model developed by Simon⁴ that was used for our gait analysis.

This study aimed to explore the effect of marker placement variation on foot and ankle kinematics of patients with RA. A model simulation study was performed to attain insight in the effect of variation of navicular and distal metatarsal I initial marker position on the assessed kinematic measures. A repeated gait measurement study was performed on three patients with RA to observe possible predicted effects of marker placement variation as seen in the model simulation.

Methods

Three female patients suffering from RA participated in this study (Fig. 1b,c,d). The three RA patients were 33, 59 and 66 years old and signed an informed consent before participation. The feet of the RA patients were each affected differently by the disease with regards to inflammation and damage. The following clinical characteristics were assessed: the Visual Analog Scale for Pain, the Joint Alignment and Motion (JAM) score, the Disease Activity

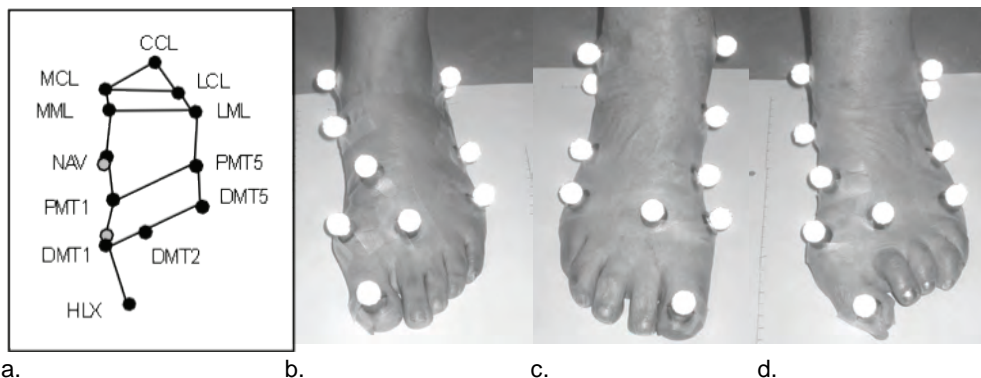


Figure 1: a. Top view of foot markers: repositioning of the original (black) navicular (NAV) and distal metatarsal I (DMT1) markers to their new (grey) position. Abbreviations for marker position: CCL posterior calcaneus, LCL lateral calcaneus, MCL medial calcaneus, LML lateral malleolus, MML medial malleolus, PMT5 and DMT5 proximal and distal metatarsal 5, PMT1 and DMT1 proximal and distal metatarsal 1, DMT2 distal metatarsal 2, HLX hallux. b,c,d. Foot of the three RA subjects with markers.

Score (DAS 28), the pain and disability sub-scores of the Foot Function Index (5-FFI), the Larsen score and the Sharp Van der Heijde score. This study received approval from local medical ethics committee.

One tester performed the gait measurements using a 6-camera video-based motion analysis system (Vicon, 370, Oxford Metrics Group). The RA patients were asked to walk at a comfortable walking speed. The gait recordings were carried out on three different occasions in two weeks time. During each occasion (session), 10 gait trials with multiple steps were recorded. A method developed by Simon was used to study foot and ankle kinematics⁴. The joint range of motion was assessed in BodyBuilder (V3.55, Oxford Metrics Limited). Details about the temporal-spatial and kinematic measures assessment are given in chapter 4.

The mean value and corresponding standard deviation (SD) of the joint angles range of motion, as function of the % gait cycle, was assessed for each session using 7 to 8 trials. The range of motion of each joint angle during the stance phase was assessed from the difference between the minimum and maximum value of the joint angle during stance. The data of one RA patients (subject N72) and session was used as input for the model. Then the initial location of the navicular and distal metatarsal I markers were varied successively with 8 mm in two directions: proximal-distal and medial-lateral (Fig. 1a). The position of the navicular marker was modified using the calcaneus segment's coordinate system and the axis between the central calcaneus point and the original navicular marker axis. In the x-

and y-direction 8 mm was added to the original position. The modified position of the distal metatarsal I marker was assessed by scaling the line between the proximal and distal metatarsal I, and the line between the distal metatarsal V and distal metatarsal I.

To explore the effect of variation in marker position between-days, the difference in minimum, maximum and range of motion value between the sessions was calculated. The natural variation in walking is assessed by means of the standard deviation: the average standard deviation was assessed from the mean standard deviation from each session and subject. The results of the repeated gait measurements were compared to the results of the model simulation study.

Results

An overview of the demographic, clinical and gait characteristics of the three RA patients is given in Table 1. For subject N72, limited damage to the hindfoot and forefoot joints was observed on X-ray. However, more extensive erosion and synovitis of the forefoot and hindfoot joints as well as tearing of the tibialis posterior tendon were observed on magnetic resonance imaging (MRI). The three RA patients varied in disease duration and disease activity. Furthermore, the disease affected different areas of the foot and ankle.

DEMOGRAPHIC AND CLINICAL SCORES	Scoring range	N72	G39	Z47
Age (years)		33	66	59
Disease duration (months)		23	224	100
Rheumatoid factor		1200	250	10
DAS 28	0-9.4	2.9	3.3	2.5
Pain Visual Analog Score (%)	0-100	28	20	12
5 FFI Pain	0-126	8	17	39
5 FFI Disability	0-126	33	39	44
Larsen score	0-15	0	4	0
SVH score	0-64	2	16	25
Joint Alignment and Motion (JAM)	0-32	12	15	4
GAIT CHARACTERISTICS	Healthy subjects mean (SD)			
Walking speed (m/s)	1.25 (0.11)	0.56	0.73	0.65
Individual Variability walking speed (m/s)	0.03	0.08	0.04	0.03
Stride length (m)	1.32 (0.08)	0.74	0.94	0.97
Individual variability stride length (m)	0.02	0.09	0.04	0.03

Table 1: Demographic, clinical and gait characteristics of the three RA subjects N72, G39 and Z47.

Difference in joint ROM between sessions (deg)	Model simulation				RA subjects		
	Nav Y	Nav X	DMT1 X	DMT 1 Y	Min	Max	Ave
Ankle dorsiflexion	0.1	0.0	0.0	0.0	0.2	2.2	1.0
Medial arch collapse	1.3	1.3	-0.2	-0.8	0.3	4.9	2.1
MTP 1 dorsiflexion	0.0	0.0	-5.2	-1.9	0.4	4.5	2.1
Sub-talar in/eversion	-0.2	0.0	0.0	0.0	0.2	2.1	1.3
Midfoot supination	-1.8	0.0	0.0	0.0	0.9	9.8	3.8
Forefoot abduction	0.0	0.0	-0.2	0.0	0.2	1.0	0.5
Forefoot spreading	-0.1	0.1	0.1	-0.1	0.8	6.4	2.7
MTP 1 abduction	0.0	0.0	0.3	-0.1	0.3	8.1	2.9
Difference in temporal-spatial between sessions							
Walking speed (m/s)	-	-	-	-	0.01	0.11	0.03
Stride length (m)	-	-	-	-	0.00	0.07	0.04
Double stance phase (%)	-	-	-	-	0.2	7.6	1.6

Table 2: Difference in joint ROM (deg) and temporal-spatial characteristics between sessions. In the model, variation of 8 mm in X (anterior-posterior) or Y (medial) direction of the navicular (NAV) and first distal metatarsal (DMT1) marker position were simulated. The repeated gait recordings were performed with 3 RA patients and the minimum (Min), maximum (Max) and average (Ave) difference in joint ROM between measurement sessions is presented.

Standard Deviation of joint angle (deg)	RA (N=3)	Simon Healthy (N=10)	Carson Healthy (N=8)
Ankle dorsiflexion	1.43	0.93	0.66
Medial arch collapse	2.24	0.65	0.69
MTP I dorsiflexion	4.07	1.37	1.95
Subtalar in/eversion	1.78	0.80	0.68
Midfoot spination	2.53	0.74	0.59
Forefoot abduction	1.51	0.55	0.57
Forefoot spreading	3.18	0.74	
MTP I abduction	2.12	0.45	1.07

Table 3: Average within session standard deviation of the joint range of motion for all patients and sessions. MTP I: first metatarso-phalangeal joint. The last two columns include findings from Simon⁴ and Carson⁵.

In the simulation study, variations in initial marker location of about 8 mm resulted in an offset of the assessed kinematic measures of up to 10° (Fig. 2): Variations in navicular marker location resulted in changes in minimum or maximum joint angle of the medial arch collapse (5°), the sub-talar joint (1.5°), and the midfoot supination (2°). Variations in initial distal metatarsal I marker resulted in changes in minimum or maximum joint angle of the medial arch collapse (4°), MTP I dorsiflexion (5°) and abduction (10°), forefoot spreading (11°), and abduction of the forefoot with respect to the hindfoot (4°). Furthermore, the marker position variation influenced the range of joint motion and thus the pattern of the joint motion (Fig. 2 a,b,c). For example, the position of the distal metatarsal I marker did not influence the joint angle during mid-stance, but up to 5° for peak MTP I dorsiflexion. The effects of variation in marker position on joint ROM were much smaller than the offset effects (Table 2). Variation in navicular marker position influenced the midfoot range of motion with 1° to 2° . The largest effect was observed for the DMT1 anterior/posterior position variation on the dorsiflexion range of motion of the MTP 1.

Also in the repeated measures of the RA patients, offset in joint angle and pattern differences were found in a specific part of the gait cycle (Table 2 and Fig. 2 d,e,f). For example, a significant difference in peak value existed between the MTP I angle in the second and third session, while this difference was not found at mid-stance. The offset in forefoot spreading and tibio-talar flexion was larger during stance- than during swing phase. However, larger offsets (5° to 15°) in the assessed kinematic measures were observed between the three sessions compared to the values predicted by the simulation. Also, most of the maximum differences in joint range of motion between the sessions were larger than those predicted by the simulation (Table 2).

During the gait recordings of one of the RA patients, the mean walking speed and stride length were smaller in the first session than in the second and third sessions: they were 0.66 m/s and 0.89 m, 0.76 m/s and 0.96 m, and 0.77 m/s and 0.96 m, respectively. Between the first and the other two sessions with more similar walking speed, larger differences were observed for most kinematic measures.

The average with-in session standard deviation, which displays the variation in natural walking, is presented in Table 3. The with-in session variation for the MTP I dorsiflexion and sub-talar eversion angle were almost as large as the maximum observed MTP I dorsiflexion variation between sessions: 4.1° compared to 4.5° and 1.8° compared to 2.1° , respectively (Table 2 and 3).

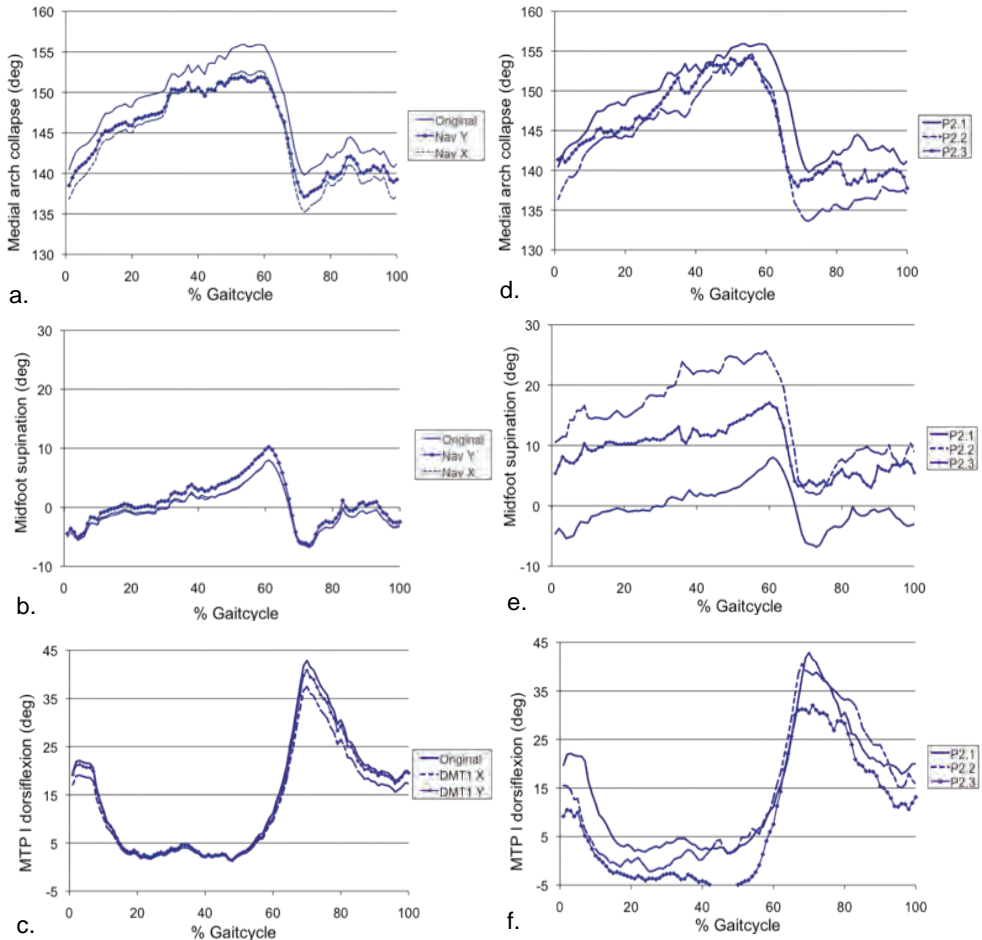


Figure 2: a,b,c Effect of navicular (NAV) and distal metatarsal I (DMT1) marker position in x- or y-direction on joint angles as function of the gait cycle (stance and swing phase); d,e,f: Joint range of motion of the medial arch collapse, midfoot supination and MTP I dorsiflexion in the three sessions of one RA patient.

Discussion

Joint range of motion offset and pattern variations were found in the three repeated gait measurements with RA patients as well as in the model simulation study as result of foot marker position variations of 8 mm. Reproducibility studies using healthy subjects have also reported a significant offset in joint range of motion^{1,2}, while the change in pattern was not reported² or reported as a minor variation^{1,3}.

In the three gait measurement sessions, observed offset and pattern variations were mostly larger than those seen in our simulation study. According to our findings, these larger variations in the joint angle pattern and offset might be explained by variation in other marker locations and by difference in walking speed and stride length. Healthy subjects increase their stride length and walking speed by increasing the rotation of the pelvis in the transverse plane or in the sagittal plane resulting in higher heel raise¹⁰. It is assumed, that walking speed will also affect other foot and ankle kinematics of healthy subjects and patients with RA.

The joint angle offset and pattern variations in our between-day measurement study were larger than those reported in studies with healthy subjects¹⁻³. Due to deformations of foot structures, the repeatability of marker placement on RA feet becomes challenging. This may increase with increasing foot deformations. Also the assessed with-in session standard deviations were higher than those reported for healthy subjects, suggesting higher variability in the natural walking pattern (Table 3).

Limitations to this study are the limited number of RA subjects and the limited number of marker placement variations. Hence statistical analysis of the results is not possible.

Conclusion

A model simulations study and three repeated gait recordings were performed to explore the effect of foot marker placement variation and repeated measures on assessed joint angles for RA patients. Our findings suggest that, in addition to the influence of marker location, the differences in joint range of motion might be explained by variations in walking speed and stride length as well as individual gait variations. Future studies should analyse the effects of repeated measures in a larger population suffering from RA as well as the potential for optimising the marker placement protocol or usage of additional foot markers.

Acknowledgements

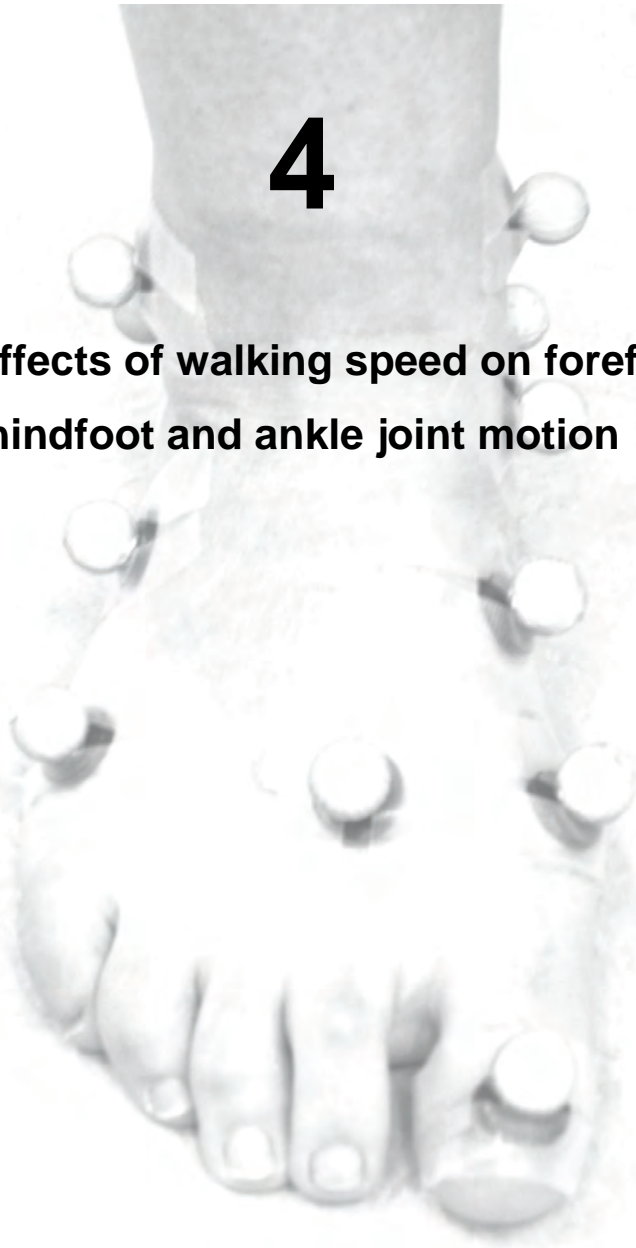
We would like to thank L. Schaake for his valuable support in the gait lab and the data post-processing. This study was funded by the Innovation Centre for Rehabilitation Technology, grant number IC-7856, The Netherlands.

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4

The effects of walking speed on forefoot, hindfoot and ankle joint motion



Dubbeldam R, Buurke JH, Simons C, Groothuis-Oudshoorn CGM, Baan H, Nene AV, Hermens H. The effects of walking speed on forefoot, hindfoot and ankle joint motion. Clin Biomech 2010; 25: 796-801

Abstract

Background. Foot and ankle joint kinematic differences have been identified between healthy subjects and subjects with various pathologies suffering from foot and ankle impairments. Changes in temporal factors such as walking speed and double stance time are also found in these pathological conditions. As such, in theory, these factors would also influence the kinematics and hence make it difficult to ascertain the effects of the disease on the kinematics. The aim of this study was to analyse foot and ankle kinematics from gait recordings of healthy subjects walking at comfortable and slower speeds.

Methods. Gait patterns of 14 healthy subjects were recorded. The subjects were first asked to walk at a comfortable speed and then at predefined speeds of 75% and 50 % of their comfortable walking speed respectively. Temporal variables were calculated. Foot and ankle joint kinematics were determined from marker-recordings.

Findings. The subjects walked at mean velocities of 1.28 m/s, 0.97 m/s and 0.65 m/s. With decreasing walking speed the minimum tibio-talar plantarflexion and maximum hallux dorsiflexion at toe-off decreased significantly between 3° and 9°. The minimum medial arch at toe-off and minimum midfoot supination at mid-stance were significantly affected by the walking speed. The corresponding individual session differences were small (1°-2°), but the reliability was high and hence the differences were considered clinically relevant.

Interpretation. Walking speed significantly affected foot and ankle kinematics. Studies aiming to improve the understanding of the effects of foot and ankle pathologies on foot and ankle kinematics should take the walking speed into account.

Introduction

Several pathologies, such as rheumatoid arthritis and diabetes mellitus, lead to foot and ankle impairments. Improved gait recording technologies and the development of foot and ankle kinematic models have made it possible to study the effect of these pathologies on foot and ankle kinematics (Khazzam et al., 2006, Khazzam et al., 2007; Turner et al., 2007, Turner et al., 2008, Weiss et al., 2008). In general, kinematic data of impaired, mostly older, subjects are compared to those of relatively young and healthy subjects and the results are used to assess the effects of pathologies on foot and ankle kinematics. Besides the kinematic differences between healthy and impaired subjects, the temporal factors such as walking speed and double stance phase are different. Walking speed and stride length is lower while double stance phase is longer for subjects with foot and ankle impairments (Canseco et al., 2008, Helliwell et al., 2007, Laroche et al., 2007, Khazzam et al., 2007, Turner et al., 2007, Turner et al. 2008, Weiss et al., 2008). In these studies, impaired subjects with rheumatoid arthritis obtained mean walking speeds ranging from 0.90 m/s to 0.96 m/s (Khazzam et al., 2007, Turner et al., 2008, Weiss et al., 2008) while subjects with ankle osteoarthritis or subjects suffering from a cerebrovascular accident tended to walk at even lower speeds of 0.3 m/s to 0.75 m/s (Chen et al., 2005, Khazzam et al., 2006, Perry et al., 1995). Both factors, the disease process and the temporal factors, are likely to influence foot and ankle kinematics and hence make it difficult to deduce the effects of individual factors on the kinematics. Several studies have reported the effect of walking speed on lower extremity kinematics, including the ankle joint (Chiu and Wang, 2007, Laroche et al., 2007, Lelas et al., 2003, van der Linden et al., 2002, Murray et al., 1984, Rosenbaum et al., 1994, Stansfield et al., 2001) but no studies were found describing foot kinematics.

The aim of this study was to show the effects of walking speed on foot and ankle kinematics in matured healthy subjects walking at comfortable and clinically relevant slower speeds. We hypothesised that with decreasing walking speed joint kinematics in terms of range of motion would significantly decrease in the sagittal, transverse and frontal planes.

Methods

Subjects

Fifteen healthy subjects, 5 males and 10 females, without foot and ankle complaints participated in this study. One male subject was excluded from the analysis due to difficulty in adapting his walking speed to 50% of his comfortable walking speed. The remaining fourteen subjects had a mean age of 43 years (range 30 to 55 years, SD 8 years). An informed consent was obtained prior to participation from each subject. This study was approved by the Medical Ethical Committee of Roessingh Rehabilitation Centre, Enschede, The Netherlands.

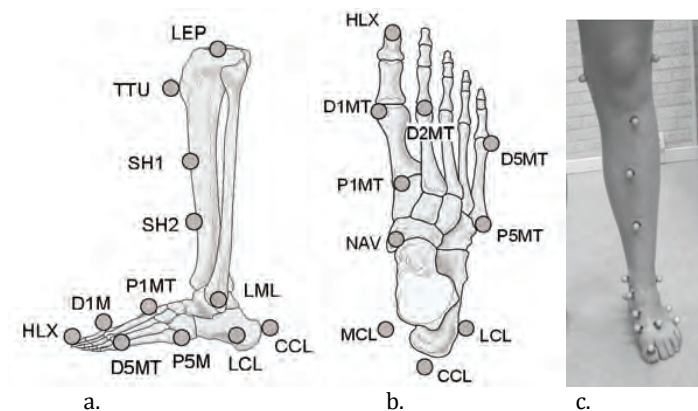


Figure 1: a. Lateral view and b. top view of marker positions on the foot and leg (Simon et al., 2006); c. Leg with markers

Protocol

Gait analysis was performed using a 6-camera video-based (1.3 megapixel, 100 Hz) motion analysis system (Vicon Nexus, Vicon Motion Systems, Oxford Metrics Group, UK). One experienced tester attached nineteen markers to the lower limbs of the subjects according to the method described by Simon (Simon et al., 2006) (see Fig. 1). For each subject, the right foot was measured in three sequential sessions between which the markers were not removed. Initially, the subjects were asked to walk at their own comfortable walking speed (V_c). In the second and third session the subjects were asked to walk at a predefined speed of 75% (V_{75}) and 50% (V_{50}) of the comfortable walking speed respectively. The walking speed was computed from the recordings, but to adjust the walking speed, it was also

measured manually during the recordings and communicated to the test subject. During each session, the recording was continued until at least 7 trials were obtained for each walking speed with less than 5% variance and within 5% of the predefined walking speed.

Data analysis

The temporal-spatial variables walking speed, step length, stride length, stride time and double-support time and stride width were assessed for each subject from the marker co-ordinate recordings in a special LabVIEW script (V7.2, National Instruments, Austin, Texas, USA). This script was also used to normalise the data to the gait cycle using the specified initial contact and toe-off indications in Vicon Nexus (Vicon Motion Systems, Oxford Metrics Group, UK). A brief description of the contents of the script is given in Appendix A. The foot and ankle joint kinematic variables shown in Table 1 were calculated using the method developed by Simon (Simon et al., 2006).

Sagittal plane	Frontal plane	Transverse plane
Tibio-talar flexion	Subtalar eversion	Leg/hindfoot external rotation
Medial arch	Mid-/hindfoot supination	Fore-/hindfoot adduction
Hallux flexion	Fore-/midfoot supination	Metatarsal (MT) I-V angle
		Hallux adduction

Table 1: Overview of assessed kinematic parameters arranged by main plane of motion.

For each subject and session, the mean value of the joint angles motion, as function of the % stance phase, was assessed using 5 to 7 trials, such that a minimum of 10 steps were incorporated in the analysis. For each subject the foot and ankle joints the maximum and minimum value and the range of motion (ROM) during the stance phase was calculated from the mean joint angle motions. The ROM was defined as the maximum minus minimum angle during stance phase. However, for the tibio-talar flexion, the ROM was calculated from the maximum dorsiflexion angle minus the maximum plantar-flexion angle at toe-off.

Statistical analysis

The statistical analyses were performed in SPSS 16.0 (SPSS Inc., Chicago, IL, USA). To test the normal distribution of the temporal-spatial and joint ROM variables, a Shapiro-Wilk

test was performed. A repeated measures ANOVA is used to test for differences in temporal factors and joint angles (maximum, minimum and ROM) between the three walking speed sessions. In case of violation of sphericity the Greenhouse-Geisser method is used. Those variables with a statistical significance of the within subject effect ($p < 0.05$), were tested post-hoc for within subject contrasts. The variables of the 75% walking speed session (V_{75}) are compared to those of the comfortable walking speed session (V_c) and 50% walking speed session (V_{50}) respectively. A sequential rejective Bonferroni correction was applied on the within subject contrasts to correct for multiple parameter testing.

The significant mean group differences between the mean joint angle values were small and to obtain a better idea of the clinical relevance of these results, an analysis was performed to study the individual differences in joint variables between the sessions for each subject as well as the reliability of the measurements. Therefore, the maximum, minimum and ROM joint angle values of each step for each subject for each session were assessed. From these step values, a mean joint angle parameter for each subject and walking speed session was calculated. The mean difference between the sessions was assessed for each subject. The group mean difference and corresponding standard deviation between the sessions were assessed in Excel (Microsoft® Excel® 2008 for Mac, Microsoft Corp., USA). The reliability of the measurement variables was assessed by relating the individual variances to the between-subject variances. The reliability values were assessed using a linear mixed model analysis in SPSS and were calculated from the co-variance parameters as follows: The reliability value equals the Intercept value divided by the Intercept value plus the residual value (Vangeneugden et al., 2004).

Results

The group's mean values of the temporal-spatial variables for the three walking speeds V_c , V_{75} and V_{50} and the corresponding standard deviation are shown in Table 2. The Shapiro-Wilk test indicated a normal distribution of the data. The temporal variables differed statistically ($p < 0.0001$) between all three walking speeds. With decreasing walking speed, the stride (step) length decreased and the stride time and double support time increased. The toe-off as function of the % gait cycle was delayed with decreasing walking speeds.

	V _c (mean (SD))	V ₇₅ (mean (SD))	V ₅₀ (mean (SD))
Stride time* (s)	1.05 (0.07)	1.18 (0.09)	1.53 (0.14)
Walking speed* (m/s)	1.28 (0.13)	0.97 (0.11)	0.65 (0.08)
Stride length* (m)	1.34 (0.10)	1.14 (0.09)	0.99 (0.09)
Stride width (m)	0.08 (0.02)	0.08 (0.02)	0.07 (0.02)
Step length* (m)	0.68 (0.06)	0.60 (0.07)	0.50 (0.05)
Double support time* (% gait cycle)	23.5 (3.6)	27.8 (3.2)	33.1 (4.1)
Toe-off* (% gait cycle)	62,1 (1.8)	64.7 (1.7)	67.2 (1.8)

* Statistically significant ($p < 0.0001$) difference in value between the three walking speeds

Table 2: Descriptive statistics of the temporal-spatial parameters (mean value and SD) for the three walking speeds.

The joint angle variables with statistically significant ($p < 0.05$) within subject effects and corresponding within subject contrasts are presented in Table 3. Statistically significant joint angle differences between sessions, after sequential rejective Bonferroni correction, are indicated with a star in Table 3. In the sagittal plane a decrease in walking speed corresponded with a statistically significant reduction of the peak value of the tibio-talar plantarflexion, a flatter medial arch and reduced hallux dorsiflexion at toe-off. In the frontal plane a significant increase in pronation of the midfoot with respect to the hindfoot was found at mid-stance at lower walking speeds. Regarding the joint ROM (maximum-minimum joint angle), lower walking speeds resulted in significantly less ROM of the tibio-talar joint, the medial arch and hallux joint in the sagittal plane and less abduction motion of the hallux in the transverse plane. When comparing the lowest walking speed (V₅₀) to the 75% walking speed (V₇₅) statistically significantly reduced ROM was found for the adduction of the forefoot with respect to the hindfoot, leg external rotation and for their corresponding peak values at toe-off, respectively. The maximum and minimum metatarsal (MT) I-V angle was statistically significantly different between the comfortable walking speed (V_c) and the 75% walking speed session (V₇₅): reduced walking speed resulted in an increase of the MT I-V angle.

				Within Subject Contrasts		Sign. Diff
	V _C Mean (SD)	V ₇₅ Mean (SD)	V ₅₀ Mean (SD)	V _C -V ₇₅	V ₇₅ -V ₅₀	
Tibio-talar ROM	18.47 (4.50)	16.45 (4.83)	14.38 (5.25)	0.03	0.01	*
Tibio-talar dorsifl max	12.26 (3.13)	13.37 (2.83)	13.85 (2.23)	0.07	0.17	
Tibio-talar dorsifl min	-6.33 (5.59)	-3.28 (6.62)	-0.77 (6.75)	0.00	0.00	*
Med arch ROM	17.87 (2.04)	16.74 (2.65)	15.42 (2.57)	0.02	0.01	*
Med arch min	128.25 (3.70)	129.21 (3.95)	130.50 (3.95)	0.00	0.01	*
Hallux dorsifl ROM	50.12 (5.42)	46.52 (6.55)	41.72 (5.58)	0.00	0.00	*
Hallux dorsifl max	51.11 (5.08)	47.34 (6.28)	42.07 (5.70)	0.00	0.00	*
Hallux dorsifl min	0.91 (2.36)	0.75 (2.63)	0.24 (3.06)	9.04	0.80	
Sup Mid-/Hindfoot min	-8.78 (6.02)	-9.72 (6.06)	-10.86 (6.26)	0.00	0.00	*
Sup Fore-/Midfoot max	-4.03 (1.97)	-4.45 (2.15)	-4.68 (2.38)	0.29	0.39	
Leg/Hindfoot rot ROM	6.11 (1.77)	5.72 (1.79)	5.04 (1.79)	0.48	0.01	
Leg/Hindfoot rot max	12.32 (3.84)	11.90 (3.65)	11.24 (3.78)	0.17	0.00	
Abd Fore-/Hindfoot ROM	10.05 (2.13)	9.38 (2.15)	8.34 (1.91)	0.10	0.00	
Abd Fore-/Hindfoot max	-12.44 (5.74)	-12.85 (5.58)	-13.70 (5.64)	0.90	0.03	
Abd Fore-/Hindfoot min	-22.49 (6.16)	-22.23 (5.90)	-22.04 (5.73)	1.95	0.56	
MT I-V angle max	14.91 (4.81)	15.40 (4.75)	15.67 (4.64)	0.04	1.71	
MT I-V angle min	4.80 (3.86)	5.40 (3.77)	5.58 (3.77)	0.01	2.21	
Hallux add ROM	7.84 (3.12)	6.96 (2.84)	5.59 (2.43)	0.02	0.00	*
Hallux add min	-21.21 (4.66)	-20.43 (4.89)	-19.28 (5.08)	0.14	0.21	

Table 3: Mean and corresponding standard deviation (SD) of joint ROM and peak values and the within subjects contrasts (values after sequential rejective Bonferroni correction) of the ANOVA post-hoc test; * indicates significant difference ($P < 0.05$) between walking speeds.

The statistically significant mean joint angle differences between the sessions ranged between 1° and 5° and up to 9° between the lowest and highest speed. The individual joint angle session differences varied between 0° and 14° and the reliability between 0.53 and 0.94 (Table 4 and Fig. 2). Four groups of joint values were observed: (i) Joint values with large individual differences with high reliability, (ii) large individual differences with moderate reliability, (iii) small individual differences with high reliability, and (iv) small individual differences and low reliability. The first group consisted of the minimum tibio-talar angle, which had good reliability ($r=0.82$) with large mean individual differences up to 6° (V_C-V_{50}).

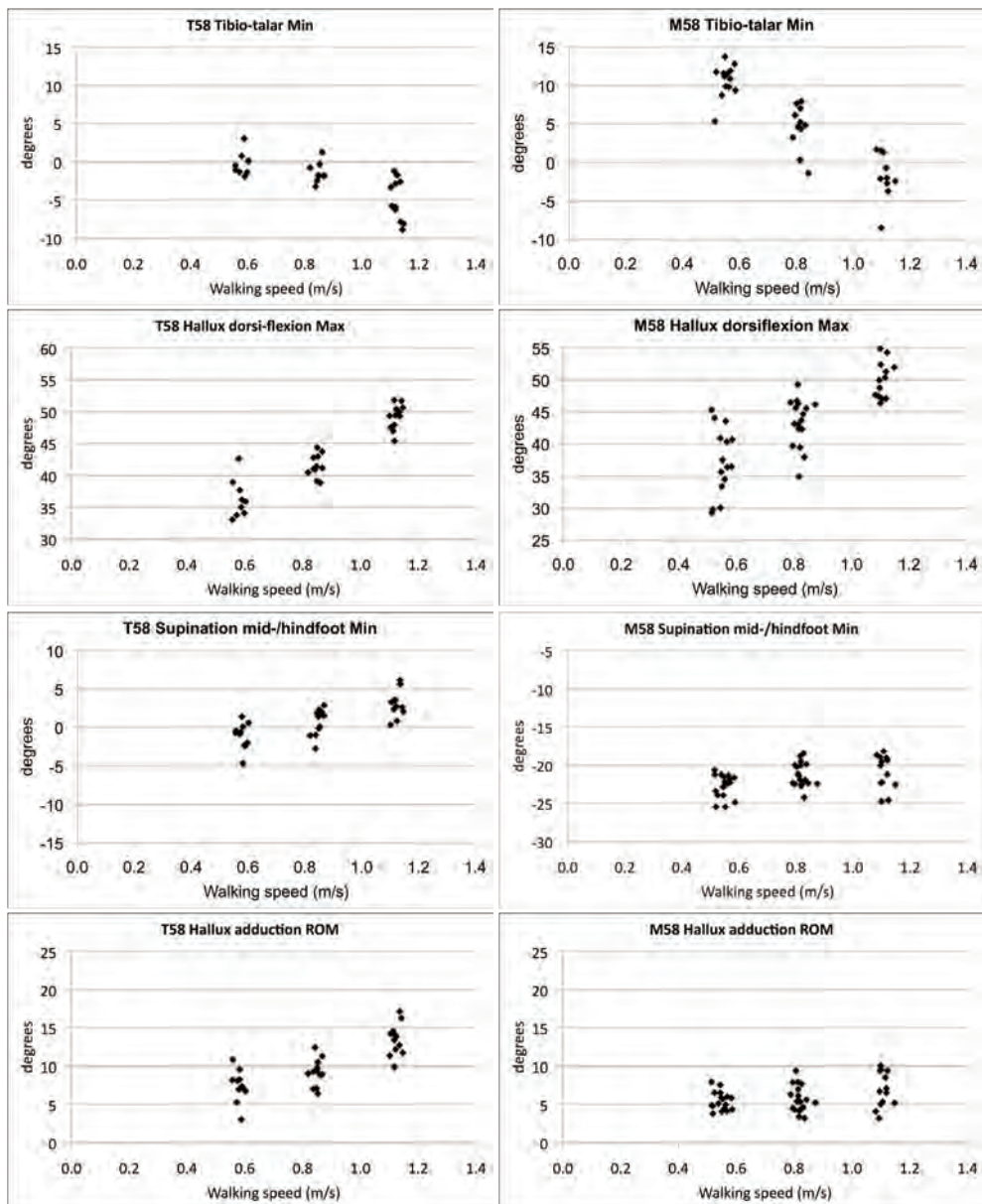


Figure 2. Typical within-subject variance of joint angle values with-in and between walking speed sessions. The values of two subjects (M58 and T58) are presented.

	Ind diff V _C -V ₅₀		Ind diff V _C -V ₇₅		Ind diff V ₇₅ -V ₅₀		Reliability
	Mean	SD	Mean	SD	Mean	SD	
Tibio-talar ROM	4.08	3.81	2.16	2.47	1.87	2.19	0.67
Tibio-talar dorsifl min	-6.21	2.93	-3.40	2.19	-2.77	1.82	0.82
Med arch ROM	1.74	2.05	0.81	1.28	0.93	1.45	0.61
Med arch min	-2.30	1.41	-1.34	1.16	-0.96	1.63	0.88
Sup Mid-/Hindfoot min	2.33	0.92	0.95	0.70	1.39	0.83	0.94
Hallux dorsifl max	9.35	3.21	4.84	2.17	4.51	2.81	0.73
Hallux add ROM	2.49	1.81	1.15	1.33	1.34	0.96	0.53
Walking speed	0.63	0.06	0.32	0.04	0.31	0.05	0.90
Stride length	0.35	0.07	0.21	0.05	0.15	0.04	0.85

Table 4: The mean and corresponding standard deviation of individual session differences (Ind diff) of those joint angle variables (degrees) that were significantly influenced by walking speed, and individual session differences of the walking speed (m/s) and stride length (m). The corresponding reliability values are presented in the last column. With V_C the comfortable walking speed session, and V₇₅ and V₅₀ the two lower walking speed sessions at 75% and 50% of V_C, respectively.

The second group consisted of the tibio-talar ROM and maximum hallux dorsiflexion, which had a moderate reliability of the data ($r=0.67$ and $r=0.73$) but high mean individual differences of 4° and 9° (V_C-V₅₀), respectively. In the third group, the minimum medial arch and midfoot supination angles had a high reliability ($r=0.88$ and $r=0.94$) with mean individual differences up to 2° (V_C-V₅₀). In the fourth group, the medial arch and hallux adduction ROM reliability was low ($r=0.61$ and 0.53) with small mean differences up to 2° (V_C-V₅₀). For the walking speed and stride length, individual differences between sessions of 0.3 m/s and 0.2 m and corresponding reliability values of 0.90 and 0.85 respectively were assessed (Table 4).

Discussion

The aim of this study was to collect and analyse foot and ankle joint kinematics in healthy subjects (30 years and older) walking at comfortable and two clinically relevant slower walking speeds. The slower speeds represent the walking speed of subjects with foot and ankle impairments resulting from various pathologies. Variation in walking speed significantly affected the foot and ankle joint ROM in the sagittal and transverse planes and it mainly influenced these joint motions at toe-off. The effect of walking speed on joint ROM

in the frontal plane was not significant, however a significant effect of walking speed on midfoot joint supination was found at mid-stance.

The joint motions assessed from the gait measurements with comfortable walking speed corresponded to the joint angle values reported by Simon (Simon et al., 2006). Variations in marker-placement are known to give variations in assessed joint angles (Carson et al., 2001, Simon et al., 2006), but to minimise such effects, one experienced tester attached the markers to the healthy subjects to prevent inter-tester variability. To prevent inter-session variability, the markers remained on the subjects during all three sessions. Hence, the influence of marker-placement on the joint neutral position was identical for all three sessions. During the measurements, the walking speed sessions were not randomised. As the two lower walking speeds were related to the comfortable walking speed, the comfortable walking speed session was measured first. In previous observations, several participants had balance problems at the 50% walking speed. Reducing the walking speed in two steps from comfortable to 50% enabled the participants to adjust their walking more naturally. The assessed cadence and stride length values were in the range of values reported in literature (Eppeland et al., 2009, Kirtley, 2006, Murray et al., 1984).

Variation in walking speed significantly affected joint motions in the sagittal plane. The trend to increase tibio-talar dorsiflexion at mid-stance and statistically significantly decrease tibio-talar plantarflexion at toe-off at lower speeds corresponds to findings reported by Lelas, Murray and Rosenbaum (Lelas et al., 2003, Murray et al., 1984, Rosenbaum et al., 1994, van der Linden et al., 2002). We found significant differences in tibio-talar plantarflexion at toe-off between all three walking speed sessions, and taking into account the results from Lelas et al. and Van der Linden et al. who analysed even more walking speeds, these differences are not linear.

In our study, an increased flattening of the medial arch with decreased walking speed was observed at toe-off. This finding may be explained by the supporting effect of the plantar fascia and the M. tibialis anterior on the medial arch at toe-off: Tension on the plantar fascia, which extends from the calcaneus to the base of the toes, may result from hallux dorsiflexion and M. gastrocnemius and M. soleus loading. The reduction in peak hallux dorsiflexion at toe-off from 47° to 37° for lower walking speeds respectively reduces the tension on the plantar structures and yields a slight flattening of the medial arch (Cheng et al., 2008, Carlson et al., 2000, Garcia et al., 2008). The M. gastrocnemius and M. Soleus relax just before toe-off for all walking speeds, hence their contribution to plantar fascia tension is nihil

at this phase (Chiu and Wang, 2007, Hof et al., 2002, Murray et al. 1984, Neptune et al., 2008). The M. tibialis anterior starts loading the foot just at toe-off at the lower walking speeds, but much before toe-off and more intensely at higher walking speeds and hence supports the medial arch around toe-off at the higher walking velocities (Hof et al. 2002, Perry, 1992).

The hallux dorsiflexion at toe-off increased with walking speed. An increase in hallux dorsiflexion at toe-off enables a larger stride length, which corresponded with our temporal spatial findings.

The frontal plane motion of the hind foot was not significantly affected by the walking speed, even though the hindfoot is initially slightly (0.5° - 1°) less everted for lower walking speeds. The M. tibialis anterior loading increases with increasing walking speed and restrains the increased external eversion moment. Significant differences in frontal plane motion only occurred in the mid foot and took place at foot loading or at mid stance but the range of motion did not differ significantly. During the loading phase of the foot, significant increases in peak supination angles of the midfoot with respect to hindfoot were found with increasing walking speed. Activity of the M. Tibialis anterior is increased for higher walking speeds at foot loading (Neptune et al., 2008) and may, due to its distal attachment to the mid-tarsal bones, increase the supination motion of the midfoot with respect to the hindfoot. Likewise, significantly less pronation motion of the forefoot with respect to mid foot occurred during mid-stance for higher walking speed. Additionally, the visco-elastic properties of the passive structures may result in increased joint stiffness for the higher walking speeds.

In the transversal plane, significant differences in joint ROM between walking speeds were only observed for the hallux adduction. More forefoot adduction motion with respect to the hind foot and more external leg rotation were observed at higher walking speeds, but were only significant between the two lower speed sessions. Perry describes the initial leg internal rotation with respect to the hind foot as a mechanism to align the ankle joint with the forward motion of the body centre of mass (Perry, 1992). At the end of the stance phase an external rotation of the leg enables the forefoot to remain on the floor while the centre of mass progresses forward. In this study, increased hallux adduction and leg rotation were related to increased stride length.

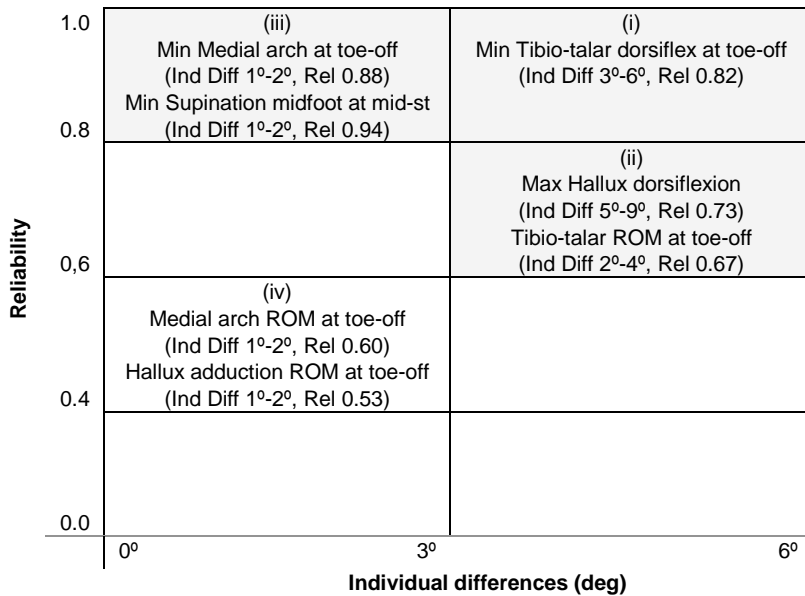


Figure 3: Clinically-relevant-matrix based on individual session differences and reliability: The grey areas were considered clinically relevant in our study.

An increase in MT I-V angle was expected at the higher walking speeds during terminal stance due to increased loading on the forefoot to generate more push-off compared to lower walking speeds (Rosenbaum et al., 1994). The contrary, however, was observed. A possible explanation for this finding could be that the increased hallux dorsiflexion and higher calf muscle activity, which result in more tension on the plantar fascia, may be able to restrain forefoot spreading for the higher walking speeds. Other factors that may contribute are increased intrinsic muscle tension and increased joint stiffness, which results from the visco-elastic soft tissue properties.

Statistically significant differences in mean joint angle values were limited to 1° to 9° between the comfortable and lower walking speeds and these differences corresponded to 5% to 20% of the joint ROM. To evaluate the clinical relevance of the results, the individual joint angle differences between the sessions and the corresponding reliabilities were analysed and the joint angle variables were assigned to one of four groups (Fig. 3). In the first and second group, (i) and (ii) in figure 3, the effects of the walking speed were assumed to be clinically relevant: The reliability was moderate to good and the mean individual differences were larger than the 3 to 5 degrees, which were suggested by Nester et al. to be

clinically relevant (Nester et al., 2007). In the third group the individual differences were small (1° - 2°) but the reliability was very high and the effects of walking speed were assumed to be clinically relevant. In the fourth group, the individual differences were small and the reliability values were low. The variance of the data and inconsistent individual differences resulted in such inconsistent values that, even though the mean joint angle values between the walking speed sessions are significantly different, these results were not considered clinically relevant.

Gait abnormalities in joints of subjects suffering from pathologies affecting the foot and ankle may be caused, to some extent, by their reduced walking speed. Clinical observations in combination with kinematic comparisons to healthy subjects walking at matched speeds (Van der Linden et al., 2002) could provide more insight in the effects of such pathologies on gait kinematics.

Conclusion

Foot and ankle joint kinematics of healthy subjects (30 years and older) were recorded at comfortable and two slower walking speeds, which represent the walking speed of subjects with foot and ankle impairments resulting from various pathologies. The walking speed had a clinically relevant influence on the minimum midfoot supination angle during the mid-stance phase, and on the minimum tibio-talar plantar-flexion angle, the tibio-talar flexion range of motion, the minimum medial arch angle and maximum hallux dorsiflexion angle during the toe-off phase. Future studies that aim to improve the understanding of the effects of pathologies on foot and ankle kinematics of impaired subjects, should take the walking speed into account.

Acknowledgements

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Appendix A: Assessment of the temporal parameters

To assess temporal factors from the marker recordings initial heel contact and toe-off can be defined by attaching a label to that specific frame in VICON workstation. In our study, initial heel contact was defined as the moment when the heel contacts the floor, and toe-off was defined as the moment when the greater toe leaves floor contact. The motion of the dorsal calcaneus marker (CCL) and the greater toe marker (HLX) in the sagittal plane were used as reference. For each trial the heel contact and toe-off of both feet were labelled by hand.

The elapsed time between two labels is assessed from the elapsed number of frames between two labels divided by the camera frequency (frames per second). Stride time was defined as the time elapsed between heel contact and the next heel contact. Foot-off, opposite foot-off and opposite foot strike as % gait cycle were assessed by dividing the elapsed number of frames from initial heel contact to foot-off, opposite foot strike, opposite foot off, respectively, by the number of frames between heel contact to next heel contact (gait-cycle) of that occurring step.

From the markers MCL, LCL and CCL a centre point of the calcaneus CCC was assessed. The stride length was calculated from the difference in x-axis location of the CCC at heel contact to the next heel contact. The step length was calculated from the difference in CCC x-axis location at heel contact and opposite foot heel contact. Stride width was defined as the difference in y-axis location of the CCL at initial heel contact and the y-axis location of the opposite heel at opposite heel contact. The walking speed was assessed by dividing stride length by stride time.



5

**Foot and ankle kinematics in
rheumatoid arthritis cannot only be explained
by alteration in walking speed**

Dubbeldam R, Nene AV, Buurke J, Groothuis-Oudshoorn CGM, Baan H, Drossaers-Bakker KW, Van de Laar MAFJ, Hermens H. Foot and ankle joint kinematics in rheumatoid arthritis cannot only be explained by alteration in walking speed. *Gait Posture* 2011; 33: 390-5

Abstract

Background. Rheumatoid arthritis (RA) manifests itself in the foot and ankle of RA patients. The foot and ankle joint kinematics of these patients differ from that of healthy subjects. However, the factors that lead to these differences are not yet fully understood. The aim of this study was to analyse the effect of walking speed and the disease process on foot and ankle joint kinematics of RA subjects.

Methods. Gait recordings of 23 RA and 14 age-matched healthy subjects were performed and their foot and ankle joint kinematics were analysed during the stance phase of the gait cycle. Stance phase characteristics of the group of RA subjects and of the group of healthy subjects were compared. The healthy subjects walked at 100% (V_c), 75% (V_{75}) and 50% (V_{50}) of their comfortable walking speed. In a multi-level linear model significant differences between the two groups due to the factors walking speed and the disease process were analysed.

Results. The hindfoot dorsiflexion, medial arch and hallux abduction motion at single-stance and toe-off were only influenced by the walking speed. The hallux maximum flexion at toe-off and the midfoot supination at single-stance were influenced by both the walking speed and the disease process. The hindfoot eversion motion at single-stance was only influenced by the disease process.

Conclusion. In conclusion, the reduction of walking speed of RA subjects compared to healthy subjects does not explain all of the observed foot and ankle kinematics differences.

Introduction

Several pathologies, such as rheumatoid arthritis (RA) and diabetes mellitus, lead to foot and ankle impairments. Improved gait recording technologies and the development of foot and ankle kinematic models have made it possible to study the effect of these pathologies on foot and ankle kinematics¹⁻⁸. In general, kinematic data of impaired, mostly older, subjects are compared to those of relatively young and healthy subjects and the results are used to assess the effects of pathologies on foot and ankle kinematics. Besides the kinematic differences between healthy and impaired subjects, the temporal factors such as walking speed and double stance phase are different: Walking speed is slower and stride length is smaller, while stance phase, including double stance phase, is longer for subjects with foot and ankle impairments. Besides the disease process, these temporal factors may influence foot and ankle kinematics and this makes it difficult to deduce the effects of the disease process on foot and ankle kinematics.

The effect of walking speed on the foot and ankle kinematics of healthy subjects has been studied^{5,9,10}. It was observed that, among others, a lower walking speed resulted in significantly less ankle plantar-flexion, medial arch flattening, hallux dorsi-flexion and hallux abduction motion at toe-off and less pronation of the midfoot at mid-stance. Similar and other changes in foot and ankle kinematics have been observed when comparing RA subjects to healthy subjects^{1,2,4-8}. However, in these studies, both groups walked at their own comfortable walking speed: The RA subjects walked slower than the healthy subjects. Hence, part of the observed kinematic differences might be attributed to the difference in walking speed. By comparing the effects of walking speed on foot and ankle kinematics of healthy subjects to the kinematics of RA subjects, the contribution of the walking speed to the kinematic differences in RA subjects may be analysed.

The aim of this study was to differentiate between the effect of the disease process and walking speed on foot and ankle kinematics of RA subjects. We hypothesised, that not all changes in RA kinematics could be explained by the walking speed alone.

Methods

Subjects

Fourteen healthy subjects without foot and ankle complaints and twenty-one age-matched RA patients (out-patient clinic) with varying foot and ankle complaints participated in this study. An informed consent was obtained from all subjects prior to participation. All patients were older than eighteen years, met the 1987-ACR criteria for rheumatoid arthritis, and had not undergone orthopedic surgery on their feet and ankles. This study received ethical approval from the local medical ethics committee. The RA subjects had a mean disease duration of 9 years (SD 7 years), a mean Larsen score¹¹ of 1.6 (SD 1.7) and a mean Sharp van der Heijde (SVH) foot score¹² of 13 (SD 12).

Protocol

Gait analysis was performed using a 6-camera video-based (1.3 megapixel, 100 Hz) motion analysis system (Vicon Nexus, Vicon Motion Systems, Oxford Metrics Group, UK). Nineteen infra-red reflective markers were attached to the lower limbs of the subject according to the method described by Simon¹³ (Fig. 1). For the RA patients one foot was measured according to the above protocol, while walking at a comfortable walking speed. For each healthy subject, the right foot was measured in three sequential sessions⁹. Initially, the subjects were asked to walk at their own comfortable walking speed (V_c). In the second and third session the subjects were asked to walk at a predefined speed of 75% (V_{75}) and 50% (V_{50}) of the comfortable walking speed, respectively. The walking speed was computed from the recordings, but to adjust the walking speed, it was also measured manually during the recordings and communicated to the test subject. During each session, the recording was continued until at least 7 trials were obtained for each walking speed with less than 5% variance and within 5% of the predefined walking speed.

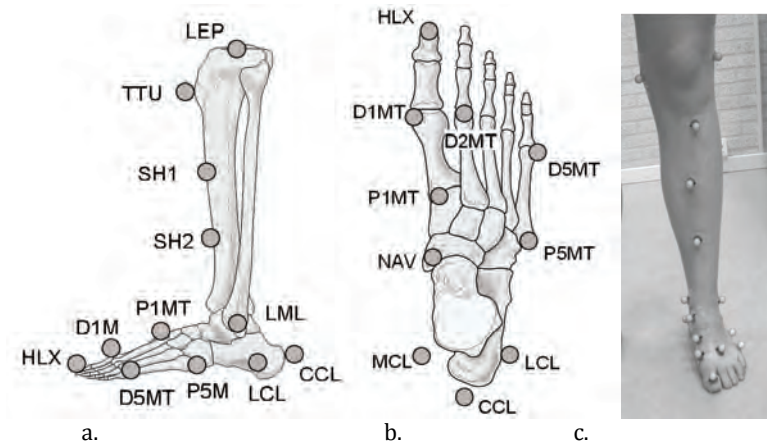


Figure 1: a. Lateral view and b. top view of marker positions on the foot and leg¹³; c. Leg with markers

Sagittal plane	Frontal plane	Transverse plane
Tibio-talar dorsiflexion	Subtalar eversion	Leg/hindfoot external rotation
Medial arch	Mid-/hindfoot supination	Fore-/hindfoot adduction
Hallux flexion	Fore-/midfoot supination	Metatarsal (MT) I-V angle
		Hallux adduction

Table 1: Overview of assessed kinematic parameters arranged by main plane of motion.

Data analysis

The temporal parameters walking speed, step length, stride length, stride width, stride time and double stance phase were assessed for each subject from the marker co-ordinate recordings in a special LabVIEW script (V7.2, National Instruments). This script was also used to normalise the data to the stance phase using the specified initial contact and toe-off indications in Vicon Nexus (Vicon Motion Systems). The foot and ankle joint kinematic parameters shown in Table 1 were calculated using the method developed by Simon¹³.

For each subject, and in case of the healthy subjects also for each session, the mean value of the joint angles motion, as function of the % stance phase, was assessed using 5 to 7 trials. The stance phase was split into three parts: foot-loading, single-stance, and toe-off. Foot-loading was defined from initial heel contact to opposite foot toe-off (double-stance),

single-stance was defined from opposite foot toe-off to opposite foot heel contact, and toe-off was defined from opposite foot heel contact to foot toe-off (double-stance). For each subject the maximum, the minimum and the range of motion (ROM) values were calculated for each joint for each part of the stance phase. The ROM was defined as the maximum minus minimum angle. Previous studies have shown that walking speed significantly influences ankle plantarflexion, medial arch, hallux dorsiflexion and hallux abduction motion during toe-off. These joint values were plotted for all healthy and RA subjects and compared optically. From the plots it was deduced if walking speed could be the only factor to explain the differences between RA and healthy subject kinematics.

In a second step, the individual contributions of the disease process and walking speed on the foot and ankle kinematics of RA subjects were analysed in more detail. The assessed ROM of the foot and ankle joints during foot-loading, single-stance and toe-off were taken into account in the analysis together with the following minimum and maximum joint angle values, which have been reported in literature to be affected by RA:

- maximum tibio-talar dorsiflexion at heel contact,
- minimum and maximum tibio-talar dorsiflexion at toe-off,
- maximum hallux dorsiflexion at toe-off,
- minimum navicular bone height during single-stance,
- minimum fore-/hindfoot supination during single-stance.

Statistical analysis

Statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). To test the normal distribution of the temporal and joint ROM variables, a Shapiro-Wilk test was performed for each group. A multi-level linear model was used to analyse the effects of walking speed and the disease process on the temporal variables and the joint kinematics. The estimates of fixed effects were assessed and the level of significance was set to $p < 0.05$. Sequential rejective Bonferroni correction was used to adjust for multiple testing.

Results

The temporal and joint variables were normally distributed according to the Shapiro-Wilk test. An independent-samples test indicated no significant difference in age between the healthy subjects and the RA group (Table 2). Both walking speed and disease process significantly ($p < 0.05$) influenced stride time, cadence, foot-off, double-stance phase, and step length. Walking speed alone influenced stride length, the disease process alone influenced stride width. The mean walking speed of the RA group was about 60% of the comfortable walking speed of the healthy subjects.

	RA subjects	Healthy subjects			Sign. of Estimates	
					Multi-level linear model ($p < 0.05$)	
	V_C	V_C	V_{75}	V_{50}	RA	V
Number of subjects	21	14				
Gender (male / female)	4m, 17f	3m, 11f				
Age (years)	46.6 (12.8)	41.6 (8.5)				
Walking speed (m/sec)	0.78 (0.14)	1.28 (0.13)	0.97 (0.11)	0.65 (0.08)		
Stride time (sec)	1.3 (0.1)	1.1 (0.1)	1.2 (0.1)	1.5 (0.1)	0.003	0.000
Foot-off (% gait)	68.1 (2.9)	62.1 (1.8)	64.7 (1.7)	67.2 (1.8)	0.005	0.000
Double-stance (% gait)	35.7 (6.2)	23.5 (3.6)	27.8 (3.2)	33.1 (4.1)	0.002	0.000
Stride length (m)	1.00 (0.15)	1.34 (0.10)	1.14 (0.09)	0.99 (0.09)	0.069	0.000
Stride width (m)	0.13 (0.03)	0.08 (0.02)	0.08 (0.09)	0.07 (0.02)	0.000	0.200
Step length (m)	0.48 (0.08)	0.68 (0.06)	0.60 (0.07)	0.50 (0.09)	0.002	0.000
Cadence (steps p. min)	93 (8)	115 (8)	102 (7)	79 (7)	0.000	0.000

Table 2: Overview of the mean and corresponding standard deviation of age and temporal-spatial variables for the RA and healthy subjects. With V_C , V_{75} and V_{50} representing 100%, 75% and 50% of the comfortable walking speed, respectively. In the last 2 columns, the statistical significance levels of the effects (Estimates in multi-level linear model, SPSS) of RA or V on the temporal factors can be found.

For joint angles that are known to be influenced by walking speed in healthy subjects, the differences between RA and healthy subjects could not be explained by walking speed alone (Fig. 2 a,b). The RA subject joint angle values that overlapped the values of the healthy subjects, are predominantly influenced by walking speed. Such was the case for the minimum tibio-talar angle at toe-off (Fig. 2a), However, for several joints, such as the hallux flexion (Fig. 2b), a visible deviation from the healthy subject values was observed for the RA values. In these cases, walking speed alone was not able to explain the observed differences between RA and healthy subjects.

The individual effects of walking speed and the disease process on foot and ankle kinematics of RA subjects were studied in more detail in a multi-level linear model (Table 3). The tibio-talar plantarflexion, medial arch collapse and hallux abduction were significantly influenced by walking speed alone (Fig. 2 a,c,d). Hallux dorsiflexion, navicular bone height, midfoot supination and leg rotation were influenced by both walking speed and the disease process. Hindfoot eversion was the only motion that was influenced by the disease process alone and not by walking speed. The joints moving in the sagittal plane, ankle flexion, medial arch and hallux flexion, were affected by walking speed during single-stance and toe-off. Also the motion of the navicular bone was significantly affected by walking speed during the end of single-stance and beginning of toe-off. The midfoot supination motion was affected by walking speed during single-stance, while the more distal forefoot and hallux abduction motions were affected by walking speed during the toe-off phase. Leg rotation was affected by walking speed during foot-loading and toe-off. The disease process significantly influenced the subtalar joint and midfoot supination during single-stance (Fig. 2 e,f): RA subjects had less range of motion compared to the healthy subjects walking at comfortable and lower walking speeds. At toe-off, the disease process significantly reduced peak hallux dorsiflexion. Less leg rotation motion with respect to the hindfoot was observed for the RA subjects, but this was not statistically significant. The mean motion of the navicular bone of RA subjects during stance coincided with the navicular motion of healthy subjects walking at a lower speed. However, as the RA subjects place their opposite-foot sooner than healthy subjects, the range of motion of the navicular bone during single-stance is smaller for RA subjects compared to healthy subjects.

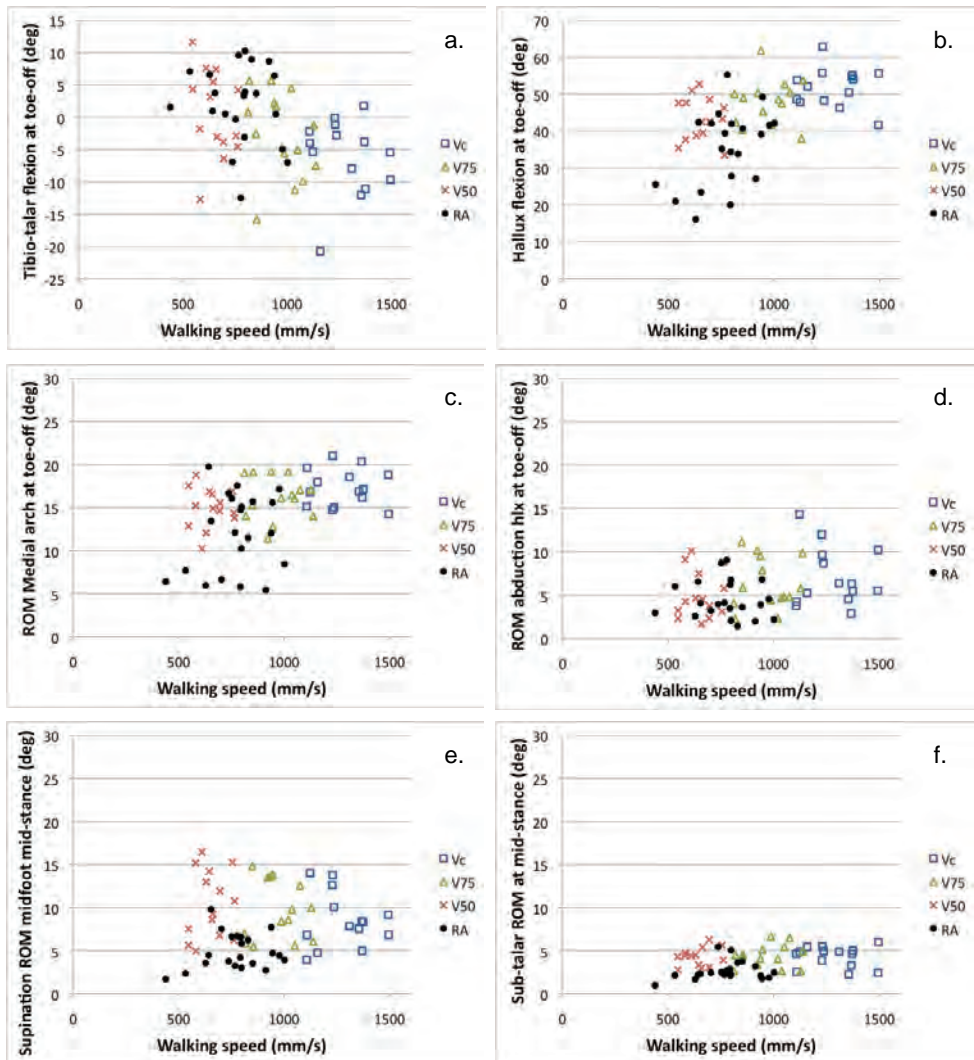


Figure 2: Joint angle values for the healthy group (for each walking speed: Vc, V75 and V50) and the RA group (RA); a. Minimum tibio-talar plantarflexion at toe-off; b. Maximum hallux dorsiflexion at toe-off; c. Medial arch range of motion at toe-off; d. Hallux abduction range of motion at toe-off; e. Forefoot supination range of motion at single-stance; f. Subtalar eversion range of motion at single-stance.

Joint	Model factor	Foot- loading		Single-stance		Toe-off		
		ROM1	Max1	ROM2	Min2	ROM3	Max3	Min3
Tibio-talar dorsiflexion	RA	0.1196	0.0477	0.0092		0.0825	0.5563	0.2157
	V	0.6335	0.0305	0.0000		0.0000	0.0001	0.0000
Medial arch	RA	0.0862		0.0034		0.0136		
	V	0.0625		0.0000		0.0000		
Hallux dorsiflexion	RA	0.4789		0.0002		0.3174	0.0018	
	V	0.0206		0.0000		0.0000	0.0000	
Navicular height	RA	0.0127		0.0000	0.9099	0.0458		
	V	0.0031		0.0000	0.9604	0.5369		
Subtalar eversion	RA	0.5667		0.0002		0.4401		
	V	0.7453		0.4054		0.5267		
Mid-/hindfoot supination	RA	0.7831		0.0000	0.4200	0.9770		
	V	0.6914		0.0001	0.0000	0.1329		
Fore-/midfoot supination	RA	0.7758		0.0761		0.1622		
	V	0.0445		0.0051		0.0005		
Fore-/Hindfoot abduction	RA	0.6153		0.3428		0.1035		
	V	0.1799		0.6292		0.0236		
MT I-V	RA	0.0276		0.7099		0.0241		
	V	0.6004		0.9758		0.9583		
Leg-hindfoot rotation	RA	0.0095		0.7860		0.0073		
	V	0.0018		0.4464		0.0010		
Hallux abduction	RA	0.8130		0.0208		0.2109		
	V	0.2878		0.4604		0.0000		

Table 3: Significance levels of the estimate of fixed effects in the multi-level linear model of the independent factors walking speed V and disease process RA on joint angle values (ROM, max, min) during the three parts of the stance phase (Foot-loading, single-stance and toe-off). In bold, the statistical significant effects of V and RA after sequential rejective Bonferroni correction ($p < 0.05$) are given.

Discussion

Foot and ankle kinematics of 21 RA subjects have been assessed and compared to the kinematics of healthy subjects at comfortable and lower walking speeds. For several joints, the joint motion of RA subjects was comparable to that of healthy subjects walking at comparable speed. But, as hypothesised, the factor walking speed alone was not able to explain all the differences in foot and ankle kinematics observed between RA and healthy subjects.

The lower walking speed of RA subjects is an effect associated with the disease process. In general, RA subjects walk at a lower speed with smaller step length while their cadence is slightly lower to that of healthy subjects walking at comfortable speed^{1,2,4,5,14}. Our spatio-temporal findings were in the range of values reported in literature. After correction for walking speed, Eppeland et al.¹ reported a smaller step length and higher cadence for RA subjects compared to healthy subjects, while no differences were observed in stance duration. The above findings coincide with the observed effects of the disease process on spatio-temporal parameters in our multi-level model. From both studies it can be concluded that the smaller step length of RA subject observed in other studies^{2,4,5,14}, is not only associated with their lower walking speed: RA subjects increase their cadence while reducing their step length compared to healthy subjects walking at similar speed.

For those joints where the kinematic differences between RA and healthy subjects could be attributed to the walking speed alone, the RA joint motion pattern is normal compared to healthy subjects. No significant differences were observed between the joint motion of the RA and healthy subjects walking at a comparable low speed for the following joint motions at toe-off: the ankle plantarflexion, the medial arch motion and the hallux abduction motion. The alterations in these joint motions in RA subjects are initially the consequence of the alteration in walking speed and are not caused directly by local disease factors such as swelling, pain or deformation. Several findings in the literature, which observe relationships between walking speed, foot angle at toe-off, first metatarso-phalangeal (MTP1) joint range of motion and pressure, and foot pain support these conclusions^{5,10,14-16}. In healthy subjects lower walking speeds are related to lower peak pressures under the MTP1 and the hallux¹⁰. Van der Leeden et al.¹⁶ found a negative relationship between peak pressure under the forefoot of RA subjects and the time needed to walk 10 m, but it was not statistically significant. The relationships between MTP 1 and hallux peak pressure and the 10 m

walking time were however not analysed. Morag and Cavanagh¹⁵ found a relationship between dynamic ankle joint range of motion, calcaneal inclination (which can be considered equivalent to first metatarsal inclination and both are indicators for medial arch height) and Choparts angle with peak MTP I pressure during walking of healthy subjects. Similar findings were reported by Laroche et al.⁵, who observed lower walking speeds and lower foot angle at toe-off for RA subjects with less MTP1 range of motion. MTP1 pressure was not measured in their study. In RA, 50-70% of the patients complain of forefoot impairments early on in the disease process¹⁷ and it may well be that RA subjects lower their walking speed and hence reduce their heel rise and flatten their medial arch to lessen the peak pressure under their MTP 1.

Several joint motions were influenced by both walking speed and the disease process or were solely influenced by the disease process. For these joints, abnormal RA joint motion was observed compared to the healthy subjects walking at comparable low speeds. Hallux dorsiflexion at toe-off was lower for healthy subjects for the smaller walking speeds, but RA subjects had even less hallux dorsiflexion at toe-off. Swelling and pain of the MTP 1 joint have been reported frequently and both features continue with increasing MTP 1 erosion, stiffness and alignment from disease onset¹⁷. Although a lower walking speed results in less required hallux dorsiflexion and decreased pressure under the MTP 1, the RA subjects show even less hallux dorsiflexion to further reduce the pressure under their MTP 1 or to compensate for their reduction in MTP1 stiffness, which may be caused by local erosion, swelling or pain. Findings in the literature support the above-mentioned theory^{7,15,18,19}. Turner and Woodburn reported the lowest hallux dorsiflexion at toe-off and highest forefoot peak pressure for a group of RA subjects with primarily forefoot damage compared to a RA group with primarily hindfoot damage and control subjects⁷. Also in healthy subjects the MTP 1 range of motion during gait has been related to peak pressure under the hallux¹⁵. Laroche et al.¹⁸ studied the effect of hallux mobility in RA subjects. They found a linear relationship between maximal active hallux dorsiflexion whilst sitting and walking speed but not between pain during gait and walking speed. In a study performed by Canseco et al.¹⁹, pre-surgical subjects with primary complaint of hallux rigidus who demonstrated pain or discomfort as well as limitation of motion, the effects of local MTP 1 impairment has been reported: The hallux rigidus subjects showed less hallux dorsiflexion at toe-off compared to their healthy subjects.

The supination motion of the midfoot during single-stance was influenced by both the walking speed and the disease process. The disease process results in synovitis and erosion of the RA midfoot and hindfoot joints and influences the stiffness of the tarsal joints , which may result in less available motion. The subtalar eversion motion during single-stance was only influenced by the disease process and was lower for RA subjects compared to healthy subjects. Turner and Woodburn ⁷ showed an increased hindfoot eversion offset for RA subjects compared to healthy subjects, especially for those RA subjects with hindfoot structural damage. The effect of RA on the hindfoot eversion range of motion was not reported. In a severely impaired RA population, Khazzam et al. ⁴ found less hindfoot eversion motion during foot loading, single-stance and toe-off compared to healthy subjects. Impairments to the subtalar joint such as swelling, pain and erosion may result in functional and structural stiffness and mal-alignment of the hindfoot. Furthermore, impairments to the posterior tibialis tendon may play a role in the RA hindfoot motion. Gait characteristics of subjects with posterior tibialis tendon dysfunction show similarities to those of RA subjects: an offset and reduction of hindfoot eversion, flattening of the medial arch and an offset in forefoot abduction ^{20,21}.

Limitations

The number of healthy and RA subjects used in this study is limited. Some of the observed differences such as a less leg rotation may become significant if the number of subjects increase. Furthermore, the disease severity of the RA subject may be of influence on the model outcome. The RA subjects in this study reported moderate disease impairments. More severely impaired RA subjects with more structural damage to their foot and ankle may show abnormal joint motion in other, additional joints of the foot or ankle.

Conclusion

Foot and ankle kinematics of 21 RA subjects have been assessed and compared to the kinematics of 14 healthy subjects walking at comfortable and lower speeds. As hypothesised, walking speed alone is not able to explain the differences in foot and ankle kinematics observed between RA and healthy subjects. In addition to the effects of lower walking speed, other RA factors such as disease activity, pain and joint damage result in abnormal joint function compared to healthy subjects, and consequently may influence foot

and ankle joint kinematics too. In our study, the disease process influenced the hallux dorsiflexion at toe-off, the hindfoot eversion motion at single-stance and the minimum supination of the midfoot at single-stance. Analysis of disease factors, which cause the reduction in walking speed and abnormal joint motions, might provide further insight in understanding the effect of RA on foot and ankle kinematics.

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6

**Kinematic coupling relationships exist
between non-adjacent segments of
the foot and ankle of healthy subjects**

Dubbeldam R, Nester C, Nene AV, Hermens HJ, Buurke JH. Kinematic coupling relationships exist between non-adjacent segments of the foot and ankle of healthy subjects. *Gait Posture* 2012, <http://dx.doi.org/10.1016/j.gaitpost.2012.06.033>

Abstract

Introduction Pathologies of foot and ankle structures affect the kinematics at the site of the impaired structure but also influence kinematics elsewhere in the foot and ankle. An understanding of kinematic coupling relationships in the foot could provide insight into mechanisms that explain differences in foot and ankle kinematics between healthy and pathological subjects. The aim of this study was to explore foot and ankle kinematic coupling relationships between adjacent and non-adjacent segments of healthy subjects and evaluate individual variability of and effect of walking speed on these relationships.

Method Gait of 14 subjects was recorded at comfortable and two slower walking speeds to assess individual foot kinematics during stance phase. A qualitative evaluation of the coupling relationships was made using angle-angle plots to determine their consistency, i.e. changes in movement direction of each segment occurred at the same time and the plot returned along the same line after the turning point. The Pearson correlation coefficient of determination (R^2) was used to provide a quantitative evaluation of coupling. Individual variability was assessed with the coefficient of variation (CV). The Friedman-test was used to test the effect of walking speed.

Results Consistent coupling relationships were observed between hindfoot in/eversion and hallux plantar/dorsiflexion (R^2 0.7, CV 0.2), between hindfoot in/eversion and forefoot ab/adduction (R^2 0.5, CV 0.3) and between leg rotation and midfoot collapse/elevation (R^2 0.5, CV 0.4). Less or non-consistent coupling relationships were observed between the other studied segments. Walking speed significantly influenced coupling relationships between hindfoot and midfoot.

Introduction

Pathologies of foot and ankle structures affect foot and ankle kinematics during gait. For example, first metatarsal-phalangeal (MTP-I) joint stiffness^{1,2}, ankle joint arthrosis³ and ankle joint arthrodesis^{4,5} influence kinematics at the affected joint. However, these localised pathologies also affected kinematics elsewhere in the foot and ankle. This may be explained by the fact that several active and passive foot structures cross multiple foot and ankle joints. Whilst passive and active structures attached to adjacent bones control the motion between these adjacent bones, passive and active structures attached to non-adjacent bones are able to influence the motion of non-adjacent bones. Passive structures such as ligaments and fascia restrain motions, while external loading and muscles move and control motions of the bones. These guiding mechanisms result in coupling of adjacent and non-adjacent bone motions. Understanding this coupling may provide insight into the full kinematic effects of localized pathologies.

Our knowledge of kinematic coupling in the foot during gait is relatively limited. Using bone-attached-markers Wolf et al. identified transverse and frontal plane coupling between adjacent and non-adjacent (mid-) tarsal bones⁶. Foot models have been used to assess coupling between different foot segments, rather than anatomical joints. Continuous coupling relationships between adjacent segments of the leg, hindfoot and forefoot have been described but not between non-adjacent segments⁷⁻¹⁰. Several reports suggest that hallux motion is related to static hindfoot eversion during standing and is influenced by a change in hindfoot motion due to a foot orthosis^{11,12}. However, Halstead et al. found that maximum hindfoot eversion and maximum toe flexion during gait did not correlate strongly ($r=0.47$)¹³. It should be noted though, that Halstead used discrete angular values from specific instances in time rather than investigating the continuous motion relationship throughout stance.

A common impact of foot and ankle pathologies is reduced walking speed, which itself affects foot and ankle kinematics^{2,14,15}. Walking speed may affect coupling due to differences in muscle activation patterns and external loading or due to visco-elastic behaviour of passive structures. As a musculoskeletal disease may influence both foot structures and walking speed, it is difficult to deduce their separate effects on joint coupling when investigating impaired subjects. It is thus important to understand the effect of walking speed on coupling in healthy feet prior to interpreting data from feet affected by musculoskeletal disease.

The aim of this study was to explore coupling between the hallux, forefoot, midfoot, hindfoot and leg in healthy subjects during the stance phase of gait. As a precursor to future research in a population with rheumatoid arthritis who walk at slower speeds, the effect of walking at 75% and 50% of comfortable walking speed was investigated.

Methods

Subjects

Following ethical committee approval, 14 healthy subjects (10 females) without foot and ankle complaints and between 30 and 60 years of age gave informed consent (mean age 43, range 30-55, standard deviation (SD) 8 years).

Protocol

As this study precludes a study of people with rheumatoid arthritis, a kinematic model designed for use in population with significant foot deformity was chosen to analyse foot kinematics¹⁶. One experienced tester attached nineteen markers to the lower extremity of the subjects. For each subject, right foot kinematics were measured using a 6-camera video-based motion analysis system (Vicon, Oxford Metrics Group, UK) at comfortable walking speed (V_{100}) and at 75% (V_{75}) and 50% (V_{50}) of the comfortable walking speed¹⁴.

Data analysis

Walking speed was assessed for each step and subject from the marker coordinate recordings and kinematic data were normalised from initial contact to toe-off (Vicon Motion Systems, Oxford Metrics Group, UK)¹⁴.

Based on prior reports of foot and ankle kinematics in people with rheumatoid arthritis¹⁷⁻¹⁹ and taking into account the attachment sites of active and passive foot structures, 6 combinations of adjacent and non-adjacent segment motions were analysed: coupling between leg, midfoot and hindfoot; and coupling between hindfoot, forefoot and hallux (Table 1).

I. Kinematic coupling relationship between	II. Kinematic coupling relationship between
Leg/hindfoot rotation - Hindfoot in/eversion	Hindfoot in/eversion – Fore-/Hindfoot ab/adduction
Hindfoot in/eversion - Medial arch	Hindfoot in/eversion – Midfoot pro/supination
Leg/hindfoot rotation - Medial arch	Hindfoot in/eversion – Hallux plantar/dorsiflexion

Table 1: Overview of to be studied adjacent and non-adjacent coupling relationships.

Several methods are available to quantify coupling (appendix A). In this study, coupling was evaluated by combining simple statistical and descriptive approaches, sensitive to changes in the direction of motion, to identify strong coupling relationships that are consistent, i.e. the motion of the segments is synchronous and coupling is independent of the different phases of stance. Using angle-angle plots, the group average of one segment motion was plotted against the motion of the associated segment. To evaluate the consistency of the coupling throughout stance, the synchronicity of the change in movement direction, e.g. the hallux changing from plantarflexion into dorsiflexion, at the same instant that the hindfoot changes from inversion to eversion, and the independency of the relationship to the stance phase were described. A coupling relationship was considered consistent if the change in movement direction of each segment occurred at the same time and the plot returned along the same line after the turning point. The assumption of linear coupling was evaluated by fitting first and second order polynomial trend lines to the angle-angle plots and by assessing the goodness of fit by means of the corresponding R-squared values.

Statistical analysis

To quantify the strength of the coupling relationships, for each step and subject bi-variate Pearson correlation-coefficients (CC) were calculated (SPSS 16.0, SPSS Inc., Chicago, IL, USA). Mean subject CC values were calculated for each coupling relationship and walking speed session from which the minimum, maximum and average coefficient of determination (R^2) for the whole group for each session was derived (Microsoft® Excel® for Mac, Microsoft Corp., USA).

The average coefficient of variation (CV) was assessed for each session to analyse the individual variability of each coupling relationship. First, a Fisher transformation into Z-domain was applied to the individual subject CC values to stabilize variance for the whole range of CC values, such that the variance of CC is not related to its mean value. The

coefficient of variation for each subject and session was defined as the standard deviation of the CC divided by the mean CC (Z-domain). For each walking speed session, a group average coefficient of variation was calculated for each coupling relationship.

A Shapiro-Wilk test evaluated the normal distribution of the subject's temporal-spatial and correlation-coefficient parameters. For non-parametric coupling relationships, a Friedman test was performed to analyse the effect of walking speed using the average correlation-coefficient values (in Z-domain) for each subject and session with rejective Bonferroni correction for multiple testing. A linear mixed-model was used to analyse the reliability of the coupling relationships, which relates the individual variability to the group variation in coupling (SPSS 16.0, SPSS Inc., Chicago, IL, USA). Each step from each subject was included in the model. The reliability of the coupling correlation-coefficients was assessed by relating the individual within-subject variances to the between-subject variances and was calculated as follows: the reliability value equals the Intercept value divided by the Intercept value plus the residual value²⁰.

Results

The healthy subjects walked at an average comfortable walking speed of 1.28 m/s and 75% and 50% of the comfortable walking speed was 0.97 m/s and 0.65 m/s, respectively.

Coupling relationships

The angle-angle plots of the group average values for all 6 coupling relationships and the R^2 values of the trend lines are presented in Figure 1. A distinct synchronous directional change of motion was observed in the plots for the relationship of the leg rotation with medial arch and hindfoot in/eversion and for the relationship of the hindfoot in/eversion with hallux plantar/dorsiflexion and forefoot ab/adduction (Fig. 1 a,b,d,e). With exception of the leg rotation - hindfoot in/eversion relationship, these plots returned along the same line and a consistent motion relationship between the segments was observed. In contrast, for the relationship between the midfoot pro/supination and hindfoot in/eversion motion: the change from midfoot pronation to supination occurred earlier than the change from hindfoot eversion to inversion (Fig. 1f). Also the medial arch collapsing motion reversed to elevation before the hindfoot eversion changed to inversion (Fig. 1c). Consequently, the relationships of the

hindfoot in/eversion with the medial arch motion and the midfoot pro/supination were not consistent.

A linear trend line was a good fit for the observed consistent coupling relationships, although the coupling relationship between hindfoot in/eversion and forefoot ab/adduction could better be described as quadratic (second order polynomial) (Fig. 1 a-f).

The average coefficients of determination of the coupling relationships are given in table 2 and the corresponding coefficients of individual variation and reliability of the correlation-coefficient are given in Table 3. The strongest coupling was found between hindfoot in/eversion and hallux plantar/dorsiflexion motion: at least 70% of the variance of the hindfoot motion could explain the variance in hallux motion for each walking speed session.

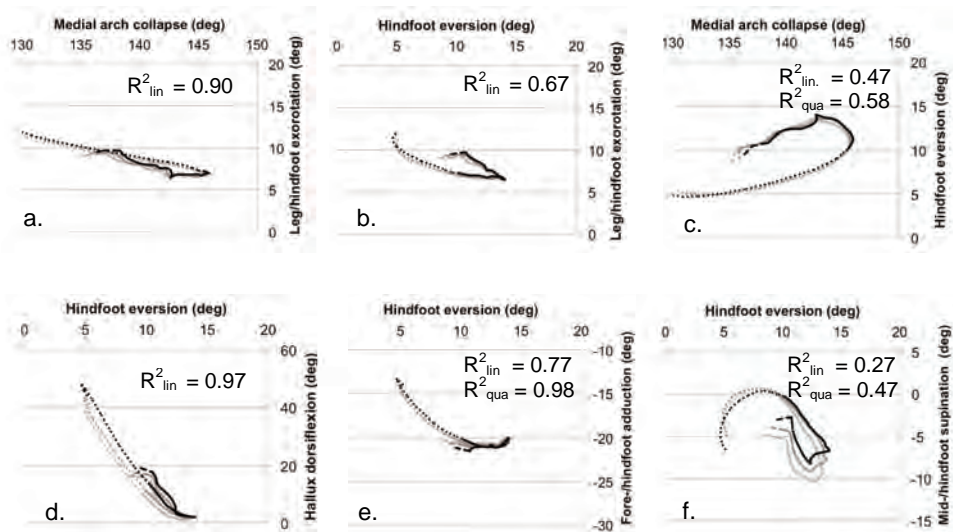


Figure 1: Angle-angle plots of the coupling relationships with linear or quadratic trend line regression coefficients (R^2_{lin} , R^2_{qua}): a. Medial arch – Leg/hindfoot rotation; b. Hindfoot in/eversion – Leg/hindfoot rotation; c. Medial arch - Hindfoot in/eversion; d. Hindfoot in/eversion – Hallux dorsi/plantarflexion; e. Hindfoot in/eversion – Fore/hindfoot ab/adduction; f. Hindfoot in/eversion – Mid/hindfoot pro/supination. The average 100%, 75% and 50% of comfortable walking speed in black, dark grey and light grey, respectively. The large striped, continuous and small striped part of the graphs represent the first double stance, single stance and second double stance phase from heel contact to toe-off.

	V ₁₀₀ (R ²)			V ₇₅ (R ²)			V ₅₀ (R ²)		
	ave	min	max	ave	min	max	ave	min	max
Leg/hindfoot rotation – Medial arch collapse	0.51	0.03	0.79	0.48	0.01	0.83	0.45	0.01	0.87
Leg/Hindfoot rotation – Hindfoot in/eversion	0.39	0.15	0.80	0.39	0.02	0.84	0.39	0.16	0.83
* Hindfoot in/eversion – Medial arch collapse	0.32	0.00	0.66	0.26	0.00	0.61	0.19	0.02	0.64
Hindfoot in/eversion – Hallux plantar/dorsiflexion	0.78	0.54	0.94	0.75	0.48	0.92	0.71	0.57	0.88
Hindfoot in/eversion – Fore/Hindfoot ab/adduction	0.51	0.24	0.84	0.50	0.24	0.82	0.48	0.29	0.75
* Hindfoot in/eversion – Midfoot pro/supination	0.22	0.10	0.73	0.32	0.04	0.73	0.42	0.00	0.85

Table 2: The group's average (ave), minimum (min) and maximum (max) coefficient of determination (R²) of the 6 assessed coupling relationships for each walking speed session. V₁₀₀ refers to the comfortable walking speed session. V₇₅ and V₅₀ refer to the sessions at 75% and 50% of the comfortable walking speed, respectively. * In first column indicates a statistically significant difference between walking speed sessions. In light grey the (quasi-) linear coupling relationships.

	Average Coefficient of Individual variation (CI)			Reliability
	V ₁₀₀	V ₇₅	V ₅₀	
Hindfoot in/eversion - Medial arch collapse	0.49	2.26	2.43	0.70
Leg/hindfoot rotation - Medial arch collapse	0.41	0.63	0.76	0.65
Leg/hindfoot rotation - Hindfoot in/eversion	0.40	0.53	0.47	0.55
Hindfoot in/eversion – Hallux plant/dorsiflexion	0.17	0.19	0.21	0.49
Hindfoot in/eversion – Fore-/Hindfoot ab/adduction	0.29	0.29	0.35	0.45
Hindfoot in/eversion – Midfoot pro/supination	0.35	0.17	1.65	0.73
Walking speed	0.02	0.02	0.04	0.90

Table 3: Average coefficient of individual subject variation and reliability of the coupling relationship correlation coefficients (in Z-domain).

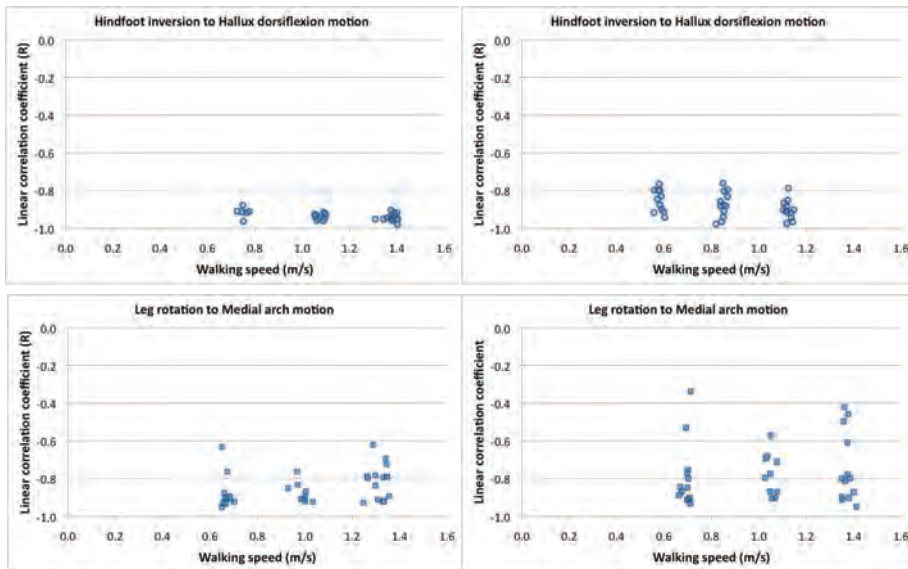


Figure 2: Top: two examples of individual variation of the correlation coefficient between the hindfoot in/eversion and hallux dors/i/plantarflexion motion. Bottom: two examples of individual variation of the correlation coefficient between the medial arch and leg/hindfoot rotation motion

Even for those subjects where this relationship was less strong, a coefficient of determination of 0.5 was apparent. The corresponding individual variation of the correlation-coefficient was small (Fig. 2) with a coefficient of variation of 0.2. For the coupling between hindfoot in/eversion and forefoot ab/adduction the average coefficient of determination was 0.5. However, lower individual values (minimum 0.24) were observed. While a linear relationship was observed between leg rotation and medial arch motion, the average coefficient of determination was 0.5, with the minimum individual value less than 0.05. The coefficient of individual variation increased from 0.4 to 0.8 with decreasing walking speed (Fig. 2). For the coupling relationship between hindfoot in/eversion and leg rotation, less than 40% of variation of one segment could explain the variation in the other with minimum individual values of 0.03. Furthermore, the individual variation was larger (0.4-0.5) compared to those of the hindfoot in/eversion relationship with the forefoot ab/adduction (0.3) or hallux plantar/dorsiflexion (0.2).

Effect of walking speed

Four of the CC values of the mean subject's coupling relationships were not normally distributed and the Friedman test was used to assess the influence of the walking speed on all coupling relationships. Statistically significant differences in coupling correlation-coefficient due to walking speed were observed for the relationships between hindfoot in/eversion motion with medial arch and midfoot pro/supination motion (Table 2). The corresponding reliabilities were high (reliability > 0.70).

Discussion

We sought to identify consistent coupling relationships that existed throughout stance between foot and ankle segments of healthy subjects. Quasi-linear coupling relationships were observed between non-adjacent foot segments, where variation of motion in one segment could explain 50% to 70% of the motion in the other segment. Statistically significant effects of walking speed on coupling relationships occurred for midfoot motion.

Kinematic coupling relationships

Consistent coupling relationships were identified between hindfoot in/eversion and forefoot ab/adduction ($R^2 = 0.5$) and hallux plantar/dorsiflexion ($R^2 = 0.7$) with small individual subject variations. The relationship between hindfoot in/eversion and forefoot ab/adduction concurs with previous reports^{7,8,10}, but may be underestimated quantitatively due to its non-linear behaviour. The strong relationship between hindfoot in/eversion and hallux plantar/dorsiflexion has not been reported before. The latter relationship has been suggested but was not found through analysis of discrete values of maximum hallux dorsiflexion and hindfoot eversion (rather than hindfoot inversion)¹¹⁻¹³.

The consistent coupling between these foot segments might be explained by function of specific structures. For example, the plantar-fascia spans the calcaneus to the head of the metatarsals and hallux and tension in the plantar-fascia is related to hallux, medial arch and hindfoot kinematics (windlass-phenomenon)²¹⁻²³. Furthermore, intrinsic hallucis muscles originate at the hindfoot and are able to influence motion of both segments. The coupling between hindfoot and hallux may offer a distinct advantage for efficient gait. The dorsiflexed position of the hallux at heel-contact, pre-tensions the plantar structures. This may result in a

functionally stiffer hindfoot joint and facilitate immediate load transfer from the leg to the floor²¹. It may also provide some resistance to hindfoot eversion and thus absorb some energy. During mid-stance, the motions of the hindfoot and hallux reverse and activation of the Tibialis posterior supports inversion of the hindfoot with respect to the leg^{24,25}. The forward progression of the centre of mass together with activation of the calf muscles and heel lift, will dorsiflex the hallux and tension plantar structures and further assist the inversion of the hindfoot prior to toe-off.

Leg rotation was not consistently related to hindfoot in/eversion motion (Fig. 1b). This finding agrees with results of other studies that report changes in the coupling between leg rotation and hindfoot in/eversion motion during different phases of stance^{7,8}. Some coupling was expected because literature indicates that passive structures alone are able to couple leg rotation and hindfoot flexion and eversion^{26,27}. A stronger ($R^2 = 0.5$) and consistent relationship was found between leg rotation and medial arch motion. The relationship between these non-adjacent segments has not been previously reported, but there is a case for the active structures having a greater influence on their coupling than passive structures. Only the tibio-navicular ligament spans the leg and midfoot segments while several active structures, Tibialis posterior and anterior and Peronei, attach the leg to the midfoot. The Tibialis posterior is able to stabilise the medial arch²⁸. Due to the medial and lateral moment arm of the Tibialis posterior and anterior and the Peronei around the ankle, the muscles provide transverse plane motion of the leg with respect to the foot²⁹.

In accordance with other studies, the frontal plane coupling relationships between hindfoot and midfoot motion were not found to be strong ($R^2 < 0.4$) with large individual variations, especially for the lower walking speed⁸⁻¹⁰. In the current study, it was observed that midfoot pronation motion changed to midfoot supination motion before the hind foot eversion motion changed to inversion during the mid-stance phase. So even if the foot is positioned on the floor, independent frontal plane motion is possible between these foot segments.

Effect of walking speed

Walking speed statistically significantly influenced coupling relationships related to the midfoot. This can be explained by the significant increase in midfoot motion in the frontal (midfoot pronation) and sagittal (medial arch flattening) plane with lower walking speeds¹⁴. Most obvious, at lower walking speeds the midfoot was able to follow the hindfoot in its

eversion motion instead of reaching the turning point to inversion motion before the hindfoot does (Fig. 1f).

Limitations

There are two important limitations to be considered. Firstly, the observed relationships between foot and ankle joints in this study are only valid for the studied activity: walking. Joint coupling depends on the performed activity and hence no conclusions should be made towards other activities²⁵. Secondly, the limitation of the correlation-coefficient approach is the fact that it assumes linear relationships. We observed several non-linear relationships and in some cases the direction of motion changed several times during stance. It would not be justifiable to use the linear correlation-coefficient as a single measure to compare such coupling relationships between joints. We addressed this problem by first evaluating the joint angle-angle graph and the linearity of the coupling relationships⁶. The correlation-method was applied to all coupling relationships to be able to compare our results with other studies, but we ensured conclusions from this study were only made for quasi-linear relationships. Apparently non-linear and not consistent motion relationships require separate investigation.

Another issue might regard the reliability of the segment motions. However, measurement reliability was good for most assessed segment motions¹⁶. Furthermore, an offset or change in pattern of an assessed segment motion would result in a shift or slope-change in the coupling graph, respectively. The character of the coupling would not change in terms of synchronicity or consistency. Hence, the effect of measurement variation on coupling is expected to be limited.

Clinical relevance

We observed consistent coupling between motion of the hindfoot, forefoot and hallux and between the leg and medial arch. The kinematic coupling of these foot segments have not been reported before and may explain how a local pathology such as first metatarsal-phalangeal joint stiffness could have wide ranging effects, such as influencing hindfoot motion. Especially in feet with more complex and multiple pathological effects, such as in rheumatoid arthritis, knowledge of coupling relationships may provide substantial insight. Furthermore, we endeavoured to relate the observed coupling relationships to several passive and active foot and

ankle structures, which join the non-adjacent segments. Disruption of one or more of these structures due to pathology yields different motion patterns^{1,3,26-28}. Understanding how pathologies affect these structures, and hence may influence the coupling between foot and ankle segments, provides insight in the observed changes in foot and ankle kinematics of impaired subjects. These insights might enable development of new treatment options.

Acknowledgements

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Appendix A: Kinematic coupling analysis methods

Several methods are available to quantify coupling. At present, the most frequently used method to analyse and quantify foot and ankle joint coupling in healthy subjects is the vector coding (coupling angle) technique⁷⁻⁹. Before this method is applied, the raw kinematic data are filtered using a 4th-order low-pass Butterworth filter to smooth the data. The coupling angle is the tangent of the joint-angle-angle plot and can be assessed at each point of the stance phase. The value and range of the coupling angle depends on the chosen assessment method. E.g. Ferber assesses an absolute tangent value, which enables quantification of the relative amount of motion between two joints but results in a loss of directional sensitivity of motion. Chang presents the coupling angle in a range of 360 degrees, which is able to define the direction of motion (in-phase, anti-phase) but may be sensitive to quantify (around 0 degrees) and analyse mean angles (in-phase is considered around 45 and around 225 degrees). A mean value, hence a linear value, is usually calculated for four sequential parts of the stance phase. The coupling angle is furthermore very sensitive to small angle changes. An exploratory study to test the applicability of this method to rheumatoid arthritis subjects indicated a high sensitivity of the assessed coupling angle to small variations in the data.

A method that proved less sensitive to such variations is the bi-variate Pearson correlation-coefficient. The correlation-coefficient represents a mean value of linear coupling and, so far, is calculated over the whole stance^{6,8}. A limitation of this method is the assumption of a linear relationship between the joint motions, which may not represent the natural behaviour of the joints considering the whole stance phase. However, the correlation-coefficient assesses the direction of motion (In or anti-phase) and its product, the coefficient of determination, is a measure of variance in motion between two joints.

A more complicated method to assess joint coupling is the continuous relative phase angle technique^{10,30}. The joint phase angle is the tangential angle of the angular displacement

and angular velocity aspect ratio ($\tan \gamma_i = \Delta \dot{\alpha}_i / \Delta \alpha_i$) and can be compared to another joints phase angle by means of a relative phase angle ($\epsilon = \gamma_1 - \gamma_2$). Before calculating the phase angles, the angular displacement and the angular velocity data need to be normalized to avoid domination of one joint over the other due to a larger range of motion or higher angular velocities. The relative phase variability appears to be a measure of agility or ability to induce co-ordination changes, which are required to adapt to a certain situation. Reduced relative phase variability has been related to lower limb impairments³⁰. However the advantage of this more complex method (with potential normalization issues) compared to the coupling angle or correlation-coefficient approaches has not yet been pointed out. In this study, our aim was to explore segment motion relationships and identify synchronous motions using descriptive and simple statistical approaches, which are sensitive to directional changes.



7

Foot and ankle kinematics in rheumatoid arthritis: the influence off foot and ankle joint and leg tendon pathologies

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Abstract

Introduction From early onset of the disease, patients with rheumatoid arthritis (RA) suffer from walking impairments. Clinically, pathologic effects of RA on foot and ankle structures have been studied, but little is known how they relate to kinematic changes during gait. The aim of this study was to explore the relationship between clinically observed pathologies of foot and ankle joints and leg tendons and the corresponding gait kinematics.

Methodology Gait of 25 subjects with varying stages of RA disease was recorded and foot and ankle kinematics were assessed. Magnetic resonance imaging was performed of each subject: first metatarsal-phalange (MTP I), midfoot and hindfoot synovitis and erosion scores and leg tendon involvement were determined. The Joint Alignment and Motion score represented daily clinical assessment. The 95% confidence intervals (CI) of the correlation coefficient of the Spearman correlation tests were used to explore the relationships between the clinical and kinematic parameters.

Results Maximum MTP I dorsiflexion at pre-swing was related to reduced MTP I passive motion, MTP I synovitis and erosion, midfoot synovitis and erosion and hindfoot erosion. Midfoot pronation range of motion during single-stance was related to subtalar alignment and Achilles tendon involvement. Hindfoot eversion range of motion during single-stance was related to subtalar alignment and peroneus longus tendon involvement. Involvement of the tibialis posterior tendon could not be identified as an independent factor influencing foot or ankle kinematics.

Conclusions Our findings suggest moderate to strong relationships between foot and ankle gait kinematics and structural pathologies.

Significance and innovations

- The results of this study are the first to demonstrate moderate to strong relationships between local foot and ankle joint pathologies and maximum first metatarsal-phalangeal dorsiflexion during gait of rheumatoid arthritis subjects. These insights may be used in future treatment and analysis.
- Our findings suggest that subtalar alignment and first metatarsal-phalangeal stiffness, both sub-scale scores of the Joint Alignment and Motion score and easily assessable in daily clinical practice, are at least moderately related to pathological foot and ankle joint kinematics. Individual monitoring of these simple clinical assessments may provide insight in foot and ankle function of rheumatoid arthritis patients during gait.
- Pathologic changes to the Achilles and peroneus longus tendon may have a moderate to strong influence on midfoot pronation and hindfoot eversion motion during the stance phase of gait, respectively. The established hypothesis of the relationships between tibialis posterior tendon pathology and midfoot and hindfoot frontal plane kinematics during gait could not be confirmed. Our findings suggest a more important relationship between the hindfoot alignment and the midfoot and hindfoot frontal plane kinematics.

Introduction

At the onset of the disease, 60% of the patients with rheumatoid arthritis (RA) suffer from walking impairments while this percentage is 40% later on in the disease¹. These impairments have been related to the effects of RA on, among others, walking speed and foot and ankle structures. Metatarsal pain, global foot pain, disease activity, foot swollen joint count and hindfoot deformity all affect and impair walking at some point during the disease process²⁻⁵. Several studies have analysed foot and ankle joint kinematics in subjects with RA during walking at comfortable speed to attain insight in gait differences compared to healthy subjects⁶⁻⁹. However, little is known about the effects of local structural pathologies on foot and ankle joint kinematics in RA subjects.

Turner analysed the effects of predominantly forefoot, hindfoot or combined deformation in RA subjects on foot and ankle kinematics and observed changes in both forefoot and hindfoot kinematics¹⁰. Laroche studied the effect of metatarso-phalangeal (MTP) stiffness on gait parameters in RA subjects¹¹. MTP stiffness was significantly related to walking speed, knee flexion and foot angle at toe-off, though the effects on foot and ankle joint kinematics were not analysed. The effects on foot and ankle kinematics of other frequently reported structural impairments such as tibialis posterior tendon involvement and ankle arthritis have been studied, but not in a RA population¹²⁻¹⁵.

A better general understanding of the effects of foot and ankle structural pathologies on foot and ankle kinematics during gait may support clinical decisions in both conservative and surgical treatment for this complex disease^{10,15-17}. In addition, for daily clinical practice a better general understanding of the relationship between easy assessable clinical scores and gait kinematics, if existing, would be of use. Assessment of structural pathologies usually requires technologies such as X-ray or magnetic resonance imaging (MRI), but a clinical score like the joint alignment of motion (JAM)¹⁸ can be easily, quickly and frequently determined and has already been related to foot function impairments^{2,19}.

The aim of this study was to explore the relationship between clinical foot and ankle assessment (JAM), structural inflammation and damage and joint kinematics of the foot and ankle during gait of subjects with varying degrees of RA.

Methods

Subjects

Twenty-five RA patients (out-patient clinic), 3 male and 22 female, with varying foot and ankle impairments and disease duration participated in this cross-sectional observational study. Subjects were eligible for this study when they met the 1987-ACR criteria for rheumatoid arthritis, were at least 17 years of age and had not undergone orthopedic surgery on their feet and ankles. Exclusion criteria for gait analysis were the following: not being able to walk without walking aid, walking at such a low speed that losing balance was an issue, and severe mobility restriction at the knee or hip joints.

The following demographic characteristics and clinical scores were collected: age, disease duration, rheumatoid factor, RA-related drug usage, Disease Activity Score (DAS) 28, Visual Analog Score (VAS) for foot and ankle pain, Foot Function Index (5-FFI), Larsen score and Sharp van der Heijde (SVH) score. The subjects were recruited consecutively and an informed consent was obtained from all subjects prior to participation. This study received ethical approval from the local medical ethics committee.

Protocol

Gait analysis was performed, with subjects walking at comfortable walking speed, using a 6 infra-red video camera based (1.3 megapixel, 100 Hz) motion analysis system (Vicon Nexus, Vicon Motion Systems, Oxford Metrics Group, UK). Nineteen infra-red reflective markers were attached to the lower limbs of the subject according to the method described by Simon²⁰ (Fig. 1). Both feet were measured according to the above protocol, but only the foot causing most discomfort was used in the analysis. During each session, 8 to 10 trials were recorded to obtain sufficient usable steps in the analysis.

Data analysis

The temporal parameters walking speed, step length, stride length, stride width, stride time and double stance phase were assessed for each subject from the marker co-ordinate recordings in a special LabVIEW script (V7.2, National Instruments). This script was also



Figure 1: a. Leg, foot and ankle marker placement according to Simon²⁰; b. Foot and ankle marker placement on a more severe deformed foot.

used to normalise the data to the stance phase using the specified initial contact and toe-off indications in Vicon Nexus (Vicon Motion Systems). The method developed by Simon was applied to assess foot and ankle kinematics²⁰. This model is able to assess kinematics of 5 foot and ankle segments, i.e. hallux, forefoot, midfoot, hindfoot and leg, and has been developed specifically for subjects with more or less severe foot deformities for which the axes of inter-segmental motion may not conform to the standard anatomical planes.

For each subject, the mean value of the joint angles motion, as function of the percent stance phase, was assessed using 6 to 7 trials. The stance phase was subdivided into three parts: foot-loading, single-stance, and pre-swing. Foot-loading was defined from initial heel contact to opposite foot toe-off (first double-stance), single-stance was defined from opposite foot toe-off to opposite foot heel contact, and pre-swing was defined from opposite foot heel contact to foot toe-off (second double-stance). For each subject the maximum, the minimum and the range of motion (ROM) values were calculated for each joint and each part of the stance phase. ROM was defined as the maximum minus minimum angle^{20,21}. Simon et al. analysed the reliability of the kinematic measures by means of the coefficient of multiple correlation (CMC)²⁰: Several of the minimum and maximum kinematic measures, especially those of the midfoot, were sensitive to an offset in the data. But for all ROM values, as well as for the maximum ankle and first metatarsal-phalangeal (MTP I) dorsiflexion, the CMC's were larger than 0.94. In this study, only the maximum first

metatarsal-phalangeal (MTP I) dorsiflexion at pre-swing, the midfoot supination-pronation ROM at single-stance and the subtalar eversion-inversion ROM at single-stance were evaluated. These foot motions were identified as being influenced by the RA disease as an independent factor in addition to the corresponding, often reduced, walking speed²².

The three kinematic parameters being influenced by RA as an independent factor were correlated with clinical parameters assessed by an experienced radiologist and rheumatologist. Synovitis and bone erosions of the MTP I, the midfoot and hindfoot were assessed by means of MRI^{16,23}. The exact MRI protocol and reliability of the method have been described in a recent publication²⁴. Bone erosion was scored from 0-10 and synovitis from 0-3. The MRI bone erosions of the proximal and distal part of the MTP I joint were combined as the MTP I erosion. Midfoot erosion was defined as the sum of the MRI bone erosion scores of the proximal metatarsals, the cuneiforme, the cuboid and the navicular bone. Hindfoot erosion was defined as the sum of the MRI bone erosion scores of the calcaneal and talar bone. MTP I synovitis was obtained directly from the MRI synovitis score for the MTP I joint. The MRI joint synovitis of the tarsometatarsal and cuneonavicular joint formed the midfoot synovitis. The MRI joint synovitis of the tibiotalar, talo(calcaneo)navicular, calcaneotalar and calcanealcuboid joint formed the hindfoot synovitis. Furthermore, involvement of the tibialis posterior, peronei, triceps surae and flexor hallucis longus tendons were assessed from MRI. The tendon involvement scores were calculated by adding the MRI tendon scores (0-1) for signal inhomogeneity, fluid (collection), thickening, enhanced signal intensity and tearing, as a sign of tenosynovitis or damage of the tendons, resulting in an ordinal scale. The joint alignment and motion (JAM)¹⁸ was assessed and the sub-scores subtalar alignment and passive motion and MTP I passive motion were analysed as individual parameters. Involvement of the MTP 2-5 joints and flexor digitorum longus was not taken into account as the MTP 2-5 were not represented in the computer model.

Statistical analysis

Statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). The minimum, maximum and mean values and corresponding standard deviation of the demographic characteristics, clinical scores and kinematic parameters were assessed. The kinematic and clinical parameters were not normally distributed. Furthermore, we anticipated that several clinical scores are interrelated due to temporal, chronological effects or the

effects of local joint damage on joint stiffness. Hence, Spearman correlation tests were performed between the clinical parameters and also between the kinematic parameters. The 95% confidence interval (CI) of the correlation coefficient (CC) was assessed and used to evaluate possible clinical parameter relationships. As it is not the aim of this study to analyse the relationships between the clinical parameters, the results will be reported, but will only be discussed in reference to the kinematic parameters.

The relationships between the kinematic and clinical parameters were evaluated with the lower and upper values of the 95% confidence interval of the Spearman correlation coefficients. All clinical parameters were included in the correlation with kinematic parameters as, at this stage, it is not clear which relationships exist between the clinical scores. As suggested by Cohen, relationships with a correlation coefficient larger than 0.3 or 0.5 are defined as moderate or strong, respectively²⁵.

Results

An overview of the descriptive statistics of the demographic characteristics, clinical scores and kinematic parameters is given in Table 1. The subjects represent all ages and disease durations, with a mean age of 51 years (range 23 - 78 years) and mean disease duration of 9 years (range 0.5 - 23 years). Eight subjects (32%) used two disease modifying anti-rheumatic drugs (DMARD), 15 subjects (60%) used one DMARD and two subjects (8%) used no RA-related drugs.

The Spearman correlation test demonstrated that the three kinematic parameters were independent. The sub-scales of the JAM were all interrelated (CI 0.0-0.7) and related to MRI scores: The subtalar motion score was related to midfoot (CI 0.1-0.7) and hindfoot erosion (CI 0.5-0.9) and synovitis (CI 0.1-0.8) as well as to tibialis posterior tendon (CI 0.1-0.7) and flexor hallucis longus tendon (CI 0.2-0.8) degeneration. The subtalar alignment score was related to hindfoot erosion (CI 0.2-0.8) and synovitis (CI 0.0-0.7) and peroneus tendon degeneration (CI 0.1-0.8). For each joint, MRI erosion and synovitis scores were strongly interrelated (CI 0.5-0.8). Erosion and synovitis of the hindfoot were related to erosion of the midfoot (CI 0.2-0.8) and degeneration of the peroneus tendon (CI 0.1-0.7) and flexor hallucis longus tendon (CI 0.1-0.8).

DEMOGRAPHIC AND CLINICAL SCORES	Scoring range	Min	Max	Mean	SD
Age (years)		23.0	78.0	51.3	15.8
Disease duration (months)		6.0	276.0	113.0	82.5
Rheumatoid factor		0	2600	216	550
DAS 28	0-9.4	1.1	6.7	3.4	1.3
Pain Visual Analog Score (%)	0-100	3.0	93.0	41.3	25.4
5 FFI Pain	0-126	0.0	75.0	30.0	19.4
5 FFI Disability	0-126	6.0	67.0	29.8	16.4
Larsen score	0-15	0.0	5.0	1.4	1.7
SVH score	0-64	0.0	39.0	12.7	10.8
Joint Alignment and Motion (JAM)					
Subtalar Motion	0-4	0.0	4.0	2.0	1.3
MTP I Motion	0-4	0.0	4.0	1.9	1.3
Subtalar Alignment	0-4	0.0	3.0	0.6	1.0
MTP I Alignment	0-4	0.0	3.0	0.8	1.1
Magnetic Resonance Imaging (MRI)					
Synovitis MTP I	0-3	0.0	3.0	2.0	1.3
Erosion MTP I	0-20	0.0	20.0	5.8	5.1
Synovitis midfoot	0-6	0.0	6.0	2.3	2.3
Erosion midfoot	0-100	0.0	73.0	15.8	20.4
Synovitis hindfoot	0-12	0.0	12.0	4.0	4.1
Erosion hindfoot	0-20	0.0	13.0	3.3	4.2
Tibialis posterior tendon	0-5	0.0	5.0	1.8	1.9
Flexor Hallucis Longus tendon	0-5	0.0	5.0	0.6	1.2
Peroneus tendon	0-5	0.0	5.0	1.2	1.6
Achilles tendon	0-5	0.0	3.0	0.3	0.7
GAIT CHARACTERISTICS					
	Healthy subjects: mean (SD)	Min	Max	Mean	SD
Walking speed (m/s)	1.25 (0.11)	0.44	1.00	0.77	0.14
Individual Variability walking speed (m/s)	0.03	0.02	0.15	0.61	
Stride length (m)	1.32 (0.08)	0.59	1.35	0.99	0.14
Individual variability stride length (m)	0.02	0.02	0.08	0.05	
Max MTP I dorsiflexion toe-off (deg)	51.1 (5.1)	16.1	55.3	34.1	10.2
Midfoot pronation ROM single-st. (deg)	8.6 (3.5)	1.7	9.8	4.8	2.0
Hindfoot eversion ROM single-st.(deg)	3.7 (1.2)	1.0	5.5	2.6	1.0

Table 1: Overview of demographic, clinical and gait characteristics. Abbreviations: DAS: Disease Activity Score, FFI: Foot Function Index, Min: minimum, Max: maximum, ROM; Range Of Motion, SD: standard deviation, SVH: Sharp- Van der Heijde score, MTP I: First metatarsal-phalangeal joint, Single-st.: single-stance

The maximum MTP I dorsiflexion at pre-swing was significantly related to local pathologies of the MTP I: a moderate to strong negative correlation coefficient (CI range -0.3 to -0.8) was found for the correlation with synovitis and erosion of the MTP I, respectively. A negative CC indicates that more MTP I erosion and inflammation resulted in less MTP I dorsiflexion at pre-swing. Furthermore, erosions of the midfoot and hindfoot and the MTP I passive motion measured clinically in the JAM moderately related to MTP I dorsiflexion at pre-swing (CI -0.1 to -0.7) (Table 2, Fig. 2).

Midfoot pronation and hindfoot eversion ROM during single-stance were not significantly related to local erosions or inflammations. However, a more everted alignment of the subtalar joint was related to less midfoot pronation and hindfoot eversion ROM (CI -0.2 to -0.8). Furthermore, the results suggest a moderate relationship between midfoot pronation motion and pathologic changes of the Achilles tendon (CI -0.0 to -0.7): More severe Achilles tendon involvement was related to more midfoot pronation motion. More severe involvement of the peroneus longus tendon was related to less hindfoot eversion motion at single-stance (CI -0.0 to -0.7). No significant relationship was observed for involvement of the tibialis posterior tendon on midfoot or hindfoot motion (Table 2, Fig. 3).

Spearman correlation test	MTP I max. dorsiflexion at toe-off		Midfoot pronation ROM at single-stance		Hindfoot eversion ROM at single-stance	
	low CI	upp CI	low CI	upp CI	low CI	upp CI
Subtalar motion JAM	-0.65	0.05	-0.57	0.19	-0.55	0.21
MTP I motion JAM	-0.75	-0.13	-0.57	0.18	-0.59	0.15
Subtalar alignment JAM	-0.67	0.02	-0.75	-0.14	-0.78	-0.20
Synovitis MTP I MRI	-0.82	-0.30	-0.41	0.39	-0.67	0.05
Erosion MTP I MRI	-0.86	-0.40	-0.65	0.07	-0.57	0.20
Synovitis Mid foot MRI	-0.69	0.00	-0.57	0.21	-0.40	0.40
Erosion Mid foot MRI	-0.77	-0.17	-0.62	0.13	-0.55	0.23
Synovitis Hind foot MRI	-0.63	0.11	-0.68	0.03	-0.34	0.46
Erosion Hind foot MRI	-0.69	0.00	-0.63	0.12	-0.51	0.29
Tibialis posterior tendon inv. MRI	-0.42	0.38	-0.32	0.48	-0.45	0.36
Flex. hall. longus tendon inv. MRI	-0.50	0.30	-0.31	0.49	-0.34	0.47
Peroneus tendon inv. MRI	-0.55	0.23	-0.59	0.17	-0.70	-0.01
Achilles tendon inv. MRI	-0.43	0.37	0.02	0.70	-0.28	0.51

Table 2: Results of the Spearman correlation tests between clinical and kinematic parameters: the lower (low) and upper (upp) values of the confidence interval (CI) of the correlation coefficient.

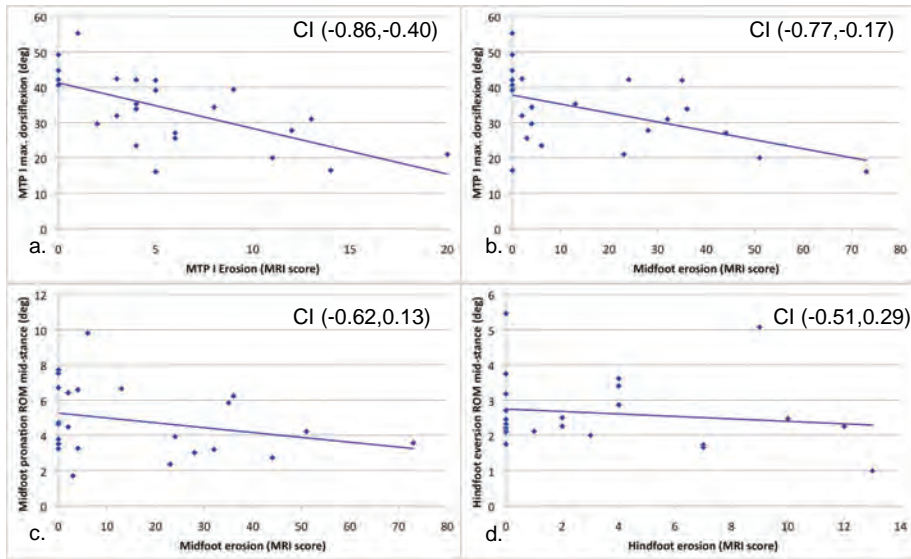


Figure 2: Individual effects of joint erosion on joint motion with corresponding linear regression line and the confidence interval (CI) (lower value, upper value) of the Spearman's correlation coefficient: a, b. Maximum MTP I dorsiflexion as function of MTP I and midfoot erosion, respectively; c. Midfoot pronation ROM as function of midfoot erosion; d. Hindfoot eversion ROM as function of hindfoot erosion.

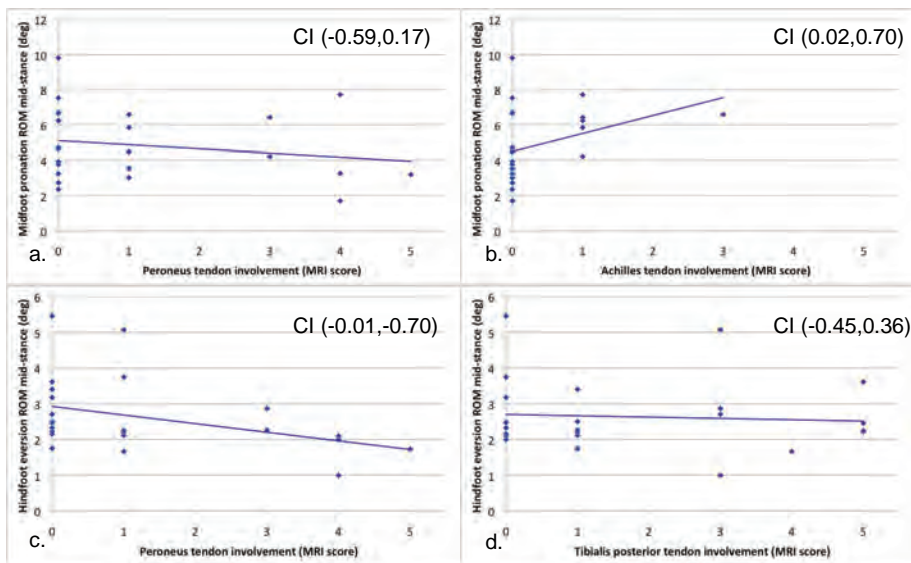


Figure 3: Individual effects of tendon involvement on midfoot (a, b) and hindfoot (c, d) kinematics with corresponding linear regression line and the confidence interval (CI) of Spearman's correlation coefficient.

Discussion

The aim of this study was to explore the relationship between clinically observed pathological changes in the joints and tendons of the foot in RA subjects and their corresponding MTP I, midfoot and hindfoot motion during gait. In addition, the relationship between sub-scores of the JAM and joint kinematics were analysed. The cross-sectional cohort consisted of RA subjects with more or less severe disease activity, pain and structural damage and they represented a broad range of RA patients. The mean kinematic data were comparable to findings by Khazzam and Turner in more or less severe RA populations^{5,6,10,22}. Although RA is a complex disease with multiple impairments to the foot and ankle, relationships between clinical and kinematic parameters were found in our cross-sectional cohort

Joint involvement

The maximum MTP I dorsiflexion at pre-swing was moderately to strongly related to MTP I mobility and by joint pathologies in the whole foot and ankle. Synovitis and erosion of the MTP I joint result in pain and or stiffness of the joint. MTP I pain may result in the desire to unload the pressure applied to the forefoot and reduce the range of MTP I motion during gait. This can be achieved, among others, by reducing stride length, which was observed in our RA subjects with pain (VAS) and which has already been observed in RA subjects with forefoot pain⁴. In healthy subjects, lower walking speed resulted in lower peak pressures under MTP I²⁶, required less MTP I dorsiflexion and ankle range of motion at pre-swing²¹, which were both related to peak pressure under MTP I and hallux²⁷. To further unload their MTP I, RA subjects increase their cadence and reduce their stride length²⁸ so, for similar walking speeds, an even lower MTP I dorsiflexion at pre-swing can be achieved. Nevertheless, in RA subjects an increased peak pressure under the MTP I was observed compared to healthy subjects and was related to damage to the forefoot in RA subjects²⁹. Also in our study lower maximum MTP I dorsiflexion at pre-swing was related to smaller stride lengths. MTP I stiffness directly limits the maximum attainable MTP I dorsiflexion during gait: Canseco reported a significant reduction of MTP I maximum dorsiflexion in subjects with hallux rigidus compared to healthy subjects³⁰ and furthermore, in RA subjects, MTP I stiffness was related to walking speed¹¹. Joint erosions of the midfoot and hindfoot seem to relate to less MTP I dorsiflexion at pre-swing. These hindfoot findings confirm earlier studies that observed effects of hindfoot osteo-arthritis (in a general population)¹⁴ or

hindfoot deformities (in a RA population)^{4,10}, on MTP I motion pre-swing and stride length. No studies were found that studied the effects of mid-foot erosion on gait parameters.

Midfoot supination-pronation and hindfoot eversion-inversion motion during the single-stance phase seem to be at least moderately related to hindfoot alignment but not to midfoot or hindfoot erosion or synovitis. Only for the more severe cases of hindfoot erosion, reduced midfoot pronation and hindfoot eversion motion were observed. The latter corresponds to similar findings reported by Turner, who only observed significant changes in hindfoot and forefoot kinematics in a group of RA subjects with severe hindfoot deformations and not in a group with mostly forefoot deformations¹⁰. Also in subjects with severe ankle osteo-arthritis changes in hindfoot kinematics were observed¹⁴. This may be explained by the fact that during gait, only a limited amount of hindfoot motion is required in the frontal plane (Figure 4a). The data suggest that only a more advanced stage of hindfoot pathologies with severe stiffness may influence and impair midfoot and hindfoot kinematics (Figure 4b). Foot posture, however, shifts the required motion with regards to the available motion (Figure 4c): a pronated foot type has been related to increase in maximum hindfoot eversion during gait in healthy and in RA subjects^{31,32}. Hence, in our study the increased hindfoot alignment of RA subjects with a more everted static posture of the hindfoot, may result in less available eversion motion during single-stance.

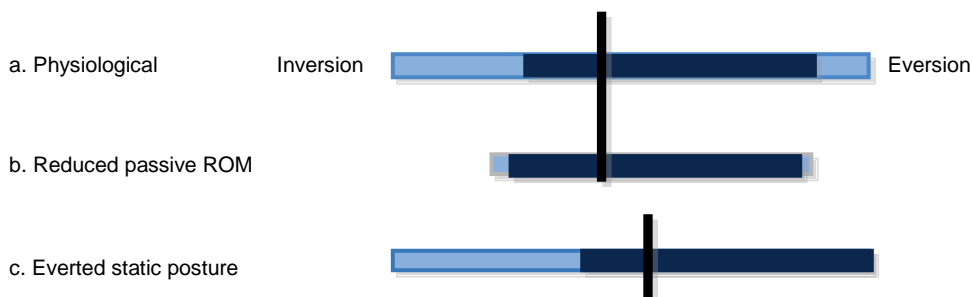


Figure 4: Hindfoot in/eversion motion with active ROM (dark blue) required during gait, available passive ROM (light blue) and posture of the hindfoot in the frontal plane (black line). a. Physiological situation: The active ROM required during gait is less than the available ROM. b. The required ROM during gait is still possible even though the available ROM is reduced as a consequence of joint stiffness. c. Due to an initial everted hindfoot posture the joint reaches it's maximum eversion value during the required active ROM.

Tendon involvement

Our findings suggest moderate to strong relationships between tendon involvements and midfoot and hindfoot motion during gait: Achilles tendon involvement was related to increased pronation motion of the midfoot. Four RA subjects were observed with MRI signal inhomogeneities and one with thickening of the Achilles tendon and for each of these subjects staining of the attachment of the plantar fascia was observed on MRI. The latter was not observed in RA subjects without Achilles tendon involvement. Several studies have reported that tensioning of the Achilles tendon results in reduced inclination of the calcaneus, flattening of the medial arch and tensioning of the plantar fascia³³⁻³⁶. Consequently, damage to the Achilles tendon or the plantar fascia may reduce the pre-tensioning capacity to the foot structures and result in more midfoot motion during single-stance. The studies including Achilles tensioning did not report on its effect on midfoot and hindfoot motion in the frontal plane.

Moderate to strong relationship between pathological changes of the peroneus longus tendon and reduced hindfoot eversion motion were observed during single- stance. In this study, involvement of the peroneus longus tendon was strongly related to the subtalar alignment sub-scale score of the JAM (CI 0.1-0.8) and to hindfoot synovitis (CI 0.1-0.7). Hindfoot joint synovitis can lead to destruction of the ankle ligaments³⁷. Both have been associated with peroneus longus tendon involvement^{38,39} and also with changes in passive ankle joint ROM and alignment^{33,40,41}. As subtalar alignment also significantly influences midfoot motion it is not clear at present, if the peroneus longus involvement and reduced midfoot motion have a causal relationship. As far as we know, there are no studies that report on the effects of local peroneus tendon pathologies on foot and ankle kinematics in subjects with or without a systemic disease. Our findings demonstrate a need for further analysis of the effects of peroneus tendon and hindfoot ligament and alignment pathologies on foot and ankle kinematics.

Tibialis posterior tendon involvement was related to the subtalar passive motion sub-score of the JAM (CI 0.1-0.7), but did not influence the midfoot supination or the hindfoot eversion motion during single-stance. Eight of our RA subjects did not have pathological involvement of their tibialis posterior tendon and another seven only had MRI signal inhomogeneities. However, also for those RA subjects with more severe involvement of the tibialis posterior tendon, no change in midfoot or hindfoot motion during single-stance was observed in our study. Other studies did report a statistically significant relationship of tibialis posterior

tendon dysfunction with forefoot and hindfoot kinematics in subjects with severe tibialis posterior tendon pathologies¹³. It must be noted though, that in these studies the subjects also had a flatfoot or significant hindfoot eversion posture, which was not always the case in our study. So possibly, the observed effects in the other studies might be attributed mostly to foot alignment. This is in agreement with the finding in our study, which demonstrates a moderate to strong relationship of the hindfoot alignment with hindfoot eversion and midfoot pronation motion. Furthermore, Imhauser⁴⁰ and Pisani⁴² demonstrate and discuss that the tibialis posterior tendon can only control and support midfoot and hindfoot motion if the hindfoot joint is stable and the ligaments are intact. However, in RA subjects the hindfoot ligaments are frequently involved in pathologies due to tarsitis³⁷. Although we did not assess the hindfoot ligaments, we did observe a relationship between tibialis posterior tendon involvement and the subtalar motion sub-scale score of the JAM.

Limitations

We analysed a cross-sectional cohort of RA subjects, with various stages of the disease and corresponding pathologies. Due to the complexity of the disease, heterogeneity of the study population and for some clinical parameters, a limited number of subjects, the analysis of relationships between clinical and gait parameters resulted in large confidence intervals. In future, it is suggested to study the effects of pathologies on kinematics in a more homogeneous study population and preferably, in a longitudinal study.

In this exploratory study, we have tried to explain several of our findings by means of other studies, which used, among others, plantar pressure and muscle strength analysis. These parameters were not measured in our study, but the suggested possible explanations might be used as starting points or hypotheses in future studies.

Furthermore, due to limitations of the used foot and ankle model, the lateral forefoot (MTP 2-5) was not taken into account in this study. As these structures are frequently impaired in RA subjects, future kinematic analysis studies should consider taking the motion of the MTP 2-5 joints or the lateral forefoot into account.

Clinical relevance

In this study, moderate to strong relationships of joint and tendon pathologies with foot and ankle kinematics were observed from the onset of the assessed joint and tendon pathologies. Even small changes in joint motion or alignment during the stance phase of gait may have functional implications such as loss of walking speed²¹, compensation or overload in foot, knee or hip joints^{26,27,43}, increased energy consumption⁴⁴ and consequently, reduced social participation^{5,45}. Deterioration of joint and tendon structures occur from the beginning of the RA disease and thus should be monitored and treated carefully.

The JAM sub-scores, MTP I passive motion and subtalar alignment, are easily measured in daily clinical practice without burden to the patient. Our findings suggest a moderate to strong relationship between JAM sub-scale scores and foot and ankle kinematics, which might make the JAM suitable for quick assessment of foot and ankle function during gait. While large JAM sub-score variability was observed between subjects, long-term individual monitoring may provide a good estimate for individual foot and ankle function during gait, as it already does for foot and ankle function during daily life^{2,19}.

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8

General discussion



The aim of this thesis was to improve our understanding of the characteristic foot and ankle kinematics observed in patients with rheumatoid arthritis (RA). Studies analysing gait of the lower limb of RA patients were systematically reviewed and their findings summarised. The effects of marker placement variation on the assessed foot and ankle joint kinematic measures were analysed and conclusions for the choice of kinematic measures were made. The effects of walking speed on foot and ankle kinematics have been determined in healthy subjects and the main effects of the disease, independent of walking speed, have been identified for RA patients. Coupling of motion of adjacent and non-adjacent segments have been assessed and evaluated in healthy subjects. And finally, pathological changes to foot and ankle structures have been related to foot kinematic measures.

Gait analysis in rheumatoid arthritis

The review included 78 studies which assessed and evaluated gait characteristics of the lower extremity of RA subjects and reported on typical plantar foot pressures, electromyography (EMG) of the leg muscles, three-dimensional joint kinematics and temporal-spatial measures. The variety in measurement methods and parameters, especially in kinematic assessment, make it difficult to compare the findings of these studies. Furthermore, most studies are cross-sectional and descriptive studies, while longitudinal data measuring the effect of the natural course of the disease or the long-term effects of interventions were not found. Plantar pressure and temporal-spatial measures have been assessed numerously to investigate the efficacy of foot orthoses [Hennessy 2011] as well as the effects of surgical interventions to the forefoot [Davys 2005, Dereymaecker 1997, Grondal 2006, Harris 1997, Mulcahy 2003]. Additionally, plantar pressure measures have been used to classify the severity of the disease [Doorn 2011, Giacomozi 2009, Schmiegel 2008] and plantar pressure measures have been related to pathological changes to foot structures [Schmiegel 2008, Tastekin 2009, Tuna 2005, Turner 2008, Van der Leeden 2006]. For RA patients, daily functional outcome measures, such as the Foot Function Index (FFI) most efficiently represent walking impairments and satisfaction levels to treatment [Van der Heijde 2010, Van der Leeden 2006]. However, for clinicians, plantar pressure and temporal-spatial measures provide details on dynamic foot loading and function during gait. At present, such measures assist the decision-making and evaluation of conservative and surgical interventions [Hamilton 2001, Grondal 2006].

Due to the continuous improvements in medication, RA subjects with less deformed feet are expected to present themselves for interventions. Such feet may require more detailed classification, assessment and monitoring of dynamic foot and ankle function to be able to provide optimal conservative and more preservative surgical interventions [Hyslop 2010, Van der Heijde 2010]. Kinematic foot and ankle measures may provide additional information on dynamic function in terms of foot segment motion. Several studies have reported gait of RA subjects and identified significant changes compared to healthy subjects [Khazzam 2007, Turner 2008, Woodburn 2004, Weiss 2008]. However, the underlying mechanisms are not yet well understood: only 4 studies analysed how clinical pathological findings and interventions related to foot and ankle kinematic measures [Keenan 1991, Long 2003, Turner 2008, Weiss 2007, Woodburn 2003]. Additional pathology related and intervention related kinematic studies as well as longitudinal studies are still required. Such studies may lead to fundamental insight into the effects of structural damage and interventions on foot and ankle kinematics and insight into the natural course of the disease with respect to affecting kinematics. This thesis is a first attempt to identify critical kinematic measures and pathological dynamic foot and ankle function. Furthermore, it is first to analyse the relationships between kinematic measures and pathological changes to local foot and ankle structures.

Assessment of foot and ankle segment kinematics

Kinematic measures need to be repeatable and reliable in order to provide useful data in a clinical and research setting. Variation in marker attachment is one of the causes for variability of the assessed kinematic measures and may be an important factor in cases of individual subject analysis, especially in cases of deformed feet. The computer model, which calculates the kinematic measures of the foot and ankle segments, prescribes the positions for marker attachments on the foot. However, the feet of the patients with RA included in this study involved local swellings, bunions and deformations at the marker attachment sites. Attachment location of the markers at the distal head of the first metatarsophalangeal (MTP I) and navicular bone were discussable and the choice of location could vary up to 8 mm in multiple directions. A model simulation study showed that variations of 8 mm in these marker attachment locations resulted in an offset of the absolute kinematic measures for which these markers are used of 2° in the frontal plane up to 5° for the sagittal plane and 10° for the transverse plane. The range of motion measures in the sagittal and frontal plane

were only slightly (0.5°) less sensitive to marker placement location. In the transverse plane, variability in range of motion measures reduced to less than 1° compared to the absolute measures. The findings of the repeated gait recordings of three RA patients were comparable to those of the model simulation. However, larger differences in range of motion between the assessed angles were observed in the repeated gait recordings for one of the three RA patients: variations of 10° for midfoot supination and up to 8° for MTP I joint abduction were observed. Apparently, other issues than just marker placement have to be considered in repeated measurements. Among others, changes in temporal-spatial measures may affect foot and ankle kinematics and thus contribute to the between-session variability. This was confirmed in our findings: larger variations in range of motion were observed between sessions with larger differences in walking speed (0.1 m/s), stride length (0.07 m) or double stance phase (8%). Therefore, it is recommended to report the corresponding variation in temporal-spatial parameters in repeatability and repeated measures (longitudinal) studies.

The advantage of using a computer model to simulate variations in marker placement is the possibility of studying specific effects of marker placement variation, such as direction of the variation, magnitude and sensitivity on the assessed kinematic measures. Such findings may assist in the definition of the optimal marker attachment location. For example, the proximal/distal position and medial/lateral position of the distal MTP I marker had the largest effect on the assessed MTP I dorsiflexion and abduction, respectively. The latter is mainly an offset problem and may be avoided by analysing range of motion data. However, an issue is the variability of 5° in assessed MTP I dorsiflexion which was predicted by the simulation as well as the gait recordings and reported by several other studies [Carson 2001, Long 2010]. Multiple foot and ankle computer models are available and each model attaches the MTP I markers to the skin on the medial side of the MTP I. Especially in arthritic feet, the distal location may be influenced by bunions and swellings. Hyslop et al. and De Mits et al. solved this problem by adding an additional marker distal to the MTP I joint line, which resulted in improved repeatability of MTP I dorsiflexion assessment in both healthy and arthritic subjects [De Mits 2011, Hyslop 2010]. Disadvantage of their method is the increase of necessary markers on the foot. While that may not be an issue in scientific settings, in a clinical setting it might be desirable to keep the numbers of markers as low as possible [Benedetti 2011]. Attachment of the distal MTP I marker to a more dorsal location may be an alternative solution, but the effects on repeatability have not been studied yet and it may lead to problems with the recording system in terms of distinguishing foot markers.

Effect of walking speed on foot and ankle kinematics

For patients with RA, significant changes in foot and ankle kinematics have been reported together with a reduction of walking speed compared to healthy subjects [Khazzam 2007, Turner 2008, Platto 1991]. Therefore, the effects of walking speed on foot and ankle kinematics were analysed in a healthy population. In a second step it was analysed if walking speed alone could explain the observed kinematic changes in RA patients.

In chapter 4, gait of 14 healthy subjects with a mean age of 43 years (range 30 to 55 years) was recorded at their own comfortable and two slower walking speeds. The foot and leg markers were attached to the healthy subjects only once, after which all three walking speed sessions were recorded in sequence. As a result, variations in assessed kinematic measures due to variations in repeated marker placement were avoided. The kinematic findings at comfortable walking speed were comparable to those reported by Simon [Simon 2006] while the effects of walking speed on MTP I dorsiflexion motion and ankle plantarflexion and eversion motion were comparable to those reported by other studies [Laroche 2007, Lelas 2003, Rosenbaum 1994]. The clinical relevance of the statistically significant findings was addressed by means of the corresponding reliability values. Reliability values can be used to distinguish subjects from each other despite measurement error [de Vet 2006] and may be assessed by means of a linear mixed model in clinical trials with repeated measures [Vangeneugden 2004]. The findings were assumed to be clinically relevant if the magnitude of the change in joint range of motion angle exceeded 3° [Nester 2007] and the reliability was good (>0.7) or if the corresponding reliability value was extremely high (>0.9) (figure 3, chapter 4). In conclusion, the differences in maximum ankle plantarflexion (3° - 6°), minimum medial arch collapse (1° - 2°) and maximum MTP I dorsiflexion (5° - 9°) were significantly and relevantly influenced by walking speed in the sagittal plane. In the frontal plane, the differences in minimum midfoot pronation between walking speed sessions were small (1° - 2°), but significant and highly reliable (0.94). The effect of walking speed on the assessed kinematic measures is only slightly larger than the observed effects due to variations in marker placement on kinematic measures. Hence, much care should be taken when attaching the markers to the feet of RA subjects, especially, when comparing individuals at different moments in time or before and after interventions. The development of marker attachment protocols dealing with bunions and swellings or finding less sensitive marker locations may improve consistent marker attachment and reduce measurement errors.

Gait of 21 patients with RA was recorded and kinematic measures were assessed. The kinematic measures of the RA patients were compared to the assessed values of the healthy subjects walking at various speeds by means of a linear mixed model (CHAPTER 5). Detailed analysis of the kinematic differences between the two groups indicated that the maximum MTP I dorsiflexion at pre-swing as well as the hindfoot eversion motion and midfoot pronation motion during mid-stance were all reduced as effect of the disease, independent of walking speed. Other studies have pointed out significant differences in additional kinematic measures between RA patients and healthy subjects, such as hindfoot plantar flexion at pre-swing or abduction motion of the MTP I [Khazzam 2007, Turner 2008]. Also in this thesis, these differences were statistically significant between the two groups, but they could be attributed to walking speed alone. Although the reduction in walking speed may impair walking in daily life, the corresponding changes in foot and ankle kinematic do not represent pathological dynamic function because healthy feet show similar function walking at lower speeds. On the contrary, however, the reductions in maximum MTP I dorsiflexion at pre-swing as well as the hindfoot eversion motion and midfoot pronation motion during mid-stance could be attributed to the disease alone and are assumed to be pathological: These motions are not observed in healthy feet walking at similar speeds, they impair normal walking and may result in local or compensatory overloading of foot and ankle structures. Therefore, it is suggested to focus further development and new interventions on addressing the pathological motions, in an attempt to improve or restore normal foot and ankle dynamic function. Such interventions may lead to improvements in daily function and discomfort, even without major improvements in temporal-spatial characteristics [Benedetti 2011].

The developments of surgical interventions on foot and ankle structures have been evidence-based and the effects of surgery have been evaluated by means of daily function or satisfaction scores [Loveday 2012, Popelka 2010, Van der Heijde 2010, Van der Krans 2006]. More recently, plantar pressure and temporal-spatial measures are successfully used to assist diagnosis and evaluation of foot and ankle function pre and post surgery [Doorn 2011, Grondal 2006, Rosenbaum 2011, Stockley 1990]. Design and evaluation of conservative intervention such as orthoses have made use of plantar pressure measures for quite some time [Barret 1976]. So far, orthoses have been successful in reducing forefoot plantar pressure and foot pain, but their effects on foot and ankle kinematics are still discussed [Loveday 2012, Hennessy 2011].

Woodburn et al. did observe positive long-term effects of hindfoot orthoses on normalizing hindfoot in/eversion motion and these improvements remained during bare foot walking [Woodburn 2003]. One might conclude that restoring normal foot posture restores normal foot function over time. Restoration of normal function over time suggests regeneration of foot and ankle structures and this is only possible if these structures are not severely impaired. Such reasoning emphasizes the importance of prescribing orthoses in an early stage of the disease. This hypothesis was confirmed by Van der Leeden et al. who analysed factors predicting outcome of orthotic usage in RA [Van der Leeden 2011]. Their study concluded that disease duration as well as age and higher baseline values for pain and disability predicted improvements in daily function. The clinical factors studied by Van der Leeden et al. included forefoot and hindfoot deformities, which were assessed by means of a structural index score as described by Platto et al. [Platto 1991]. Also total swollen foot joint count was studied. The investigated clinical factors did not influence the outcome of orthoses usage, but perhaps the crucial clinical factors were not studied or were lost in average scorings. Fundamental knowledge of the effects of pathological change of foot and ankle structures on dynamic function is still missing to effectively study and improve conservative and surgical interventions. Iaquinto et al. used an advanced computer foot and ankle modelling to study the effects of specific surgical interventions on kinematics [Iaquinto 2011]. Although such modelling studies will provide insight and offer guidelines for clinical studies, they need to be validated. Therefore, the next step in this thesis was to analyse and improve the general understanding of the causes for the observed kinematic changes in RA.

Role of pathological structural changes on foot and ankle kinematics

RA affects multiple active and passive structures. These structures, such as the plantar foot ligaments attach to adjacent and non-adjacent bony segments and may influence coupling of motion of foot and ankle bony segments. In chapter 6, the relationships between the motions of adjacent and non-adjacent foot and ankle segments were analysed in healthy subjects. Quasi-linear coupling relationship was found between hindfoot eversion and MTP I plantarflexion motion, hindfoot eversion and forefoot adduction and also between leg rotation and medial arch motion. These coupling relationships appeared to be stronger and more consistent than coupling between other (non-) adjacent segments. The coupling between hindfoot eversion and MTP I plantarflexion demonstrated little differences between the subjects and also a small variation with-in the subjects. Mostly passive structures such

as the plantar ligaments and plantar fascia may explain the strong coupling between hindfoot eversion and MTP I plantarflexion and forefoot adduction motion [Caravaggi 2009, Carlson 2000, Cheung 2006]. Between midfoot and leg only the tibio-navicular ligament can provide coupling. However, multiple active structures such as the tibialis posterior and anterior and the peroneii, attach to leg and midfoot. General timing of their activation pattern and moment arms make it tenable that these muscles may control motions of these segments with respect to each other [Ivanenko 2002, McCullough 2011, Neptune 2008].

These findings, and the findings regarding the effects of walking speed may explain how a local pathology may have wide-ranging effects on foot and ankle kinematics, such as have been reported in gait studies of impaired subjects [Canseco 2008, Khazzam 2006]. For example, Canseco et al. observed a reduction of maximum MTP I dorsiflexion at pre-swing in a population with Hallux rigidus, as expected. However, they also reported corresponding significant changes in hindfoot eversion motion. Khazzam et al. observed reduced motion of the ankle during gait of subjects with ankle arthrosis. They also reported a reduced walking speed and stride length, which may explain the observed reduction in maximum MTP I dorsiflexion at pre-swing. In patients with RA similar effects were reported. Early RA subjects already tend to walk at lower speeds compared to healthy subjects and Turner reported a reduction of heel rise in a RA population with mainly forefoot issues [Turner 2006]. In a RA population with severe deformations to mainly the forefoot, also kinematic changes in hindfoot were observed, and vice-versa [Turner 2008].

In chapter 7, the relationships between pathological changes of active and passive foot and ankle structures of RA patients and their corresponding MTP I dorsiflexion, midfoot pronation and hindfoot eversion were studied. Local synovitis and erosion of the MTP I and midfoot joints related to reduced maximum MTP I dorsiflexion at pre-swing. Also hindfoot erosion tended to reduce maximum MTP I dorsiflexion. While the effects of MTP I stiffness and erosion on MTP I motion may be expected [Canseco 2008, Laroche 2007], similar effects of hindfoot erosion on MTP I motion have been reported as well [Khazzam 2006, Turner 2008]. The strong motion coupling between hindfoot and MTP I observed in healthy subjects in this thesis (CHAPTER 6) or related lower walking speeds found in the other studies might explain these findings. In this thesis however, hindfoot erosion was not related to walking speed. Future studies should evaluate the underlying mechanisms of coupling

between hindfoot and MTP I and evaluate if this strong natural coupling remains intact in subjects with foot and ankle impairments.

Midfoot pronation and hindfoot eversion range of motion at single-stance (mid-stance) were not influenced by local damage to the joints, but only by pathological changes to the Achilles and peroneus tendon, respectively. Only five RA patients demonstrated Achilles tendon involvement and for each of these patients staining of the attachment of the plantar fascia was observed with Magnetic Resonance Imaging (MRI). The latter was not the case for the other RA patients. This again indicated an important role for the plantar structures on foot and ankle motion. It might be hypothesized that loss of the integrity of the plantar structures results in an increased pathological motion of the midfoot to compensate for the loss of natural coupling between MTP I (and forefoot) and hindfoot. Only recently the occurrence of plantar fasciitis and other pathological changes to plantar structures spanning from hindfoot to forefoot and MTP I in RA have received more attention, which is supported by technological improvements in MRI [Balen 2001, Potter 2009, Riente 2011, Wakefield 2008]. Meanwhile, several modeling studies have demonstrated the important function of the plantar structures on stabilizing and pre-tensioning the foot [Caravaggi 2009 and 2010, Cheung 2006]. Treatment of subjects with impairments to plantar structures is well advanced [Campbell 1974, Cole 2005, Goff 2011]. The findings of this thesis suggest that an early detection and registration of pathologies of plantar structures in RA might result in timely and effective conservative interventions.

Pathological changes to the tibialis posterior tendon did not influence the midfoot or hindfoot motion during single-stance. This may seem to be contrary to the expectation based on kinematic observations of gait of subjects with tibialis posterior tendon dysfunction [Ness 2008, Tome 2006]. However in those cases also severe eversion posture of the foot was reported. In this study, the RA patients with subtalar misalignment also displayed moderate to large changes in midfoot pronation and hindfoot eversion motion. Furthermore, Imhauser demonstrated that the tibialis posterior can only function if the ligamentous structures of the hindfoot and midfoot are intact [Imhauser 2004]. Ligamentous structures are frequently affected in RA patients and thus the stability of the foot will be impaired [Loveday 2012, Wiener-Ogilvie 1999]. Data on pathological changes of ligamentous structures of the RA patients were not available in this thesis. Hence it was not possible to evaluate their effect on foot and ankle stability or motion during gait at present.

This study is the first gait study to question the previously suggested importance of pathological changes of the tibialis posterior on midfoot and hindfoot kinematics in RA. The findings emphasize the importance of stability and normal alignment or foot posture and suggest pathological changes to other leg tendons may be important as well. To maintain a normal posture and function, ligaments need to be intact. Our findings agree with surgical intervention strategies for flexible pes plano valgus and (RA) subjects with tibialis posterior dysfunction. In those cases attention is paid to the alignment of foot posture or isolated joint arthrodesis in order to stabilise the foot and optimise post-surgical outcome [Pisani 2010, Popelka 2010, Van der Heijde 2010, Van der Krans 2006]. Such interventions may be good for severely deformed feet, but in early RA with less deformed feet, less rigorous joint preserving stabilizing surgical measures need to be developed and conservative stabilizing interventions need to be improved. Furthermore, the onset and long-term development of pathological changes to the leg tendons of RA patients has not been analysed, even though Keenan et al. related changes in muscle activation pattern of multiple leg muscles in RA subjects to hindfoot valgus posture [Keenan 1991]. Several studies have reported on the occurrence of leg tendon pathologies in RA [Bouysset 1995, Gerster 1977, Helliwell 2007, Wakefield 2008]. However, only recently Verhulst et al. reported normal values for ultrasonic measures of leg tendons in healthy subjects and hence provide reference values for studies on tendon pathologies [Verhulst 2011]. In a cadaver study, Bohne et al. demonstrated that other leg muscles than the tibialis posterior tendon may be worth studying in RA [Bohne 1997]: the peroneus longus not only has a function in stabilizing the longitudinal and transverse arch, but it also contributes to restraining varus forces acting upon the first metatarsal bone. The peroneus may have a similar role in RA or other feet with midfoot instability [Ellis 2010, Loveday 2012, Van der Krans 2006]. Further studies are required to investigate the independent role of pathological changes of tendinous and ligamentous structures on foot and ankle kinematics.

The sub-scales of the Joint Alignment and Motion (JAM) could be related to kinematic changes in RA: MTP I stiffness was related to maximum MTP I dorsiflexion and subtalar alignment was related to midfoot and hindfoot motion at single-stance. The effect of MTP I stiffness on MTP I kinematics corresponds to findings in literature [Canseco 2008, Laroche 2006 and 2007]. The effect of subtalar alignment has been discussed above. The JAM is scored by visual inspection. Potentially, static imaging techniques may provide a better measure for scoring hindfoot alignment.

Conclusions

This thesis demonstrates that walking speed has a clinically significant effect on foot and ankle kinematics and that walking speed should be taken into account when analyzing or monitoring foot and ankle kinematics of subjects with or without impaired gait. Walking speed was accounted for in this gait study with RA patients and healthy subjects and the kinematic differences observed in the RA patients could not be explained by the corresponding reduction in walking speed alone. Many kinematic changes have been observed and reported for patients with RA, which makes analyses of causal relationships difficult. By accounting for walking speed in this cross-sectional RA study, pathological kinematic function of the RA foot could be defined more specifically as mainly a reduction of hindfoot and midfoot motion in the frontal plane during single-stance and dorsiflexion motion of the MTP I joint at pre-swing. These findings might enable more specific future analyses of the relationships between RA gait and pathological changes to foot and ankle structures as well as the effects of interventions.

This thesis was first to study the relationship between multiple local or segmental pathological changes of active and passive foot and ankle structures and the corresponding foot and ankle kinematics. The kinematic changes were all, more or less, related to hindfoot alignment. Local structural joint pathologies influenced MTP I motion, while the Achilles and peroneus tendon influenced midfoot and hindfoot motion. The analysis was performed in a cross-sectional study. Hence, no causal relationships can be made. However, these findings provide hypotheses or starting points for future gait research in more homogenous RA populations or in long-term RA studies.

This thesis does not support previous reports on the effect of tibialis posterior dysfunction on hindfoot eversion motion during gait. While there was an effect of peroneus tendon involvement on hindfoot eversion motion, this may be the consequence of a corresponding decline in hindfoot alignment, as these parameters were all interrelated. These findings suggest that foot posture is a crucial factor for foot function in RA subjects. Normal dynamic foot function requires a complex and delicate equilibrium between stability and mobility. Future studies should look into more preserving techniques to maintain foot stability from and early point in the disease.

While the plantar structures were not studied directly in this thesis, the findings suggest that they have an important role in motion coupling between forefoot and hindfoot during gait. As a result, if plantar structures are intact, a reduced motion of the forefoot may result in a

corresponding reduced motion in the hindfoot and vice-versa. If plantar structures are impaired, compensatory motions may occur in the midfoot, as have been observed in this thesis for RA subjects affected by pathological changes of plantar structures. The role and importance of the plantar structures need to be confirmed by future studies. Development of new conservative interventions, that focus on restoring or supporting the function of the plantar structures during gait should be considered.

MTP I stiffness and subtalar alignment, both sub-scores of the JAM, were moderately related to changes in MTP I, midfoot and hindfoot kinematics. The JAM is a clinical measure, easily assessed in daily practice and hence may enable therapists a fast assessment of potential gait impairments. Individual differences such as natural joint laxity and increased stiffness due to natural degeneration (age), will influence the JAM sub-scales. Future studies should evaluate if the JAM prediction of gait impairments can be improved when assessing the JAM sub-scales for subjects with RA on the long-term.

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Summary

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Samenvatting

SUMMARY

Background

From an early stage of the disease 40% to 60% of the Rheumatoid arthritis (RA) patients suffer from walking impairments such as pain, diminished mobility and problems with daily activities. These walking impairments relate to pathological changes of foot and ankle structures, which also occur from an early stage of the disease. Walking may be characterised by temporal-spatial, foot plantar pressure and foot and ankle kinematic measures. The temporal-spatial and plantar pressure measures and their relationship to walking impairments and pathological changes of foot and ankle structures have been studied for patients with RA. These gait measures are used together with daily functional impairment scores and structural involvement scores to support the decision and evaluation process of surgical and conventional interventions. With the recent development of optical recording technologies and detailed foot and ankle computer models, typical RA foot and ankle kinematic measures have been assessed and reported, but they are not yet regularly used in a clinical setting. Gait analysis of kinematic measures of the hip, knee and ankle contribute significantly and successfully to the diagnosis and evaluation process of subjects impaired by a cerebral vascular accident or cerebral palsy. For RA patients, the relationship between kinematics and walking impairments or pathological changes of foot and ankle structures are not yet fully understood. Such fundamental knowledge is required to be able to support the development and evaluation of more effective interventions, which aim to improve or restore normal foot and ankle kinematic function. The aim of this thesis was to improve our understanding of the causes of the alterations in foot and ankle kinematics of patients with RA compared to healthy subjects.

Methodology

A review was performed on studies analysing lower limb kinematics during gait of RA subjects. The quality of these studies and their conclusions were analysed (CHAPTER 2). The analysis of foot and ankle kinematics requires a repeatable assessment method, which has been proven for kinematic range of motion measures in healthy subjects. In RA feet, however, deformities and swellings may be present and during preliminary measurements, the positions of the markers on the distal end of the first metatarsal and navicular bone were discussed. At the time of the measurements, no repeatability study on assessment of foot

kinematics of RA patients had been performed. Therefore, the effects of variation in repeated marker placement on more or less severely deformed RA feet was analysed (CHAPTER 3). The marker placement variation was simulated by means of a computer model and validated only by repeated measures on 3 patients with RA. Hence, no statistical analysis was performed. From these findings, however, choices for kinematic measures were made and conclusions on marker positioning on severely deformed feet were drawn.

Gait of 23 RA patients with various stages of disease severity and gait of 14 healthy age-matched subjects was recorded. Their foot and ankle kinematic measures were assessed by means of a 5-segmented foot and ankle model consisting of segments for the leg, hindfoot, midfoot, forefoot and hallux. First, the effects of walking speed on foot and ankle kinematic measures in healthy subjects were analysed by means of a repeated measures ANOVA (CHAPTER 4). Reliability was assessed by means of a linear mixed model to evaluate clinical significance of the findings. For the healthy subjects, foot and ankle kinematic measures were assessed for three walking speeds: at comfortable walking speed and at 70% and 50% of the comfortable walking speed, respectively. The assessed kinematic measures of the RA patients walking only at their own comfortable speed were compared to those from the healthy subjects walking at three different speeds. Graphical observations indicated that walking speed alone could not explain the observed kinematic differences between RA patients and healthy subjects. Therefore, in a second step, a linear mixed model was used to assess the independent contribution of the factor 'walking speed' and the factor 'disease' on foot and ankle kinematic measures of RA patients (CHAPTER 5). The kinematic measures that were influenced by the factor disease were identified and used to study the relationships between kinematic and clinical measures (CHAPTER 7).

As an intermediate step, coupling between motions of adjacent and non-adjacent foot and ankle segments were studied in healthy subjects by means of Pearson correlation tests and corresponding coefficient of variation (CHAPTER 6). Several passive and active structures are attached to (non-) adjacent foot and ankle segments and will influence the relative motions between these segments. These findings could provide insight in underlying mechanisms of the observed RA foot and ankle kinematics. For example, motion coupling between segments might explain how a change in motion in one segment, which is affected by a local pathology, affects motion of a more distal or proximal segment. As part of another thesis, Dr. Hetty Baan assessed clinical measures for 25 patients with RA. From her extensive database, the erosion and synovitis scores of the first metatarsal-phalange (MTP I), midfoot and hindfoot joints and the involvement scores of the leg tendons were deduced

and included in this thesis. The joint and tendon scores were determined from Magnetic Resonance Imaging (MRI). Furthermore, hindfoot and MTP I sub-scales of the Joint Alignment and Motion (JAM) were included. Clinical scores related to MTP II-V and the lesser toes were not taken into account, as the model did not provide assessment of their kinematic measures. The clinical and kinematic scores were tested for inter-dependency by means of Spearman correlation tests. The relationship between the kinematic and clinical parameters was studied by means of the Spearman correlation tests. In this explorative study, the upper and lower values of the 95% confidence intervals for the correlation coefficients were assessed and reported. Relationships with a correlation coefficient larger than 0.3 or 0.5 are defined as moderate or strong, respectively.

Results

The literature review included 78 studies. The quality of the studies was mostly scored as moderate due to the relatively small sample size compared to the required number of subjects to ascertain high quality for clinical effect studies (>50 subjects). But also non-optimal methodology and analysis influenced the quality: as mentioned in the background section, gait measures were not compared to clinically meaningful scores for function or damage and repeatability of the methodology was not addressed. Furthermore, more uniformity in methodology, especially in kinematic measures, would facilitate comparisons between studies. The conclusions for temporal-spatial measures were consistent and a reduction in walking speed, stride length and single-stance time were observed for patients with RA compared to healthy subjects. Increased cadence was observed for the RA patients to compensate for the shorted step length compared to healthy subjects walking at similar speeds. Higher pressures were observed under the heads of metatarsal II-V and several pressure measures could be related to clinical scores such as pain. Changes in kinematic measures of the hindfoot, forefoot and first metatarsal-phalange (MTP I) were observed for the RA patients compared to healthy subjects. Different studies analysed different measures, but generally observed were: a reduction of hindfoot plantarflexion and MTP I dorsiflexion at pre-swing, reduction of maximum forefoot abduction and an abnormal shift to hindfoot eversion during the stance phase. No studies related the kinematic changes of the foot and ankle to daily function or clinical damage scores, only one study evaluated the effects of (forefoot) surgery on foot kinematics during gait and another analysed the effects of orthoses on foot kinematics.

Variation in marker position on the foot resulted in an offset (up to 10 °) of the assessed joint motion and in a less pronounced change in pattern (up to 5°) of the joint motion as function of the stance-phase. Variation in marker placement in the computer model predicted similar findings as the gait recordings. Most sensitive were the assessed MTP I plantar/dorsiflexion (5°) to variation in position of the distal MTP I marker in proximal-distal direction and the midfoot pro/supination (2°) to variation in position of the navicular marker in medial-lateral direction. But due to the presence of bunions, swelling or deformation, placement of the distal metatarsal I marker and navicular marker often conflicted with the prescribed position of the marker placement protocol.

Gait of 14 healthy subjects was recorded at their own comfortable and two slower walking speeds of 1.28 m/s, 0.97 m/s and 0.65 m/s, respectively. The effects of walking speed were significant and clinically relevant for the assessed maximum ankle plantarflexion (3°-6°), minimum medial arch collapse (1°-2°) and maximum MTP I dorsiflexion (5°-9°) in the sagittal plane. In the frontal plane, the differences in minimum midfoot pronation between walking speed sessions were small (1°-2°), but significant and highly reliable (0.94).

The independent contribution of the factor walking speed and disease were assessed in a linear mixed model. The model included the kinematic measures from 21 RA patients walking at their own comfortable speed and of 14 healthy subjects walking at comfortable and the two lower walking speeds. The results indicated that the factor walking speed alone influenced hindfoot plantarflexion, midfoot medial arch motion, leg rotation and forefoot abduction motion at pre-swing. MTP I dorsiflexion at pre-swing and midfoot supination motion at single-stance were influenced by both walking speed and the disease, while the disease alone influenced hindfoot eversion motion during single-stance.

In healthy subjects, strong and consistent quasi-linear coupling was observed between hindfoot eversion and MTP I plantarflexion motion and individual variation in coupling was small (mean coefficient of determination R^2 0.8 and coefficient of variation CV 0.2). Coupling between leg rotation and midfoot medial arch motion seemed consistent, but was less strong (R^2 0.5) and showed much more individual differences (R^2 0.1-0.8) and variability (CV 0.4). Coupling between adjacent segments was less consistent, with large individual differences (R^2 0.2-0.8) and more individual variation (CV 0.4-0.5).

The relationships between clinical and kinematic measures were assessed. A reduction of maximum MTP I dorsiflexion at pre-swing was moderately to strongly related to increased erosion and synovitis of MTP I joint (CI 0.3,0.8), erosion of the midfoot joints (CI 0.2,0.8)

and hindfoot joints (CI 0.0,0.7). Increased midfoot pronation motion during single-stance was related to increased involvement of the Achilles tendon (CI 0.0,0.7). Reduced hindfoot eversion motion during single-stance was related to increased involvement of the peroneus tendon (CI 0.0,0.7). The sub-scales of the JAM were also related to the kinematic measures: reduced MTP I motion resulted in reduced MTP I dorsiflexion pre-swing (CI 0.1,0.8) and reduced alignment of the hindfoot resulted in reduced midfoot pronation motion (CI 0.1,0.8) and hindfoot eversion motion (CI 0.2,0.8) at single-stance. The findings suggest that tibialis posterior tendon involvement was not related to midfoot pronation (CI -0.3,0.5) or hindfoot eversion (CI -0.5,0.4) in this study.

Conclusions

Limited knowledge is available regarding the underlying mechanisms for the observed changes in foot and ankle kinematics and how interventions affect these abnormal motions in RA.

Repeatability of assessed foot and ankle kinematic measures is lower for severely deformed feet compared to normal feet due to variation in marker position on the foot. Especially, the kinematic measures for the midfoot and MTP I dorsiflexion are sensitive to marker position variation. The protocols for marker placement need to be optimised for more or less severely deformed feet. For example, the repeatability of the assessed MTP I dorsiflexion may be optimised by attaching the distal metatarsal I marker more dorsally or by adding an extra marker distal to the MTP I joint.

Walking speed significantly influences foot and ankle kinematics, but cannot explain all observed kinematic differences between RA and healthy subjects. The disease influences maximum MTP I dorsiflexion at pre-swing and midfoot pronation motion and hindfoot eversion motion at single-stance, independent from walking speed. These kinematic measures were not observed for healthy subjects walking at similar walking speeds. Therefore, they are assumed pathological and should be addressed by interventions with priority.

The motions of hindfoot eversion and MTP I plantarflexion were strongly and consistently coupled for healthy subjects. Passive structures such as the plantar fascia and ligaments attach these two foot segments. Consequently, if a pathological change to a local structure

impairs motion of one segment, their coupling in motion will influence the motion of the other segment indirectly. On the other hand, if a disease affects the plantar structures, coupling of motion between MTP I and hindfoot motion is reduced or lost and compensative motion of another segment such as the midfoot may be required.

Clinical findings could be related to changes in kinematic measures in this cross-sectional observational study with 25 RA patients. Pathological changes to local and more proximal joints were related to changes in MTP I dorsiflexion at pre-swing. Hindfoot alignment and involvement of the Achilles tendon were related to midfoot pronation. All five individual cases with Achilles tendon involvement also suffered from involvement of the plantar structures, which was not observed in the other RA patients. Taking the findings of the coupling study into regard as well, it was concluded that future studies should investigate the role of plantar structures in foot and ankle kinematics of RA patients. Furthermore, hindfoot alignment and involvement of the peroneus tendon were related to reduced hindfoot eversion motion. These two clinical parameters were also interrelated. No effects were found for the tibialis posterior tendon. Future studies should investigate the relationships between foot and ankle alignment and leg tendons with kinematic measures in a more homogenous RA population or in longitudinal RA studies.

SAMENVATTING

Achtergrond

Al in een vroeg stadium van de ziekte lijdt 40% tot 60% van de reumatoïde artritis (RA) patiënten aan loopstoornissen zoals pijn, verminderde mobiliteit en problemen met de dagelijkse activiteiten. Deze loopstoornissen zijn gerelateerd aan pathologische veranderingen van voet- en enkelstructuren, die ook al in een vroeg stadium van de ziekte voorkomen. Lopen wordt gekenmerkt door plantaire druk, ruimte-tijd en kinematische parameters. De plantaire druk en ruimte-tijd parameters en hun relatie met loopstoornissen en pathologische veranderingen van de voet en enkel zijn reeds uitvoerig bestudeerd bij patiënten met RA. Deze parameters worden samen met de scores van ervaren dagelijkse functionele beperking en pathologische veranderingen gebruikt bij de keuze voor en het evaluatie proces van chirurgische en conventionele ingrepen. Met behulp van recente ontwikkelingen in de gangbeeldanalyse van optische meettechnieken en gedetailleerde voet en enkel computermodellen, zijn de typische gewrichtsbewegingen van de RA voet en enkel tijdens lopen geanalyseerd en beschreven. Deze techniek wordt echter nog niet regelmatig gebruikt in de kliniek. Gangbeeldanalyse van gewrichtsbewegingen van de heup, knie en enkel dragen in belangrijke mate en met succes bij aan de diagnose en evaluatie van patiënten met een beroerte of cerebrale parese. Voor patiënten met RA zijn de relaties tussen gewrichtsbewegingen en loopstoornissen of pathologische veranderingen van de voet en enkel nog niet voldoende bestudeerd. Deze fundamentele kennis is nodig ter ondersteuning van de ontwikkeling en evaluatie van meer effectieve interventies, die gericht zijn op verbetering of herstel van een normale dynamische functie van de voet en enkel. Het doel van dit proefschrift was om meer inzicht te krijgen in de oorzaken van de veranderingen in de voet en enkel gewrichtsbewegingen van RA patiënten ten opzichte van gezonde proefpersonen.

Methodologie

Een literatuuronderzoek naar bestaande gangbeeld studies van patiënten met RA werd uitgevoerd. De kwaliteit van deze studies en hun conclusies werden geanalyseerd en beschreven (HOOFDSTUK 2). De analyse van voet en enkel gewrichtsbewegingen vereist een goede reproduceerbaarheid van de parameters van de meting. Voor gezonde personen is reeds aangetoond dat de gangbeeldanalyse van de voet en enkel bewegingen

herhaalbaar is. Echter, bij RA voeten kunnen misvormingen en zwellingen aanwezig zijn die de positie van de marker kunnen beïnvloeden. Tijdens eerste proefmetingen bij RA patiënten bleek dat de precieze positionering van markers ter hoogte van het distale os metatarsale I en het os naviculare discutabel was. Op het moment van deze metingen waren nog geen gangbeeld reproduceerbaarheid-studies uitgevoerd bij RA patiënten. Daarom werd het effect van variatie in herhaalde markerplaatsing op meer of minder ernstig misvormde voeten van 3 RA patiënten geanalyseerd (HOOFDSTUK 3). Aanvullend werd de variatie in markerpositie gesimuleerd door een computermodel. Door het beperkt aantal proefpersonen werd geen statistische analyse uitgevoerd. Met behulp van de resultaten werden keuzes gemaakt voor de in de vervolg studies te gebruiken kinematische parameters en werden conclusies getrokken over markerpositionering op ernstig misvormde voeten.

Het gangbeeld werd geregistreerd van 23 RA patiënten met verschillende ziektestadia en van 14 gezonde proefpersonen van gelijke leeftijd. De voet en enkel gewrichtsbewegingen zijn berekend met behulp van een gedetailleerd voet en enkel computermodel bestaande uit 5 segmenten: onderbeen, achtervoet, middenvoet, voorvoet en hallux. In eerste instantie werden de effecten van loopsnelheid op de voet en enkel gewrichtsbewegingen bij gezonde proefpersonen geanalyseerd door middel van een herhaalde-metingen-ANOVA (HOOFDSTUK 4). De voet en enkel gewrichtsbewegingen van de gezonde proefpersonen werden geregistreerd en geanalyseerd bij drie loopsnelheden: comfortabele loopsnelheid en 70% en 50% van de comfortabele loopsnelheid. De betrouwbaarheid werd bepaald om de klinische betekenis van de bevindingen te toetsen. Dit is gedaan aan de hand van een lineair-mixed-model. De ganganalyse van de RA patiënten is uitgevoerd bij een door henzelf gekozen comfortabele snelheid. De gewrichtsbewegingen van de RA voeten en enkels werden vergeleken met die van de gezonde proefpersonen bij de drie verschillende snelheden. Uit bestudering van de grafieken bleek dat de loopsnelheid alleen niet de waargenomen verschillen in gewrichtsbewegingen tussen de RA patiënten en gezonde proefpersonen kon verklaren. Daarom werd in een tweede stap een lineair-mixed-model gebruikt om de onafhankelijke bijdrage van de factor 'loopsnelheid' en de factor 'ziekte' op de voet en enkel gewrichtsbewegingen van RA patiënten te analyseren (HOOFDSTUK 5).

De gewrichtsbewegingen die werden beïnvloed door de factor 'ziekte' werden geïdentificeerd en gebruikt om de relaties tussen gewrichtsbewegingen en klinische parameters te bestuderen (HOOFDSTUK 7). Als tussenstap werden de koppelingen tussen de bewegingen van aangrenzende en niet-aangrenzende voet- en enkelsegmenten

onderzocht bij gezonde proefpersonen. Daarvoor is gebruik gemaakt van de Pearson correlatie-test (determinatiecoëfficiënt R^2) en de variatiecoëfficiënt (CV) (HOOFDSTUK 6). Verschillende actieve en passieve structuren zijn bevestigd aan (niet) aangrenzende voet- en enkelsegmenten en beïnvloeden de relatieve bewegingen tussen deze segmenten. De bevindingen kunnen inzicht geven in de onderliggende mechanismen van de geobserveerde RA voet en enkel gewrichtsbewegingen. Aan de hand van koppeling tussen segmentbewegingen is het bijvoorbeeld mogelijk uit te leggen hoe een verandering in de beweging in één segment, die wordt beïnvloed door een lokale pathologie, beweging van een meer distaal of proximale gelegen segment beïnvloedt. Als onderdeel van een andere studie heeft dr. Hetty Baan verschillende klinische scores van 25 RA patiënten gemeten en geanalyseerd. Van haar uitgebreide database zijn in dit proefschrift gebruikt: de erosie en synovitis scores van het eerste metatarsale-phalange (MTP I) gewricht, de middenvoet en achtervoet gewrichten en ook de letsel scores van pezen van spieren van het onderbeen welke aanhechten op de voet (HOOFDSTUK 7). De pees- en gewrichtscores werden vastgesteld op basis van Magnetic Resonance Imaging (MRI). Verder werden sub-scores van de Joint Alignment en Motion (JAM) voor de achtervoet en MTP I inbegrepen. De klinische bevindingen die betrekking hebben op de MTP II-V en de kleinere tenen zijn niet meegenomen in deze studie omdat het computermodel deze gewrichtsbewegingen niet berekent. De klinische en kinematische scores werden getest op onderlinge afhankelijkheid door middel van Spearman correlatietests. De relaties tussen de kinematische en klinische parameters werd bestudeerd door middel van Spearman correlatietests. In deze explorerende studie zijn de laagste en hoogste waarde van de 95% betrouwbaarheidsintervallen (BI) van de correlatie-coëfficiënten geëvalueerd en beschreven. Relaties met een correlatie-coëfficiënt van meer dan 0.3 of 0.5 worden gedefinieerd als matig of sterk, respectievelijk.

Resultaten

Het literatuuronderzoek omvatte 78 studies. De kwaliteit van de studies werd voornamelijk als matig gescoord als gevolg van de relatief kleine steekproef in vergelijking met het hoog aantal proefpersonen (> 50 personen) welke vereist is voor een hoge kwaliteit klinische effect studie. Maar ook de gekozen methodologie en analyse beïnvloedden de kwaliteit: loopstoornissen werden niet vergeleken met klinisch relevante scores voor de functie en of pathologische veranderingen en de reproduceerbaarheid van de methodologie kwam niet

aan de orde. Bovendien zou meer uniformiteit in methodologie, met name in de berekening en analyse van kinematische parameters, de vergelijking tussen studies verbeteren. De conclusies voor ruimte-tijd parameters kwamen overeen en er werd bij RA patiënten een vermindering van de loopsnelheid, verkleining van de paslengte en verkorting van de single-stance tijd waargenomen in vergelijking met gezonde proefpersonen. In vergelijking met gezonde personen die lopen bij een vergelijkbare snelheid, werd bij RA patiënten een verhoogde cadans ter compensatie van een kleinere staplengte waargenomen. Hogere drukken werden waargenomen onder de kopjes van metatarsale II-V en een aantal druk parameters konden worden gerelateerd aan klinische scores, zoals pijn. Veranderingen in de bewegingen van de achtervoet, voorvoet en MTP I werden waargenomen bij RA patiënten in vergelijking met gezonde proefpersonen. De verschillende gangbeeld studies onderzochten verschillende kinematische parameters, maar over het algemeen werd het volgende waargenomen: een vermindering van de achtervoet plantarflexie en MTP I dorsaalflexie bij pre-swing, afname van de maximale voorvoet abductie en een abnormale verschuiving naar achtervoet eversie tijdens de standfase. Er werden geen studies gevonden die de relatie tussen de kinematische veranderingen en de klinische scores voor het dagelijkse functioneren of pathologische veranderingen bestudeerden. Slechts één studie evalueerde het effect van (voorvoet) operaties aan de voet op gewrichtsbewegingen tijdens lopen en slechts één studie analyseerde het effect van orthesen op gewrichtsbewegingen van de voet.

Variatie in markerpositie op de voet van 3 RA patiënten resulteerde in een offset (tot 10°) van de berekende gewrichtsbewegingen en in een verandering in patroon (maximaal 5°) van de gewrichtsbewegingen als functie van de standfase. De simulaties in markerpositie in het computermodel voorspelden soortgelijke bevindingen. De meest gevoelige gewrichtsbewegingen voor variatie in markerpositie waren de MTP I plantair/dorsaalflexie (5°) als gevolg van variatie in de proximaal-distaal positie van de distale metatarsale I marker en de middenvoet pro/supinatie (2°) als gevolg van variatie in de mediaal-lateraal positie van de naviculare marker. Door de aanwezigheid van eeltknobbels, zwellingen en of vervormingen was de plaatsing van de distale metatarsale I marker en navicular marker vaak niet in overeenkomst met de voorgeschreven positie in het markerplaatsing protocol.

Het lopen van 14 gezonde proefpersonen werd opgenomen bij hun eigen comfortabele en twee langzamere loopsnelheden van gemiddeld 1.28 m/s, 0.97 m/s en 0.65 m/s, respectievelijk. Het effect van loopsnelheid was significant en klinisch relevant in het sagittale vlak voor de maximale enkel plantairflexie (3° - 6°), minimale mediale boog (1° - 2°)

en een maximale MTP I dorsaalflexie (5° - 9°). In het frontale vlak waren de verschillen in minimale middenvoet pronatie tussen loopsnelheid sessies klein (1° - 2°), maar significant verschillend en uiterst betrouwbaar (0.94).

De onafhankelijke bijdrage van de factoren 'loopsnelheid' en 'ziekte' werd onderzocht in een lineair-mixed-model. De input van het lineair-mixed-model omvatte de kinematische parameters van 21 RA patiënten die lopen op hun eigen comfortabele snelheid en de kinematische parameters van 14 gezonde proefpersonen die lopen op een comfortabele en twee langzamere snelheden. De resultaten toonden aan dat de factor 'loopsnelheid' alleen de achtervoet plantairflexie, de inzakking van de mediale boog, de onderbeen rotatie en de voorvoet abductiebeweging tijdens pre-swing beïnvloedde. De MTP I dorsaalflexie tijdens pre-swing en de middenvoet supinatiebeweging tijdens single-stance werden beïnvloed door zowel de factor 'loopsnelheid' als de factor 'ziekte'. De factor 'ziekte' alleen beïnvloedde de achtervoet eversiebeweging tijdens single-stance.

Bij gezonde personen werd een sterke en consistente quasi-lineaire koppeling waargenomen tussen de achtervoet eversiebeweging en de MTP I plantairflexiebeweging (gemiddelde determinatiecoëfficiënt R^2 0.8). De individuele variatie in deze koppeling was klein (variatiecoëfficiënt CV 0,2). Koppeling tussen de onderbeen rotatie en de inzakking van de mediale boog was consistent, maar was minder sterk (R^2 0,5) en toonde veel meer individuele verschillen (R^2 0,1-0,8) en variabiliteit (CV 0,4). Koppeling tussen naast elkaar liggende segmenten was minder consistent, met grote individuele verschillen (R^2 0,2-0,8) en meer individuele variatie (CV 0,4-0,5).

De relaties tussen klinische en kinematische parameters zijn geanalyseerd. Een vermindering van de maximale MTP I dorsaalflexie op pre-swing was matig tot sterk gecorreleerd aan toegenomen erosie en synovitis van het MTP I gewricht (BI 0.3,0.8), erosie van de middenvoet gewrichten (BI 0.2,0.8) en achtervoet gewrichten (BI 0.0,0.7). Een toename van de middenvoet pronatie tijdens single-stance was gecorreleerd aan een pathologische veranderingen van de achillespees (BI 0.0,0.7). Afname van de eversiebeweging van de achtervoet tijdens single-stance was gecorreleerd aan pathologische veranderingen van de peroneus pees (BI 0.0,0.7). De sub-schalen van de JAM waren ook gecorreleerd aan veranderingen in gewrichtsbewegingen: een afname van de beweeglijkheid van het MTP I gewricht resulteerde in een afname van de MTP I dorsaalflexie tijdens pre-swing (BI 0.1,0.8) en een slechtere uitlijning van de achtervoet resulteerde in een afname van de middenvoet pronatiebeweging (BI 0.1,0.8) en achtervoet

eversiebeweging (BI 0.2,0.8) tijdens single-stance. In deze studie waren de pathologische veranderingen van de tibialis posterior pees niet gecorreleerd aan veranderingen in middenvoet pronatiebeweging (BI -0.3,0.5) of achtervoet eversiebeweging (BI -0.5,0.4).

Conclusies

Er is slechts beperkte kennis beschikbaar over de onderliggende mechanismen voor de waargenomen veranderingen in de voet en enkel gewrichtsbewegingen in RA en hoe chirurgische en conventionele interventies deze abnormale bewegingen beïnvloeden.

Reproduceerbaarheid van de gemeten en berekende voet en enkel kinematische parameters is minder goed voor ernstig misvormde voeten dan voor normale voeten. Dit is een gevolg van, onder andere, een hogere variatie in de markerplaatsing op de voet. Vooral de kinematische parameters voor de middenvoet en MTP I dorsaalflexie zijn gevoelig voor variatie in markerpositie. De protocollen voor markerplaatsing moeten worden geoptimaliseerd voor meer of minder ernstig misvormde voeten. Zo kan bijvoorbeeld de reproduceerbaarheid van de MTP I dorsaalflexie worden geoptimaliseerd door het meer dorsaal plaatsen van de distale metatarsale I marker of door het aanbrengen van een extra marker distaal van het MTP I gewricht op de hallux.

Loopsnelheid beïnvloedt de voet en enkel gewrichtsbewegingen, maar kan niet alle waargenomen kinematische verschillen tussen RA en gezonde proefpersonen verklaren. Onafhankelijk van de factor 'loopsnelheid' beïnvloedt de factor 'ziekte' de maximale MTP I dorsaalflexie tijdens pre-swing en de middenvoet pronatiebeweging en achtervoet eversiebeweging tijdens single-stance. Een dergelijke verandering in gewrichtsbewegingen werden niet waargenomen bij gezonde personen die bij eenzelfde snelheid lopen. Daarom wordt aangenomen dat deze veranderingen in gewrichtsbewegingen van pathologische aard zijn en met prioriteit moeten worden behandeld door middel van conventionele of chirurgische interventies.

De koppeling tussen de bewegingen van de achtervoet eversie en MTP I plantairflexie was sterk en consistent voor gezonde proefpersonen. Passieve structuren zoals de fascia plantaris en de plantaire ligamenten verbinden deze twee voetsegmenten. Derhalve zal een pathologische verandering van een lokale structuur van één dezer segmenten niet alleen de beweging van dat ene segment beïnvloeden maar ook, door de koppelingsrelatie, indirect

de beweging van het andere segment. Anderzijds zal een pathologische verandering van de plantaire structuren de koppeling tussen de MTP I en achtervoet beweging beïnvloeden en kunnen compensatoire bewegingen nodig zijn van een ander segment zoals de middenvoet.

In de cross-sectionele observatiestudie met 25 RA patiënten konden enkele klinische bevindingen gerelateerd worden aan veranderingen in gewrichtsbewegingen: pathologische veranderingen van het lokale gewricht en van de meer proximaal gelegen gewrichten werden gecorreleerd aan een afname van de MTP I dorsaalflexie tijdens pre-swing. De stand van de achtervoet en pathologische veranderingen van de achillespees werden gecorreleerd aan een afname van middenvoet pronatie. Alle 5 RA patiënten met pathologische veranderingen van de achillespees hadden ook pathologische veranderingen van plantaire structuren. Dergelijke pathologische veranderingen werden niet geobserveerd bij de andere RA patiënten. Naar aanleiding van deze bevindingen en de bevindingen uit het koppelingsonderzoek, wordt geconcludeerd dat in toekomstige studies de rol van plantaire structuren op de gewrichtsbewegingen van RA patiënten moet worden onderzocht. Verder werden zowel de stand (uitlijning) van de achtervoet als pathologische veranderingen van de peroneus pees gerelateerd aan een afname van de achtervoet eversiebeweging. De twee klinische parameters waren ook onderling gecorreleerd. Er werden echter geen effecten op gewrichtsbewegingen gevonden voor pathologische veranderingen van de tibialis posterior pees. Toekomstige studies dienen verder in te gaan op de effecten van veranderde stand van de voet en enkel (uitlijning) en pathologische veranderingen van de pezen van het onderbeen op veranderingen in gewrichtsbewegingen in een meer homogene RA populatie of tijdens longitudinale RA studies.



Dankwoord

Dankwoord

Er zijn veel mensen die in de afgelopen jaren in meer of mindere mate bijgedragen hebben aan de totstandkoming van dit proefschrift. Een ieder hartelijk bedankt, een aantal mensen in het bijzonder.

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Dear Chris, thank you for helping me understand the findings of the kinematic coupling study. I felt very welcome in Salford and am grateful for your time and support in writing the article together. It took some time, but I think it was worth the effort to get these ideas out into the world.

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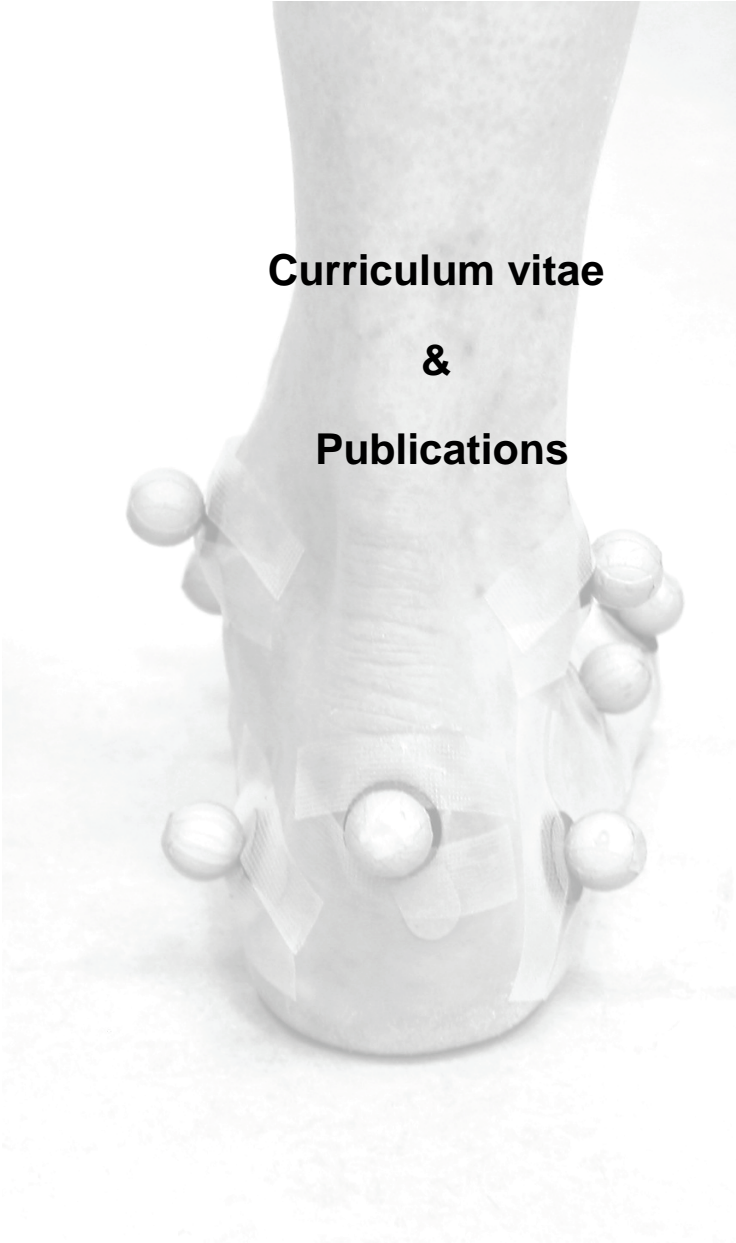
Mijn lieve familie, dank jullie wel voor jullie steun en interesse gedurende de afgelopen jaren. Oma's oppas voor de kinderen en twee jaar lang wekelijkse logeren bij Suzanne in Utrecht zijn slechts enkele van vele voorbeelden.

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Ja mijn lieve kinderen, er is weer meer tijd!

**Curriculum vitae
&
Publications**



Curriculum Vitae

Rosemary Dubbeldam is geboren op 9 juli 1972 te Den Helder. Na vijf jaar voorbereidend wetenschappelijk onderwijs (VWO) op het Johannes College te Den Helder, heeft zij het examen jaar in 1990 afgesloten op het Werenfridius College te Hoorn. Zij is gestart met de studie Luchtvaart- en Ruimtevaarttechniek in Delft en is afgestudeerd in 1996. Daarna heeft zij gewerkt bij Delphi Automotive Systems in Wuppertal, Duitsland, aan de ontwikkeling van airbags voor de automobiel industrie. Bij Delphi werd er tijd vrijgemaakt voor onderzoek: bijvoorbeeld om samen te werken met de biomechanica afdeling van de Universiteit van Bochum en Universiteit Eindhoven aan de ontwikkeling van voet en knie computermodellen, die gebruikt worden in botsingssimulatie.

In 2003 heeft zij besloten tijdelijk uit het bedrijfsleven te stappen om meer tijd te hebben voor haar kinderen en om zich verder te ontwikkelen. Zij heeft een jaar gestudeerd aan de faculteit Biomedische wetenschappen van de Universiteit Twente. In 2004 is zij gestart met de deeltijd opleiding Fysiotherapie aan de Hogeschool Thim van der Laan in Utrecht en heeft deze in 2007 afgerond. Vanaf 2009 is zij één dag in de week werkzaam als fysiotherapeut in een kleine particuliere praktijk in Duitsland. Sinds 2005 is zij in deeltijd werkzaam als onderzoeker bij Roessingh Research and Development (RRD) in Enschede. De uitgevoerde gangbeeld metingen van patiënten met reumatische artritis voor de afdeling reumatologie van het Medisch Spectrum Twente, vormden uiteindelijk de basis voor dit promotieonderzoek. In 2011 is zij bij RRD begonnen met een nieuw onderzoek wat betrekking heeft op de balanshandhaving van oudere fietsers.

Naast bovenstaande werkzaamheden is zij trainer bij de gymnastiek vereniging TuS Wüllen in Ahaus, Duitsland. Daar begeleidt zij sinds 2006 drie keer in de week de jonge talenten van de turnafdeling.

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