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SENSITIVITY OF PREDICTED MUSCLE FORCES TO THE ANATOMICAL VARIABILITY OF THE MUSCULOSKELETAL GEOMETRY

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SUMMARY
The purpose of this study was to investigate the sensitivity of predicted muscle forces to perturbation of the musculoskeletal geometry based on the normal, anatomical variability of muscle points extracted from magnetic resonance images. Comparison with previous research [1] shows that the anatomical variability of muscle points varies between muscle points, emphasizing the importance of muscle point specific perturbations.

INTRODUCTION
Musculoskeletal models are often used for advanced biomechanical analyses. The accuracy of these models relies on the definition of correct geometrical, inertial and musculotendon parameters. Several sensitivity analyses of these model parameters have recently been performed: The sensitivity of muscle forces to perturbations of the musculotendon parameters has previously been investigated [1] and was highest for the tendon slack length. When studying the sensitivity of muscle forces to the musculoskeletal geometry by perturbing each individual muscle attachment and via point by 1 cm in every direction, muscle forces of the plantar flexors were most sensitive to perturbation of the insertion of the Achilles tendon [2]. However, the applied fixed perturbation of 1 cm might not reflect the true anatomical variability of these muscle points. Therefore, the purpose of this study was to investigate the sensitivity of predicted muscle forces to perturbation of the musculoskeletal geometry based on the normal, anatomical variability of muscle attachments extracted from medical imaging, instead of a fixed perturbation.

METHODS
We used the generic gait2392 model in OpenSim [3]. The model consisted of 12 rigid body segments, 11 joints, 23 degrees of freedom (DOF) and 86 Hill-type musculotendon actuators (MTA). A gait analysis was performed for one female subject (23yrs, 1.73m, 63kg) on a split belt treadmill (Forcelink, Culemborg, The Netherlands) during a trial of normal walking (4km/h). Data acquisition consisted of 3D motion capture with 2 Krypton cameras (Nikon Metrology, Leuven, Belgium), force registration by treadmill-embedded force sensors and electromyography (Zero-wire EMG, Aurion, Milan, Italy).

The generic model was scaled based on a static trial. Inverse kinematics were solved for one gait cycle of the right leg by Kalman smoothing [4] and dynamic consistency was increased by applying the Residual Reduction Algorithm [3]. Finally, a static optimization algorithm that minimizes the sum of muscle activations squared was performed to calculate muscle forces at each time instant. For each individual muscle, the time instant of maximal muscle force over the gait cycle was determined.

The variability range of the muscle attachment points was determined on six MRI-based personalized musculoskeletal models of normal control subjects. These six models were created using in house developed software [5] and contained subject-specific bones of pelvis, bilateral femur and tibia as well as the paths of the bilateral MTA of all hip and upper leg muscles. For each muscle attachment point, the muscle point type was defined, being origin (o), pseudo origin (po, most distal intermediate point on proximal segment), pseudo insertion (pi, most proximal intermediate point on the distal segment) or insertion (i). Expressing the location of the muscle point relative to its bone coordinate system, allows an easy transfer to the scaled generic model. These attachment points define a three-dimensional box representative of the anatomical variability for each muscle.

For this sensitivity analysis, a set of 13 muscle attachments was then perturbed repeatedly within its own anatomical variability range using a uniform Latin hypercube method. The sampling was defined independent of the perturbation direction (x, y and z). Perturbing within the anatomical variability of the muscle attachment point has the advantage that the size of the perturbation is based on accurate information extracted from medical imaging. The number of perturbations was determined based on convergence of the output variables: i.e. when the mean standard deviation of the muscle force at the time instant of nominal maximal muscle force over the last ten percent of the simulations is within two percent of the mean standard deviation of the muscle force over the entire set of perturbations. If all muscle forces converged within the two percent range, the muscle point was not further perturbed. For all perturbations, muscle forces converged within 200 simulations.

Sensitivity of the muscle force was expressed in two indices [2]. These were calculated at the time instant of maximal

muscle force in the nominal, unperturbed simulation. Firstly, the local sensitivity index (LSI), quantifying the effect of a perturbation on the muscle of the perturbed MTA:

$$\text{LSI} = \frac{\sum_{i=pert} \left| F^{MTA}_{perturbed,i}(t) - F^{MTA}_{generic,i}(t) \right|}{\sum_{i=pert} F^{MTA}_{generic,i}(t)} 100\%.$$

Secondly, the overall sensitivity (OSI), quantifying the effect of a perturbation on the muscle forces of all unperturbed MTA:

$$\text{OSI} = \frac{\sum_{i\neq pert} \left| F^{MTA}_{perturbed,i}(t) - F^{MTA}_{generic,i}(t) \right|}{\sum_{i\neq pert} F^{MTA}_{generic,i}(t)} 100\%.$$

with $F^{MTA}_{generic,i}(t)$ and $F^{MTA}_{perturbed,i}(t)$ being the nominal and perturbed muscle force, produced by the perturbed (i=pert) and unperturbed (i≠pert) MTA at the time instant (t) of maximal muscle force of the perturbed muscle in the nominal simulation.

RESULTS AND DISCUSSION

The unique value of this study lies in the use of the anatomical variability of muscle points to determine an accurate perturbation size and in the use of statistical methods to sample the anatomical range. Hence, the sensitivities we calculate better reflect the expected errors when using a generic instead of subject-specific model of the musculoskeletal geometry. The range of anatomical variability and sensitivity indices for the perturbed muscles are listed in Table 1. The largest variability is found for sartorius (3.26cm, pi, x), semitendinosus (3.17cm, pi, y) and gluteus medius anterior (3.16cm, o, x). The smallest ranges are found for biceps femoris (0.07cm, o, y), sartorius (0.09cm, pi, z) and (0.34cm, o, y). The OSI was highest for gluteus medius anterior (4.66%, o), iliacus (1.96%, po) and gluteus medius anterior (1.80%, i). Higher OSI values indicate that the muscle forces of the unperturbed muscles were more affected by the anatomical perturbations. The OSI was lowest for sartorius (0.08%, pi), semitendinosus (0.14%, pi) and sartorius (0.15%, o). The LSI was highest for gluteus medius anterior (44%, o), gluteus minimus anterior (32.80%, o) and piriformis (25.49%, i). Higher LSI values indicate that the muscle force of the perturbed muscle was more affected by the anatomical perturbations. The LSI was lowest for iliacus (2.72%, pi), semimembranosus (5.14%, pi) and gluteus medius posterior (6.21%, i). There is no clear relation between LSI and OSI values.

In general, the anatomical variability of muscle points tends to be smaller than the fixed perturbation used in previous research [2], where an absolute range of 2 cm was applied in all directions. We observe a muscle-specific, directional dependency of the variability. Our sensitivity indices differ from the results of Carbone et al. resulting in a different sensitivity ordering. These differences result from differences between used models (gait2392 vs Twente Lower Extremity Model), applied perturbation size (within anatomical variability vs fixed), number of applied perturbations (multiple vs two per dimension) and calculation of indices (at the time instant of maximal force vs over the entire gait cycle).

In future research, the study will be extended to include the anatomical variation of and sensitivity of all MTA in the MRI-based model. Further, the effect of the perturbations on the muscles' contribution to the joint moment will be investigated.

CONCLUSIONS

When performing a sensitivity analysis on the musculotendon geometry, perturbations should be determined on the anatomical variability. Perturbations within this anatomical variability better reflect the errors made when using a generic model to study a specific subject than fixed perturbations.

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Table 1: Absolute variability ranges for each dimension (x, y and z) and sensitivity indices of the perturbed muscles

Muscle	Type	X (cm)	Y (cm)	Z (cm)	OSI (%)	LSI (%)
Gluteus medius anterior	o	3.16	0.34	0.71	4.66	44.00
Iliacus	pi	1.95	2.00	1.34	1.96	8.38
Gluteus medius anterior	i	1.81	1.75	0.96	1.80	12.45
Iliacus	po	1.86	0.72	1.48	1.67	2.72
Gluteus medius posterior	i	2.71	0.85	1.53	1.22	6.21
Semimembranosus	pi	1.69	2.33	1.16	0.92	5.14
Biceps femoris caput longum	o	1.69	0.07	2.59	0.77	9.28
Gluteus minimus anterior	o	2.23	0.51	1.09	0.58	32.80
Piriformis	i	1.57	1.25	0.72	0.55	25.49
Adductor longus	o	1.19	0.84	0.92	0.37	6.54
Sartorius	o	1.85	0.89	1.95	0.15	6.54
Semitendinosus	pi	1.69	3.17	0.84	0.14	9.80
Sartorius	pi	3.26	1.94	0.09	0.08	7.14