Non-rigid deformation to include subject-specific detail in musculoskeletal models of CP children with proximal femoral deformity and its effect on muscle and contact forces during gait

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To account for proximal femoral deformities in children with cerebral palsy (CP), subject-specific musculoskeletal models are needed. Non-rigid deformation (NRD) deforms generic onto personalized bone geometry and thereby transforms the muscle points. The goal of this study was to determine to what extent the models and simulation outcomes in CP patients differ when including subject-specific detail using NRD or Magnetic Resonance Imaging (MRI)-based models. The NRD models slightly overestimated hip contact forces compared to MRI models and differences in muscle point positions and moment arm lengths (MALs) remained, although differences were smaller than for the generic model.

Keywords: subject-specific; MRI; non-rigid deformation; musculoskeletal modelling

Introduction

Musculoskeletal models (MSM) that present a three-dimensional, mathematical description of the human body can be used supplementary to clinical gait analysis to investigate parameters that cannot be measured directly in vivo, such as muscle moment arm length (MAL), musculotendon length (MTL), muscle forces and joint contact forces. Most often, generic MSMs are used, which are based on cadaveric datasets and are representative for subjects with normal anatomy and anthropometrical properties (Delp et al. 1990; Damsgaard et al. 2006; Andersen et al. 2009; Arnold et al. 2010; Modenese et al. 2011).

Children with cerebral palsy (CP) often present proximal femoral bone deformities, such as an increased femoral anteversion (FA) and neck-shaft angle (NSA). These bone deformities can affect the MAL of the muscle with respect to the hip joint. As generic MSMs do not account for bone deformities, they are not suitable to represent musculoskeletal geometry in children

with CP (Blemker et al. 2007; Scheys, Van Campenhout, et al. 2008). To represent such a population correctly, models that incorporate more subject-specific details are needed.

To accommodate for more subject-specific detail, personalized MSMs created using medical imaging, such as magnetic resonance imaging (MRI) (Arnold et al. 2000; Blemker et al. 2007; Scheys et al. 2009; Scheys et al. 2011; Correa et al. 2011; Hainisch et al. 2012; Tsai et al. 2012; Modenese et al. 2016; Wesseling et al. 2016) and computed tomography (CT) (Lenaerts et al. 2009; Mellon et al. 2013; Pellikaan et al. 2014; Bartels et al. 2015; Martelli et al. 2015; Marra et al. 2016) allow including a high level of detail in the MSM as bone geometry, muscle paths and joint center locations can be personalized.

Image-based modeling is however very time demanding, as manual segmentation of the bones and muscle paths is required. Therefore, different methods have been developed that allow semi-automatic personalization. Recently, non-rigid deformation (NRD) methods have been proposed that create MSMs by deforming the generic bone geometry onto personalized bone geometry and subsequently transforming the different muscle points (Scheys et al. 2009; Hausselle et al. 2012; Valente et al. 2014; Pellikaan et al. 2014; Chen et al. 2016; Marra et al. 2016). However, image-based techniques allow determining these locations based on the acquired images, whereas NRD techniques use mathematical algorithms to approximate their location.

Personalized musculoskeletal geometry is known to affect muscle MAL and MTL estimations (Scheys, Spaepen, et al. 2008; Scheys et al. 2011; Correa et al. 2011). As MALs determine the functionality of the muscles, muscle forces calculated during dynamic simulations of gait will be sensitive to changes in MAL (Carbone et al. 2012). As muscle forces largely affect joint loading (Correa et al. 2010; Steele et al. 2012; Carriero et al. 2012), it will be affected by the different levels of personalized musculoskeletal geometry that is used. However, Correa et al. suggested that generic and personalized MSMs yield similar muscle

function during dynamic simulations of gait (Correa et al. 2011). In contrast, a clear effect of including personalized geometry using MRI-based models on the magnitude and orientation of calculated hip contact loading was shown (Bosmans et al. 2014). However, it remains unknown to what extent the approximation of subject-specific detail by using NRD, will affect the calculated hip contact forces in patients with proximal femoral deformities. Therefore, the goal of our study was to define the effect of personalization based on MRI and NRD on muscle point positions, moment arm lengths and consequently the muscle and hip contact forces in patients with proximal femoral deformities during gait. We hypothesize that the modifications of the musculotendon points introduced by the NRD technique yield representative estimates in patients with proximal femoral deformity. If the estimated hip loading only minimally differs from the MRI model, this would suggest that NRD MSMs could serve as less time demanding, but valid alternatives for image-based MSMs to estimate hip joint loading in CP patients.

Material and methods

Subjects

Seven subjects diagnosed with diplegic CP (8-12 yrs.) participated in this study. All subjects were clinically diagnosed with an increased FA (ranging from 23° to 56°; normal range 20° to 24° (Fabry et al. 1973)) and NSA (ranging from 133° to 157°; normal range 129° to 130° (Zippel 1971)) (table 1). All subjects could walk independently without the aid of orthotic or supporting devices. Exclusion criteria were: surgical interventions performed prior to this study or receiving botulinum toxin treatment in the previous six months, obesity and pronounced foot deformities. All procedures were approved by the local ethical committee and the subjects' parents gave written informed consent.

Experimental data collection

For all subjects, reflective skin mounted markers were placed on bony landmarks according to the MOCAP-protocol (Software for Interactive Musculoskeletal Modeling (SIMM), Motion Analysis Corp., Santa Rosa, USA). This protocol was expanded with extra cluster markers on both femora and tibiae. All marker positions were outlined with a marker on the subjects' skin. A static trial and gait data were collected during barefoot walking at self-selected speed for each subject. Eight Vicon cameras were used to capture the three-dimensional marker trajectories (100 Hz, Vicon, Oxford Metrics, Oxford, UK). Two force platforms embedded in the walkway were used to measure the ground reaction forces (1500 Hz, Advanced Mechanical Technology Inc., Watertown, MA).

In addition, MRI data of the lower extremities were collected. A series of five axial images were acquired (1.5T Philips MRI scanner) with the subjects lying supine with extended knees. A full-leg image was created by combining the overlapping image series. To allow coupling of the kinematic data and the MRI data, radio opaque, non-ferromagnetic markers were placed prior to the MRI scan on the outlined marker position of the reflective markers (Scheys et al. 2006).

Musculoskeletal modeling

Generic model

For each subject, a generic model (figure 1) with 14 segments, 19 degrees of freedom and 88 musculotendon actuators (Delp et al. 1990) was scaled based on a static trial (Software for Interactive Musculoskeletal Modeling (SIMM), Motion Analysis Corp., Santa Rosa, CA, US).

Magnetic resonance imaging (MRI) based model

MRI models were defined for all subjects based on the acquired MR images using a dedicated workflow (figure 1) (Scheys et al. 2006). Bone structures of the pelvis, femora, patellae and

tibiae were segmented from the images (Mimics Innovation Suite, Materialise N.V., Leuven, Belgium). The hip joint center was determined by fitting a sphere to the femoral head using an iterative closest point algorithm (Besl & McKay 1992). The knee joint was modelled as a sliding hinge joint (Yamaguchi & Zajac 1989), where the knee axis was based on the geometry of the distal femur, by connecting the centers of two spheres fitted to the lateral and medial posterior condyles. Segmental coordinate frames were defined for the bone meshes (Wu et al. 2002) and marker coordinates, based on the radio opaque markers in the MR images, were expressed in the respective segmental coordinate frames. Next, the muscle points of all hip and knee actuating muscles were identified in the MR images (Scheys et al. 2006). The number of muscle points were defined similar to the generic model. The muscle points of all distal tibia and foot muscles as well as the ankle joint center were the same in the scaled generic and MRI models.

Non-rigidly deformed model (NRD)

For the NRD model (figure 1), the generic pelvis, femora and proximal tibiae bone geometries and muscle points were transformed onto the bone geometries as segmented from the MR images using an advanced non-rigid deformation procedure (Materialise N.V., Leuven, Belgium). To acquire the deformed bone geometries, an elastic surface registration approach was used (Danckaers et al. 2014). Next, a thin-plate splines deformation field (Bookstein 1989) was computed from the obtained pair of corresponding meshes to deform the muscle points. The hip joint center was defined as in the MRI model. Generic knee joint position and functions were scaled based on the MRI-based femur dimensions, to compensate for possible errors in segment length between the scaled generic and MRI-based femur. Muscle points of all distal tibia and foot muscles as well as the ankle joint center were adopted from the scaled generic model.

For all three model types, a wrapping surface based on the bone geometry of the distal femur defined the dynamic via-points of the knee extensors and prevented the muscles from penetrating the bone geometry. The musculotendon parameters (i.e. optimal fiber length and tendon slack length) of the generic model were linearly scaled based on the MTL in anatomical position in the respective models (Delp et al. 2007). For each model, the maximal isometric force of each musculotendon actuator was scaled based on the body mass of the subject.

Dynamic simulations of gait

For each subject, dynamic simulations of gait were generated in OpenSim 3.0 (Delp et al. 2007) using all three model types. Joint angles during gait were calculated using Kalman smoothing (De Groote et al. 2008), where model markers were fitted to the experimental marker trajectories with a least squares optimization. Joint moments were calculated using inverse dynamics. Static optimization was used to estimate muscle forces, while minimizing the sum of squared muscle activations (Anderson & Pandy 2001). Hip contact forces were calculated with the joint reaction analysis (Steele et al. 2012) and normalized to body weight (BW). Hip contact force orientation was calculated using the contact force components (figure 2).

Data analysis

Data of the 14 limbs were treated as independent data sets and averaged for each limb over the gait cycle. The results of the MRI models are used as reference to compare the results between the three model types. Differences in muscle point location with respect to the MRI model were calculated for the generic and NRD models. The first and second peak of the resultant hip contact force was calculated (P1 and P2 respectively) and the difference with the MRI model in MAL and muscle forces were calculated for the generic and NRD models. In addition, the contact force components (i.e. antero-posterior, supero-inferior and medio-lateral component)

at the times of the peaks were determined. Hip contact force magnitude and orientation were compared using a Friedman test ($p < 0.05$). When significant differences were found, a multiple comparison using Bonferroni correction identified the significant differences between the model types.

A subset of 12 muscles that deliver the highest maximal force in the MRI model was selected (thereby presenting all muscles that deliver at least 3.75 N/kg in the MRI model). For this subset, the MALs and muscle forces as well as the difference in muscle point location on the relevant segments (i.e. pelvis, femur or proximal tibia) are presented in the results. A complete overview is presented in Table 1 of the supplementary materials.

Results

Muscle points

Over all muscles, the average difference in 3D muscle point position between the scaled generic and MRI models is 2.19cm, while the NRD points differ on average 1.73cm from the MRI model (supplementary material table S1). For the selected subset (figure 3), the differences between the models are smaller (average difference with MRI of 1.60cm and 1.34cm for the generic and NRD points respectively). The differences in these muscles are largest in the superior-inferior direction, with on average the generic and NRD points being positioned more anteriorly, superiorly and laterally compared to the MRI points (figure 3). For the selected subset, the generic points are positioned between 1.42cm posteriorly and 1.39cm anteriorly, 2.52cm inferiorly and 1.32cm superiorly, 0.45cm medially and 1.85cm laterally with respect to the MRI model, while the difference with the NRD points range between 1.35cm posteriorly and 1.08cm anteriorly, 3.05cm inferiorly and 0.98cm superiorly, 1.41cm medially and 1.30cm laterally.

Moment arm length

When considering all hip MALs during gait, average RMS differences with the MRI model are larger for generic than NRD models (supplementary material table S2). The maximal absolute difference in MALs between the generic and MRI models is 3.34cm, while for the NRD models the difference is maximally 2.13cm. For the selected subset, also large differences between models exist at P1 and P2 (figure 4). For the knee, differences in MALs are smaller and similar for the NRD and generic models (maximal RMS difference with MRI of 1.45cm and 1.34cm for the NRD and generic models respectively). Differences in ankle MALs are only very small (average RMS difference with MRI of 0.03cm for the NRD and generic models), as ankle kinematics only showed small differences and muscle paths on the distal tibia and foot were not personalized.

Muscle forces

The average RMS difference in muscle forces with the MRI model are similar for the generic and NRD models (supplementary material table S2). From the selected subset of muscles, the large underestimation of gluteus medius anterior force at P1 in the generic model (average difference of 6.0N/kg with the MRI model) is decreased in the NRD model (average difference of 0.39N/kg with the MRI model; figure 5). In contrast, for other muscles, e.g. the vastii and semimembranosus, the difference increases. At P2, the difference in muscle forces with the MRI model is overall smaller for the NRD than the generic model (maximal absolute difference for the selected subset of 6.53N/kg for the generic and 3.08N/kg for the NRD model; figure 5).

Hip contact forces

The hip contact force magnitude at P1 is not significantly different between the generic, NRD and MRI models (3.97BW, 4.59BW and 4.17BW for the generic, NRD and MRI models respectively; figure 6A). At P2, the hip contact force magnitude of the NRD model is not significantly different from MRI (4.99BW and 5.50BW for the MRI and NRD models respectively), however the generic model calculates significantly lower contact forces

(3.15BW). For the different force components (figures 6B and 6C), the NRD contact forces are significantly increased compared to the MRI model in the anterior/posterior (1.30BW vs 0.91BW at P1 and 0.76BW vs 0.41BW at P2) and medial/lateral (1.00BW vs 0.70BW at P1) directions. These changes in force components affect the hip contact force orientation (figure 6D and 6E), presenting a significantly more anterior orientation at P1 for the NRD compared to the MRI model (17.6° vs 13.4° in the sagittal plane).

Discussion

The goal of this study is to determine to what extent the approximation of subject-specific detail, by using a non-rigidly deformed MSM, will affect the muscle point positions, moment arm lengths and calculated muscle and hip contact forces during gait in patients with proximal femoral deformities. Peak hip contact force magnitudes are similar for the NRD and MRI models, making NRD hip loading more comparable to MRI than the generic models. However, NRD is not capable of fully correcting differences in the muscle points and MALs with the MRI models.

Indeed, the NRD models compensate for the underestimated hip loading magnitude calculated by the generic model, but results in slightly increased hip loading compared to MRI models, with an increased loading of 0.42BW and 0.51BW at the first and second peak in contact force respectively (figure 6). At the first peak, specifically the anterior/posterior and medial/lateral components, and thereby the inclination in the sagittal plane, significantly exceed the MRI model (figure 6). This indicates the inclusion of NRD muscle points fails to include sufficient subject-specific detail, although loading magnitude is more comparable to MRI than for the generic model.

These differences relate to differences in muscle points, as NRD muscle points are on average 1.73cm different from the MRI model, which is slightly larger than the 1.5cm difference between NRD techniques and cadaveric data that has been reported before (Pellikaan

et al. 2014). This difference also exceeds the inter- and intra-observer variability that is expected when creating MRI-based models (0.56cm and 0.69cm respectively) (Scheys et al. 2009). For 74% of the NRD muscle points, the 3D difference with the MRI points is smaller than for the generic points (supplementary material table S1). Similarly, for the hip MALs, for 78%, 81% and 81% of the hip flexion, adduction and rotation MALs respectively, the RMS difference with the MRI MALs is smaller for the NRD than the generic models (supplementary material table S2). This indicates NRD results in muscle point locations and hip MALs more comparable to MRI. However, differences in calculated muscle forces with the MRI models during gait remain. In particular, the hip flexors force, i.e. mm. psoas, iliacus and rectus femoris, calculated using the NRD model still show large differences with the MRI forces, specifically at terminal stance.

The knee and ankle MALs differ from the MRI-based model, despite the fact that the distal lower leg and ankle muscle points were taken from the generic model. For the knee flexion MAL, differences with the MRI model are similar for the NRD and generic models, despite the muscle points spanning the knee joint are altered in the NRD model. Also small differences are found in ankle MALs, despite the muscle points of the ankle spanning muscles are not altered. These differences result from the small differences in kinematics (supplementary material figure S1; average difference between the MRI and NRD kinematics of 2°) and knee axis definition.

As a result, muscle forces calculated for the hip muscles of the NRD model were in general more comparable to the MRI model than the generic model. Interestingly, differences in lower leg muscle forces were large for both models. Previous research already showed that several lower leg muscles, e.g. mm. soleus and medial gastrocnemius, were sensitive to changes in muscle points of other muscles (Bosmans et al. 2015). Indeed, the m. soleus and medial gastrocnemius force were increased for both the NRD and generic models compared to MRI

(supplementary material table S2). This indicates that the NRD model is not able to estimate muscle points well enough to avoid a large effect on unaltered muscles.

A limitation of the present study is that we used the MRI-based model as a golden standard. Regarding hip joint loading, a better golden standard is the use of instrumented hip prostheses (Bergmann et al. 2001; Damm et al. 2015). However, in the current population of children with CP with proximal femoral deformities this is not feasible. As all geometrical components of the MRI models were directly segmented from the subjects' individual imaging data, we may assume that this data is more representative for patients with proximal femoral deformities compared to the other model types. A limitation for the use of the NRD model is that it still requires MRI acquisition and segmentation of the bones, therefore still requiring substantial pre-processing efforts. However, as segmenting muscle paths requires most time in creating the MRI model (Scheys et al., 2009), the use of NRD would still result in a substantial gain in time investment.

In conclusion, the current study evaluated the representativeness of bone geometry based personalization methods, in particular non-rigid deformation, to estimate hip joint loading in a population presenting proximal femoral deformity. However, differences in muscle point location and MALs remain due to differences in the defined muscle lines-of-action. Therefore, the NRD MSMs in their present form cannot serve as less time demanding alternatives for image-based MSMs to estimate hip joint loading in this patient group. Nevertheless, NRD may yield a good initial guess for following user-guided modifications based on MR-images.

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Table 1. Summary of the subjects' anthropometrical parameters. For each subject the gender, age (in years), height (in cm), weight (in kg), clinical diagnosis, femoral anteversion angle (in degrees) and neck-shaft angle (in degrees) is listed.

	Subject 1		Subject 2		Subject 3		Subject 4		Subject 5		Subject 6		Subject 7	
Gender	♂		♂		♂		♀		♀		♂		♂	
Age (years)	11		10		12		10		10		8		10	
Height (cm)	144.2		136.3		149.4		136.1		142.3		132.3		134.9	
Weight (kg)	32.7		27.8		38.3		34.2		31.8		26		24.4	
Diagnosis	Diplegic		Diplegic		Diplegic		Diplegic		Diplegic		Diplegic		Diplegic	
	L	R	L	R	L	R	L	R	L	R	L	R	L	R
Anteversion angle (°)	25	28	56	56	33	37	23	30	33	42	41	40	44	48
Neck-shaft angle (°)	140	143	157	156	138	138	137	133	146	150	147	142	142	136

Figure captions

Figure 1. The origin of the different parameters in all three of the models used. The parameters were adopted from the generic model, scaled from the generic model based on the new muscle or segment length, subject-specifically determined from MR images or non-rigidly deformed (NRD) based on the bone geometry.

Figure 2. Definition of the inclination angles of the resultant hip contact force on the right hip. Ax is defined as the angle between the superior-inferior axis of the segmental reference frame (Y) and the resultant vector in the frontal plane. Ay is defined as the angle between the medio-lateral axis of the segmental reference frame (Z) and the resultant vector in the transversal plane. Az is defined as the angle between the superior-inferior axis of the segmental reference frame (Y) and the resultant vector in the sagittal plane.

Figure 3. Difference with the MRI muscle points positions in 3D, anterior-posterior, superior-inferior and medial-lateral directions. A positive value represents a more posterior, inferior and medial placement of the generic and NRD models with respect to the MRI model. p1 until p5 indicate the number of the muscle point for each muscle, starting at the origin.

Figure 4. Difference with the MRI model in moment arm length for all degrees of freedom at the first and second peak in hip contact force (P1 and P2 respectively). Positive values represent a larger moment arm towards extension, adduction and internal rotation for the generic and NRD models with respect to the MRI model.

Figure 5. Difference with the MRI model in muscle force production at the first and second peak in hip contact force. Positive values represent an increased force production for the generic and NRD models with respect to the MRI model.

Figure 6. Magnitude of (A) the two resultant peaks (normalized to bodyweight (BW)), (B and C) the three components (normalized to bodyweight (BW)) and (D and E) the inclination angles (°) of the resultant hip contact force vector. The definition of the angles is explained in figure 2. Significant results ($p < 0.05$) are indicated with an asterix (*).

Table 1. Summary of the subjects' anthropometrical parameters. For each subject the gender, age (in years), height (in cm), weight (in kg), clinical diagnosis, femoral anteversion angle (in degrees) and neck-shaft angle (in degrees) is listed.

	Subject 1		Subject 2		Subject 3		Subject 4		Subject 5		Subject 6		Subject 7	
Gender	♂		♂		♂		♀		♀		♂		♂	
Age (years)	11		10		12		10		10		8		10	
Height (cm)	144.2		136.3		149.4		136.1		142.3		132.3		134.9	
Weight (kg)	32.7		27.8		38.3		34.2		31.8		26		24.4	
Diagnosis	Diplegic		Diplegic		Diplegic		Diplegic		Diplegic		Diplegic		Diplegic	
	L	R	L	R	L	R	L	R	L	R	L	R	L	R
Anteversion angle (°)	25	28	56	56	33	37	23	30	33	42	41	40	44	48
Neck-shaft angle (°)	140	143	157	156	138	138	137	133	146	150	147	142	142	136

	GENERIC	NRD	MRI

GEOMETRY	Generic	MRI	MRI
MARKERS	Generic	MRI	MRI
MUSCLE POINTS			
Pelvis	Generic	NRD	MRI
Femur	Generic	NRD	MRI
Proximal Tibia	Generic	NRD	MRI
Distal Tibia	Generic	Scaled generic	Scaled generic
Foot	Generic	Scaled generic	Scaled generic
MT PARAMETERS	Generic	Scaled generic	Scaled generic
HIP JOINT CENTER	Generic	MRI	MRI
KNEE AXIS	Generic	Scaled generic	MRI

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Figure 2. Definition of the inclination angles of the resultant hip contact force on the right hip. A_x is defined as the angle between the superior-inferior axis of the segmental reference frame (Y) and the resultant vector in the frontal plane. A_y is defined as the angle between the medio-lateral axis of the segmental reference frame (Z) and the resultant vector in the transversal plane. A_z is defined as the angle between the superior-inferior axis of the segmental reference frame (Y) and the resultant vector in the sagittal plane.

Figure 3. Difference with the MRI muscle points positions in 3D, anterior-posterior, superior-inferior and medial-lateral directions. A positive value represents a more posterior, inferior and medial placement of the generic and NRD models with respect to the MRI model. p1 until p5 indicate the number of the muscle point for each muscle, starting at the origin.

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