CHAPTER I

General introduction
Walking is one of the most important activities in daily life, as it enables participation in daily life activities. Although walking seems an easy task for most people, it is a delicate combination of movements of the different parts of the body. When a central neurological disorder such as cerebral palsy (CP) affects motor control, and consequently walking ability, the complexity of walking becomes apparent. In pediatric rehabilitation medicine, an important treatment goal is to acquire, maintain or improve walking ability of children with CP. To this end, one of the most common interventions in these patients is the use of an ankle foot orthosis (AFO). Evidence for the efficacy of these orthoses to improve gait in children with CP is however considered ambiguous, as both positive and negative effects have been reported. This thesis will focus on how efficacy of AFOs in CP might be improved.

CEREBRAL PALSY

With a prevalence of 2-3 per 1000 live births, CP is the most common cause of children’s disability in Western Europe\(^\text{[1-3]}\). It is described as “a group of permanent disorders of the development of movement and posture, causing activity limitations, that are attributed to a non-progressive disturbance that occurred in the developing fetal or infant brain”\(^\text{[1,4]}\). Several etiological factors could underlie CP and are typical for a particular time of onset: prenatal (e.g. intoxication), perinatal (e.g. infarction), and postnatal (e.g. infection)\(^\text{[3,5]}\). There are several risk factors for CP, such as prematurity, infection in the mother and/or child, and intrapartum asphyxia\(^\text{[6]}\).

The term CP covers a broad variety of clinical presentations, which can be categorized into groups or classes. First, CP can be described in terms of motor disorders, with spastic, ataxic, and dyskinetic sub-types\(^\text{[5]}\). A mix of types may also occur, in which the dominant type defines the motor disorder classification\(^\text{[4,2]}\). The type that will be discussed in this thesis is the spastic CP, which is the most common type as it accounts for approximately 80 percent of the patients with CP\(^\text{[3]}\). Spastic CP is defined as a posture- and movement-dependent muscle tone regulation impairment\(^\text{[5]}\), which can be divided into impaired muscle control and impaired biomechanical muscle properties\(^\text{[5,8]}\). Impaired muscle control includes both deficit symptoms (e.g. muscle weakness and loss of selective motor control), and excess symptoms, such as spasticity\(^\text{[9]}\) and muscle co-contractions\(^\text{[5]}\). Impaired biomechanical muscle properties include increased muscle stiffness and abnormal muscle length\(^\text{[10,11]}\). Consequently, children with spastic CP have a risk to develop secondary impairments, such as joint contractures and bony deformities\(^\text{[12]}\). As a second categorization, spastic CP can be classified based on disease distribution\(^\text{[3]}\).
Children with unilateral CP are affected on one side, while bilateral CP involves both sides of the body\(^\text{[5-13]}\). Third, the level of impaired overall motor functioning in children with CP can be categorized with the Gross Motor Function Classification System\(^\text{[14]}\) (GMFCS). The GMFCS describes five levels of motor functioning, where lower levels indicate better motor function. Levels IV and V describe the group of children who are not able to walk independently. This thesis is focused on children with GMFCS levels I-III, i.e. referring to children who are able to walk independently with or without restrictions (level I and II respectively), or with a walking device (level III). Although the majority of children with CP (approximately 70\%) are able to walk with or without assistive devices, motor impairments often lead to walking limitations\(^\text{[5]}\). In pediatric rehabilitation medicine, an important treatment goal is to acquire, maintain or improve walking ability of children with CP.

**GAIT**

**The gait cycle**

Gait is described by different phases of one leg (i.e. the leading leg) within a gait cycle. One gait cycle, or stride, starts with initial contact, which refers to the first contact of the foot with the ground and ends with the same leg hitting the ground again. Each stride is divided into a stance phase and a swing phase, where the stance phase accounts for approximately 60\% of the gait cycle. These two main phases can be sub-divided into separate events, such as midstance (see Figure 1.1). Push-off describes the leg’s transition from the stance phase into the swing phase.

**Normal gait**

Each phase of the gait cycle is characterized by a specific position and orientation of the body’s segments and joints. In relation to these orientations, the ground reaction force, i.e. the force exerted by the ground on the body, acts on the joints. A close alignment of the ground reaction force to the joint rotation centers results in low net moments, and accordingly, in low muscle forces to maintain posture and balance. The course of the ground reaction force and its alignment to the joint rotation centers during normal gait are shown in Figure 1.1.
Figure 1.1. The gait cycle, divided into the stance phase (i.e. initial contact to toe-off) and the swing phase (toe-off to initial contact). The phase between initial contact and contralateral toe-off is referred to as the loading response. Following loading response, the leading leg progresses towards midstance, which is defined as the moment of the contralateral leg passing the stance leg. The contralateral leg swings in front of the leading leg, until contralateral initial contact occurs. Within a small period of double support, the weight is shifted from the trailing leg to the contralateral leg, also referred to as preswing or push off. This is followed by the moment of toe-off, which concludes the leg’s transition from the stance phase into the swing phase. In swing, the leg passes the contralateral leg at contralateral midstance to continue to initial contact to start a new gait cycle. The magenta line indicates the course of the ground reaction force, and its alignment with respect to the joints during normal walking. The center of pressure starts at the heel and slowly progresses towards the hallux as the stance phase continues.

Abbreviations: IC, initial contact; cTO, contralateral toe-off; MSt, midstance; cIC, contralateral initial contact; TO, toe-off; cMst, contralateral midstance.
Adequate functioning of the ankle and foot is essential for normal walking, and can be described in terms of rockers\cite{15}. The first rocker, also called heel rocker, represents the time span from the first heel contact (i.e. initial contact) to full contact of the foot with the surface. This involves lowering of the foot to the surface, which is controlled by eccentric contraction of the ankle dorsiflexor muscles. During the second rocker (ankle rocker), the tibia progresses over the foot, which remains flat on the ground. This is due to an eccentric contraction of the ankle plantar flexor muscles and allows continued forward movement of the body. The third rocker (forefoot rocker) represents the phase from contralateral initial contact to toe-off. At this stage, a large burst of power is generated about the ankle, which is due to a fast shortening (concentric contraction) of the plantar flexor muscles resulting in plantar flexion movement.

In addition to sufficient rocker functions, knee joint function in the sagittal plane is also considered an important feature during gait. The knee acts like a shock absorber as it flexes during early stance, while maximal extension is reached just before contralateral initial contact occurs. Using the force of the plantar flexion during the third rocker (push-off), and psoas muscle activation, the knee and hip will flex to reach sufficient clearance of the foot during the swing phase.

Normal gait is a complex yet highly energy efficient process\cite{16}. Several biomechanical adjustments are used by the body to minimize the energy consumption [J·kg·min⁻¹] during walking, such as a minimal excursion of the center of mass, and transfer of energy between segments by bi-articular muscles\cite{16}. The energy consumed in relation to the covered distance is also dependent on a person’s walking speed, expressed by the energy cost of walking [J·kg·m⁻¹] (also referred to as gait efficiency) and calculated by dividing the energy consumption by walking speed. Healthy individuals select a comfortable walking speed at which gait efficiency is maximal\cite{17}. In healthy children, gait efficiency improves with age until adulthood\cite{17,18}.
Gait in cerebral palsy

Due to symptoms of impaired motor control, muscle weakness, abnormal joint position, decreased joint range of motion, and a decreased muscle length, gait is often hampered in CP\textsuperscript{[16]}. The clinical representation of gait in CP is very heterogeneous, and therefore several efforts have been made to categorize these into gait patterns\textsuperscript{[19]}. In the Netherlands, the classification of Becher\textsuperscript{[5,20]} is generally used for gait in spastic CP. This classification describes five gait types, mainly based on the deviations of the knee and ankle joint angles at midstance (see Figure 1.2). Gait type 1 describes a gait pattern characterized by a normal stance phase, but insufficient foot lift during the swing phase. Gait types 2 and 3 show hyperextension of the knee, respectively with or without full foot contact. Gait types 4 and 5 describe a pattern with excessive knee flexion, either with ankle plantar flexion (type 4) or excessive dorsiflexion (type 5). This thesis only discusses children who walk in gait types 4 or 5.

The ankle and foot rocker functions are impaired in most CP walking types. Weakness of the dorsiflexor muscles, for example, commonly causes mid- or forefoot contact during the first rocker. Consequently, the tibia is positioned excessively inclined already in the beginning of stance, allowing no forward tibia progression during the second rocker, and an excessively flexed knee joint at this stage. This effect is frequently enhanced by weakness of the plantar flexor muscles. The abnormal second rocker function leads to the posterior alignment of the ground reaction force with respect to the knee joint rotation center, and accordingly, in an increased knee moment. The push-off power is also often impaired as a result of abnormal ankle joint moments in late stance. The rapid plantar flexion movement that is needed for an effective push-off is impeded by the persistent

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{gait_types.png}
\caption{The gait types according to the classification of Becher. This thesis focuses on the gait that are characterized by excessive knee flexion, either without foot contact (type 4) or with full foot contact (type 5) at midstance.}
\end{figure}
knee flexion and posterior alignment of the ground reaction force with respect to the knee joint rotation center in late stance. Abnormal timing of plantar flexion movement (i.e. early or late heel rise)\cite{16}, caused by short calf muscles, plantar flexor weakness or impaired muscle activation\cite{31}, can further deteriorate the third rocker function. A reduced push-off prevents a rapid movement of knee and hip into flexion,\cite{16} resulting in inadequate clearance, and insufficient knee extension at the end of the swing phase. The reduced knee extension during this phase leads to mid- or forefoot contact at initial contact, consequently reducing step length. As muscle shortening in spastic CP occurs according to the movement pattern, it seems apparent that gait deviations are related to an impaired muscle length\cite{20}. In turn, this may reduce the (passive) range of motion of the adjacent joints, i.e limited muscle stretch, which has been shown to be an important cause in the development of muscle contractures\cite{19}. Muscle contractures negatively affect the gait deviations\cite{16}, leading to a vicious circle in which gait further deteriorates over time.

The underlying impairments often limit walking ability in CP, as gait deviations are associated with increased energy consumption. This especially applies to children walking with excessive knee flexion during stance, as these children are liable to show deterioration of walking in (pre-)puberty\cite{22,23}, and their gait patterns are particularly energy consuming\cite{17,24}. In fact, it has been shown that walking energy consumption in CP can be two to three times higher compared to typically developing children\cite{17,24-26}. To minimize the increase in energy consumption, patients often lower their walking speed to maintain walking over longer distances\cite{25,26}. As such, an increased walking energy cost is commonly observed, which reflects poor gait efficiency\cite{25,26}. Although the nature of the association between underlying impairments, gait deviations and the increased energy consumption during walking in CP is not yet unraveled, abnormal knee and ankle kinematics and kinetics during gait are considered key features. First, the increased internal knee extension moment require high muscle forces to maintain posture\cite{27}, which could be related to a higher energy consumption during walking\cite{17,28}. Second, reduced ankle range of motion and ankle push-off power generation have been shown associated with a lower walking speed, which subsequently increases walking energy cost\cite{29-31}. To compensate for the reduced ankle push-off, power is often generated in the hip joint around toe off\cite{16,32,33}. This has been shown to be mechanically less efficient\cite{29,34}, and is thus likely to further increase the walking energy cost.
Chapter I

IMPROVING GAIT IN CEREBRAL PALSY

Treatment with AFOs

An ankle foot orthosis (AFO) is a commonly applied rehabilitation intervention in children with CP to maintain muscle length (i.e. passive range of motion), as well as to maintain or improve stability, standing, and/or walking ability[35]. An AFO is a medical device that imposes a mechanical constraint to the ankle and foot, aiming to compensate for a loss of function (i.e. resisting forces that act upon the body), or to counteract an excess of function (i.e. resisting forces from within the body). As such, an AFO can directly affect movements of the ankle and foot, and, dependent on its design, it can also stabilize the knee and hip joints[36]. AFOs are available in various different designs, e.g. hinged or non-hinged, and with a ventral shell or dorsal shell. In addition, AFOs can be made of different materials like carbon fiber or polypropylene. Consequently, each AFO holds specific mechanical properties, such as stiffness around the ankle. When prescribing an AFO, its design and mechanical properties should counteract the patient’s underlying impairments, and be designed such that it counteracts the specific gait deviations as much as possible, aiming to effectively improve gait.

AFO efficacy in cerebral palsy

The efficacy of AFOs on gait can be described in terms of its mechanical effects (i.e. gait biomechanics), and/or in terms of the patient’s gain in walking ability (e.g. gait efficiency)[37]. In general, the effects of AFOs on gait have been widely investigated, with studies mainly evaluating the efficacy of AFOs on gait biomechanics. These studies generally report improvements in terms of spatio-temporal parameters[38-45] and joint kinematics[38,40,44,46] and kinetics[40,41,43,46]. Although improvement of gait biomechanics has been shown to be closely coupled to improvement of gait efficiency[47], also in the context of orthotic interventions[40,46,47], evidence for the efficacy of AFOs on gait efficiency remains inconclusive[48].

These ambiguous results within AFO research have been acknowledged in some reviews[48-50], where various gaps in current literature have been addressed. First, the AFO’s efficacy is expected to be largely dependent on the match between the AFO’s mechanical properties and patient’s specific underlying impairments. Sufficient description of participants, especially in terms of motor impairments and gait patterns is however mostly lacking. Also the AFOs used in studies are described with global reference to design and materials, and rarely described in terms of mechanical properties[48-50].

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The absence of such information hampers to unravel the nature of the optimal match between the patient and the AFO, and to define the causes of the AFO’s (in)efficacy. Moreover, a variety of AFOs in relation to the underlying impairments and gait deviations of participants is introduced by differences in the prescription process, which is currently largely dependent on clinical experience as clear prescription guidelines are scarce. The insufficient information and variety between studies prevents a fair comparison of results, and reduces the potential to perform meta-analyses to provide more substantial evidence to improve prescription guidelines. Evidence for AFO efficacy in CP could be improved by good quality research using strong designs that can control for confounding factors, providing unambiguous characteristics of the participants’ walking biomechanics and the mechanical properties of the applied AFOs.

Another problem within AFO research concerns the lack of consistency in outcomes to report AFO efficacy. To evaluate of the effects AFOs on gait, Brehm et al. suggested a core set of outcomes, covering measures on all domains of the International Classification of Functioning, Disability and Health (IFC) framework. This is the common framework for the assessment of functioning and treatment planning of patients in rehabilitation medicine. The ICF framework uses the domains of ‘body functions and structures’ ‘activities’ and ‘participation’ to describe the impact of a disease or disability on human functioning, which can also be affected by ‘personal factors’, and ‘environmental factors’. The domain ‘body functions and structures’ describes a person’s functioning on the level of the physiological functions of body systems and the body’s anatomical structures. The ‘activity’ domain describes human functioning in terms of daily-life activities, and can be sub-divided into the capacity and performance qualifiers. The first refers to what a person can do in, for example, a laboratory setting, while the latter describes what a person actually does in day-to-day life. The ‘participation’ domain refers to a person’s participation in daily life situations, such as sports, and social events.

From the patient’s perspective, it is most relevant to assess the effect of an AFO on outcome measures that express the gain for the patient; for example, a measure that quantifies walking capacity such as walking speed or walking energy cost. Additionally, an assessment of daily walking activity (i.e. walking performance) may give insight in the patient’s functioning in daily life. The effects of an AFO on gait biomechanics, assessed with a 3D gait analysis, can also be evaluated, representing the biomechanical functioning of an AFO (i.e. at level of body functions and structures). It has been suggested that outcome measures in studies on AFO efficacy should cover both the activity level and the level of body functions and structures. This could reveal mutual relations between
outcome measures, giving insight the underlying working mechanism of AFOs, which may contribute to proving the efficacy of a treatment algorithm, i.e. how to prescribe a well-matched AFO\textsuperscript{37}.

**Optimizing AFO treatment**

Several factors that could improve AFO treatment in order to prescribe a well-matched AFO have been addressed in the literature, some of which will be discussed in this thesis.

**Adjusting the AFO alignment**

Firstly, literature suggests that an appropriate orientation of the shank (i.e. close to normal) during midstance is a main determinant for efficient walking. In normal walking, the shank is 10 to 12 degrees inclined with respect to the vertical at midstance, therewith positioning the knee joint in the middle of the base of support. It is assumed that this facilitates balance and appropriate ground reaction force alignment with respect to the knee and hip joints, and therefore contributes to conservation of energy\textsuperscript{54}. Healthy individuals have the ability to adapt the orientation of the body segments to achieve adequate alignment independent from the footwear they are wearing as long as it allows ankle range of motion.

When wearing an AFO, for most AFOs the ankle is fixed into a pre-defined angle determined by the AFO’s neutral angle (i.e. the angle of the AFO when no force is applied). As ankle range of motion is restricted, the orientation of the shank at midstance is now defined by the combination of the AFO’s neutral angle, and the shoe’s heel-sole differential, i.e. the difference in height between the heel and the forefoot. Adjusting the heel-sole differential of the AFO-footwear combination is therefore expected to influence the orientation of the shank during walking. Subsequently, adjusting the AFO alignment could impact on the efficacy of the AFO, which is considered to be affected by the (mal-)alignment of the ground reaction force to the lower limb joint rotation centers\textsuperscript{36,55,56}. Although recently more interest has been shown in the AFO alignment in CP, evidence for the effects are lacking, and evaluating the alignment is currently not completely incorporated into clinical practice\textsuperscript{55}.

To successfully implement a proper evaluation of the AFO’s alignment into the prescription process in CP, a parameter to quantify the AFO alignment seems required. The Shank-to-Vertical-Angle (SVA) has been proposed as a relatively simple control
parameter to evaluate the effects of adaptations to the heel-sole differential\(^{[54]}\). Although effects of such adjustments, as quantified by the SVA, have already reported in some studies\(^{[55]}\), the response of the SVA to manipulations to the AFO-footwear combination and its relation to joint kinematics and kinetics have not been investigated so far.

**AFO stiffness**

Secondly, children walking with excessive knee flexion in stance are typically prescribed with a rigid ventral shell AFO that is manufactured with a rigid footplate\(^{[57]}\). This type of AFO aims to reduce knee flexion by shifting the ground reaction force anterior to the knee joint rotation center, to create an external knee extensor moment in stance, which is done through a force by muscular contraction of the ankle plantar flexors in normal gait. Literature shows that rigid AFOs can effectively reduce knee flexion during stance\(^{[43]}\), which may contribute to walking energy cost improvement\(^{[46]}\). However, the rigid properties also impede walking by impairing the rocker functions. This especially accounts for the third rocker, as the rigid AFO obstructs plantar flexion, therewith reducing push-off power\(^{[42,58-61]}\). As ankle range of motion and push-off power are considered key features for efficient gait\(^{[29,31]}\), this could negatively impact on the walking energy cost.

The AFO’s impeding effect on third rocker function could be reduced by using spring-like AFOs. Research has shown that spring-like AFOs (e.g. carbon fiber AFOs) can improve the gait pattern, while less constraining voluntary push-off\(^{[62,63]}\), which might be beneficial in terms of the walking energy cost\(^{[29,35]}\). Model studies\(^{[64]}\), as well as studies in healthy adults\(^{[65]}\) and adult patient populations\(^{[66,67]}\), already showed that both joint kinematics and kinetics, as well as the walking efficiency can be influenced by applying spring-like AFOs with different degrees of stiffness. As a result, gait efficiency could be maximized by choosing the appropriate AFO stiffness for each individual patient\(^{[66]}\). This individual approach of selecting an appropriate AFO stiffness may also apply to children with CP who walk with excessive knee flexion. It is thought that an optimal AFO stiffness, which is the stiffness that results in maximized gait efficiency, could be found. This optimum is expected to reflect the trade-off between a sufficient reduction of the knee flexion and minimal obstruction of third rocker function, although this hypothesis has not yet been investigated.
Chapter I

Acclimatizing to a new AFO

Thirdly, AFO efficacy is often assessed by its effect on gait biomechanics, as the mechanical constraint of the AFO is primarily expected to alter the gait pattern in terms of joint kinematics and kinetics, and eventually the overall gait performance. When applying an AFO, it could be expected that children with CP may need time to improve their gait pattern to the AFO by adjusting their muscle activation pattern (i.e. motor learning) to the new ankle mechanics\[68\]. When evaluating effects of an AFO on gait, acclimatization time for the gait pattern to adapt to the mechanical constraints as induced by a new AFO is therefore generally recommended to comply with the learning effect\[50\]. Accordingly, most testing protocols in research studies allow for acclimatization, although the permitted time varies between six weeks and less than one day\[50\]. While inadequate acclimatization time has been reported as a potential confounding factor for the efficacy of AFOs in some studies\[39,69\], it is unknown whether such an acclimatization period is actually required to reliably assess gait biomechanics of a newly prescribed AFO.

In summary, AFOs are widely used to improve gait in children with CP. Scientific evidence for the effectiveness of AFOs is however scarce and inconclusive. Insight in underlying working mechanisms of AFOs is also lacking. Considering the variation in reported effects of AFOs on gait in CP, an individual approach to optimize AFO prescription seems essential to maximize treatment efficacy.

AIM

This thesis aims to evaluate factors that can guide an individual optimization of AFO prescription in order to maximize AFO efficacy in children with CP who walk with excessive knee flexion in stance.

OUTLINE

The chapters of this thesis are primarily based on results of the AFO-CP trial, which was initiated to get insight in underlying working mechanisms of AFOs and to provide evidence for AFO effectiveness in children with CP walking with excessive knee flexion in stance. The study specifically aimed to individually optimize AFO stiffness to maximize the gait efficiency in these children. The protocol of the AFO-CP study is described in Chapter II.
In Chapter III, an instrumented treadmill was used to investigate the Shank-to-Vertical Angle as a parameter to evaluate the tuning process within AFO prescription. This study was performed in healthy adults and describes the effects of adjusting heel height and footplate stiffness of an AFO-footwear combination (i.e. AFO and shoes) on the Shank-to-Vertical Angle and lower limb joint angles and moments.

In Chapter IV, the BRUCE instrument was used to measure the mechanical properties of an adjustable spring-hinged AFO to assess its potential use in children with spastic CP. The spring-hinged AFO was set into different stiffness configurations, of which the mechanical characteristics were measured and discussed in relation to AFO function in children with CP walking with excessive knee flexion.

The effects of a rigid AFO and two spring-like AFO configurations of the spring-hinged AFO on gait were investigated in Chapter V. The effects of the AFOs were compared to walking with shoes-only. In addition to relevant biomechanical parameters and walking energy cost, also AFO contributions to ankle work were calculated.

In Chapter VI, the results of the stiffness variations on gait were used to select the optimal AFO stiffness for each patient. This selection was based on the maximal knee extension in stance and walking energy cost while walking with the different AFOs. Children wore their optimal AFO for three months, after which effect of the stiffness-based optimization on daily life activity was assessed.

Chapter VII investigates the effects of an acclimatization period to wearing a newly prescribed AFO on gait biomechanics in children with CP. Although an acclimatization time for the gait pattern to adapt to the new AFO is generally applied, the actual need for such acclimatization to reliably assess the effects of an AFO on gait biomechanics is not known. This chapter evaluates the effects of an AFO directly after tuning, and four weeks later in a subset of relevant biomechanical gait parameters.

In Chapter VIII the overall aim of this thesis is discussed and directions for future research are given.
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