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Balance control during walking: a two perspective exploratory study

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Abstract

Achtergrond Patiënten met een neuromusculaire aandoening benoemen een gebrekkige balans tijdens lopen als meest voorkomende limitatie om dagelijkse activiteiten te kunnen uitvoeren. Het is daarom cruciaal om inzicht te krijgen hoe balans tijdens lopen wordt gereguleerd. Een regel van Hof voor een stabiele controller voor lopen in robots is mogelijk ook toepasselijk voor stabiel lopen in mensen. Hierbij moet het drukpunt (CoP) op een vaste afstand van het geëxtrapoleerde massamiddelpunt (XCoM) worden geplaatst. De XCoM is een combinatie van positie en snelheid van het massamiddelpunt (CoM). De regel is gebaseerd op het simpelste biomechanisch model voor lopen, een omgekeerde slinger. Tijdens mechanisch verstoord lopen, controleren mensen hun balans door de afstand tussen CoP en XCoM constant te houden. Ook tijdens onverstoord lopen lijkt balans op deze manier gehandhaafd te worden. Twee strategieën om de CoP op vaste afstand van de XCoM te plaatsen zijn voet plaatsing (FP) strategie en enkel strategie tijdens de enkele standsfase (SS).

Doel Het doel was om balans controle tijdens lopen te onderzoeken vanuit twee perspectieven. In hoofdstuk 2 is vanuit klinisch perspectief onderzocht of patiënten met de ziekte van Charcot-Marie-Tooth (CMT) een aangedane voet plaatsing en enkel strategie hadden en of deze patiënten een hogere marge van stabiliteit (MoS) hadden in vergelijking met gezonde controles (HC). In hoofdstuk 3 is onderzocht of een model kon lopen op een vergelijkbare manier als gezonde mensen, gebruikmakend van Hof's regel.

Methode Hoofdstuk 2: CMT patiënten (n=17) en HC (n=10) voerden een twee-minuut loop taak (2MWT) en een precisie stap taak (PST) uit op comfortabele snelheid. De primaire uitkomstmaten waren de MoS en de laterale FP en SS relaties (FP_{ml} en SS_{ml}). Van iedere relatie werd de Pearsons correlatie coëfficiënt (ρ), intercept, helling en de residuen berekend.

Hoofdstuk 3: loopkarakteristieken (CoM amplitude, loopsnelheid en stapduur) van HC (n=10) werden vergeleken met die van modelsimulaties. Het standbeen was gemodelleerd als lineaire omgekeerde slinger en het zwaaibeen als slinger. Het model werd gedwongen om de CoP op vaste afstand van de XCoM te plaatsen en zijn staptijd werd gekozen zodat energetische kosten minimaal waren. De stapbreedte en staplengte werd gefit op die van gezonde controles.

Resultaten Hoofdstuk 2: de mediane $FP_{ml,\rho}$ en $SS_{ml,\rho}$ waren respectievelijk 0.78 en -0.57. De FP_{ml} uitkomstmaten (p>0.4) en de MoS (p=0.245) waren niet verschillend tussen CMT en HC. Van de SS_{ml} uitkomstmaten waren de residuen (p=0.01) en intercept (p=0.02) kleiner en de helling was minder steil (p<0.001) in CMT vergeleken met HC.

Hoofdstuk 3: er waren geen significante verschillen gevonden tussen het model en HC in de CoM amplitude (p=0.064), loopsnelheid (p=0.427), stapduur (p=0.212), stap-breedte (p=0.678) en stap-lengte (p=0.623).

Discussie Mensen gebruiken FP en SS strategie om de CoP op een vaste afstand van de XCoM te plaatsen tijdens het lopen, gebaseerd op de hoge correlaties. Op comfortabele loopsnelheid leken CMT patiënten geen aangedane FP_{ml} strategie te hebben maar wel een aangedane SS_{ml} strategie. Echter, dit kon ook veroorzaakt zijn door het verschil in loopsnelheid. Hoofdstuk 3 bevestigde dat het plaatsen van de CoP op vaste afstand van de XCoM belangrijk is en liet zien dat energetische efficiëntie ook een belangrijk aspect is van lopen. Het model zou idealiter gebruikt kunnen worden in onderzoek naar balans tijdens het ontwijken van obstakels.

Contents

1| General introduction

Balance control

Balance control is important for safe ambulation. Neuromuscular disorders affecting the lower limb, such as stroke, Charcot-Marie-Tooth disease and multiple sclerosis, often affect balance control (Winter, 1995; Tyson *et al.*, 2006; Ramdharry *et al.*, 2018). Impaired walking balance is the most common limitation to perform daily activities and it is linked to falling and injury (Newitt, Barnett and Crowe, 2016). Therefore, improving balance control is essential to many patients with neuromuscular disorders during rehabilitation.

A basic underlying principle of balance control is that a human body (or any other system) is in balance when its centre of mass (CoM) vertical projection is within the base of support (BoS). However, this concept is only true for static situations whereas in dynamic situations the velocity of the CoM should also be taken into account. Therefore, Hof et al. proposed an extended concept of balance control during dynamic situations (Hof, Gazendam and Sinke, 2005). The extrapolated centre of mass (XCoM) as introduced here takes into account the CoM vertical projection and the CoM horizontal velocity. Dynamic stability is then defined as keeping the XCoM within the BoS. The XCoM can be moved by moving the centre of pressure (CoP) which can be done either by moving the CoP within the BoS, using weight-shifting and ankle strategies, or by taking a step.

Defining balance control during walking is more difficult than defining standing balance, because the XCoM can be out of the BoS during walking without jeopardizing balance. Hof found a simple rule to achieve stable walking in bipedal humanoid robots: the CoP should be located at a fixed distance posterior and lateral to the XCoM at the time of foot contact (Hof, 2008). Hof's rule originates from the study on controllers for stable bipedal walking in robots and is called constant offset control (Kajita and Tani, 1991; Hof, 2008; Wight, 2008; Bruijn and Van Dieën, 2018; Vlutters, Van Asseldonk and van der Kooij, 2018).

Constant offset control is also used by humans during mechanically perturbed walking (Hof, Vermerris and Gjaltema, 2010; Vlutters, Van Asseldonk and Van Der Kooij, 2016; Vlutters, Van Asseldonk and van der Kooij, 2018). Hof and colleagues found lateral stepping responses in accordance with constant offset control theory (Hof, Vermerris and Gjaltema, 2010) while Vlutters found strong relations (R^2>0.9) between CoP and CoM velocity in both the sagittal and frontal plane (Vlutters, Van Asseldonk and van der Kooij, 2018). Another study from Hof found that humans may also use constant offset control during regular walking , which is unperturbed walking (Hof *et al.*, 2007).

The studies on perturbed walking used mechanical perturbations that were given as pushes or pulls onto the pelvis, which can be seen as pushes or pulls from other individuals in daily life (Hof, Vermerris and Gjaltema, 2010; Vlutters, Van Asseldonk and Van Der Kooij, 2016; Vlutters, Van Asseldonk and van der Kooij, 2018). Other more common scenarios in which individuals have to recover balance are when obstacles (e.g. a banana peel) need to be avoided or when one should aim for specific stepping locations. Since these perturbations are common in daily life, it is important to understand how individuals respond to such perturbations. A precision stepping task was developed at the Sint Maartenskliniek in which participants are instructed to step precisely on rectangular targets that are projected onto the treadmill belt. The task was developed in order to study the ability of individuals to adjust their steps. Interestingly, patients with balance impairments and healthy individuals had similar performance on this task. To gain insight in what exactly is controlled during the precision stepping task, it could be studied if constant offset control is used.

Balance control measures

For both clinical and scientific purposes, it is crucial to understand the underlying principles of balance control in patients with balance difficulties and healthy individuals. Therefore, it is important that balance control can be quantified. However, a uniform and best way to quantify balance control during walking is lacking. Currently existing balance control measures are based on clinical evaluation or laboratory measurements. Clinical measures such as the Berg Balance Scale (BBS) (Berg *et al.*, 1992) and the Timed Up & Go test (TUG) (Faria, Teixeira-Salmela and Nadeau, 2013) focus on assessment of functional balance aspects. These functional assessments can provide insight into the severity of balance impairment and resulting daily life struggles. Unfortunately, they do not provide insight into what causes balance impairment and how balance control is regulated. Laboratory-based measures can do this and the majority of them is based on XCoM and constant offset control theories (Hof, Gazendam and Sinke, 2005; Hof, 2008; Vlutters, Van Asseldonk and van der Kooij, 2018; Luijten, 2019).

The most frequently studied balance measure during walking is the margin of stability (MoS) (McAndrew Young and Dingwell, 2012; Hak *et al.*, 2013; Van Meulen *et al.*, 2016; Tesio and Rota, 2019). The MoS refers to the shortest distance between the XCoM and the boundaries of the BoS. An advantage of the MoS is that it has biomechanical meaning as it is directly related to the minimal impulse needed to bring a subject out of balance. Disadvantages are its dependency on walking speed and most importantly, that it is unclear how the MoS is regulated. Other measures derivate from the MoS and are for instance percentage positive MoS and MoS asymmetry (Van Meulen *et al.*, 2016). The current perspective is that a lower MoS after perturbation indicates an actual risk for falling, while an increased MoS indicates a protective attitude, reflecting latent instability (Tesio and Rota, 2019).

Strategies for balance control

Hof, Vlutters and an unpublished study discussed the various strategies to achieve constant offset control (Hof *et al.*, 2007; Hof, Vermerris and Gjaltema, 2010; Vlutters, Van Asseldonk and Van Der Kooij, 2016; Luijten, 2019). In essence, two main strategies can be distinguished. The first is controlling the location of the feet and is referred to as foot placement strategy. It can be thought of as a feedforward control mechanism, including estimation of the CoM position and velocity and using these estimates to predict foot placement. The second, called ankle strategy, is believed to fine-tune balance by controlling the CoP (Hof *et al.*, 2007).

Foot placement (FP) strategy is defined as the relation between foot placement and the XCoM or CoM velocity (Vlutters, Van Asseldonk and Van Der Kooij, 2016; Luijten, 2019). Here, foot placement was either the position of the foot or the lateral CoP. So far, FP has been studied in the frontal plane and not in the sagittal plane. Findings suggested a worse FP strategy in stroke patients. (Luijten, 2019) Vlutters and colleagues found that the strength of the FP relation depended on the definition of FP, especially for the sagittal plane. The strongest relation was found between the CoP-CoM distance at toe-off and the CoM velocity at heel strike (R^2=0.982) in comparison to the weakest relation between foot-CoM distance and CoM velocity at heel strike (R^2=0.281), both for slow walking (Vlutters, Van Asseldonk and Van Der Kooij, 2016).

Ankle strategy is by many defined as the relation between initial XCoM-CoP distance and CoP movement (Hof *et al.*, 2007; Hof, Vermerris and Gjaltema, 2010; Luijten, 2019). Because CoP movement is often studied during the single stance phase, the ankle strategy is commonly referred to as single stance (SS) strategy. Hof reported that Pearson's correlation coefficients of the affected side of transtibial amputees ranging were lower than those of healthy individuals. In line with this finding, Luijten found negligible Pearson's correlation coefficients of the paretic side of stroke patients compared to moderate correlations in healthy individuals.

FP and SS strategy are interdependent, meaning that incorrect foot placement can be compensated for by movement of the CoP during single stance (Hof, Vermerris and Gjaltema, 2010; Vlutters, Van Asseldonk and Van Der Kooij, 2016; Fettrow, Reimann, Grenet, Thompson, *et al.*, 2019; Luijten, 2019). It is thought that that the contribution of SS strategy is particularly important in AP direction (Vlutters, Van Asseldonk and Van Der Kooij, 2016). Furthermore, some evidence suggests that SS is used more during slow walking and FP strategy more during fast walking (Fettrow, Reimann, Grenet, Thompson, *et al.*, 2019).

Modelling balance control

Due to the plenty possible actions and combinations of actions to keep balance, it is difficult to get full grasp on how balance is controlled during walking. Moreover, walking itself is already a highly complex task and walking characteristics depend on the objective and environment (e.g. an individual with rush and walking in an empty room or in a room filled with obstacles). Therefore, simplification of balance control during walking using a modelling approach is useful. The constant offset control theory is based on such a simplification using an inverted pendulum model which is a point mass on a massless leg with a single contact point on the ground. The model can be extended or changed in many ways. For instance, a walking model can have a stance leg and swing leg, which can be modelled respectively as an inverted pendulum and a hanging pendulum. In absence of any control action (added energy to the pendulums) the pendulums move according to their passive dynamics. Similarly, humans exploit their passive dynamics instead of struggling against inertial forces generated during movement (Kuo, 2007; Kuo and Donelan, 2010).

Aim

The common goal of the two chapters is to explore constant offset control as a balance control mechanism during walking in humans. In chapter 2, strategies to achieve constant offset control will be viewed from a clinical perspective, by comparing them between healthy individuals and Charcot-Marie-Tooth (CMT) patients during regular walking. In chapter 3, a walking model implemented with constant offset control will be used to simulate regular walking in healthy individuals.

The ultimate goal of chapter 2 is to investigate if CMT patients have impaired balance control during walking which would be reflected by differences in the MoS, FP and SS strategy between CMT patients and healthy individuals. We were primarily interested in the use of the strategies in the frontal plane because constant offset control theory is most extensively studied in the frontal plane. Therefore, the primary aim of chapter 2 is <u>to study if the MoS, lateral FP strategy and lateral SS strategy are different between CMT patients and healthy individuals</u>.

The following additional questions were addressed:

1. Do humans use FP and SS strategy during regular walking?
    - 1.1. In frontal plane
    - 1.2. In sagittal plane
2. Are the FP and SS strategy (and MoS) different between CMT patients and healthy individuals?
    - 2.1. In frontal plane (primary aim)
    - 2.2. In sagittal plane (MoS excluded)
3. Are the FP and SS strategy (and MoS) different between regular walking and a precision stepping task?
    - 3.1. In frontal plane
    - 3.2. In sagittal plane (MoS excluded)

The aim of chapter 3 is <u>to investigate if a walking model is able to walk with similar gait characteristics as those observed in healthy individuals during regular walking</u>. Ideally, the walking model could in the future be used to predict human-like responses to perturbations.

2| Balance control strategies

2.1. Abstract

Introduction Majority of patients with Charcot-Marie-Tooth disease (CMT) experience frequent falls. Next to foot drops and muscle weakness, impaired balance control is one of the factors contributing to falls in these patients. So far, no studies have been published on balance control during walking in CMT patients. The primary aim was therefore to compare the lateral foot placement (FP) strategy, single stance (SS) strategy and MoS between CMT patients and healthy controls (HC). In addition, the effect of a precision stepping task was studied.

Methods CMT patients (n=17) and HC (n=10) performed a fixed speed two-minute walk test (2MWT) and a precision stepping task (PST) at comfortable speed. FP was defined as the relation between the CoP and CoM velocity. SS was defined as the relation between the initial CoP-XCoM distance and the CoP movement. Pearson's correlation coefficient (ρ), slope, intercept and the norm of the residuals were calculated from the linear relations. A two-way mixed ANOVA was performed to reveal effects of group and condition.

Results The median $FP_{ml,\rho}$ and $SS_{ml,\rho}$ were respectively 0.78 and -0.57. The FP_{ml} outcomes ($p>0.4$) and the MoS ($p=0.245$) were not significantly different between CMT patients and HC. Of the SS_{ml} outcomes the residuals ($p=0.01$) and intercept ($p=0.02$) were smaller and slope was less steep ($p=0.0002$) in CMT patients. Furthermore, almost all FP and SS outcomes were significantly different between conditions (2MWT vs PST). The MoS was not different between conditions ($p=0.828$).

Conclusion The high correlations suggested that humans use FP and SS strategies during regular walking. CMT patients do not have impaired lateral FP strategy and no larger MoS compared to HC during walking at comfortable speed. The seemingly impaired lateral SS strategy in CMT patients, might be caused by the difference in walking speed between CMT and HC. Furthermore, FP and SS strategies were used less during the PST in both ML and AP directions.

2.2. Abbreviations

CMT	Charcot-Marie-Tooth disease
HC	healthy controls
ML	mediolateral
AP	anteroposterior
CoP	centre of pressure
CoM	centre of mass
XCoM	extrapolated centre of mass
BoS	base of support
MoS	margin of stability
FP	foot placement
SS	single stance
2MWT	two-minute walk test
PST	precision stepping task

2.3. Introduction

Charcot-Marie-Tooth disease (CMT), also known as hereditary motor sensory neuropathy, affects 1 in 2500 individuals and is the most common inherited neuromuscular disorder (Murphy *et al.*, 2013). Patients experience distal muscle weakness and sensory loss, caused by degeneration of sensory and motor neurons. As a consequence, half of patients report difficulty in walking, which is primarily caused by a foot drop in swing and reduced calf power at push off (Kennedy, Carroll and McGinley, 2016). Majority of patients report falls and almost half of patients fall at least once every month (Ramdharry *et al.*, 2018). Foot drops and muscle weakness are thought to contribute to nearly a quarter of the falls (Ramdharry *et al.*, 2018). Due to the reported high fall risk, reduced standing and postural balance in these patients, it is expected that balance control during walking is impaired (Lencioni *et al.*, 2015; Maria *et al.*, 2018). So far, no studies have been published on balance control during walking in these patients.

A uniform and best way to quantify balance control during walking is lacking. A recurrent measure that quantifies balance control during walking is the margin of stability (MoS). Disadvantages of the MoS are its velocity dependency and ambiguous interpretation. Therefore, other measures should be explored such as the foot placement (FP) and single stance (SS) relations, which are believed to reflect constant offset control strategies. From these linear relations, parameters can be calculated including Pearson's correlation coefficients, intercept, slope and the residuals of the fit.

Neither the MoS, the FP nor SS have been studied in CMT patients. With the ultimate goal of investigating if balance control during walking is impaired in CMT patients, our primary aim is to compare the MoS and the parameters of the lateral FP and lateral SS relation between CMT patients and healthy individuals during regular walking. In parallel with the primary aim, the FP and SS strategies used in the sagittal plane will be compared between groups. It is expected that CMT patients abide less by the constant offset control manner of FP due to a foot drop that is often seen in these patients (Newman *et al.*, 2007). Furthermore, it is expected that CMT patients use SS strategy less than healthy individuals due to distal muscle weakness and ankle-foot deformities in CMT patients (Newman *et al.*, 2007). Altogether, it is hypothesized that the strategies are used less by CMT patients and that this is reflected by weaker correlations, smaller residuals, less steep slopes or at least one of these compared to healthy individuals. The MoS is hypothesized to be larger in CMT patients, based on findings on larger step width (Don *et al.*, 2007).

In addition, we were interested in how balance is controlled when humans have to continuously adjust their steps while walking. Such a task was developed and it was called the precision stepping task (PST). During the PST, participants are constrained to step on pre-defined locations which vary in mediolateral and anteroposterior direction. Another aim was to investigate if humans use FP and SS strategy less during the PST. It is expected that FP strategy is used less and that the compensational SS strategy is used more in the PST compared to regular walking

2.4. Methods

Participants

In total 27 participants (17 CMT patients, 10 healthy controls) visited the Sint Maartenskliniek in Nijmegen once and gave written informed consent. The experimental set-up was part of a larger study and was approved by the local medical ethics committee. Eligibility criteria for patients were having CMT disease and being able to walk independently without a walking aid – with both orthopaedic and conventional shoes. Patients were excluded if they had other disorders influencing the gait pattern or if they had a recent surgery on the lower extremities (<1 year). Healthy controls were excluded if they had lower extremity pain, deformities or balance difficulties.

Equipment

The Gait Real-time Analysis Interactive Lab (GRAIL, Motek Medical BV, the Netherlands) at the Sint Maartenskliniek was used. The GRAIL is a dual belt treadmill embedded with two plates. Motion capture data was measured with VICON (10 infra-red cameras, sample rate 100 Hz, Oxford UK). The precision stepping task was developed in D-flow software (Motek Medical BV).

Measurement procedure

Twenty reflective markers were placed according to the Plug-in Gait lower body model. Safety was guaranteed by using a safety harness connected to the ceiling.

The experiment consisted of 3 tasks. Prior to the 3 tasks, participants performed three practice trials to get familiar with treadmill walking. In the first task, participants performed a two-minute walk test in self-paced mode to determine comfortable walking speed, step length and width. In the second task, participants performed a two-minute walk test (2MWT)) at fixed speed set to comfortable speed. In the third task, subjects performed a two-minute precision stepping task (PST) which consisted of walking with continuous step adjustments at fixed comfortable speed. CMT patients performed all measurements on orthopaedic shoes, while healthy controls walked on conventional shoes. To prevent that the determined walking speed was too fast for CMT patients to perform the PST, there was one trial in between the self-paced and fixed speed walking only for CMT patients. During this trial, comfortable walking speed was gradually increased until 120% was reached. If patients were able to walk comfortably at 120% of comfortable speed, fixed walking speed was set to the predetermined walking speed. If not, fixed walking speed was set to 90% of comfortable walking speed, to ensure that patients were able perform the PST.

During the PST, pre-defined rectangular targets (same length and width of shoes) were projected on the treadmill and moved backwards along with the treadmill belt (figure 1). Participants practiced at least once, and were instructed to step as precisely as possible on the targets. The AP distance between subsequent targets was either the pre-determined step length, 20% smaller or 20% larger. The ML distance between subsequent targets was set to twice the step width, 5 cm smaller or 5 cm larger.

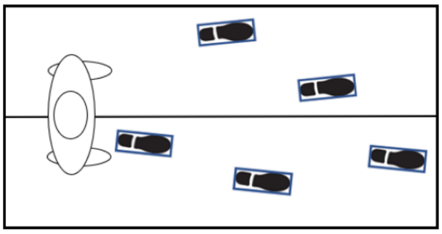


Figure 1| Schematic representation of the precision stepping task (PST)

Data analysis

Labelling and gap filling of the marker data was done in Vicon Nexus 2.7.2. Subsequent data analysis was done in MATLAB R2019b. Marker and force plate data were filtered with a zero lag, second-order low-pass Butterworth filter with cut-off frequencies of 10 Hz and 7 Hz, respectively. For each participant, the first 20 seconds were removed from analysis to remove the starting phase of walking. The subsequent 120 steps (60 left and 60 right steps) were used for analysis.

Gait events were detected using the foot markers. The force plate and marker data were used to respectively calculate the CoP (Winter, 2009), the CoM (and XCoM). The CoM was calculated by taking the average of the four pelvis markers (Whittle, 1997). The XCoM position was calculated as in equation 1a (Hof, Gazendam and Sinke, 2005; Hof, 2008). The global CoP, CoM and XCoM were calculated using the velocity of the treadmill belt which was updated every step.

$$XCoM = CoM + \frac{C\dot{o}M}{\omega_0} \qquad (1)$$

In which:

ω_0 = Eigen frequency of the participant ($\sqrt{g/l_0}$)
g = gravitational acceleration
l_0 = maximum height of the CoM
$C\dot{o}M$= CoM velocity

Foot placement (FP)

In previous studies, FP was based on the linear relation between the global CoP position and the global XCoM position making it depended on the position of the participant on the treadmill. As a result, participants that show more variety would in this case get higher Pearson's correlation coefficients. To prevent this, the FP was defined as the linear relation between the CoP with respect to the CoM and the maximal CoM velocity prior to heel strike (eq. 2).

$$CoP_{mean} - CoM_{HS} = \frac{\dot{CoM}_{max}}{\omega_0} + B \qquad (2)$$

In which:

CoP_{mean} = mean CoP position during single stance
CoM_{HS} = CoM position at heel strike
$C\dot{o}M_{max}$ = max CoM velocity prior to heel strike
B = constant offset

In figure 2A, the CoP_{mean}, CoM_{HS} and $C\dot{o}M_{max}$ quantities in the frontal plane are visualized for a single subject. In figure 2B, the FP_{ml} relations of the left and right steps are visualized. A similar figure for the FP_{ap} is given in Appendix 1. The anterior and lateral direction was the positive direction for all quantities.

Single stance (SS)

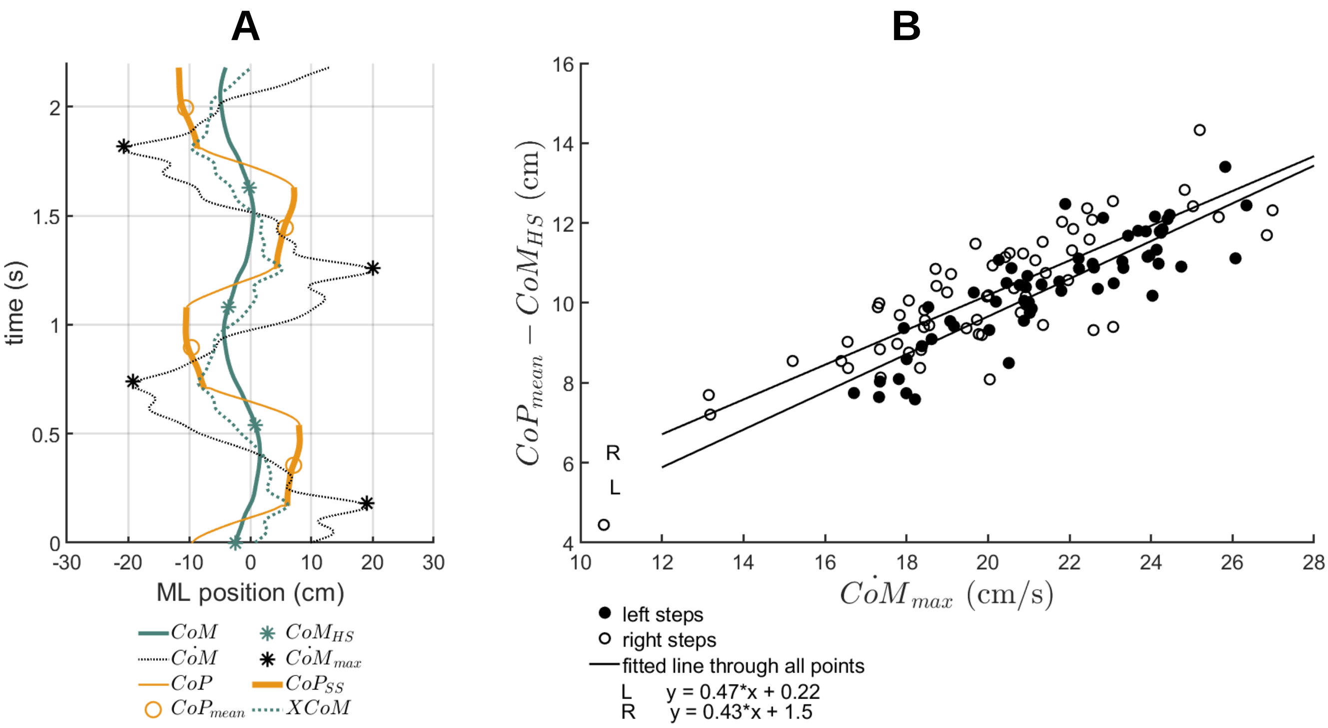
The SS was defined as the linear relation between CoP_{mov} and η_{init}. CoP_{mov} was the movement of the CoP calculated as the difference in CoP location between start and end of single stance. η_{init} was the distance between the CoP at toe off and the maximal XCoM prior to heel strike. A visualization of these quantities in the frontal plane for a single subject can be found in figure 3A. The SS_{ml} relation is visualized in figure 3B. In the frontal plane, positive values for η_{init} and CoP_{mov} indicated respectively a lateral CoP location with respect to the $XCoM_{max}$ and a lateral movement of the CoP. In AP direction, positive values for η_{init} and $CoP_{,motion}$ indicated respectively an anterior CoP location with respect to the $XCoM_{max}$ and a forward movement of the CoP (see Appendix 1 for a visualization).

FP and SS outcomes

The linear relations of the FP and SS were similarly analysed. Through the left and right steps two lines (first order polynomial) were fitted as shown in figures 2B and 3B. The outcomes of the fit were calculated for left and right steps separately and then averaged to end up with one value for each outcome: (i) norm of the residuals (FP_{res} and SS_{res}) as the mean Euclidean distance, (ii) Pearson's correlation coefficient (FP_{ρ} and SS_{ρ}), (iii) intercept (FP_{ic} and SS_{ic}) and (iv) slope (FP_{slope} and SS_{slope}). The FP_{res} and SS_{res} represented the goodness of fit of the fitted lines to the point clouds. The FP_{ic} and FP_{slope} represented respectively the constant offset value and the Eigenfrequency inverse. The SS_{ic} and SS_{slope} represented how much the CoP is moved during single stance. The Pearson's correlation coefficient indicated the strength of the relation and those ranging from 0.00 to 0.30 were interpreted as negligible, 0.30 to 0.50 as low, 0.50 to 0.70 as moderate, 0.70 to 0.90 as high and 0.90 to 1.00 as very high [19].

Margin of stability (MoS)

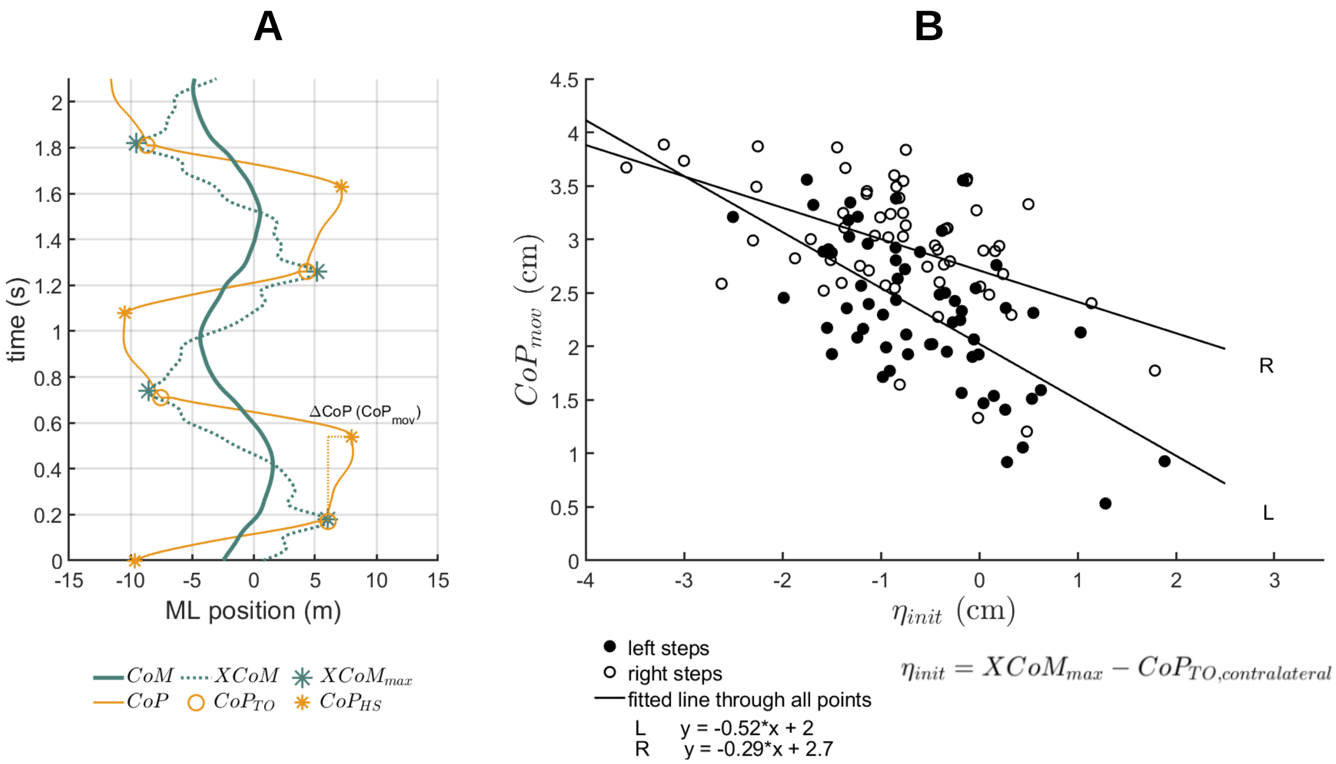
The MoS was calculated for the stance phase of each step. The maximum lateral CoP during single stance phase was chosen as an approximation of the lateral boundary of the foot. The MoS was then calculated as the difference between the maximum lateral CoP and the maximum lateral XCoM during stance phase.



Abbreviations:

CoM = centre of mass | CoP = centre of pressure | CoP_{mean} = mean CoP during single stance
HS = heel strike | SS = single stance phase

Figure 2| The mediolateral foot placement (FP_{ml}) for a single subject. **A)** The centre of mass (CoM), centre of mass velocity ($\dot{CoM}$), centre of pressure (CoP) in the frontal plane over time. **B)** The point clouds and fitted lines of the FP_{ml} relation of the left and right steps.



Abbreviations:

CoM = centre of mass | CoP = centre of pressure | XCoM = extrapolated centre of mass
HS = heel strike | TO = toe off

Figure 3| The mediolateral single stance (SS_{ml}) for a single subject. **A)** The centre of mass (CoM), extrapolated centre of mass ($XCoM$), centre of pressure (CoP) in the frontal plane over time. **B)** The point clouds and fitted lines of the SS_{ml} relation of the left and right steps.

Statistical analysis

Statistical analysis was done in MATLAB R2019b. Histograms and boxplots were visually inspected and a Kolmogorov-Smirnov test was performed to test for normality. Two-sample t-tests and a Chi-squared test were done to test for significant differences in subject characteristics. To test if there were significant differences in gait characteristics between the groups and between walking conditions, a two-way mixed ANOVA was performed. In a mixed ANOVA main effects of a between-subjects factor (group) and a within-subjects factor (walking condition) can be analysed.

The MoS, FP and SS outcomes were tested on significant differences by performing a two-way mixed ANOVA, despite if the outcome was normally distributed or not. In total 16 mixed ANOVA's were performed on the norm of the residuals, Pearson's correlation coefficient, intercept and slope of the FP and SS correlations in ML and AP direction. Bonferroni correction was applied. To our knowledge, there was no similar but non-parametric test available and it was argued that the mixed ANOVA is sufficiently robust to cope with our data. If there was a significant interaction effect, pairwise comparisons were done. In that case, depending on the outcome being normally distributed or not, either a 2-sample t-test or a 2-sample Mann-Whitney U test was performed.

2.5. Results

Subject and gait characteristics

2 of the 17 CMT patients were excluded for data-analyses due to needing support from the sidebars during the tasks. Subject characteristics were not significantly different between groups (see table 1). Of the gait characteristics, walking speed ($p<0.0001$, $F=24.214$) and stride time ($p=0.009$, $F=8.078$) were significantly lower in CMT patients than in HC. Step width was significantly larger ($p<0.0001$, $F=66.818$) in PST condition than in 2MWT condition.

Table 1| Subject characteristics, displayed as mean (SD)

	Healthy controls	CMT patients	p
Gender (F / M)	4 / 6	5 / 10	0.734
Age (years)	51.2 (12)	49.6 (14.8)	0.778
Height (m)	1.75 (0.070)	1.80 (0.095)	0.206
Mass (kg)	84.4 (15)	83.8 (19)	0.929
BMI	27.3 (3.2)	25.8 (4.6)	0.378

Table 2| Gait characteristics, displayed as mean (± SD). *p<0.05 / **p<0.001 / ***p<0.0001

	2MWT		PST		p	
	HC	CMT	HC	CMT	group	condition
speed (m/s)	1.26 (0.24)	0.82 (0.23)	1.28 (0.23)	0.81 (0.22)	<0.0001***	0.662
step width (cm)	0.15 (0.03)	0.16 (0.05)	0.21 (0.04)	0.22 (0.06)	0.694	<0.0001***
Stride time (s)	1.08 (0.08)	1.17 (0.07)	1.08 (0.08)	1.18 (0.08)	0.009*	0.548

Mediolateral balance strategies

An example

Typical examples of the FP_{ml} and SS_{ml} of a single healthy subject are shown in figure 4. The point clouds of the left and right steps and the corresponding fitted lines are shown. The $FP_{\rho,ml}$ for the left and right steps were 0.76 and 0.77 ($p<0.0001$). The $SS_{\rho,ml}$ for the left and right steps were respectively –0.69 and –0.7 ($p<0.0001$). The $FP_{res,ml}$ and $SS_{res,ml}$ averaged for left and right steps were respectively 0.68 and 0.51 cm.

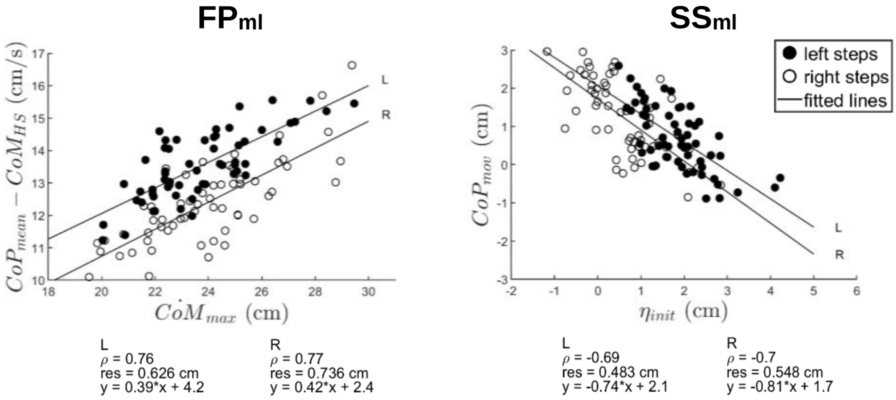


Figure 4| The point clouds of the FP_{ml} and SS_{ml} of a single healthy subject during regular walking. The high Pearson's correlation correlations (ρ) are evidence that humans use FP and SS strategies in the frontal plane.

FP_{ml} strategy

Boxplots of FP_{ml} outcomes are given in figure 5. Mean differences between groups and conditions of the FP_{ml} and SS_{ml} outcomes are given in table 4. The two-way mixed ANOVA's revealed no main effect of group, but they did reveal main effects of condition on $FP_{res,ml}$ ($p<0.0001$, $F=329.94$), $FP_{\rho,ml}$ ($p<0.0001$, $F=40.56$) and $FP_{slope,ml}$ ($p=0.0001$, $F=35.29$). In the PST condition the $FP_{res,ml}$, $FP_{\rho,ml}$ and $FP_{slope,ml}$ were larger.

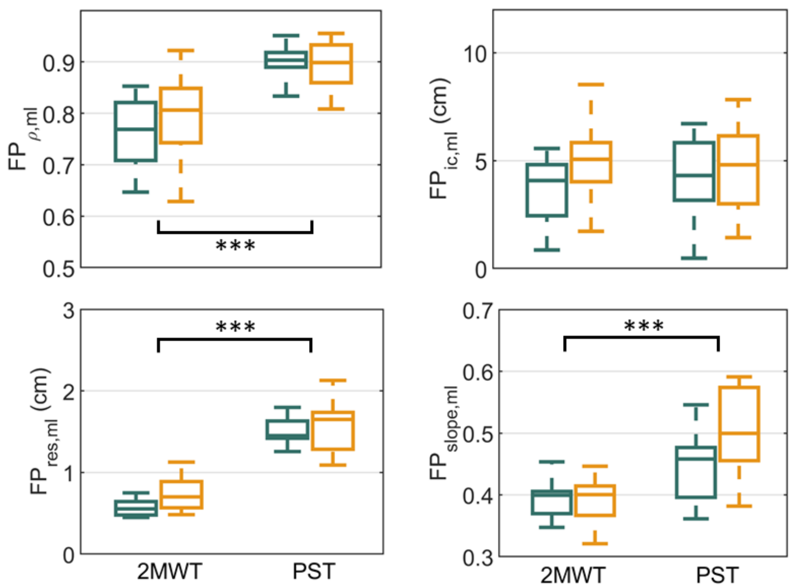


Figure 5| Boxplots of the parameters of the ML foot placement (FP) relation of healthy controls (**green**) and Charcot-Marie-Tooth (CMT) patients (**yellow**) during the 2MWT and PST. *p<0.05 / **p≤0.01 / *** p≤0.0001

SS_{ml} strategy

Boxplots of SS_{ml} outcomes are given in figure 6. The two-way mixed ANOVA's revealed significant main effects of group on $SS_{res,ml}$ (p=0.010, F=15.67) and $SS_{ic,ml}$ (p=0.020, F=13.431) and main effects of condition on $SS_{res,ml}$ (p<0.0001, F=75.29) and $SS_{\rho,ml}$ (p<0.0001, F=23.12). For $SS_{slope,ml}$ a significant interaction effect was found (p<0.001).

The $SS_{res,ml}$ and $SS_{ic,ml}$ were smaller in CMT than in HC. The $SS_{res,ml}$ and $SS_{\rho,ml}$ were larger in the PST condition than in the 2MWT condition. Post-hoc analyses revealed a less steep $SS_{slope,ml}$ in CMT compared to HC only in the 2MWT condition (p<0.001). Furthermore, the $SS_{slope,ml}$ was found to be significantly less steep in the PST condition (p<0.0001).

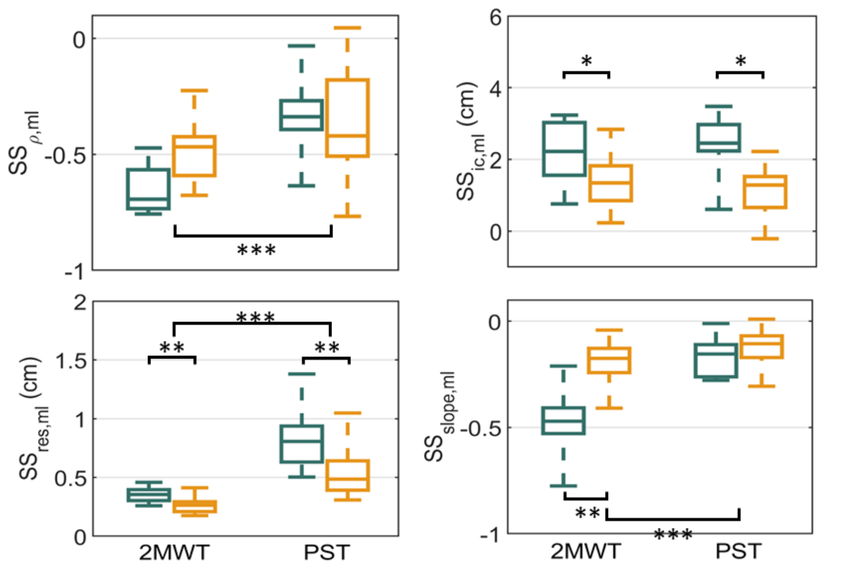


Figure 6| Boxplots of the parameters of the ML single stance (SS) relation of healthy controls (**green**) and Charcot-Marie-Tooth (CMT) patients (**yellow**) during the 2MWT and PST. *p<0.05 / **p≤0.01 / *** p≤0.0001

Table 4| Differences in FP_{ml} and SS_{ml} outcomes between groups and walking conditions. In addition, the two-way mixed ANOVA p-values for the main effects and the interaction effects are given.

		group		condition		interaction	Post-hoc
		difference CMT-HC*	p	difference PST-2MWT*	p	p	
ML FP	***ρ***	0.01 (2%)	0.405	0.12 (16%)	<0.0001	4.1103	
	Intercept (cm)	0.77 (20%)	3.835	0.07 (2%)	14.097	3.0181	
	Slope	0.03 (7%)	0.843	0.08 (21%)	0.0001	0.7899	
	Res. (cm)	0.12 (12%)	1.869	0.89 (137%)	<0.0001	5.516	
ML SS	***ρ*****	-0.07 (-15%)	0.210	-0.21 (-37%)	<0.0001	0.563	
	Intercept (cm)	-1.01 (-44%)	0.020	0.03 (1%)	13.27	1.305	
	Slope**	-0.17 (-51%)	0.005	-0.20 (-58%)	<0.0001	0.0002	CMT_{2mwt} <HC_{2mwt} (p=0.0002) PST<2MWT (p<0.0001)
	Res. (cm)	-0.19 (-33%)	0.010	0.38 (-124%)	<0.0001	0.536	

significant p-values are highlighted

* *differences are displayed as absolute differences (and percentage differences as (CMT-HC)/HC or (PST-2MWT)/2MWT)*

** *Pearson's correlation coefficients and slope were negative. Differences were multiplied with -1, so that a positive difference means a stronger correlation and steeper slope in the CMT group or PST condition*

MoS

The two-way mixed ANOVA revealed no main effect of group (p=0.245, F=1.421) and no main effect of condition (p=0.828, F=0.048). Boxplots of the MoS are shown in figure 7.

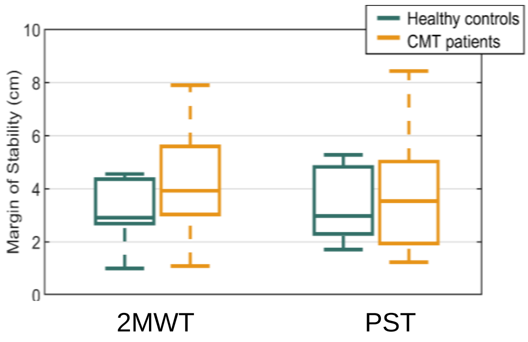


Figure 7| Boxplots of the margin of stability (MoS) of healthy controls (**green**) and Charcot-Marie-Tooth (CMT) patients (**yellow**), during regular walking (2MWT) and the precision stepping task (PST)

Anteroposterior balance strategies

An example

An example of the FP_{ap} and SS_{ap} of a single healthy subject is given in figure 8. The $FP_{\rho,ap}$ for left and right steps were respectively 0.57 and 0.63 (p<0.0001). The $FP_{\rho,ap}$ for the left and right steps were respectively -0.64 and -0.73 (p<0.0001). The $FP_{res,ap}$ and $SS_{res,ap}$ averaged for left and right steps were respectively 0.95 and 1.28 cm.

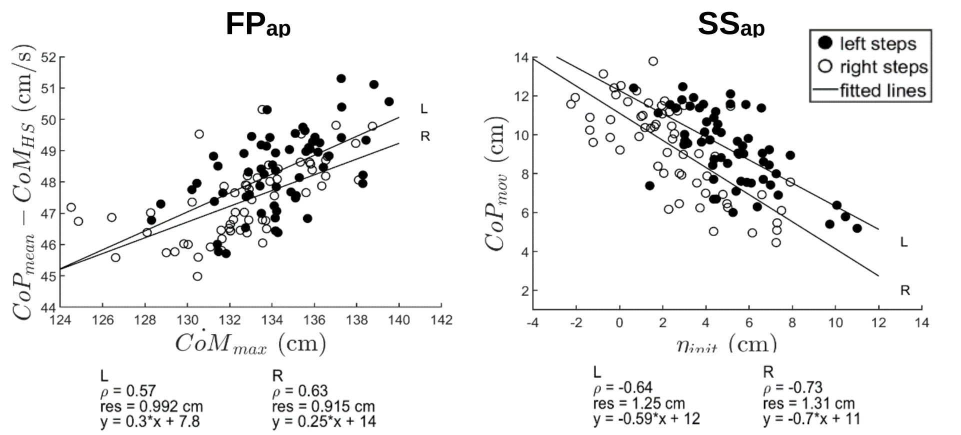


Figure 8| The point clouds of the FP_{ap} and SS_{ap} of a single healthy subject during regular walking. The moderate to high Pearson's correlation correlations (ρ) are evidence that humans can use FP and SS strategies in the sagittal plane.

FP_{ap} strategy

In table 5 mean differences of FP_{ap} and SS_{ap} outcomes between groups and conditions are given. The two-way mixed ANOVA's revealed no main effect of group, but did reveal main effects of condition on the $FP_{res,ap}$ (p<0.0001, F=128.29). The $FP_{res,ap}$ was larger in the PST condition.

Post-hoc analyses were done because interaction effects on $FP_{\rho,ap}$, $FP_{ic,ap}$ and $FP_{slope,ap}$, were revealed. The CMT patients had a smaller $FP_{\rho,ap}$ (p=0.0005), a larger $FP_{ic,ap}$ (p=0.0002) and a less steep $FP_{slope,ap}$ (p=0.0006) than HC, only in PST condition. HC had a smaller $FP_{ic,ap}$ (p=0.031) and a steeper $FP_{slope,ap}$ (p=0.031) in the PST condition compared to the 2MWT condition.

SS_{ap} strategy

The two-way mixed ANOVA's revealed a main effect of group on $SS_{ic,ap}$ ($p=0.041$, $F=11.537$) and main effects of condition on $SS_{res,ap}$ ($p<0.0001$, $F=71.25$), $SS_{\rho,ap}$ ($p<0.0001$, $F=28.44$) and $SS_{slope,ap}$ ($p=0.0012$, $F=23.513$). The $SS_{ic,ap}$ was smaller in CMT than in HC. In the PST condition the $SS_{res,ap}$ was larger, the $SS_{\rho,ap}$ was smaller and the $SS_{slope,ap}$ was less steep compared to the 2MWT condition.

Table 5| Differences in AP FP and SS outcomes between groups (CMT patients versus healthy controls) and walking condition (PST versus 2MWT), including the two-way mixed ANOVA p-values for the main effects and the interaction effects.

		group		condition		interaction	Post-hoc
		difference CMT-HC*	p	difference PST-2MWT*	p	p	
AP FP	*ρ*	-0.14 (-23%)	0.0064	-0.04 (-7%)	0.183	0.0053	CMT_{PST} <HC_{PST} (p<0.0001)
	Intercept (cm)	6.76 (73%)	0.299	-3.55 (-25%)	1.243	<0.0001	CMT_{PST} >HC_{PST} (p<0.001) PST_{HC} < $2MWT_{HC}$ (p=0.031)
	Slope	-0.05 (-20%)	0.904	0.01 (3%)	14.579	0.0005	CMT_{PST} <HC_{PST} (p<0.001) PST_{HC} > $2MWT_{HC}$ (p=0.031)
	Res. (cm)	0.03 (2%)	12.849	1.53 (172%)	<0.0001	12.849	
AP SS	*ρ***	0.02 (8%)	0.552	-0.26 (-56%)	<0.0001	2.865	
	Intercept (cm)	-3.96 (-47%)	0.041	-0.86 (-12%)	1.376	2.948	
	Slope**	-0.03 (-12%)	10.502	-0.24 (-64%)	0.0012	1.497	
	Res. (cm)	-0.05 (-4%)	13.466	0.80 (90%)	<0.0001	9.501	

significant p-values are highlighted

* *differences are displayed as absolute differences (and percentage differences as (CMT-HC)/HC) or (PST-2MWT)/2MWT)*

** *Pearson's correlation coefficients and slope were negative. Differences were multiplied with -1, so that a positive difference means a stronger correlation and steeper slope in the CMT group or PST condition*

2.6. Discussion

The ultimate goal was to investigate if CMT patients have impaired balance control during walking. Our primary aim was to compare the MoS and the parameters of the FP_{ml} and SS_{ml} relations between CMT patients and healthy individuals during regular walking. Based on finding no group differences on any of the FP_{ml} outcomes, patients did not use less FP_{ml} strategy in order to achieve constant offset control than healthy individuals. Patients did seem to use less SS_{ml} strategy represented by a lower intercept and less steep slope of the SS_{ml} linear relation in the patient group compared to healthy individuals. However, the less used SS_{ml} strategy can also be caused by the walking speed difference between groups.

Mediolateral balance strategies

Humans use FP and SS strategies in the frontal plane during regular walking

The high Pearson's correlations confirmed that humans use FP_{ml} and SS_{ml} strategy. The median $FP_{\rho,ml}$ and $SS_{\rho,ml}$ were respectively 0.78 and –0.57. It is sensible that stronger correlations were found for the FP strategy because it was based on a true linear relation (equation 2) with intercept and slope representing the constant offset value and the Eigenfrequency inverse. In contrast, the SS strategy was not based on a true linear relation. In fact, CoP movement is constrained by the outer boundaries of the foot.

CMT patients do not have impaired FP strategy at preferred walking speed

The FP_{ml} outcomes were not significantly different between CMT patients and healthy individuals. This finding was not in line with the expectation that patients would use less FP strategy. Theoretically, the FP reflects one's ability to plan or position the feet according to constant offset control. Our findings suggest that foot placement strategy was not impaired in CMT patients at preferred walking speed, meaning that this strategy might not be affected by peripheral muscle weakness and a resulting foot drop.

So far, the FP_{ml} has not been studied in patient populations other than in stroke patients (Luijten, 2019). Significant and large differences (60%) were found between the paretic side of stroke patients and healthy controls on the FP_{ml} relation. It was not strange that our findings were not in line with the significant and large differences found in stroke patients, considering that CMT is a less severe and peripheral disorder.

Walking speed is known to affect many balance control measures. We were interested in balance control measures at comfortable speed, because it represents best the daily life struggle with balance control. However, potential effects of walking speed on our findings should be considered because preferred walking speed of CMT patients (0.82 m/s) was much slower than in healthy individuals (1.26 m/s). Luijten found that halving the walking speed in healthy controls led to smaller FP ellipse widths (resembling residuals) and a larger FP ellipse angle (resembling slope). Hypothetically, smaller residuals of healthy controls could have been found if they had walked with a slower speed, resulting in a larger and perhaps significant difference between groups. Still, the comparison at comfortable but different speed was relevant, because you would expect foot placement strategy of slow walking patients to be worse than those of fast walking healthy controls.

No hard evidence for impaired SS strategy in CMT patients

Of the SS_{ml} outcomes, residuals and intercepts were smaller and slope was less steep in CMT patients. The SS_{ml} reflects how much an individual adjusts the CoP during the single stance phase and represents lateral ankle strategy. The smaller intercept in patients suggests that they move their CoP less than healthy controls if CoP was placed exactly on the XCoM. The less steep slope in patients also suggest less CoP movement during single stance in patients compared to healthy individuals. The smaller residuals in patients (33% smaller than in healthy controls) represent better fits of the linear relation. However, residuals were difficult to interpret now that the linear relation of patients was different from that of healthy controls. Taken together, patients seem to use less SS_{ml} strategy, which was in line with our hypothesis.

Unfortunately, walking speed has made interpretation of the SS outcomes difficult. Halving the walking speed in healthy controls led to smaller SS ellipse widths (resembling residuals) and a less steep SS ellipse angle (resembling slope). Therefore, slow walking is likely to result in smaller residuals and a less steep slope of the SS_{ml} relation. Effectively, the lesser use of SS_{ml} strategy in patients is potentially caused by the slower walking speed of patients. Thus, it is unclear if patients have impaired ankle strategy during walking as walking speed has potentially biased our results on the SS_{ml}.

No evidence for a larger MoS in CMT patients

The MoS was not different between CMT patients and healthy individuals which was not in line with our expectation that the MoS would be larger in CMT patients. CMT patients do not seem to increase their MoS as a protective mechanism. However, walking speed may have biased the results because the MoS depends on walking speed. The CMT patients in this study had a lower preferred walking speed and larger stride time compared to healthy individuals. Stride time has a negative effect on the MoS (Hak *et al.*, 2013). Hypothetically, if healthy controls walked with the same slow walking speed as patients approximating similar stride time, a lower MoS in healthy controls could have been found. Because the dependency of the MoS on walking speed is well established in literature, it is still expected that CMT patients have a larger MoS compared to healthy individuals, when walking with the same speed.

FP and SS strategies are used less in the precision stepping task

Another aim was to study the effect of walking condition. The Pearson's correlation coefficients, residuals and slope of the FP_{ml} relation were all larger during the precision stepping task than during regular walking. The larger correlations are thought to be caused by the induced variety during precision stepping. The slope during precision stepping was larger and was not anymore of the same magnitude as the Eigenfrequency inverse as you would expect it to be. The residuals were more than twice as large in the precision stepping task, suggesting larger variability in foot placement. Altogether, results suggest that in the precision stepping task individuals abide less by foot placement according to constant offset control, which was in line with our hypothesis.

Of the SS_{ml} relation, the Pearson's correlation coefficient was smaller, the slope was less steep and residuals were larger during the precision stepping task than during regular walking. All of these outcomes reflect that SS_{ml} strategy was used less in the PST which was contradicting our hypothesis. It was evident that SS_{ml} strategy does not compensate for the poor foot placement in the precision stepping task.

The MoS was not different between conditions despite step width being significantly larger in the precision stepping task compared to regular walking,. This finding was conflicting with literature findings of an increased MoS for wider steps in healthy individuals (McAndrew Young and Dingwell, 2012).

Anteroposterior balance strategies

Humans use FP and SS strategies in the sagittal plane during regular walking

The high $FP_{\rho,ap}$ (0.56) and moderate $SS_{\rho,ap}$ (-0.45) confirmed that humans use FP and SS strategy in the sagittal plane during regular walking. Again, weaker correlations were found for the SS strategy. Furthermore, the FP and SS relations seem to be weaker in the sagittal plane compared to the frontal plane. That FP relation was weaker in the sagittal plane compared to the frontal plane was in line with findings from Vlutters and colleagues. They found lower coefficients of determination (R^2) in the sagittal plane than in the frontal plane. One potential explanation was that constant offset control in the sagittal plane can be achieved by compensating in the next steps. In contrast, in the frontal plane it is undesirable to compensate for poor FP in the next steps because it would likely result in more lateral variation of the CoM trajectory. One would consequently not be able to walk in a straight line, which is undesirable.

The weaker SS in the sagittal plane compared to the horizontal plane, was contradicting our expectations that especially AP ankle strategy is important. Moreover, the CoP can shift more in AP direction than in ML direction due to fact that the foot length is larger than the foot width. One plausible explanation of finding a weaker SS relation in the sagittal plane is that CoP location could be less accurately measures in AP direction due to having more AP shear forces (caused by sliding of the treadmill belt and person over the force plates in the walking direction).

FP and SS strategies in the sagittal plane are used less in the precision stepping task

In parallel with the ML balance measures, the FP_{ap} and SS_{ap} relations were compared between group and conditions. Healthy individuals altered their FP_{ap} strategy in the precision stepping task, evidenced by a smaller intercept and steeper slope in this condition compared to regular walking in the healthy group. There were no differences in FP_{ap} outcomes between conditions in the CMT group, suggesting that patients did not alter the FP_{ap} strategy. As a consequence of healthy individuals altering their strategy between conditions, they had different FP_{ap} outcomes than patients in the precision stepping task. Furthermore, the FP_{ap} residuals were larger in the precision stepping task for both groups. This finding indicates that both healthy individuals and patients have more variety in their FP during precision stepping which follows logically from imposing more variety in stepping locations.

Of the SS_{ap} outcomes, the intercept was significantly lower in CMT patients. Most likely, this finding was caused by the different walking speed of patients and healthy individuals as the AP constant offset value is expected to depend on walking speed. When comparing conditions, the Pearson's correlation coefficient and intercept were smaller and the residuals were larger in the precision stepping task. These findings suggest that SS strategy in the sagittal plane was used less in the precision stepping task compared to regular walking.

It was important to take the difference in step width between conditions into consideration. Step width was larger in the precision stepping task. Therefore, it was unclear if the differences in strategies during the precision stepping task was caused by the larger step width, the step adjustments or by the combination of both. Interpretation of these results were therefore confined to this specific task.

Conclusion

Our findings confirm that humans use foot placement and single stance strategies in order to achieve constant offset control in the frontal and sagittal planes. Charcot-Marie-Tooth patients do not have impaired lateral foot placement strategy at preferred walking speed. However, patients might use single stance strategy less than healthy individuals, which would be a logical consequence of distal muscle weakness. These findings together with the finding of similar margin of stability in patients and healthy individuals should be carefully interpreted, because the slower preferred walking speed in patients potentially biased our results. Hence, it was concluded that no hard and unambiguous evidence was found for impaired strategies in patients. Furthermore, it was evident that both foot placement and single stance strategy were used less during a precision stepping task in both mediolateral and anteroposterior directions.

3| Walking model

3.1. Abstract

Introduction: A walking model implemented with energetic costs and an constant offset constraint, can replicate human-like stepping responses after perturbations. Although the walking model was able to replicate human-like step location and timing after perturbation, it failed to replicate the steady state gait characteristics. The aim was therefore to study if steady state gait characteristics of the walking model can replicate observational data of regular walking in healthy controls (HC).

Methods: The walking model consisted of a linear inverted pendulum (LIP) and a hanging pendulum representing stance and swing leg, respectively. The model was implemented with costs for step transitions and leg swing with corresponding gains k_{sts} and k_s. The model was fitted onto observational data of a two-minute walk test of HC (n=10). The step width and step length of the model were optimized for those of HC. In the optimization step k_{sts} was set to 1. The constant offsets (B_x and B_y) and gains for leg swing cost (k_{sx} and k_{sy}) were optimized. The amplitude of the Centre of Mass (CoM), walking speed, step time, step width and step length were compared between subjects and the fitted walking model. Depending on normality of the outcome, either a paired t-test or a Wilcoxon signed rank test was performed.

Results: There were no significant differences in the CoM amplitude (p=0.064), walking speed (p=0.427), step duration (p=0.212), step width (p=0.678) and step length (p=0.623) between the model and healthy individuals.

Conclusion: The walking model was able to similarly walk as healthy individuals, which is an important first step to show that the model could be used for various applications.

3.2. Abbreviations

HC	healthy controls
ML	mediolateral
AP	anteroposterior
CoP	centre of pressure
CoM	centre of mass
XCoM	extrapolated centre of mass
2MWT	two-minute walk test
LIP	linear inverted pendulum
$B_{x/y}$	constant offset value (ML/AP)
$k_{sx/sy/sts}$	gain for ML leg swing cost/ AP leg swing cost / step-to-step transition cost

3.3. Introduction

The linear inverted pendulum (LIP) is widely used in research on gait analysis with majority of studies aiming to achieve human-like gait in bipedal robots (Hof, 2008). Some studies use such a model to predict balance recovery responses of humans during perturbed walking (Vlutters, Van Asseldonk and Van Der Kooij, no date; Hof, Vermerris and Gjaltema, 2010; Matthis and Fajen, 2013). Vlutters and colleagues studied a walking model implemented with energetic costs for leg swing and step transition (Vlutters, Van Asseldonk and Van Der Kooij, no date). Foot placement of the model was constrained to a fixed distance with respect to the extrapolated Centre of Mass (XCoM). They found that the model was able to output human-like timing and locations of steps following lateral mechanical perturbations. Their results implied that the constant offset constraint and energetic cost are important for balance recovery responses during sideward perturbed walking. However, the model failed to replicate stepping locations following anteroposterior perturbations because it could not replicate human steps that did not correspond to constant offset control. Furthermore, the model failed to replicate human-like step locations, step timing and walking speed of steady state.

In daily life, mechanical perturbations can be considered as pushed or pulls received from other individuals. However, a more common scenario is having to deal with obstacles on the floor or even dealing with rough terrain such as a rocky trail. More importantly, such scenarios are the cause of nearly 20% of falls in Charcot-Marie-Tooth patients whereas only 2% of falls is caused by external perturbations (Ramdharry *et al.*, 2018). Therefore, it is crucial to understand how balance is controlled during walking on terrain with obstacles. One study found that humans exploit the biomechanics of gait in order to walk energetically efficient during walking over a terrain with virtual obstacles (Matthis and Fajen, 2013). Their results indicated that optimizing energetic efficiency is one important aspect of dealing with a terrain with obstacles. Perhaps, a second important aspect could be to control lateral stability using constant offset control. Therefore, it would be useful to simulate behaviour of the walking model in response to obstacles and to see if it can replicate human responses.

It is evident that the walking model used by Vlutters can replicate step location and timing in humans during perturbed walking (Vlutters, Van Asseldonk and Van Der Kooij, no date). However, it is unclear how the model performs during regular walking. Therefore, the aim was to investigate if a model is able to walk with similar gait characteristics as observed in healthy individuals during regular walking. For this purpose, the amplitude of the centre of mass (CoM), the walking speed and step duration were compared between healthy individuals and the model. It is hypothesised that the model can replicate human-like gait to some extent but that it cannot identically match the gait pattern due to its simplicity. Ideally, the walking model could be used in future research to see if it can predict human-like behaviour during obstacle avoidance.

3.4. Methods

The walking model presented in Vlutters study was adapted (Vlutters, Van Asseldonk and Van Der Kooij, no date). The model consisted of a LIP representing the stance leg and a single hanging pendulum representing the swing leg. The CoM height was fixed as a result of linearization. There was no double support phase, meaning that there was an instantaneous exchange between the single support phase of the left and right leg. For simplicity, the swing leg dynamics were treated independently from the stance leg dynamics so that they do not affect each others motion.

Stance leg – linear inverted pendulum model

A LIP was used to model the stance leg. Equations 1 and 2 are the solution to the equations of motion of the 3D LIP assuming a constant CoP position during pendulum swing. From these equations the final stance phase position and velocity of the CoM can be calculated.

$$r_{CoM,f} = \begin{bmatrix} x_{CoM,f} \\ y_{CoM,f} \\ z_{CoM,f} \end{bmatrix} = r_{CoP} + \left(r_{CoM,i} - r_{CoP}\right)\cosh(\omega_o t) + \frac{\dot{r}_{CoM,i}}{\omega_o}\sinh\,(\omega_o t) \tag{1}$$

$$\dot{r}_{CoM,f} = \left(r_{CoM,i} - r_{CoP}\right)\omega_o\; sinh(\omega_o t) + \dot{r}_{CoM,i}\; cosh\,(\omega_o t) \tag{2}$$

In which:

ω_o = Eigenfrequency ($\sqrt{g/l_0}$)

r_{CoP} = CoP position

$r_{CoM,i}$ = initial CoM position

$\dot{r}_{CoM,i}$ = initial CoM velocity

Swing leg – hanging pendulum model

The swing leg was modelled as a hanging pendulum that could rotate around the x and y axis which were decoupled. The equations of motion of the swing leg are given by equation 3 and was used to calculate the hip moment (M_H). We let the angle of the swing leg change from toe-off ($t = 0$) to heel strike ($t = tf$) using a cosine wave according to equation 4. The angular velocity of the swing leg was calculated as the second derivative of the swing leg angle.

$$M_H = m_s l_s^2 \ddot{\theta} + m_s\, g\, l_s \sin\,(\theta) \tag{3}$$

$$\theta = \theta_i + A - A\, cos\,(\frac{2\pi t}{2t_f}) \tag{4}$$

$$A = \frac{\theta_f - \theta_i}{2}$$

In which:

g = gravitational acceleration

m_s = swing leg mass

l_s = distance from hip joint to swing leg mass

θ = swing leg angle

$\ddot{\theta}$ = swing leg angular velocity

A = swing leg amplitude

Costs

Energetic costs for (1) leg swing and (2) step-to-step transition are taken into account. The leg swing cost was related to any motion other than the natural dynamics of the swing leg. The leg swing cost (E_s) in ML and AP direction was calculated as the sum of the absolute required hip torque during swing (equation 5) using equation 3.

$$E_s = \int_{t=0}^{t_f} |M_H|\; dt \tag{5}$$

The step-to-step transition cost was based on the impact during the transition between subsequent steps. The larger the impact between steps, the larger the step-to-step transition cost. The impact was large when the difference in vertical CoM velocity before and after impact was large. However, the vertical CoM velocity is in fact zero due to linearization of the model. It was therefore assumed that the vertical CoM velocity is related to the stance leg angle and can be calculated from equation 6. The CoM vertical velocity after impact depends on the angle between legs as in equation 7. Finally, the step-to-step transition cost (E_{sts}) is given by equation 8 and depends on the total mass (set to that of the subject) and the CoM vertical velocity before and after impact.

$$\dot{z}^-{}_{CoM} = -\frac{(x_{CoM,f} - x_{CoP,i})\,\dot{x}_{CoM,f} + (y_{CoM,f} - y_{CoP,i})\,\dot{y}_{CoM,f}}{l} \tag{6}$$

$$|\dot{z}^+{}_{CoM}| = |\dot{z}^-{}_{CoM}|\cos\,(\alpha) \tag{7}$$

$$E_{sts} = 0.5m(\,|\dot{z}_{CoM}^-| - |\dot{z}^+{}_{CoM}|)^2 \tag{8}$$

In which:

$\dot{z}_{CoM}$ = CoM vertical velocity
$\dot{z}^{-}_{CoM}$ = CoM vertical velocity prior to impact
$\dot{z}^{+}_{CoM}$ = CoM vertical velocity after impact
α = angle between legs
m = total mass of the model

Simulations

Simulations ran in MATLAB R2019b in discrete time with a fixed time step of 10^{-3} s. A prediction horizon of 1 s per step was used over which the net cost was calculated as a weighted sum of the swing cost and step-to-step transition cost. The time instance corresponding to the minimum net cost was chosen as the optimal time of heel strike (t_f):

$$t_f = min_t[k_{sx}\, E_{sx} + k_{sy}E_{sy} + k_{sts}E_{sts}] \quad (9)$$

In which:
k_{sx} = gain for ML leg swing cost
k_{sy} = gain for AP leg swing cost
k_{sts} = gain for step-to-step transition cost

Individual costs needed to be calculated for every time instance in the prediction horizon in order to calculate the net cost. For every step the leading foot was placed at a constant distance with respect to the XCoM (equation 10). After that, the final swing leg angle could be calculated using the leading foot position (equation 11). These steps were needed in order to calculate the step-to-step transition cost. The model starts on the left leg and is upright. Initial CoP position, CoM position and velocity, and swing leg angle were set to zero. Initial conditions did not affect the steady state gait characteristics of the walking model.

$$\mathrm{f_L} = \mathrm{r_{CoM,f}} + \frac{1}{\omega_o}\,\dot{\mathrm{r}}_{\mathrm{CoM,f}} + \mathrm{B} \quad (10)$$

$$\theta_f = \tan^{-1}\left(\frac{f_L}{l}\right) \quad (11)$$

In which:
f_L = leading foot position
l = leg length
$\mathrm{B} = \begin{bmatrix} B_x \\ B_y \end{bmatrix}$ = constant offset values

Optimization of walking model towards observational data

The walking model was optimized towards observational data of healthy controls during a two-minute walk test at comfortable, fixed speed (2MWT). See the method section of chapter 2 for an explanation of experimental procedures. The first 20 steps of the 2MWT were excluded and the subsequent 150 steps were used for data-analysis. The CoM height, Eigen frequency and mass of the legs of the model were set to those of the subject during the 2MWT. The model was simulated to make 150 steps. The steady state gait of the simulation was subsequently optimized to fit the mean step width and step length of the healthy subject. Equation 12 gives the optimization function which outputs the sum of the step width and step length differences between the walking model and the subject expressed in a percentage.

$$f_{optim} = \frac{|SW_{subj} - SW_{model}|}{SW_{subj}} + \frac{|SL_{subj} - SL_{model}|}{SL_{subj}} \quad (12)$$

In which:
SW_{subj} = mean step width of subject
SW_{model} = steady state step width of model
SL_{subj} = mean step length of subject
SL_{model} = steady state step length of model

The input parameter k_{sts} was set to 1 for each subject so that other gains were relative with respect to k_{sts}. All other input parameters (B_x, B_y, k_{sx} and k_{sy}) were optimized. The optimization function needed a starting point for these four input parameters. The starting points for the constant offsets were subject-specific. The starting point of B_x was set to the intercepts of chapter 2 (measured during the 2MWT). The starting point of B_y was calculated according to equation 13. The starting points of the gain for swing leg (k_{sx} and k_{sy}) were both set to 5, based on the cost landscape (explained in Appendix 2).

$$B_y = -\frac{SL_{subj}}{e^{\omega_0 T_S - 1}} \qquad (T_s = \text{stepping time}) \qquad (13)$$

Statistical analysis

Descriptive statistics of the outcomes of the model and subjects and the pairwise differences were calculated. Depending on normality of the outcome (checked similarly as in chapter 2) mean and SD or median and interquartile range (IQR) were calculated. A paired t-test or a Wilcoxon signed rank test was performed on each outcome, depending on the normality of the pairwise differences.

3.5. Results

The model converged to a steady state gait after a few steps for all healthy controls. The first and last six steps and CoM trajectory of a single subject and the model are shown in figure 1. The parameters that result in optimal step length and step width are given in table 1. B_x and B_y were in the range of [1.38 to 3.74 cm] and [-28.6 to -8.5 cm] respectively. The leg swing gains k_{sx} and k_{sy} were in the range of [4.17 to 6.83] and [3.77 to 6.19] respectively.

The Wilcoxon rank sum tests revealed no differences between the steady state gait characteristics of the model and those observed in healthy individuals. Outcomes and pairwise differences were not normally distributed. In table 2 median and IQR of all outcomes and pairwise differences are given as well as corresponding p-values. Figure 2 visualizes the boxplots of CoM amplitude, walking speed and step duration.

Table 1| Optimized simulation input parameters and starting points

Subject		1	2	3	4	5	6	7	8	9	10
B_x (cm)	*starting point*	3.33	3.80	4.16	5.29	4.93	4.35	2.61	1.39	1.20	5.60
	optimized	3.02	2.95	2.08	3.50	3.10	2.71	2.05	1.75	1.38	3,74
B_y (cm)	*starting point*	-13.2	-14.9	-18.0	-13.2	-20.8	-13.8	-24.4	-14.8	-10.7	-20.6
	optimized	-15.7	-16.8	-23.5	-16.8	-25.9	-16.2	-28.6	-11.9	-8.5	-24,8
k_{sx}		5,12	5.15	5.60	6.83	5.68	5.57	4.17	6.20	5.26	6.18
k_{sy}		4,60	5.29	5.04	3.77	6.19	5.15	5.80	3.97	5.08	6.18

Table 2| Gait characteristics of the healthy controls and the linear inverted pendulum model (LIP). Pairwise differences between healthy controls and the LIP and corresponding p-values are given. Values are displayed as median (IQR).

	Healthy controls	LIP	Pairwise difference		p-value
			absolute (LIP-HC)	percentage (LIP-HC)/HC (%)	
CoM amplitude (cm)	5.64 [3.51; 5.93]	4.22 [2.72; 4.58]	-1.16 [-1.76; -0.79]	-21 [-31; -14]	0.064
Walking speed (m/s)	1.21 [1.13; 1.50]	1.29 [1.16; 1.64]	0.12 [0.03; 0.15]	10 [3; 12]	0.427
Step duration (s)	0.54 [0.51; 0.56]	0.50 [0.44; 0.52]	-0.05 [-0.07; -0.02]	-9 [-13; -4]	0.212
Step width (cm)	15.61 [12.40; 18.42]	15.76 [12.57; 18.65]	0.17 [0.13; 0.23]	1 [1; 1]	0.678
Step length (cm)	66.92 [60.42; 70.41]	68.47 [65.65; 71.64]	1.15 [0.56; 2.38]	2 [1; 4]	0.623

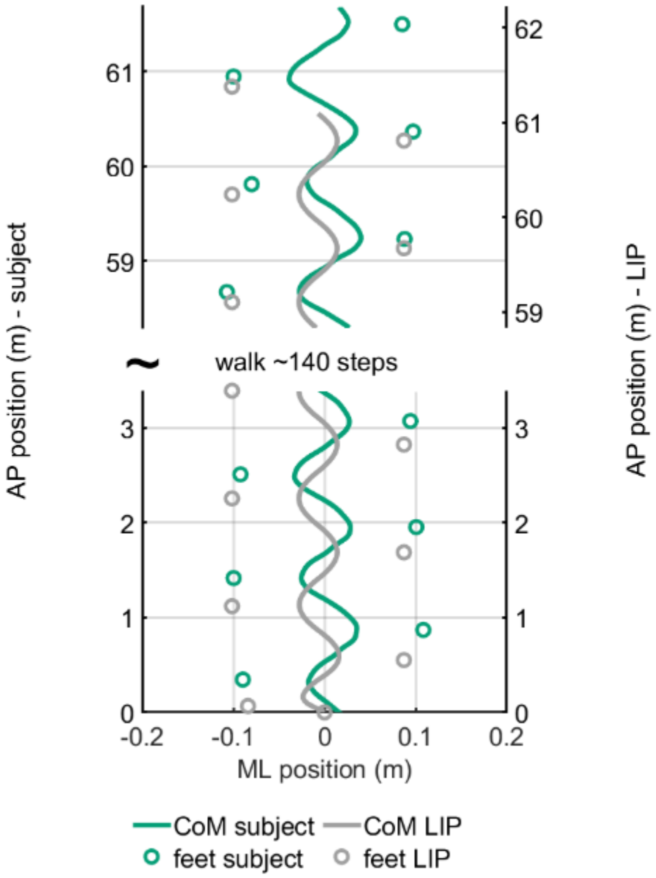


Figure 1| The CoM trajectory and stepping locations of a single subject and model (LIP) during regular walking. The subject and model walk in positive AP direction.

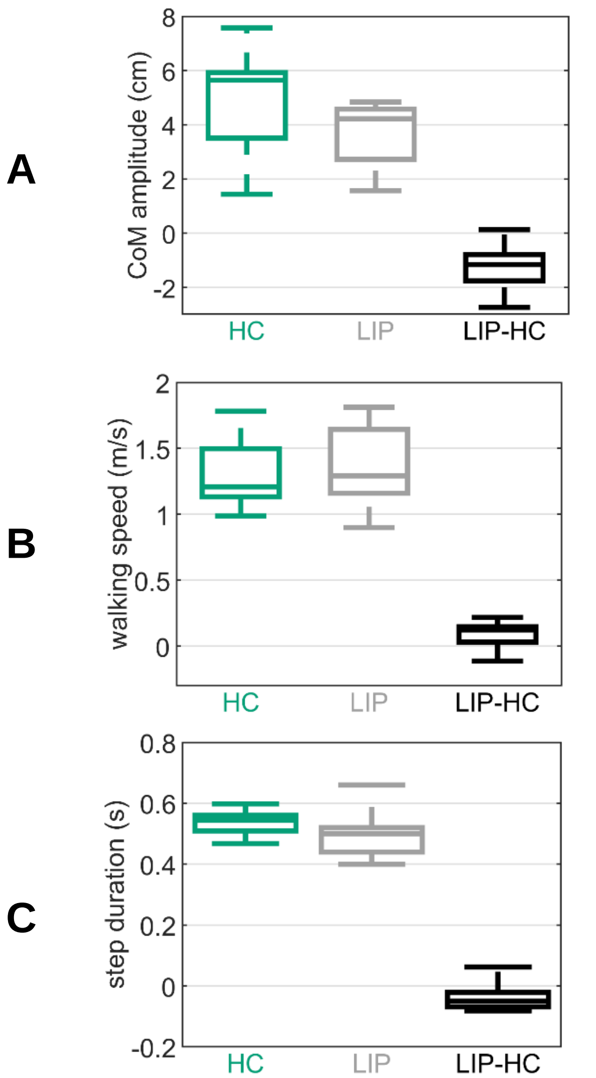


Figure 2| Boxplots of healthy controls (HC), the model (LIP) and pairwise differences. The model has steady state gait characteristics similar to those of humans. **A)** CoM amplitude, **B)** walking speed and **C)** step duration.

3.6. Discussion

The aim was to investigate if a walking model was able to walk with human-like gait characteristics during regular walking. The gait characteristics of the model were not significantly different than those observed in healthy individuals which was in line with our hypothesis. As a consequence, constant offset control and energetic costs for leg swing and step transitions are important during regular walking.

Although combining constant offset control theory and energetic cost did not result in identical matches of the simulated and observed gait pattern, this was not considered feasible nor realistic. Any human movement is characterized by variability which is caused by underlying neuromotor processes that are inherently noisy (Bartlett, Wheat and Robins, 2007; Faisal, Selen and Wolpert, 2008). So despite the difference in CoM amplitude between the model and observational data, it is though that regular walking is in essence a combination of optimizing energetic efficiency and maintaining laterally stable using constant offset control. Further support for this idea was given by a study that found that humans harness passive dynamic properties in the sagittal plane in order to walk energetically efficient, whereas in the frontal plane active control is needed in order to stabilize lateral motion (Bauby and Kuo, 2000).

The constant offset values that resulted in optimal step width and step length were realistic. The lateral constant offsets were ranging from 1.38 to 3.74 cm, meaning that the model stepped minimally with a fixed distance of 1.38 cm to maximally 3.74 cm lateral to the XCoM. The AP constant offset ranged from -28.6 to -8.5 cm. These offsets follow logically from the starting points that were used in model optimization. The starting points were the observed mean intercepts of the FP relations in chapter 2, representing the observed ML and AP constant offset values in healthy individuals.

The gains for the leg swing cost ranged from 4.17 to 6.83 in frontal plane and of 3.77 to 6.19 in the sagittal plane. Thus, both gains were approximately 5 times larger than the step-to-step transition gain, meaning that swinging the leg not according to passive dynamics was more costly than the impact of step transitions. Compared to the gains of 0.1174 (k_{sx}) and 0.2585 (k_{sy}) of Vlutters and colleagues, our gains for leg swing costs were relatively high. The relatively high gains may be partially explained by the difference in walking speed between the studies. Whereas the model walked with a median speed of 1.21 m/s in our study, it walked with an average speed of 1.01 m/s in the other study. It is expected that the impact between subsequent steps is larger for faster walking and therefore, the step-to-step transition cost was presumably higher in our study.

One important observation was that the model seem to have difficulty to approximate the CoM trajectory of some healthy individuals. Although not significantly different, the simulated CoM amplitude was as a consequence 1.16 cm (21%) smaller compared to the CoM amplitude of healthy individuals. For attempts to further improve optimization of the model, it is strongly recommended to fit the CoM trajectory – as a whole – of the model on that of the healthy individual.

This study was a crucial step for validating the walking model during regular walking. A logical next step would be to simulate self-paced regular walking. Ultimately, the walking model could be used in research on balance responses to various perturbations. Vlutters and colleagues have used the model in research on mechanically perturbed walking. They found that the model was able to output similar stepping responses as humans after being perturbed. Their results indicated that constant offset control and costs for leg swing and step transitions are important for controlling balance during perturbed walking. It would be interesting to see how the model responds to nonmechanical perturbations such as obstacles. Such a perturbation seems to be more common in daily life than a push or pull to the body. If the model would be able to output human-like responses to obstacles, then these responses can be explained by the combination of constant offset control and energetic efficiency.

Conclusion

Altogether, the model was able to walk in a similar way as healthy individuals implying that constant offset control and energetic efficiency are important during regular walking. Due to not finding any differences in the gait characteristics between model and healthy individuals, the model could be used for research on balance responses to perturbations. Though, attempts to further tune the model in order to better approximate human-like gait are encouraged. Ultimately, the model could be altered to study balance responses to obstacles.

4| General discussion

The ultimate goal was to study if constant offset control was used as a balance control mechanism during regular walking in humans. The novelty of this research was that no perturbations were applied and that both the frontal plane and sagittal plane were studied. In chapter 2, a clinical perspective was taken by investigating two strategies to achieve constant offset control in healthy individuals and patients with Charcot-Marie-Tooth disease. The use of foot placement and single stance strategies during regular walking was proven by moderate to high median Pearson's correlation coefficients in both groups. There was no hard and unambiguous evidence that the strategies were used less by these patients. In chapter 3, a modelling perspective was taken to investigate if a model implemented with constant offset control could replicate human-like gait. The model was able to walk with similar gait characteristics as observed in healthy individuals.

Constant offset control is used by humans during regular walking

Taken the findings of chapter 2 and chapter 3 together, it was reasonably shown that constant offset control was used in the frontal and sagittal plane during regular walking in humans. In chapter 2, the outcomes reflected if constant offset control was used whereas constant offset control by humans was used as an assumption in chapter 3. Either approach led to the same conclusion regarding the use of constant offset control by humans during regular walking. Nevertheless, the different chapters gave us different additional insights.

Chapter 2 showed that constant offset control can be achieved using foot placement strategy and single stance strategy. In chapter 3, no distinction was made between different strategies. Rather the sum of all strategies to achieve perfect constant offset control was subject of study in chapter 3. For future research, it is recommended to explore the potential of multiple linear regression in order to study the contribution of each possible strategy to constant offset control.

Constant offset control seems more important for frontal plane stability

Based on the weaker correlations found for the sagittal plane in the experimental data described in chapter 2, it seems that constant offset control is especially important to control stability in the frontal plane. This was in line with research in which foot placement was not significantly altered in response to anteroposterior perturbations (Vlutters, Van Asseldonk and Van Der Kooij, 2016). Although chapter 3 did not give us that insight, the walking model could potentially support the hypothesis. For that purpose, the walking model should be altered so that it does not constrain the CoP to an anteroposterior fixed distance from the XCoM. This implicates that the anteroposterior CoP should be set in some other way.

Trade-off between stability and energetic efficiency

Not only constant offset control is important for regular walking. Optimizing energetic efficiency and stabilizing lateral motion are believed to be key aspects in balance recovery responses to mechanical perturbations (Vlutters, Van Asseldonk and Van Der Kooij, 2016). Chapter 3 showed the importance of these aspects during regular walking as well, because no significant differences were found between the gait characteristics of the model and those observed in healthy individuals.

There seems to be a trade-off between stability and energetic efficiency, which depends on the circumstances. When stability is challenging, it is more important to stabilize walking. When stability is not necessarily challenging and a person intends to walk for a long time, it is more important to optimize energetic efficiency. An example of a condition in which stability is challenging is split-belt treadmill walking. Sanchez and colleagues found that humans initially step further forward on the slow belt than on the fast belt causing step length asymmetry which is believed to improve stability (Sanchez *et al.*, 2019). However, the asymmetry is reduced with practice, enabling humans to reduce metabolic costs. Another example in which energetic efficiency is less important is during a precision stepping task. Such a task was performed by the participants in chapter 2. Both healthy individuals and Charcot-Marie-Tooth patients used foot placement and single stance strategies less during precision stepping compared to regular walking. The lesser use of strategies to achieve constant offset control during the precision stepping task suggests that stability is not optimized during this task. It is thought that accuracy of movement is optimized during precision stepping as participants were instructed to step as precisely as possible on the stepping targets.

Since walking is a context dependent activity, it is crucial to study healthy individuals and patients not only during regular walking but also during other walking conditions. Rough terrains are common causes of falls in patients with balance difficulties (Ramdharry *et al.*, 2018). Therefore, it is important to know how humans deal with obstacles and rough terrains. In rough terrains some stepping locations are hazardous but an individual is free to choose where to place his feet outside of the hazardous locations. It would be interesting to see if the model from chapter 3 is able to predict human-like stepping responses in such a scenario. Chapter 3 aided as the first step of validating the walking model that can ultimately be used to investigate this matter.

Future research

Future research on balance control during walking should focus on a number of aspects. As described earlier, it should be investigated whether the contribution of each strategy to constant offset control can be calculated. If this would be possible, for instance using multiple linear regression, the effect of walking speed on the strategy contributions should be studied. Some evidence suggests that ankle strategy is used relatively more during slow walking, whereas foot placement is used relatively more during fast walking (Fettrow, Reimann, Grenet, Crenshaw, *et al.*, 2019). Knowing how walking speed and other gait characteristics independently influence the strategies would help to unambiguously interpret the strategies in the future.

It would be crucial to understand how balance is controlled during an obstacle avoidance task. One approach to study the control of balance in response to obstacles is to alter the walking model of chapter 3. This could potentially be done by adding costs for hazardous stepping locations which are set to obstacle positions from observational data. If the model would output similar responses to obstacles as observed in healthy individuals, it would suggest that constant offset control and optimizing energetic efficiency are important aspects in obstacle avoidance.

In addition to understanding balance control during walking, foot placement and single stance strategies can be useful to assess and evaluate someone’s balance. A good assessment tool is valid, reliable and sensitive to small changes. Therefore, the foot placement and single stance outcomes should be tested on these three aspects. In order to test validity, the outcomes should be compared between healthy individuals and patients with obvious balance difficulties during walking. It should be additionally studied if the outcomes correlate with currently used clinical measures for balance assessment.

Finally, future precision stepping tasks could focus on step adjustments in either the frontal or the sagittal plane. Possibly, such tasks could give insight into how humans independently control stability in these planes.

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6| Appendices

Appendix 1

Anteroposterior FP and SS relations

Figure A1 | Anteroposterior foot placement (FP_{ap}). **A)** The quantities on which the FP_{ap} is based. **B)** The point clouds and fitted lines of the FP_{ap} relation of the left and right steps.

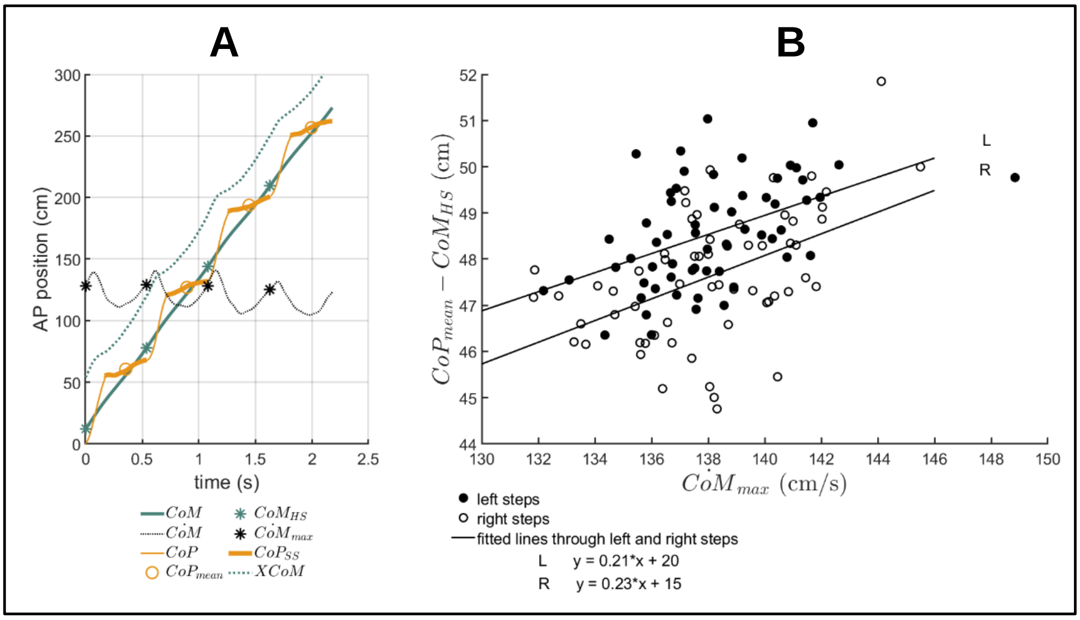
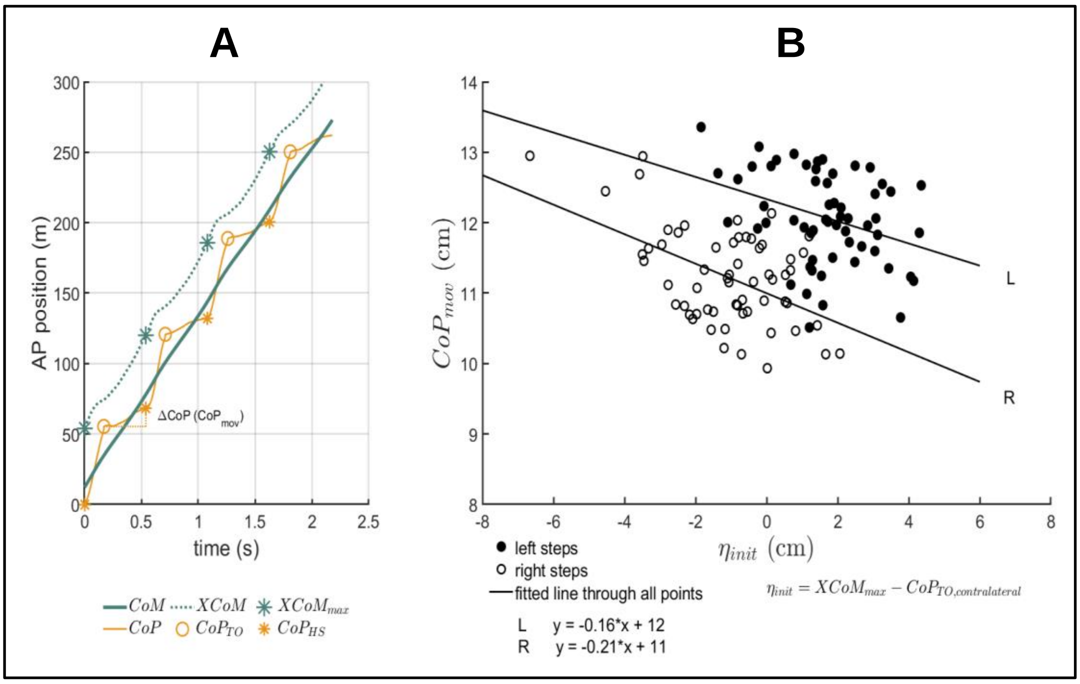


Figure A2 | Anteroposterior single stance (SS_{ap}). **A)** The quantities on which the SS_{ap} relation is based. **B)** The point clouds and fitted lines of the SS_{ml} relation of the left and right steps.



Abbreviations:
CoM = centre of mass
CoP = centre of pressure
CoP_{mean} = mean CoP during single stance
XCoM = extrapolated centre of mass
HS = heel strike
TO = toe off
SS = single stance phase

Appendix 2

Cost landscape

The gains for leg swing cost (k_{sx} and k_{sy}) were chosen according to the cost landscape of the combined error of step width and step length. In other words, the effect of different combinations of k_{sx} and k_{sy} on foot placement resemblance was studied.

The effect of different combinations of gains were studied while the other input parameters (B_x and B_y) were set to their starting points. We chose to look at the effect of gains ranging from 0 to 8. The cost was the weighted sum (in the percentage) of the step width and step length differences between the model and healthy individuals (equation 12 of chapter 2). This resulted in the cost landscape as shown in the left subplot of figure A3. We simultaneously charted the cost landscape of the CoM amplitude difference between model and healthy individuals, resulting in the cost landscape shown in the right subplot of figure A3.

As can be seen from figure A3, the both costs were relatively small if k_{sx} and k_{sy} were set to 2. However, the sum of the step length and step width of the model was 60% larger or smaller than that of the subject for these gains. Therefore, we optimized parameters B_x and B_y using these gains. Then, we used these again to optimize the gains k_{sx} and k_{sy} and this resulted in the cost landscapes shown in figure A4.

As can be seen from figure A4, the costs for step width and step length differences are reduced by using the optimized constant offset values (B_x and B_y). The minimal cost is now 11% compared to 60% when the starting points for these parameters were used. The cost here is minimal if the gains are both set to 5. Therefore, the starting points of the gains was set to 5.

Figure A3| The effect of k_{sx} and k_{sy} on the cost landscapes using the starting points of B_x and B_y. **A)** the cost landscape is the percentage weighted sum of step width and step length differences. **B)** the cost landscape is the difference in CoM amplitude in cm.

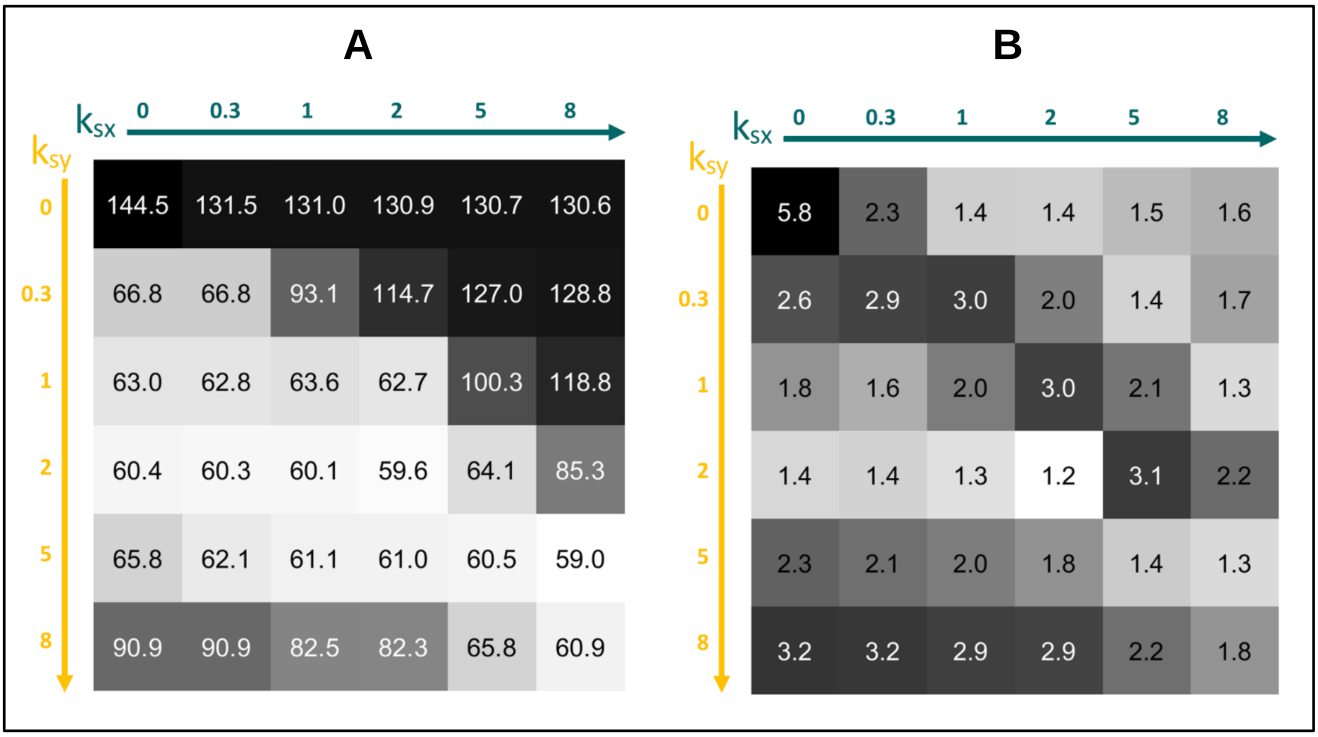
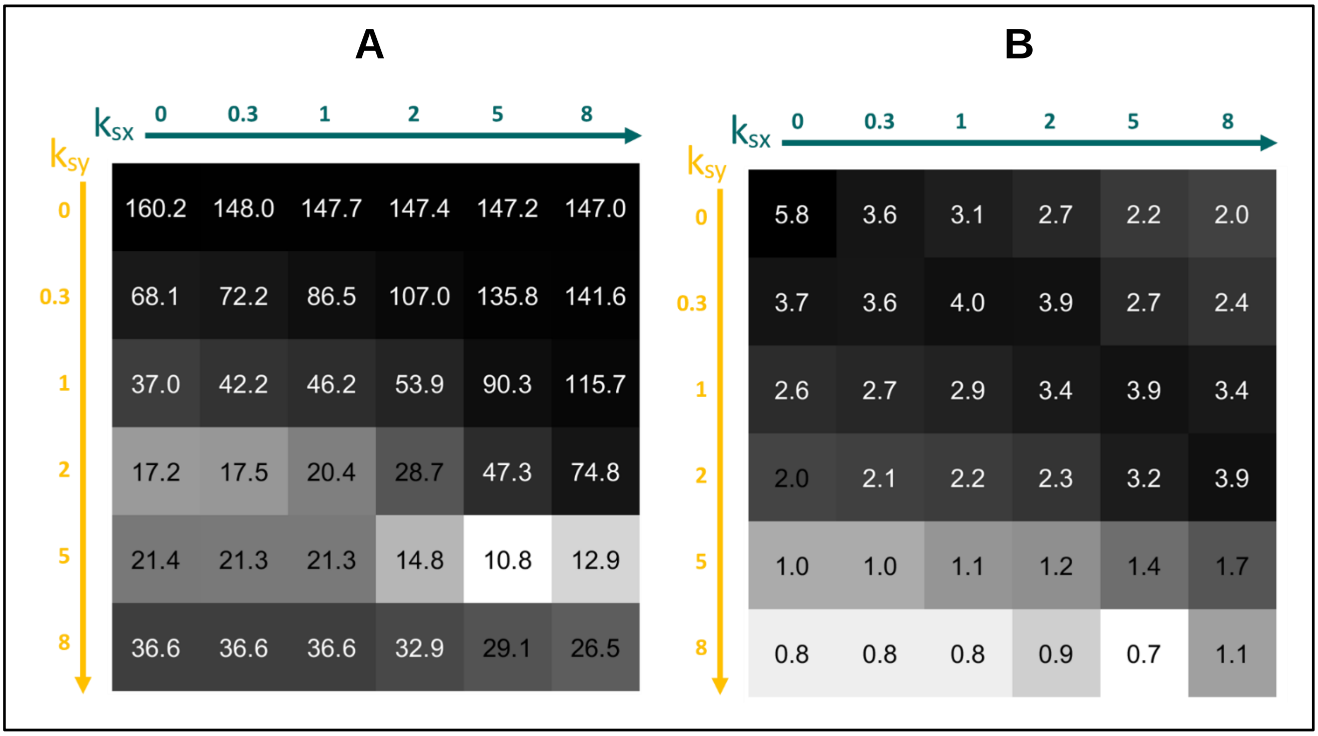


Figure A4| The effect of k_{sx} and k_{sy} on the cost landscapes using optimized values for B_x and B_y. **A)** the cost landscape is the percentage weighted sum of step width and step length differences. **B)** the cost landscape is the difference in CoM amplitude in cm.



Appendix 3

GRAIL floor projector

Background

At the St. Maartenskliniek (SMK), Nijmegen, the Gait Real-time Analysis Interactive Lab (GRAIL, Motek Medical BV) is used for clinical and scientific purposes. One of the many features of the GRAIL is that it can project objects onto the treadmill belt. It is used for projection of obstacles and targets which has to be avoided or hit by patients or research participants. Two software applications that are integrated inside the GRAIL are D-Flow and Vicon Nexus. D-Flow is used to control the GRAIL and to output data that are not directly related to standard gait analysis, including for instance the position of obstacles projected on the floor and treadmill-belt speed. Vicon Nexus is used to measure and output gait-related data, including electromyography, forces, motion capture using infrared markers. Vicon Nexus is a validated tool for gait-analysis (ref). Despite that D-Flow is not validated for research purposes, it is already used to measure the position of floor projections. Inaccuracies in the position of these obstacles were noticed by researchers at the SMK and the rehabilitation department of the Radboudumc.

Aim

To make an inventory of possible causes and solutions for the noticed inaccurate measurement of the position of floor projections. And, if possible, to implement solutions for better measurements.

Method

We approached the problem in two ways:

1| Post-measurement analysis:

As mentioned, a researcher had noticed the inaccuracy in her measurements of floor projections. She noticed this by finding results of stepping error (with respect to the floor projection) in healthy participants that were contradicting with stepping error seen in videos of the measurements. I confirmed this finding by using her code for analysis (MATLAB R2019b). The first step was therefore to see if there were any errors in the analysis that might have contributed to the inaccuracy. Two pitfalls were emphasized:

1.1| Rotation of floor projected objects

1.2| Synchronization of D-Flow and Vicon data

Two methods were studied:

<u>a) aligning signals using the cross-correlation between signals</u>

This method was the current synchronization method of the researchers at the SMK. The cross-correlation was calculated between the D marker coordinates and the V marker coordinates. For example, the cross-correlation was calculated between the D and V X coordinate of the right ankle marker. Subsequently, the delay between signals, calculated as the delay that resulted in the largest cross-correlation, was used to align the signals.

<u>b) matching identical marker coordinates of Vicon and D-Flow</u>

This method had to be developed. D had an internal clock and the internal time was outputted, whereas V had no internal time. At least it was not outputted to the c3d file as far as we know. Another difficulty was that D floor projection and marker data were not in the same file and did not have the same time-axis. The following steps were taken to end with a time-axis for V, so that all D signals could be interpolated on the V time-scale.

1. D marker data was rounded to the same nr of decimals as V data
2. for each V marker on each frame (k), we attempted to find a matching marker (with identical marker coordinates) in the D marker data
3. when a match was found, V-time at the k^{th} frame was set to the D-time of the matching marker coordinate
4. when no match was found for any marker, V-time at the k^{th} frame was set to NaN
5. gaps (the NaNs) in the time-axis of size 1 was interpolated
6. this resulted in a V time axis
7. all D signals including floor projection data were interpolated using the new V time axis.

2| Measurements on GRAIL:

Measurements were two-fold and were subsequently analysed (MATLAB R2019b)

2.1| Static measurements

Static measurements were done to study if the floor projection was accurate while the treadmill belt and the projected obstacles had zero velocity. A marker was placed on the treadmill belt. Marker position was measured with Vicon, streamed to D-Flow and a circle of the same size as the marker was projected onto the treadmill. A second marker was placed on the projection of the first marker and that was again measured in Vicon. Marker coordinates were subtracted to calculate the static difference of D-Flow output position and real position. This was repeated multiple times. Anteroposterior and mediolateral position was varied to study the effect of position on the treadmill on the static inaccuracy.

2.2| Dynamic measurements

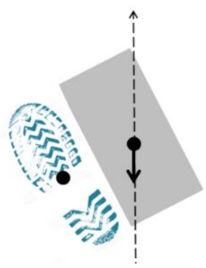
Dynamic measurements were done to study the effect of treadmill and projection velocity on the accuracy of projection. For this purpose, a phototransistor was plugged into the AD converted of Vicon and it was placed approximately in the origin of the Vicon coordinate system. A marker was placed on the phototransistor to measure the exact position, without affecting the sensibility to light. Within D-Flow, a rectangular object (20X20 cm) was made to move with a certain speed along the walking direction. We were able to detect when the object passed the phototransistor from the phototransistor signal.

Results

1| Post-measurement analysis:

1.1| Rotation of floor projected objects

In a precision stepping task that was already in use, targets were projected on the treadmill on which the participant had to step. Targets were rotated to match the alignment of the feet of the participant. The rotation was not taken into account yet in the calculations.



1.2| Synchronization of D-Flow and Vicon data

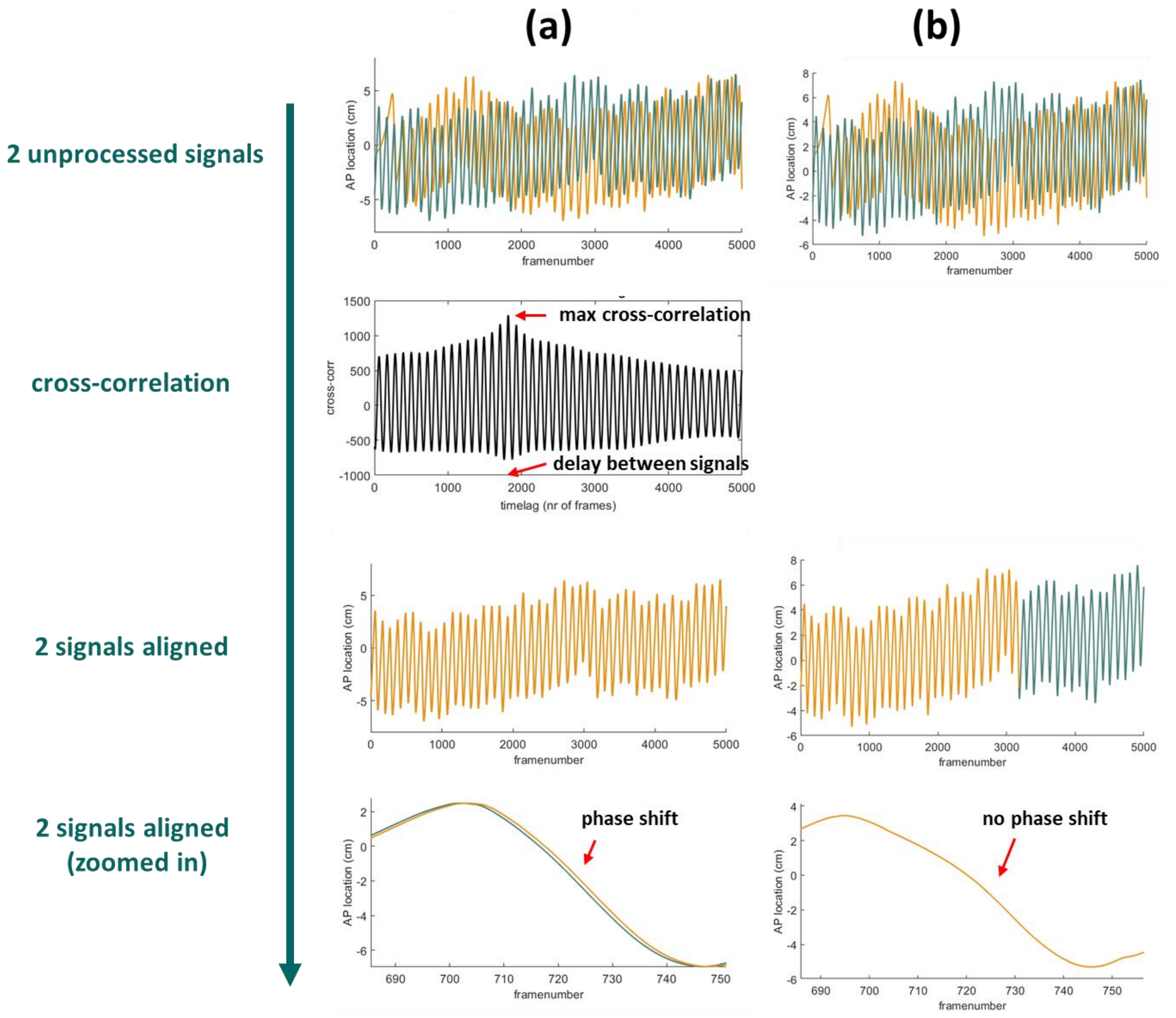
<u>a) aligning signals using the cross-correlation between signals</u>

Using the cross-correlation resulted in a phase shift between signals. It seemed that D skipped a few samples at random moments in time resulting in the phase shift. Whereas two signals should be identical after synchronization, they were not. The maximal difference between the marker coordinates was in the order of 5 mm. Therefore, this method was not recommended.

<u>b) matching identical marker coordinates of Vicon and D-Flow</u>

Matching identical marker coordinates resulted in a correct synchronization of the data as can be seen in the figure below.

In the figure below both methods (a and b) are visualized. In the lower left graph, the mentioned phase shift resulted from method *a* can be seen, whereas no phase shift is seen using method *b*. Therefore, it was preferred to use method *b.*



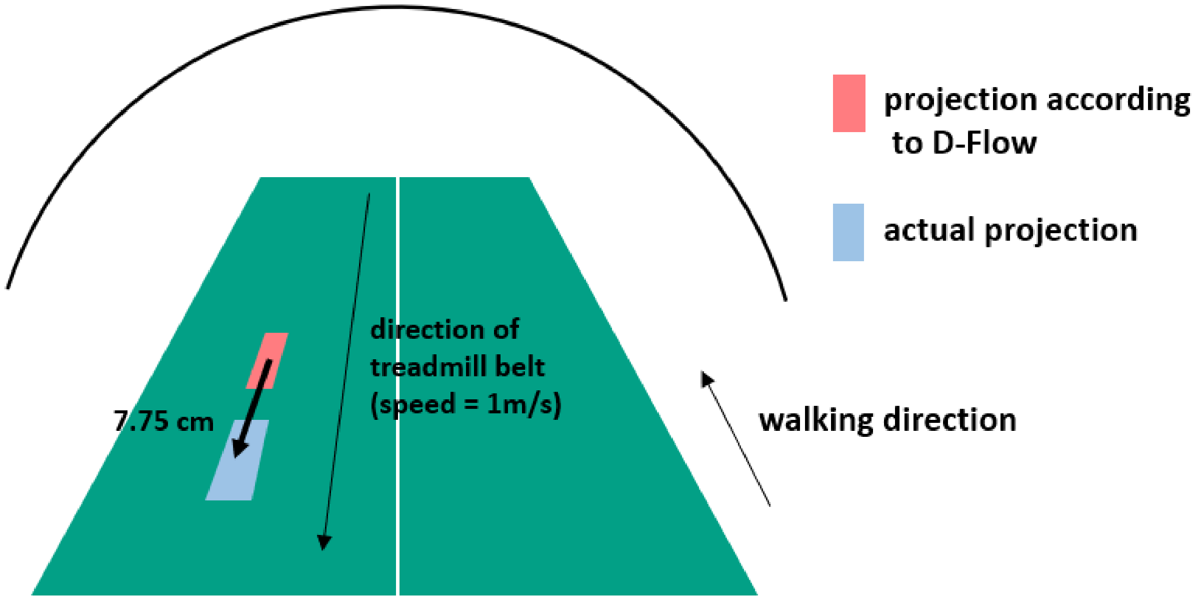
2| Measurements on GRAIL:

2.1| Static measurements

An offset of 7.78 cm was found between the position of the projection according to D-Flow and the actual projection, in which the actual position was posterior to the screen of the GRAIL. The static error was fixed by Motek Medical BV.

2.2| Dynamic measurements

A delay of 77.5 milliseconds was found, meaning that for a treadmill belt velocity of 1 m/s the position of the projection according to D-Flow was 7.75 cm located from the actual projection. The dynamic and static inaccuracies were in such directions that they (up to some extend) cancelled each other out. The situation is schematically represented in the figure below.



Recommendations

- Take into account rotation of target projections on the floor/treadmill belt.
- Be aware of the fact that Vicon is a validated tool for research purposes whereas <u>D-Flow is not a validated tool</u>.
- Use a proper method to synchronize D-Flow signals with Vicon signals. A method that seems to work well is synchronizing signals by <u>matching identical marker coordinates of Vicon and D-Flow</u>. It will allow you to interpolate all kinds of signals to the same time-axis of Vicon.
- Note that there is a <u>delay in the floor projector of 77.5 milliseconds</u>. The error of the projections on the treadmill belt therefore depend on walking speed. When you are interested in the ability of participants to step precisely on targets or to avoid obstacles presented on the floor, carefully consider these delays and how they will affect the research outcomes.
- It is expected that projections onto the screen are delayed as well.