The effect of muscle atrophy in people with unilateral transtibial amputation for three activities

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The effect of muscle atrophy in people with unilateral transtibial amputation for three activities: gait alone does not tell the whole story

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Abstract:

Amputation imposes significant challenges in locomotion to millions of people with limb loss worldwide. The decline in the use of the residual limb results in muscle atrophy that affects musculoskeletal dynamics in daily activities. The aim of this study was to quantify the lower limb muscle volume discrepancy based on magnetic resonance (MR) imaging and to combine this with motion analysis and musculoskeletal modelling to quantify the effects in the dynamics of key activities of daily living. Eight male participants with traumatic unilateral transtibial amputation were recruited who were at least six months after receiving their definitive prostheses. The muscle volume discrepancies were found to be largest at the knee extensors (35%, $p=0.008$), followed by the hip abductors (17%, $p=0.008$). Daily activities (level walking, standing up from a chair and ascending one step) were measured in a motion analysis laboratory and muscle and joint forces quantified using a detailed musculoskeletal model for people with unilateral transtibial amputation which was calibrated in terms of the muscle volume discrepancies post-amputation at a subject-specific level. Knee extensor muscle forces were lower at the residual limb than the intact limb for all activities ($p\leq0.008$); residual limb muscle forces of the hip abductors ($p\leq0.031$) and adductors ($p\leq0.031$) were lower for standing-up and ascending one step. While the reduced knee extensor force has been reported by other studies, our results suggest a new biomechanically-based mitigation strategy to improve functional mobility, which could be achieved through strengthening of the hip abd/adductor muscles.

Keywords:

Transtibial amputation; activities of daily living; muscle volume; muscle function

Introduction

Amputation imposes significant challenges in locomotion to millions of people with limb loss worldwide (Moxey et al., 2011). The main aim in rehabilitation is to restore and preserve maximum independence of mobility (indoor and outdoor). Studies show that of the 85% of those with limb loss who are fitted with a prosthesis, only 5% use their prosthesis for more than half of their waking hours (Jordan et al., 2012; Geertzen et al., 2001). This low use of the residual limb results in muscle atrophy (Lilija and Oberg, 1997). Typically, the residual muscle volume reduces by 17 to 35% in the first six months post-amputation in people with a unilateral transtibial amputation and stabilises after approximately 100 days (Lilija and Oberg, 1997; Sanders and Fatone, 2011a).

Despite many studies to quantify the reduction of residual limb volume post-amputation, how muscle atrophy affects musculoskeletal dynamics in daily activities remains unclear. Muscle volume is an important determinant of muscle strength and joint moment generating capacity (Fukunaga et al., 2001, 1992; Knarr et al., 2013; Lloyd et al., 2010). The loss of muscle volume may lead to a compensatory strategy that favours the intact over the residual limb in daily activities. This is evidenced by the decreased joint moment, power and ground reaction force (GRF) at the residual limb when compared to the intact limb during level walking (Czerniecki et al., 1991; Jarvis et al., 2016; Orekhov et al., 2019). The reduction in the residual limb's moment, power and force also suggests a protective mechanism since the soft tissues of residual limbs following lower-limb amputation are vulnerable to damage (Beyaert et al., 2008; Esposito et al., 2014; Burke et al., 1978; Bramley et al., 2021). Consequently and collectively, this results in a greater knee contact force on the intact limb in gait (Ding et al., 2020; Miller et al., 2017), which is likely related to a higher prevalence of knee joint pain and osteoarthritis among people with limb loss that then further limits their mobility in the long term (Lemaire and Fisher, 1994; Struyf et al., 2009).

While gait analysis studies have reported the main kinematic/kinetic deficits during level walking among people with limb loss, the able-bodied literature shows that activities such as standing up from a chair and stair ascent and descent are better predictors of independence and are more challenging (van Der Kruk et al., 2021). Although studies exist looking at different activities (Actis et al., 2018; Harper et al., 2018; Honegger et al., 2021), there are no studies that have conducted a combined analysis of the biomechanics of those with limb loss in these key tasks of daily living, whilst incorporating direct measures of muscle atrophy.

Musculoskeletal modelling provides an ideal framework to quantify muscle and joint contact forces during activities of daily living. Such models take as input measured motion and GRF to formulate the equations of motion; solving these yields muscle forces and joint forces. In the musculoskeletal modelling pipeline, a static optimisation is used to solve muscle redundancy based on a pre-defined criterion, such as minimising the sum of cubed muscle activation (Crowninshield and Brand, 1981). For people with limb loss, the model must be modified to represent the muscle volume discrepancies between the intact and residual limbs in order to provide a better estimation of the musculoskeletal function. This modification could be achieved by a detailed model calibration from medical imaging (such as MRI) which allows the quantification of muscle volumes. Therefore, the purpose of this study was to: quantify the lower limb muscle volume discrepancies between the residual limb and the intact limb based on MR imaging; and to use these to quantify the differences in muscle and joint loading during activities of daily living (level walking, standing-up from a chair and ascending one step) in people with unilateral transtibial amputation.

2. Method

2.1 Participants

The study was approved by the Imperial College Research Ethics Committee (Reference 16IC3562) and the NHS Research Ethics Committee (REC reference 16/LO/1715). Written informed consent was obtained from each participant. Eight male participants with traumatic unilateral transtibial amputation were recruited with the following inclusion criteria: at least six months after receiving their definitive prostheses, and capable of walking for twelve minutes continuously without walking aids. Their motion and MRI data were collected in a single-visit to the Charing Cross Hospital, Imperial College Healthcare Trust, UK. Participant characteristics are shown in Table 1.

Insert Table 1

2.2 Motion data

Motion data were collected in a motion laboratory (Charing Cross Hospital, Imperial College Healthcare Trust, UK) equipped with a 10-camera optical motion capture system (100 Hz, Vicon, Oxford, UK) and three force plates (1000 Hz, Kistler Type 9286B; Kistler Instruments Ltd, Winterthur, Switzerland). Reflective markers were placed bilaterally on the anterior/posterior superior iliac spine (A/PSIS), medial/lateral femoral epicondyles, medial/lateral malleoli, second/fifth metatarsal heads, and lateral and posterior aspect of the calcaneus. Clusters of four markers each were also placed bilaterally on the shank and thigh. On the residual limb side, the medial/lateral malleoli, second/fifth metatarsal heads, and lateral and posterior aspect of the calcaneus were placed on the prosthesis such that the markers were symmetrical with the intact limb. On completion of a static standing trial in an anatomical position, participants were asked to walk at a self-selected pace, stand up from a chair and ascend one step. These were selected as they are daily activities that can be performed independently. Standardised instructions were used for all participants (Supplementary Materials, Table S1) and each activity was repeated three times (step-ascending was repeated three times for each leading limb; and was repeated six times for both limbs). Surface electromyography (EMG; 1000 Hz, Trigon, Delsys, Boston, USA) was recorded from five bilateral muscles: gluteus medius, vastus lateralis, rectus femoris, biceps femoris long head and semitendinosus. The electrodes were placed with an orientation parallel to the muscle fibres according to Perotto (2011).

2.3 MRI data

Following the motion study, MRI data were collected from all participants using a 3.0 T MRI scanner (Verio Siemens AG, Erlangen, Germany) in a T1-weighted, 3D VIBE (volumetric interpolated breath-hold examination) sequence. Axial images were obtained contiguously from the iliac crest to the end of the intact foot. Imaging parameters were: field of view 450 × 450 mm^2; in plane resolution 1.406 ×1.406 mm; and slice thickness 1 mm. The total image acquisition time per subject was approximately 40 minutes.

Bone and soft tissue were segmented (Figure 1) by one experienced operator using Mimics (Mimics 17.0, Materialise, Belgium). First, sets of axial images were automatically registered, providing a field of view of the entire limb. Then, the borders of bones (femur, tibia and fibula) and lower limb muscles were manually delineated from the axial images. To facilitate the process, the interpolation function was applied approximately every five slices. Afterwards, muscle volumes were calculated from the automatic construction of the 3D shapes. The intra-operator error of the muscle volume, which was calculated as the volume differences of the same muscle when manually segmented four times, was 1.8 % (Henson et al., 2021). This is slightly higher than the volume error reported for the segmentation of simple phantom shapes (< 0.5 %, Handsfield et al., 2014) but less than that reported for complex shapes (< 3 %, Mitsiopoulos et al., 1998). Eighteen lower limb muscles were further divided into six groups based on their main functional action (Sartori et al., 2012): knee flexors (biceps femoris (long head and short head), semimembranosus and semitendinosus), knee extensors (rectus femoris, vastus intermedius, vastus lateralis and vastus medialis), hip abductors (gluteus medius, gluteus minimus and tensor fasciae latae), hip adductors (adductor brevis, adductor longus, adductor magnus, gracilise and pectineus), hip flexors (iliacus and psoas major) and hip extensors (gluteus maximus). The muscle group volume was defined as the sum of individual muscle volumes for each group.

Insert Figure 1

2.4 Musculoskeletal model

Musculoskeletal models of people with unilateral transtibial amputation were created using an open-source musculoskeletal modelling software FreeBody (V2.1, Cleather and Bull, 2015). It has been previously validated in the literature for predicting muscle and joint contact forces during various activities of daily living (Ding et al., 2016). Briefly, each limb consisted of four rigid segments, 15 kinematic degrees of freedom (DOFs), and 163 muscle elements representing 38 muscles. Each muscle was modelled as an ideal force generator and its force was proportional to its maximal isometric force, which was equal to the physiological cross-sectional area (PCSA) multiplied by the maximum muscle stress (60 N/cm^2, Rajagopal et al., 2016).

The intact limb was modelled upon linear scaling of a musculoskeletal anatomical model (M2), which was found to be closest to the limb loss cohort in terms of mass and limb length in a publicly available musculoskeletal atlas (http://www.msksoftware.org.uk, Ding et al., 2019). The dataset of M2 provided bone geometry (coordinates of joints, tibiofemoral contact points and wrapping objects), muscle geometry (attachments sites, via points and PCSA) and the segmented bone surfaces from MRI. The scaling factors used for the pelvis, thigh, shank and foot are the ratios of the intersegmental length and width measured from the reflective markers in the standing trial to intersegmental length and width in the underlying dataset of M2 (Nolte, et al., 2016). Modifications were made to the contralateral limb as follows: muscles crossing the ankle joint were removed; the tibia surface was then aligned to the tibia surface of M2 such that the re-attachment site of gastrocnemius after the myodesis stabilisation procedure was estimated on M2 (Potter, 2011). The muscle PCSA from the intact limb was considered as a baseline whilst the PCSA from the residual limb was calculated by multiplying a coefficient, which was defined as the muscle volume ratio between the residual and intact limbs. The optimisation function of the residual limb was therefore formulated as:

$$\min[\sum_{j\in M_{group}}(\frac{F_j}{C_j F_{jmax}})^3+\sum_{i\in M/(M_{group})}(\frac{f_i}{f_{imax}})^3]$$

where F and F_{max} are the muscle force and the maximal muscle force, respectively; F_{max} is based on the baseline of the intact limb; M $(M=i+j)$ is the list of all muscles in the residual limb; c_j $(j=6)$ the coefficient of muscle group for the knee flexors; knee extensors; hip abductors; hip adductors; hip flexors; and hip extensors.

2.5 Data analysis and statistics

Data post-processing was performed using Matlab (MathWorks, Inc., Natick, USA). All kinetics data were time normalised to a full cycle consisting of 101 data points. One gait cycle was defined by consecutive heel strikes of the same leg. The standing-up cycle started at the seat-off whilst the single step ascent started at the foot-off as defined based on force plates at the seat and floor, respectively (when the vertical force component dropped to zero); they both ended with the subject standing still as defined based on the velocity of markers on the superior iliac spine.

Recorded EMG data and modelled muscle activations were normalized to the maximum value of individual muscle in all activities, and therefore both varied between 0 (fully deactivated) and 1 (fully activated). Their differences were quantitatively evaluated using Sprague and Geers metric of magnitude (M), phase (P) and combined (C) errors (Schwer, 2007), which quantified the magnitude and phase error independently, while the combined error was computed as the root of the sum of squares of M and P. The interpretation of the Sprague and Geers metric is as follows (Klemt et.al., 2019):

$0 < C < 0.15$ excellent similarity;

$0.15 < C < 0.30$ very good similarity;

0. $30 < C < 0.45$ good similarity;

$0.45 < C < 0.60$ moderate similarity;

and $C > 0.6$ no similarity.

The discrepancies between limbs were investigated: discrete data (i.e., muscle volume) were assessed by the Wilcoxon Signed Rank test ($\alpha = 0.05$) whilst the continuous data (i.e., ground reaction force and its vertical, anterior-posterior and lateral-medial components, joint moments, muscle forces and joint contact forces) during dynamic tasks were assessed by spatial parameter mapping (SPM) analysis (non-parametric, one-sample paired t-test), in which the t-statistic is calculated as a function of time (SPM {t}). A critical threshold (t*) was determined based on the vector-field smoothness and temporal gradients of the continuous data. Regions of ground reaction forces, muscle forces and joint forces for which SPM {t} exceeded the critical threshold, were considered as statistically significant differences. The computations were conducted using “SPM1D”, a free and open-source software package for SPM (available at www.tpataky.net/spm1d).

3. Results

Muscle group volumes of the knee extensors, hip abductors and hip adductors were significantly lower (p = 0.008) at the residual limbs than at the intact limbs (Table 2). The differences were largest for the knee extensors (-34.7%), followed by the hip abductors (-12.9%).

(Insert Table 2)

These significant differences were predominantly due to the vertical component of the ground reaction force (Figure 2: 0-8% of gait, 0-30% of standing-up and 50-66% of step-ascending).

(Insert Figure 2)

Only knee extension moments were lower at the residual limbs for all activities (Figure 3: 6–16% of gait; 1-42% of standing-up and 47-73% of ascending one step).

The combined errors between the modelled muscle activations and measured EMG signals were in the range of 0.18 to 0.37, demonstrating a good and very good similarity with the measured muscle activity (Supplementary Materials, Table S2 and Figure S2). Hip abductors and hip adductors were lower during the standing-up and ascending one step tasks (Figures 4-6), yet there were no differences in gait (Figure 4). Knee joint contact forces were lower at the residual limb during the first peak of gait and the peaks in standing-up and ascending one step (Figure 7).

4. Discussion

This is the first study to have determined muscle volume reductions at the residual limb when compared to the intact limb for people with unilateral transtibial amputation and used this to explore its effect on musculoskeletal dynamics for three different activities of daily living.

The volume reduction found here is in the range of previous findings based on alternative methods, which was 17-39% for all muscles (Lilija and Oberg, 1997, Sherk et al., 2010) and was 22% for quadriceps femoris (Schmalz et al. 2001).

In dynamic activities, standing up from a chair and ascending one step are more challenging than gait for those with limb loss as shown by the higher joint moments required in the sagittal plane (Figure 3: the peak knee extension moment was approximately double when ascending one step). Knee extension moments were significantly lower at the residual limbs than the intact limbs when the peak, vertical GRF occurred (Figure 2). This may be attributed to the muscle atrophy of the knee extensors. As a result, knee extensor forces were found to be lower during the generation of vertical support at standing-up and ascending one step (Figures 5 and 6). It is widely acknowledged that the knee extensors contribute to the peak of ground reaction force during weight acceptance in order to complete knee extension. The reduced knee extension moments at the residual limb may occur to protect it from the increased shear force in mechanically demanding tasks (Šlajpah et al., 2013) – the protective mechanism may be inevitable since the soft tissues at the residuum-prosthesis interface are not suitable for load-bearing and consequently, will exacerbate the progressive loss of the knee extensor function.

The anterior-posterior GRF component is comprised of braking (negative) and propulsive (positive) regions. Due to the loss of soleus and gastrocnemius, people with limb amputation would use their prosthetic feet to achieve braking and propulsion. Participants in our study were all equipped with definitive, energy storage and return (ESAR) prosthetic feet (Table 1). No significant differences were found in the propulsive region between the intact and residual limbs (e.g., the late stance of gait). This is consistent with available literature that the ESAR feet commonly produce an increased propulsive force due to the keel-spring in the prosthesis, although this does not replace the active musculature of the natural limb (Hafner et al., 2002). The braking forces were lower in ascending one step when compared to the intact limb. This may be due to the incapability of the ESAR feet in braking especially in activities that consume higher energy, or a compensation mechanism that reduced residual leg braking may be beneficial to increase net propulsion in the absence of ankle muscles as proposed by Silverman et al. (2008). Our findings highlight that conclusions on people with limb loss function made from gait alone do not provide sufficient information.

The atrophy of hip abductor/adductors, as identified from MR imaging, weakened its function in the higher demand activities measured here. In the sagittal plane, muscles that contribute to vertical support also dominate during stair ambulation (Pandy et al., 2010; Lin et al., 2015). So hip abductors could potentially compensate for the loss of the gastrocnemius and soleus, which mainly dominate vertical support in late stance. Our study found no significant between-limb differences in late stance and, hence, didn't suggest a strengthening of gluteus medius at this phase. Hip abductors could also coordinate with knee extensors in weight acceptance (Ellis et al., 2014; Pandy et al., 2010). For people with transtibial amputation, reduced knee flexion at the residual limb was well documented from loading response to pre-swing. This could be an effective strategy in maintaining socket fit and function, and therefore decreasing the compressive and shear force at the socket-stump interface (Commean et al., 1997). Thus, the vertical support could be provided by the skeleton with a straighter knee rather than the knee extensors with a flexed knee as in a non-amputee gait. Moreover, Lin et al., (2015) have shown that in stair ascent, most of the forward acceleration during the first half of the stance phase was generated by gluteus medius. During weight acceptance in three activities, vertical ground reaction forces were significantly lower at the residual limbs than at the intact limbs. While strengthening of the hip abductors has been suggested to improve mediolateral balance during level walking and standing (Nadollek et al., 2002; Crozara et al., 2019), our results have implications for hip abductor interventions, particularly at the weight acceptance phase, to compensate for the weakness of the knee extensors.

There are some limitations to this study. First, the small number of participants limits the capability to generalise the results to a broader population of those with limb loss. Secondly, the cause of amputation in our participants is trauma at a relatively young age. More participants would have enabled the investigation of how population factors such as age, cause of amputation and amputation level might affect muscle atrophy and the consequent loss of musculoskeletal function. Third, while muscle volume is a major determinant of the force generating capability of a muscle, other factors such as muscle architecture changes can influence the muscle force (Charles et al., 2019; Renström et al., 1983), which are not detectable based on our current MRI sequencing. Fourth, in the motion study, our participants were asked to ascend one step. This may not be representative of a stair-climbing activity in daily living which often consists of braking and forward propulsion phases. However, the peaks of braking GRF were comparable to other studies of people with lower limb loss (Schmalz and Blumentritt, 2007). Also, the normalised EMG activity in our study was used as a validation of the predicted muscle activation by comparing their temporal and spatial features. Researchers have found that significant variations exist due to the selection of peak EMG amplitude in the normalisation and the variations may be greater than the variations between limbs (Rouffet et al., 2008). As the maximal EMG amplitudes were not from a voluntary contraction or a high-intensity dynamic movement, normalised EMG was not used for the assessment of between-limb differences. Residual limb muscle atrophy is associated with disuse and denervation; the former is a function of reduced muscle volume and mass while the latter would be identified by reduced contractile elements and muscle activity (Vander et al., 2008; Bramley et al., 2021). In our study, we assumed that disuse is the main cause of muscle atrophy. Due to the abovementioned limitation in EMG normalisation, the contribution of reduced muscle activity to muscle function was not considered. Finally, we also did not incorporate intrinsic muscle properties which could be formatted by considering the muscle excitation-activation relationship and muscle-tendon force-length-velocity relationship in our modelling. It is known that this assumption may affect the peak magnitudes of the muscle and joint contact forces, however, these have been shown to have little influence on the trend of these force estimates (Lin et al., 2012; Modenese et al., 2018).

In conclusion, this study used musculoskeletal modelling and MRI measurements to investigate how muscle atrophy in the residual limb affected musculoskeletal dynamics for three activities of daily living for people with unilateral transtibial amputation. Mechanical asymmetry was found including asymmetrical GRF and joint contact forces in activities of level walking, standing-up and ascending one step. The study also found significant differences in muscle activation that were more prevalent for activities other than gait, demonstrating that more highly loaded activities should be incorporated in such analyses as gait alone is unlikely to identify clinically-relevant information. We propose that these results suggest a biomechanically-based mitigation to improve functional mobility, which could be achieved through strengthening of the hip abductor/adductor muscle in the early post-amputation stage.

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Competing interests

The authors declare that they have no competing interests.

References

Actis, J.A., Nolasco, L.A., Gates, D.H., Silverman, A.K., 2018. Lumbar loads and trunk kinematics in people with a transtibial amputation during sit-to-stand. J. Biomech. 69, 1-9.

Ardestani, M.M., Moazen, M., 2016. How human gait responds to muscle impairment in total knee arthroplasty patients: Muscular compensations and articular perturbations. J. Biomech. 49, 1620–1633.

Beyaert, C., Grumillier, C., Martinet, N., Paysant, J., André, J.M., 2008. Compensatory mechanism involving the knee joint of the intact limb during gait in unilateral below-knee amputees. Gait Posture. 28(2), 278-284.

Bramley, J.L., Worsley, P.R., Bader, D.L., Everitt, C., Darekar, A., King, L., Dickinson, A.S., 2021. Changes in tissue composition and load response after transtibial amputation indicate biomechanical adaptation. Ann Biomed Eng, 49(12), 3176-3188.

Buis, A.W.P., Condon, B., Brennan, D., McHugh, B., Hadley, D., 2006. Magnetic resonance imaging technology in transtibial socket research: A pilot study. J. Rehabil. Res. Dev. 43, 883–890.

Burke, M.J., Roman, V., Wright, V., 1978. Bone and joint changes in lower limb amputees. Ann. Rheum. Dis. 37(3), 252-254.

Charles, J.P., Suntaxi, F., Anderst, W.J., 2019. In vivo human lower limb muscle architecture dataset obtained using diffusion tensor imaging. PLoS One. 14, 1–18.

Crozara, L.F., Marques, N.R., LaRoche, D.P., Pereira, A.J., Silva, F.C., Flores, R.C., Payão, S.L., 2019. Hip extension power and abduction power asymmetry as independent predictors of walking speed in individuals with unilateral lower-limb amputation. Gait Posture. 70, 383-388.

Crowninshield, R.D., Brand, R.A., 1981. A physiologically based criterion of muscle force prediction in locomotion. J. Biomech. 14(11), 793-801.

Cleather, D.J., Bull, A.M.J., 2015. The development of a musculoskeletal model of the lower limb: introducing Freebody. R.Soc.Open Sci. 2(6), 140449.

Commean, P.K., Smith, K.E., Vannier, M.W., 1997. Lower extremity residual limb slippage within the prosthesis. Arch. Phys. M. 78(5), 476-485.

Czerniecki, J.M., Gitter, A., Munro, C., 1991. Joint moment and muscle power output characteristics of below-knee amputees during running: The influence of energy storing prosthetic feet. J. Biomech. 24(1), 63-75.

Ding, Z., Javis, H., Bennett, A., Baker, R., Bull, A.M.J, 2021. Higher Knee Contact Forces Might Underlie Increased Osteoarthritis Rates in High Functioning Amputees: A Pilot Study. J. Orthop. Res. 39(4), 850-860.

Ding, Z., Nolte, D., Kit Tsang, C., Cleather, D.J., Kedgley, A.E., Bull, A.M.J., 2016. In Vivo Knee Contact Force Prediction Using Patient-Specific Musculoskeletal Geometry in a Segment-Based Computational Model. J. Biomech. Eng. 138, 021018.

Ding, Z., Tsang, C.K., Nolte, D., Kedgley, A.E., Bull, A.M.J., 2019. Improving musculoskeletal model scaling using an anatomical atlas: the importance of gender and anthropometric similarity to quantify joint reaction forces. IEEE Trans. Biomed. Eng. 66(12), 3444-3456.

Edwards, D.S., Guthrie, H.C., Yousaf, S., Cranley, M., Rogers, B.A., Clasper, J.C., 2016. Trauma-related amputations in war and at a civilian major trauma centre-comparison of care, outcome and the challenges ahead. Injury. 47(8), 1806-1810.

Ellis, R.G., Sumner, B.J., Kram, R., 2014. Muscle contributions to propulsion and braking during walking and running: insight from external force perturbations. Gait Posture, 40(4), 594-599.

Esposito, E.R., Wilken, J.M., 2014. The relationship between pelvis–trunk coordination and low back pain in individuals with transfemoral amputations. Gait Posture, 40(4), 640-646.

Fukunaga, T., Miyatani, M., Tachi, M., Kouzaki, M., Kawakami, Y., Kanehisa, H., 2001. Muscle volume is a major determinant of joint torque in humans. Acta Physiol. Scand. 172, 249–255.

Fukunaga, T., Roy, R.R., Shellock, F.G., Hodgson, J.A., Day, M.K., Lee, P.L., Kwong- Fu, H., Edgerton, V.R., 1992. Physiological cross- sectional area of human leg muscles based on magnetic resonance imaging. J. Orthop. Res. 10, 926–934.

Geertzen, J.H.B., Martina, J.D., Rietman, H.S., 2001. Lower limb amputation part 2: Rehabilitation- A 10 year literature review. Prosthet Orthot Int. 25(1), 14-20

Hafner, B.J., Sanders, J.E., Czerniecki, J., 2002. Energy storage and return prostheses: Does patient perception correlate with biomechanical analysis? Clin. Biomech. 17, 325–344.

Handsfield, G.G., Meyer, C.H., Hart, J.M., Abel, M.F., Blemker, S.S., 2014. Relationships of 35 lower limb muscles to height and body mass quantified using MRI. J. Biomech. 47, 631–638.

Harper, N.G., Wilken, J.M., Neptune, R.R., 2018. Muscle function and coordination of amputee stair ascent. J.Biomech. Eng. 140(12).

Henson, D.P., Edgar, C., Ding, Z., Sivapuratharasu, B., Le Feuvre, P., Finnegan, M.E., Quest, R., McGregor, A.H., Bull, A.M.J., 2021. Understanding lower limb muscle volume adaptations to amputation. J. Biomech. 125, p.110599.

Honegger, J.D., Actis, J.A., Gates, D.H., Silverman, A.K., Munson, A.H. and Petrella, A.J., 2021. Development of a multiscale model of the human lumbar spine for investigation of tissue loads in people with and without a transtibial amputation during sit-to stand. BMMB, 20(1), 339-358.

Isakov, E., Burger, H., Gregoric, M., Marinccek, C., 1996. Stump length as related to atrophy and strength of the thigh muscles in trans-tibial amputees. Prosthet. Orthot. Int. 20(2), 96-100.

Jarvis, H.L., Bennett, A.N., Twiste, M., Phillip, R.D., Etherington, J., Baker, R., 2016. Temporal spatial and metabolic measures of walking in highly functional individuals with lower limb amputations. Arch. Phys. Med. Rehabil. 98(7), 1389-1399.

John, C.T., Seth, A., Schwartz, M.H., Delp, S.L., 2012. Contributions of muscles to mediolateral ground reaction force over a range of walking speeds. J. Biomech. 45, 2438–2443.

Jordan, R.W., Marks, A., Higman, D., 2012. The cost of major lower limb amputation: A 12-year experience. Prosthet. Orthot. Int. 36, 430–434.

Klemt, C., Nolte, D., Ding, Z., Rane, L., Quest, R.A., Finnegan, M.E., Walker, M., Reilly, P., Bull, A.M.J., 2019. Anthropometric scaling of anatomical datasets for subject-specific musculoskeletal modelling of the shoulder. Ann Biomed Eng.47(4), 924-936.

Knarr, B. A., Ramsay, J. W., Buchanan, T. S., Higginson, J. S., Binder- Macleod, S. A., 2013. Muscle volume as a predictor of maximum force generating ability in the plantar flexors post- stroke. Muscle & nerve, 48(6), 971-976.

Lin, Y.C., Dorn, T.W., Schache, A.G., Pandy, M.G., 2012. Comparison of different methods for estimating muscle forces in human movement. Proc. Inst. Mech. Eng. H: J. Eng. Med, 226(2), 103-112.

Lin, Y.C., Fok, L.A., Schache, A.G., Pandy, M.G., 2015. Muscle coordination of support, progression and balance during stair ambulation. J. Biomech. 48(2), 340-347.

Lemaire, E.D., Fisher, F.R., 1994. Osteoarthritis and elderly amputee gait. Arch. Phys. Med. Rehabil. 75, 1094–1099.

Lilja, M., Öberg, T., 1997. Proper time for definitive transtibial prosthetic fitting. J Prosthet Orthot. 9(2), 90.

Lloyd, C.H., Stanhope, S.J., Davis, I.S., Royer, T.D., 2010. Strength asymmetry and osteoarthritis risk factors in unilateral trans-tibial, amputee gait. Gait Posture. 32, 296–300.

Marra, M. A., Vanheule, V., Fluit, R., Koopman, B. H., Rasmussen, J., Verdonschot, N., Andersen, M. S., 2015. A subject-specific musculoskeletal modeling framework to predict in vivo mechanics of total knee arthroplasty. J.Biomech. Eng. 137(2), 020904.

Miller, R.H., Krupenevich, R.L., Pruziner, A.L., Wolf, E.J., Schnall, B.L., 2017. Medial knee joint contact force in the intact limb during walking in recently ambulatory service members with unilateral limb loss: a cross-sectional study. PeerJ. 5, e2960.

Mitsiopoulos, N., Baumgartner, R.N., Heymsfield, S.B., Lyons, W., Gallagher, D., Ross, R., 1998. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J. Appl. Physiol. 85, 115–122.

Modenese, L., Montefiori, E., Wang, A., Wesarg, S., Viceconti, M., Mazzà, C., 2018. Investigation of the dependence of joint contact forces on musculotendon parameters using a codified workflow for image-based modelling. J. Biomechanics, 73, 108-118.

Moxey, P.W., Gogalniceanu, P., Hinchliffe, R.J., Loftus, I.M., Jones, K.J., Thompson, M.M., Holt, P.J., 2011. Lower extremity amputations - a review of global variability in incidence. Diabet. Med. 28, 1144–1153.

Nadollek, H., Brauer, S., Isles, R., 2002. Outcomes after trans- tibial amputation: the relationship between quiet stance ability, strength of hip abductor muscles and gait. Physiother. Res. Int. 7(4), 203-214.

Nolte, D., Tsang, C.K., Zhang, K.Y., Ding, Z., Kedgley, A.E., Bull, A.M., 2016. Non-linear scaling of a musculoskeletal model of the lower limb using statistical shape models. J. Biomech, 49(14), 3576-3581.

Orekhov, G., Matt Robinson, A., Hazelwood, S.J., Klisch, S.M., 2019. Knee joint biomechanics in transtibial amputees in gait, cycling, and elliptical training. PLoS One. 14, 6–10.

Pandy, M.G., Lin, Y.C., Kim, H.J., 2010. Muscle coordination of mediolateral balance in normal walking. J. Biomech. 43, 2055–2064.

Perotto, A.O., 2011. Anatomical Guide for the Electromyographer – the Limbs and Trunk, 5 ed. Charles C Thomas Publisher LTD.

Rajagopal, A., Dembia, C.L., DeMers, M.S., Delp, D.D., Hicks, J.L., Delp, S.L., 2016. Full-body musculoskeletal model for muscle-driven simulation of human gait. IEEE Trans. Biomed. Eng, 63(10), 2068-2079.

Renström, P., Grimby, G., Morelli, B., Palmertz, B., 1983. Thigh muscle atrophy in below-knee amputees. Scand. J. Rehabil. Med. Suppl. 9, 150–162.

Rouffet, D.M., Hautier, C.A., 2008. EMG normalization to study muscle activation in cycling. J Electromyogr Kinesiol, 18(5), 866-878.

Sanders, J.E., Fatone, S., 2011. Residual limb volume change: Systematic review of measurement and management, JRRD. 48(8), p.949.

Sartori, M., Reggiani, M., Farina, D., Lloyd, D.G., 2012. EMG-Driven Forward-Dynamic Estimation of Muscle Force and Joint Moment about Multiple Degrees of Freedom in the Human Lower Extremity. PLoS One. 7, e52618

Schmalz, T., Blumentritt, S., 2007. Biomechanical analysis of stair ambulation in lower limb amputees, Gait Posture. 25(2), 267–278.

Schmalz, T., Blumentritt, S., Reimers, C.D., 2001. Selective thigh muscle atrophy in trans-tibial amputees: An ultrasonographic study. Arch. Orthop. Trauma Surg. 121, 307–312.

Schwer, L.E., 2007. Validation metrics for response histories: Perspectives and case studies. Eng. Comput. 23, 295–309.

Sherk, V.D., Bemben, M.G., Bemben, D.A., 2010. Interlimb Muscle and Fat Comparisons in Persons With Lower-Limb Amputation. Arch. Phys. Med. Rehabil. 91, 1077–1081.

Silverman, A.K., Fey, N.P., Portillo, A., Walden, J.G., Bosker, G., Neptune, R.R., 2008. Compensatory mechanisms in below-knee amputee gait in response to increasing steady-state walking speeds. Gait & posture, 28(4), 602-609.

Šlajpah, S., Kamnik, R., Burger, H., Bajd, T., Munih, M., 2013. Asymmetry in sit-to-stand movement in patients following transtibial amputation and healthy individuals. Int. J. Rehabil. Res. 36, 275–283.

Smith, K.E., Vannier, M.W., Commean, P.K., 1995. Spiral CT Volumetry of Below-Knee Residua. IEEE Trans. Rehabil. Eng. 3, 235–241.

Struyf, P.A., van Heugten, C.M., Hitters, M.W., Smeets, R.J., 2009. The Prevalence of Osteoarthritis of the Intact Hip and Knee Among Traumatic Leg Amputees. Arch. Phys. Med. Rehabil. 90, 440–446.

Tintle, L.S.M., Baechler, L.M.F., Nanos III, C.G.P., Forsberg, L.J.A. and Potter, M.B.K., 2010, Traumatic and trauma-related amputations: Part II: Upper extremity and future directions. JBJS, 92(18), 2934-2945.

Vander, A.J., Sherman, J.H., Luciano, D.S. and Van Wynsberghe, D.M., 1990. Human physiology: the mechanisms of body function. New York: McGraw-Hill. pp. 208.

van Der Kruk, E., Silverman, A.K., Reilly, P., Bull, A.M.J., 2021. Compensation due to age-related decline in sit-to-stand and sit-to-walk. J. Biomech. 122, 110411.

Figure 1. Segmentation of muscle volumes from MR images. (a) pelvis cross section, (b) thigh cross section, and 3D reconstructions with (c) anterior view and (d) posterior view. Abbreviations: AL, adductor longus; AM, adductor magnus; BF, biceps femoris; Gr, gracilis; IL, iliacus; PS, psoas major; RF, rectus femoris; SM, semimembranosus; ST, semitendinosus; VI, vastus intermedius; VL, vastus lateralis and VM, vastus medialis.

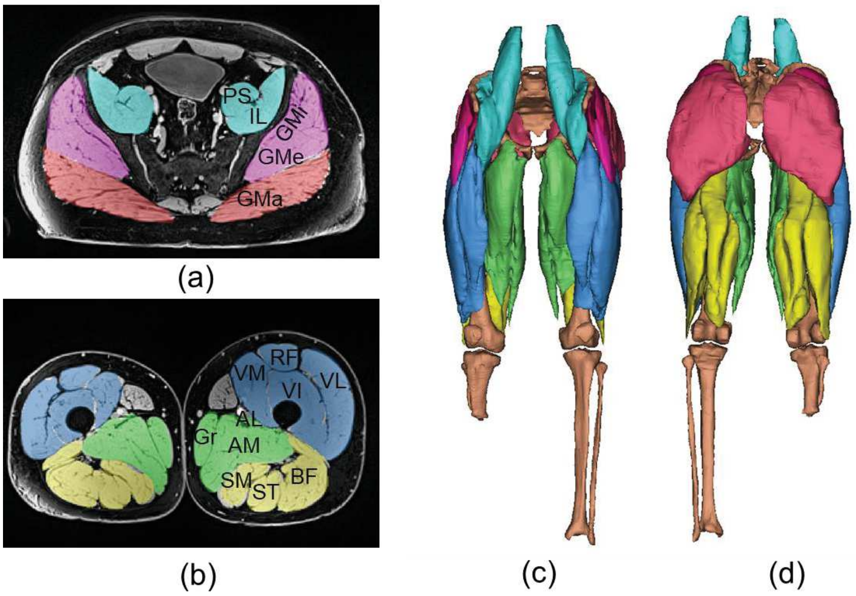


Figure 2 Body weight normalised ground reaction force components (vertical, anterior/posterior and lateral/medial) for people with unilateral transtibial amputation across three activities (the intact limb is black and the residual limb is red; for the activity of step-ascending the intact and residual limbs are both leading limbs; n=8) with spatial parameter mapping (SPM) analysis (non-parametric, one-sample paired t-test). The grey regions represent significant differences.

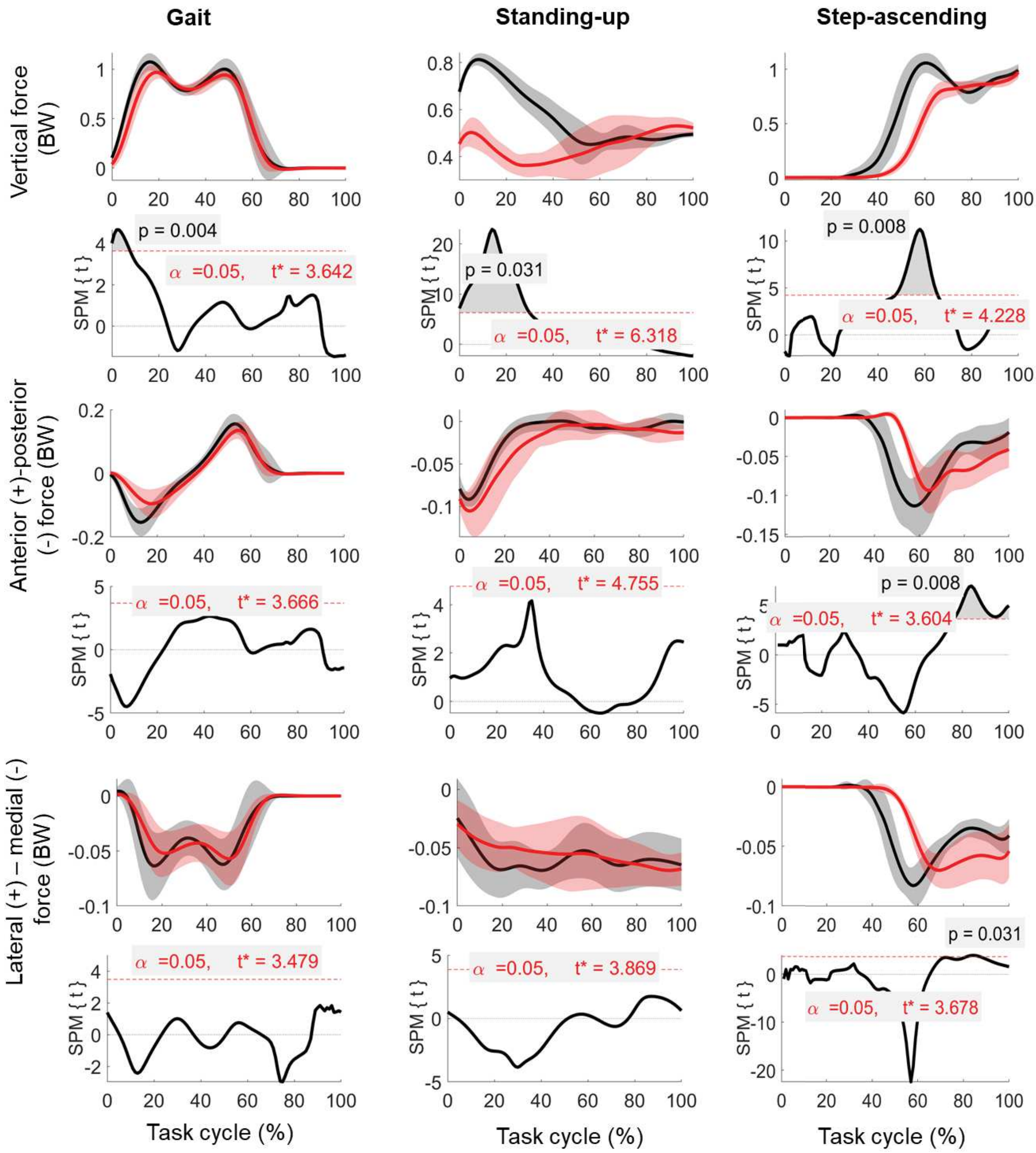
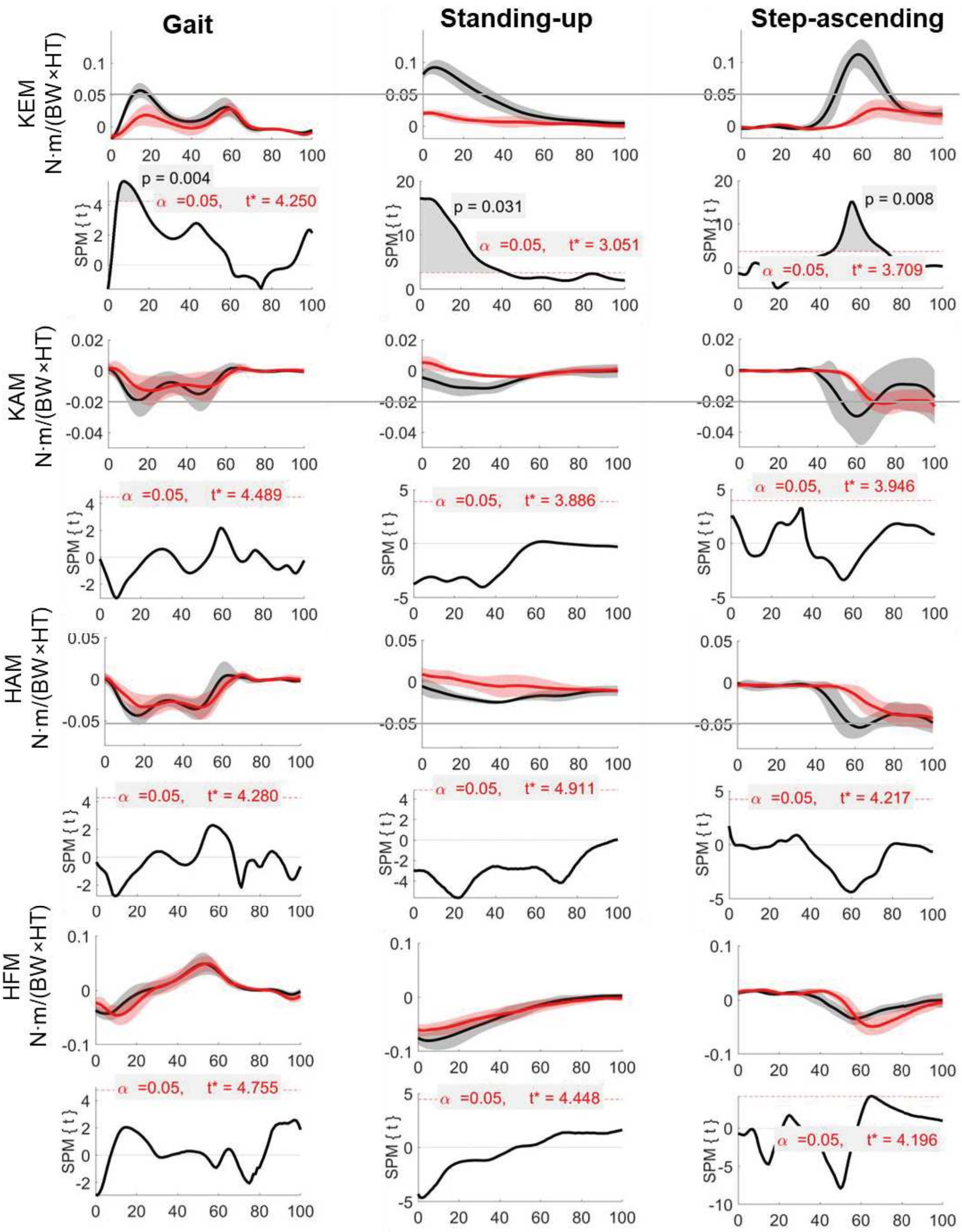


Figure 3: Body weight times height normalised joint moments at the knee and hip for people with unilateral transtibial amputation across three activities (the intact limb is black and the residual limb is red; for the activity of step-ascending the intact and residual limbs are both leading limbs; n=8); knee extension (KEM), knee adduction (KAM), hip adduction (HAM) and hip flexion (HFM) with spatial parameter mapping (SPM) analysis (non-parametric, one-sample paired t-test). The grey regions represent significant differences.



Gait
Standing-up
Step-ascending
KEM
N·m/(BW×HT)
KAM
N·m/(BW×HT)
HAM
N·m/(BW×HT)
HFM
N·m/(BW×HT)
SPM{t}
p = 0.004
α =0.05, t* = 4.250
p = 0.031
α =0.05, t* = 3.051
p = 0.008
α =0.05, t* = 3.709
α =0.05, t* = 4.489
α =0.05, t* = 3.886
α =0.05, t* = 3.946
α =0.05, t* = 4.280
α =0.05, t* = 4.911
α =0.05, t* = 4.217
α =0.05, t* = 4.755
α =0.05, t* = 4.448
α =0.05, t* = 4.196

Figure 4: Gait body weight normalised muscle forces aggregated into six groups: knee flexors, knee extensors, hip abductors, hip adductors, hip flexors and hip extensors for people with unilateral transtibial amputation (the intact limb is black and the residual limb is red, n=8) with spatial parameter mapping (SPM) analysis (non-parametric, one-sample paired t-test). The grey regions represent significant differences.

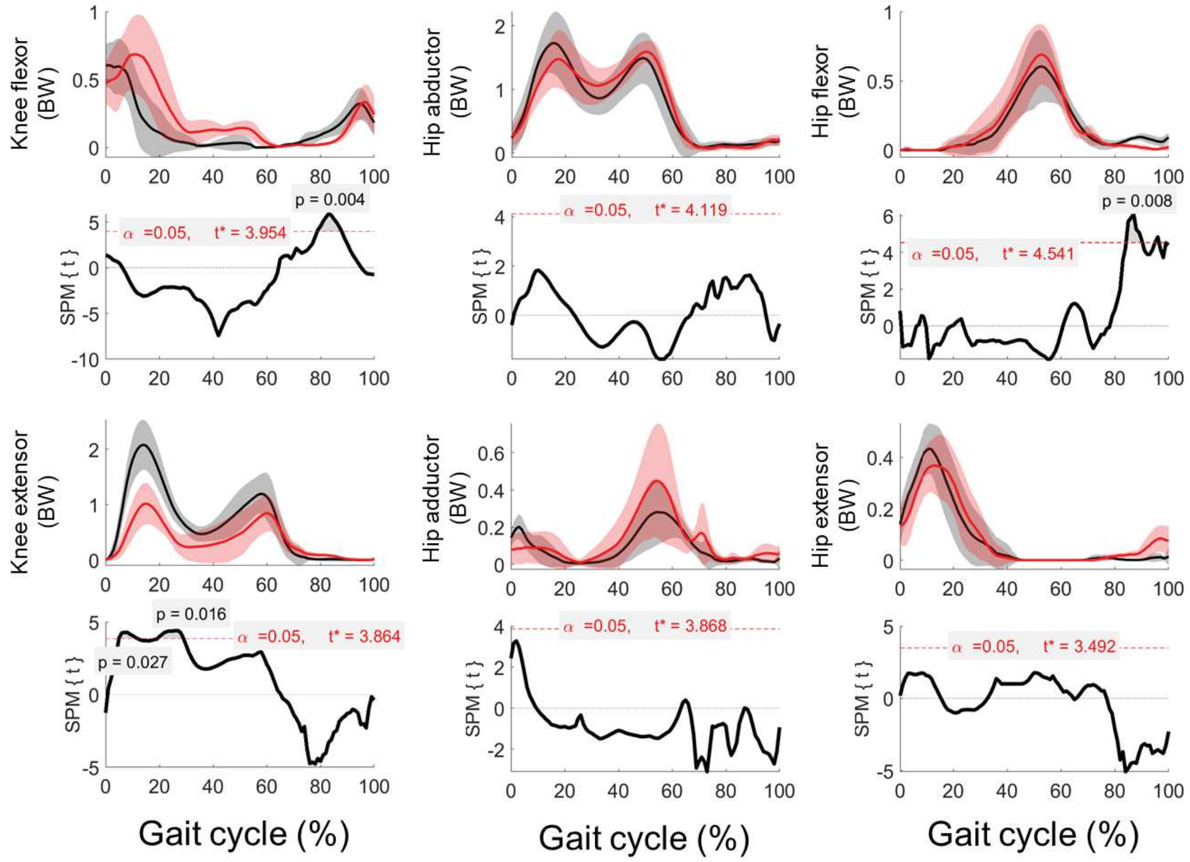


Figure 5: Standing-up body weight normalised muscle forces aggregated into six groups: knee flexors, knee extensors, hip abductors, hip adductors, hip flexors and hip extensors for people with unilateral transtibial amputation (the intact limb is black and the residual limb is red, n=8) with spatial parameter mapping (SPM) analysis (non-parametric, one-sample paired t-test). The grey regions represent significant differences.

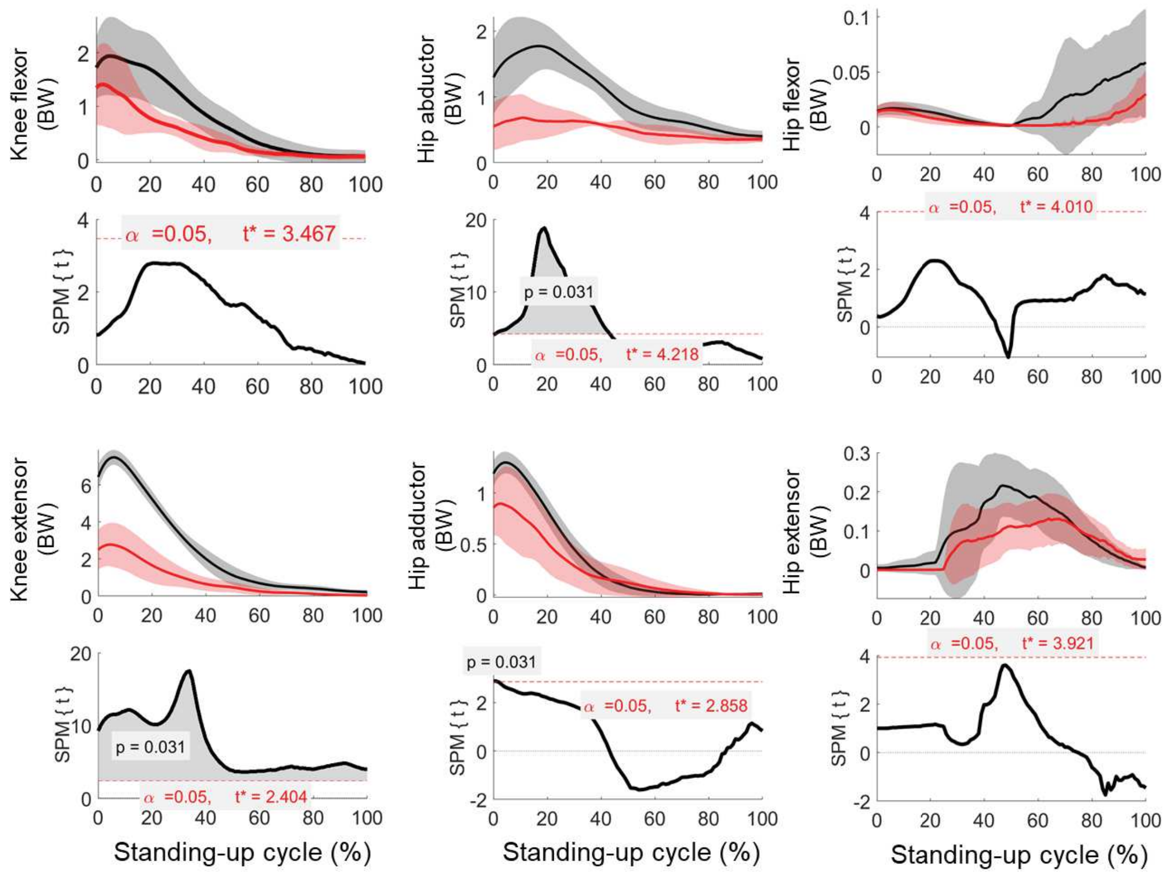


Figure 6: Step-ascending body weight normalised muscle forces aggregated into six groups: knee flexors, knee extensors, hip abductors, hip adductors, hip flexors and hip extensors for people with unilateral transtibial amputation (the intact limb is black and the residual limb is red; the intact and residual limbs are both the leading limbs; n=8) with spatial parameter mapping (SPM) analysis (non-parametric, one-sample paired t-test). The grey regions represent significant differences.

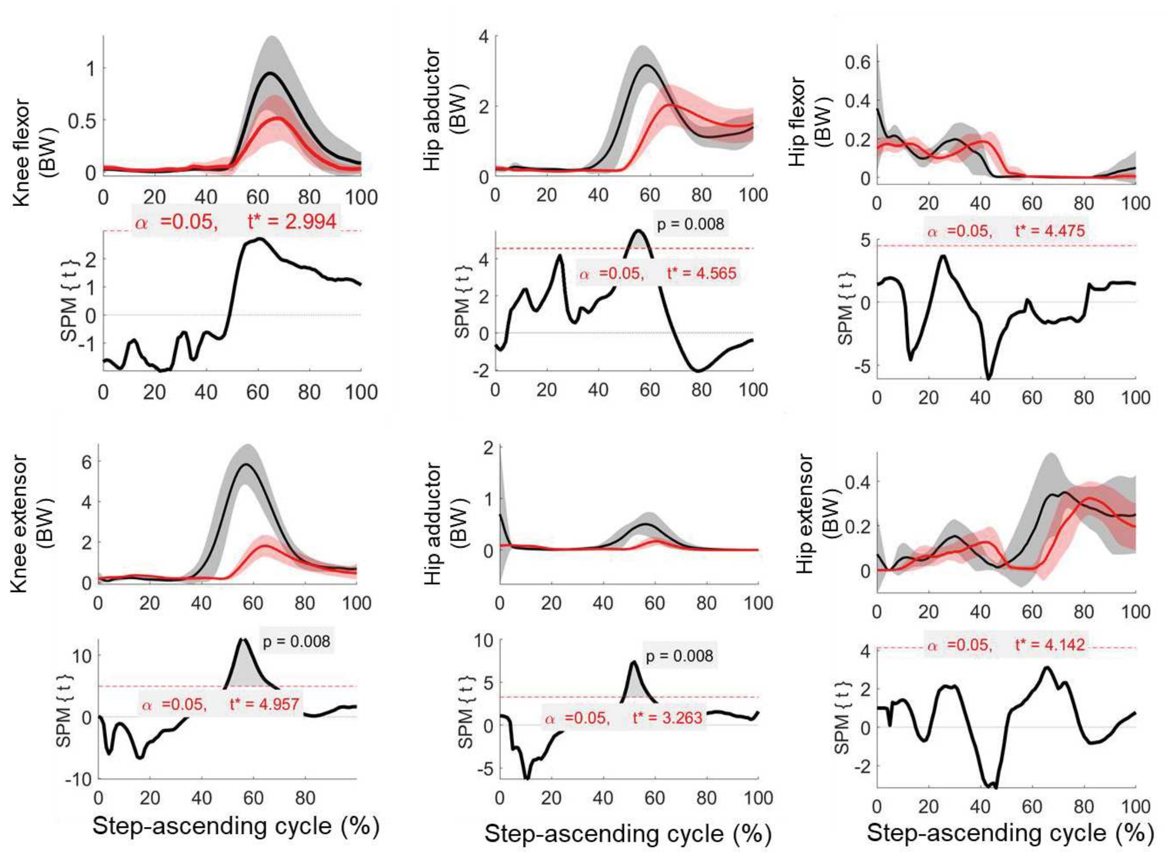


Figure 7: Body weight normalised knee joint contact forces for people with unilateral transtibial amputation (the intact limb is black and the residual limb is red; for the activity of step-ascending the intact and residual limbs are both leading limbs; n=8) with spatial parameter mapping (SPM) analysis (non-parametric, one-sample paired t-test). The grey regions represent significant differences.

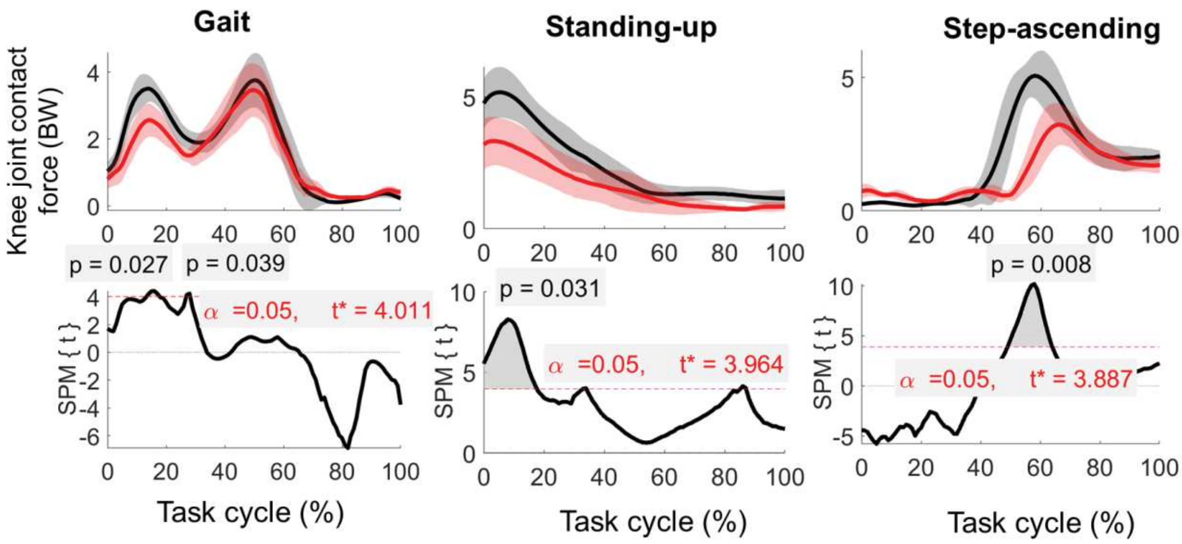


Table 1: Participant characteristics

Participant	Side of amputation	Age (years)	Height (m)*	Mass (kg)*	Time since amputation (months)	Cause of amputation ¶	Co-morbidities	Prosthetic foot
1	Left	33	1.78	84.4	29	IED	--	Vari-Flex XC Rotate (Ossur, Iceland)
2	Left	32	1.82	98.0	77	IED	--	Freedom THRIVE (Ottobock, Germany)
3	Left	37	1.85	94.3	98	IED	--	EchelonVT (Blatchford, UK)
4	Left	34	1.81	81.4	97	Gunshot	--	RUSH ROGUE (Proteor USA, USA)
5	Right	33	1.80	101.6	107	IED	--	Vari-Flex XC Rotate (Ossur, Iceland)
6	Left	34	1.83	84.0	10	Other	--	Pro-Flex Pivot (Ossur, Iceland)
7	Right	32	1.76	76.7	39	IED	Screw in ankle	Vari-Flex XC Rotate (Ossur, Iceland)
8	Left	33	1.77	79.2	100	IED	Screw in ankle	Elite Blade (Blatchford, UK)
Mean (SD)	--	33.5 (1.6)	1.80 (0.03)	87.5 (9.3)	70 (38)	--	--	--

*Height and mass were measured whilst wearing their prosthesis.

¶IED, improvised explosive device.

Table 2 Muscle group volumes at the intact and residual limbs. Knee flexors refer to biceps femoris (long head and short head), semimembranosus and semitendinosus; knee extensors refer to rectus femoris, vastus intermedius, vastus lateralis and vastus medialis; hip abductors refer to gluteus medius, gluteus minimus and tensor fasciae latae; hip adductors refer to adductor brevis, adductor longus, adductor magnus, gracilise and pectineus; hip flexors refer to iliacus and psoas major and hip extensors refer to gluteus maximus.

	Muscle group volumes (cm^3)											
	Knee flexors		Knee extensors		Hip abductors		Hip adductors		Hip flexors		Hip extensors	
	Intact	residual	Intact	residual	Intact	residual	Intact	residual	Intact	residual	Intact	residual
1	903	845	2087	1578	609	585	1003	946	414	460	1120	1174
2	1034	804	2975	1494	742	596	1483	1306	458	426	1494	1077
3	978	922	2621	1582	777	620	1115	1049	472	483	1327	1319
4	739	796	1998	1446	650	589	1002	968	470	475	945	897
5	1134	1129	2666	1734	684	624	1556	1469	582	633	1402	1251
6	937	812	2626	1542	674	546	1338	1225	545	536	1258	1134
7	1005	854	2322	1864	589	562	1471	1435	413	393	952	973
8	729	700	2066	1395	543	465	1231	1144	418	435	1036	859
Mean	933	858	2420	1579	658	573	1275	1193	471	480	1192	1085
(SD)	140	126	354	154	78	51	221	201	63	75	209	166
p-value[a]	0.055		**0.008**		**0.008**		**0.008**		0.461		0.109	
Significant % difference from intact to residual limb	--		-34.7		-12.9		-6.4		--		--	

[a.] *p*-value was from Wilcoxon Signed Rank test ($\alpha = 0.05$).

Bold indicates a significant difference.

Supplementary Materials

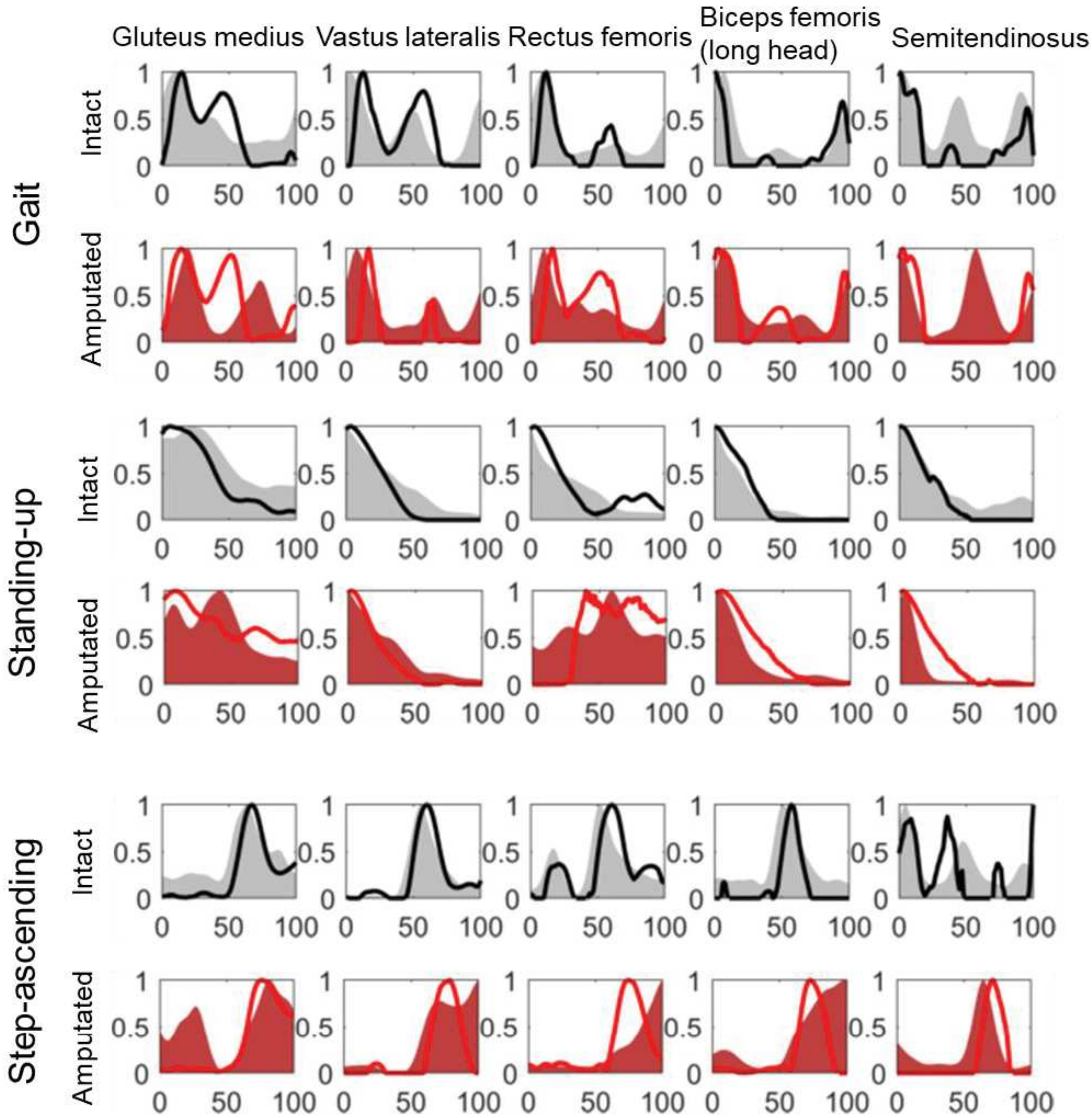
Table S1: Procedure and instruction of tasks

Tasks	Procedure	Instruction
Walking at a self-selected speed	Participants walk along a 6m walkway at a comfortable speed. They are asked to walk as naturally as possible with as much practice as they wish. 3 x walking with left & right foot contact with force plates.	“When you will hear, ‘GO’, please walk to the end of the walkway as you would usually walk at your preferred speed with your arms relaxed by your side and looking ahead.”
Standing up from a chair	Participants are seated with each foot positioned on one of two force plates hip width apart. Chair height is adjusted to allow each participant’s thigh to be horizontal and their shank vertical. 3 x standing-up task	“When you will hear ‘GO’, please stand up with your arms crossed over your chest and remain standing. You will perform this movement in what you consider a normal way, at your own preferred speed”
Ascending a single stair	The stair was composed of one single step (step height: 16 cm, step depth: 60 cm) without handrail support. 3 x stair-ascending task of each limb; in total 6 x stair-ascending task of both limbs	“When you will hear ‘GO’, please climb up the stair at your own preferred speed using one limb, followed by the contralateral limb so that you can stand still on the stair”

Table S2: Quantitative magnitude (M), phase (P) and combined (C) errors between modelled muscle activations and measured EMG for the gluteus medius, vastus lateralis, rectus femoris, biceps femoris (long head) and semitendinosus during activities, where 0<C<0.15 indicates excellent similarity; 0.15<C<0.30, very good similarity; 0.30<C<0.45, good similarity; 0.45<C<0.60 moderate similarity and C>0.60, no similarity (Klemt et.al., 2019).

		Gait			Standing-up			Stair-climbing		
		M	*P*	*C*	*M*	*P*	*C*	*M*	*P*	*C*
Gluteus medius	Intact	-0.06	0.18	0.19	-0.16	0.10	0.19	-0.19	0.14	0.24
	Residual	0.19	0.24	0.31	0.03	0.11	0.11	-0.16	0.18	0.24
Vastus lateralis	Intact	-0.05	0.24	0.25	-0.03	0.10	0.11	-0.03	0.11	0.12
	Residual	-0.27	0.30	0.37	-0.07	0.09	0.11	-0.18	0.21	0.28
Rectus femoris	Intact	-0.18	0.20	0.27	0.11	0.12	0.16	-0.03	0.17	0.17
	Residual	0.05	0.22	0.22	0.07	0.16	0.18	0.20	0.27	0.34
Biceps femoris (long head)	Intact	-0.20	0.19	0.28	0.16	0.05	0.17	-0.29	0.20	0.35
	Residual	-0.01	0.11	0.11	0.23	0.09	0.25	-0.25	0.25	0.36
Semitendinosus	Intact	-0.31	0.19	0.37	-0.09	0.10	0.14	-0.07	0.24	0.25
	Residual	-0.20	0.29	0.35	0.30	0.14	0.33	-0.09	0.25	0.26

Figure S1: Comparison of muscle activations derived from musculoskeletal modelling (solid line) and measured EMG (shaded area) in one representative subject. EMG data were individually normalised to the maximum recorded signal of each muscle during the activities and modelled muscle activations were defined to be between 0 (fully deactivated) and 1 (fully activated) in terms of the peak value predicted during the activities.



Conflict of interest statement

The authors declare that there are no financial or personal relationships with people of organisations that have inappropriately influenced this work.