ASSESSMENT OF EFFECTIVENESS OF MUSCLE LENGTHENING SURGERY IN CEREBRAL PALSY USING MUSCULOSKELETAL MODELING

by

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I, Eda Biricik, hereby certify that I am aware of the Academic Ethics and Integrity Policy issued by the Council of Higher Education (YÖK) and I fully acknowledge all the consequences due to its violation by plagiarism or any other way.

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ABSTRACT

ASSESSMENT OF EFFECTIVENESS OF MUSCLE LENGTHENING SURGERY IN CEREBRAL PALSY USING MUSCULOSKELETAL MODELING

Cerebral Palsy is a permanent movement disorder that manifests itself at early childhood, as poor coordination, and gait difficulty due to muscle spasticity and/or contracture. Excessive knee flexion during gait e.g., crouch gait is a common impairment and often corrected by hamstring lengthening surgery. Such crouch gait is presumed to originate from shortness (i.e., contracture) and/or slowness in lengthening (i.e., spasticity) of affected muscles and remedial surgery is considered to improve gait by increasing muscle length or its velocity. However, a third group of patients who neither has short nor slow hamstrings pre-operatively can still undergo surgery. The aim of the thesis is to investigate whether the gait of those patients improved after the surgery by testing the hypotheses: post-operatively, (i) the knee joint movement is improved (ii), the hip joint movement is deteriorated (iii), the gait deviation index (GDI) is increased (iv), muscle unit length do not change, and (v) pre-operative psoas muscle lengths were shorter. Findings showed that mean knee angle decreased significantly at the initial contact (0-3%), terminal stance (28-43%), and the terminal swing phases (95-100%) ($p<0.05$). No significant effects were detected in the hip angle or the GDI. Additionally, no significant changes in the hamstring muscle lengths were found. Only half of the patients had shorter psoas muscle lengths pre-operatively. In conclusion, the excessive knee flexion of the patients was decreased without negatively affecting hip movement or gait overall. The improvement in the knee angle was achieved without any change in the muscle length of the hamstrings, suggesting that an isometric position shift of the target muscle occurs, which may be ascribed to post-surgical alterations in the epimuscular connections.

Keywords: Hamstring lengthening surgery, Remedial surgery, Spasticity, Contracture, OpenSim, Musculoskeletal modeling, Psoas, Lengthening velocity, Muscle shortness, Cerebral Palsy.

ÖZET

SEREBRAL PALSİDE KAS UZATMA AMELİYATININ ETKİNLİĞİNİN KAS-İSKELET MODELLEMEYLE DEĞERLENDİRİLMESİ

Serebral palsi, erken çocukluk döneminde kendini kas spastisitesi ve/veya kontraktürü sebebiyle zayıf koordinasyon ve yürüme güçlüğü olarak gösteren kalıcı bir hareket bozukluğudur. Yürüyüş sırasında aşırı diz fleksiyonu, yani çömelme yürüyüşü, en çok karşılaşılan yürüyüş bozukluklarından biridir ve sıklıkla hamstring uzatma ameliyatı ile düzeltilir. Bu tür çömelme yürüyüşünün, etkilenen kasların kısalığından (yani kontraktür) ve/veya uzamadaki yavaşlıktan (yani spastisiteden) kaynaklandığı varsayılır ve iyileştirici cerrahinin, kas uzunluğunu veya hızını artırarak yürüyüşü iyileştirdiği kabul edilir. Ancak ameliyat öncesi ne kısa ne de yavaş hamstringleri olan üçüncü bir grup hasta yine de ameliyat olabilir. Bu tezin amacı, bu hastaların yürüyüşlerinin ameliyattan sonra düzelip düzelmediğini şu hipotezlerle araştırmaktır: ameliyat sonrası, (i) diz eklemi hareketi düzeldi (ii) kalça eklemi hareketi bozuldu (iii) yürüyüş sapma indeksi (GDI) arttı (iv) hamstring kaslarının birim uzunluğu değişmedi ve (v) ameliyat öncesi psoas kas uzunlukları daha kısaydı. Bulgular, ortalama diz açısının ilk temasta (%0-3), son duruşta (%28-43) ve son salınım fazlarında (%95-100) anlamlı olarak azaldığını gösterdi ($p<0.05$). Kalça açısında veya GDI'de önemli bir etki tespit edilmedi. Ek olarak, hamstring kas uzunluklarında önemli bir değişiklik bulunmadı. Hastaların sadece yarısında ameliyat öncesi daha kısa psoas kas uzunlukları vardı. Sonuç olarak, hastaların aşırı diz fleksiyonu, genel olarak kalça hareketini veya yürüyüşünü olumsuz etkilemeden azaltıldı. Diz açısındaki iyileşme, hamstringlerin kas uzunluğunda herhangi bir değişiklik olmadan elde edildi, bu da, epimusküler bağlantılardaki cerrahi sonrası değişikliklere atfedilebilecek olan hedef kasta izometrik bir pozisyon kayması meydana geldiğini düşündürdü.

Anahtar Sözcükler: Hamstring uzatma ameliyatı, İyileştirici cerrahi, Spastisite, Kontraktür, OpenSim, Kas-iskelet modellemesi, Psoas, Uzama hızı, Kas kısalığı, Serebral Palsi.

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LIST OF ABBREVIATIONS

CP	Cerebral Palsy
CNS	Central Nervous System
UMN	Upper Motor Neuron
PNS	Peripheral Nervous System
LMN	Lower Motor Neurons
ECM	Extracellular Matrix
MFT	Myofascial Force Transmission
EMFT	Epimuscular Myofascial Force Transmission
MTU	Muscle-tendon Unit
EDL	Extensor Digitorum Longus
GGI	Gillette Gait Index
GDI	Gait Deviation Index
TD	Typically Developing
ASIS	Anterior Superior Iliac Spines
SD	Standard Deviation
GC	Gait Cycle
SM	Semimembranosus
Ps	Psoas

1. INTRODUCTION

1.1 Cerebral palsy

Cerebral palsy (CP) or cerebral palsies[1] encapsulates a wild range of neurodisability. The widely accepted definition proposed by Rosenbaum is:

> Cerebral palsy describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior, by epilepsy and by secondary musculoskeletal problems[2].

Not only the high prevalence of the disorder [3], but also the increased survival rates [4],[5] draw the attention of the science community to improve the life quality of these patients.

Cerebral palsy originates from the injury of the healthy brain tissue in the pre- or the post-natal period and formation of non-progressive brain lesions which are defined as "static encephalopathy" [6]. Although the brain lesions are static, the musculoskeletal pathology is progressive and varies greatly with the location and the severity of the injury [7].

The varying nature of the pathology required classification systems. One of the common classifications is based on the locations of the affected limbs i.e., topographical. Figure 1.1 shows the topographical classification of the cerebral palsy in accordance with the Surveillance of Cerebral Palsy Europe (SCPE) [8].

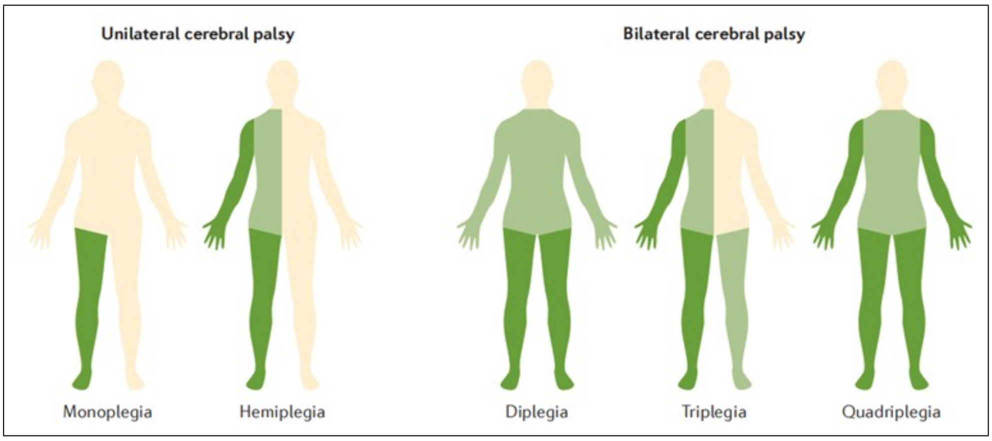


Figure 1.1: Topographical classification of the cerebral palsy [9].

Although, lesions on the central nervous system (CNS) affects the upper motor neurons (UMN) the adverse effects seen in the peripheral nervous system (PNS). The injury at the UMN affects the lower motor neurons (LMN) through different paths and results in the various symptoms observed in CP patients, as shown in the figure 1.2.

The contractures are one of the most common pathologies observed in the CP patients. The prevalence of contractures has even led to the disease being referred as "short muscle disease" in time [10]. The most concise definition of the contracture is the narrowed range of motion of the joints that has a significant impact on the gait of the patient. When the range of motion of a joint is limited due to contractures several parts of that joint is affected, including the ligaments, joint capsule, tendons, and muscles [11].

When studying the consequences of the contracture on the muscles, the muscle tissue is examined under two sub-groups: the contractile tissue and the connective tissue. The contractile tissue consists of actin and myosin myofilaments that generates the active force by cross-bridge theory. Sarcomeres containing myofilaments are added in series to create myofibrils and induce muscle growth. Several studies state that immature type of myofibrils and decreased number of satellite cells limit the growth capacity of the spastic muscle [12][13].

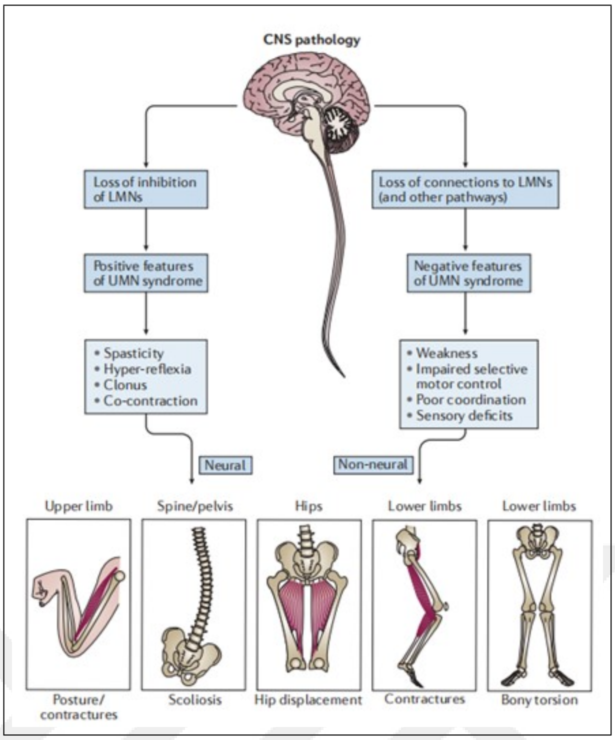


Figure 1.2: The outcomes of the UMN injury on PNS [9].

Insufficient number of sarcomeres added in series fail to keep up with the bone growth and resulted in the longer sarcomere lengths in the short muscles [14]. A contradicting study shows that spastic muscle does not demonstrate a shifted force-length curve towards the shorter sarcomere lengths, as a longer sarcomere should [15][20] which debates whether the decreased number of sarcomeres are the main problem behind limited joint movement i.e., contractures.

On the other hand, connective tissue in the muscle is also highly affected by the UMN syndrome. The connective tissue mostly consists of collagen reinforced extracellular matrix (ECM) accompanied with other non-collagenous molecules [16]. The abnormal posture i.e., flexed joint position that induced by spasticity, leads to structural alteration in the ECM [11].

One of the mostly mentioned alteration is the relative increase of the collagen amount compared to the contractile tissue [11][14][17]. Considering the contractures as a relative immobility, increased stiffness in the ECM is also attributed to the abnormal cross-linking of the collagen fibers [11].

All these articles study the ECM in the muscles and investigate the interactions between muscle fibers within the bundle i.e., myofascial force transmission (MFT) [18]. However, the connective tissue comprises of the endomysium, perimysium and the epimysium that interacts with not only the neighboring muscles but the surrounding non-muscular structures as well [19]. Epimuscular myofascial force transmission (EMFT) defines that interaction's effect on the force exertion [21][22]. Many studies in the literature indicate the presence of the EMFT in the human muscles [23][24][25]. Although, EMFT increases the force exertion significantly in the CP patients [26], its possible effects on the limited joint angle during the gait only shown in an intra-operative study [15]. EMFT's effect on contracture of a joint during gait still requires further investigation.

1.2 Muscle lengthening surgery

Muscles of the CP patients are accepted short namely, unable to stretch which causes decrease in the achievable range of motion i.e., contracture. The muscle lengthening surgery, also known as remedial surgery [27], muscle release [28] and aponeurotomy [29], is one of the frequently used treatment method to diminish the contracture. The hamstring lengthening surgery is one of the surgeries that is done to correct the abnormal knee angle in the sagittal plane leads to crouch gait in the CP patients.

Crouch gait or, excessive knee flexion during the gait is often attributed to the shortness of hamstrings and hamstring lengthening surgery aims to diminish the effect of shortness by increasing the muscle-tendon unit (MTU) length [30].

However, following studies showed that not all CP patients with crouch gait has shorter hamstrings, in fact they often have of normal length or longer hamstrings compared to typically developing children [31]. A classification study also indicated that hamstring lengthening surgery improves the gait of the patient through different mechanisms. While patients with short hamstrings increased MTU lengths post-operatively, patients with low lengthening velocity of hamstrings increased the velocity post-operatively [30].

Yet there was a third group, whom does not have short or slow hamstrings and still benefitted from the surgery [30][32]. These findings indicate that there is different mechanism that muscle lengthening surgery works on which may also have a major influence on the crouch gait of the CP patients.

Although the main intension is to elongate the MTU length in muscle lengthening surgery, a partial fasciotomy (i.e., preparatory dissection) is performed to expose the target muscle [33]. An in-situ animal study of the muscle lengthening surgery showed that there are significant effects of surgery on the target and non-target muscles which can be attributed to the EMFT [27].

1.3 Importance of classification

Orthopedic surgeries performed on the CP patients generally conducted in a "single event multilevel surgeries" i.e., applying several surgical interventions at the same time including osteotomies and lengthening of the hip and calf muscles [34].

In the case of hamstrings, due to the biarticular nature of the muscles, effects of the other surgeries on hamstrings are unpredictable. Additionally, although the observable pathology is similar (e.g., crouch gait) the reason behind may differ [30]. Mentioned studies have proven that a course classification is required for studies investigating the effects of muscle lengthening surgeries.

1.4 Gait improvement parameters

In this thesis improvement in the gait of CP patients were analyzed from three different aspect, considering the biarticular nature of the hamstring muscles. The angle changes in the sagittal plane of the knee and hip joints due to surgery were investigated separately and a gait score was used to represent the change in the total gait.

1.4.1 Knee angle in sagittal plane

In the hamstring lengthening surgery, the main pathology addressed is the increased knee flexion or excessive resistance to knee extension during the gait, especially at the initial contact phase. As an indicator of the crouch gait, the knee angle in the sagittal plane reflects the severity of the pathology.

1.4.2 Hip angle in sagittal plane

Hamstrings are biarticular muscles which manipulate hip and knee joint at the same time. A similar study conducted on extensor digitorum longus (EDL) of rats showed that muscle lengthening surgery have significant effect on the non-intervened side as well [27]. Additionally, reported increased anterior pelvic tilt in the CP patients after the hamstring lengthening surgery [35][38] supports the importance of examination of the hip angle in the sagittal plane as a gait improvement parameter.

1.4.2.1 The psoas muscle . The psoas muscle (i.e., psoas major) is a biarticular muscle which origins from the thoracic and lumbar vertebrae(T12-L4) and ends at the lesser trochanter of femur. Although psoas' main function is hip flexion, it also influences the trunk's position with respect to the pelvis. A musculoskeletal model study revealed that patients whose gait improved after hamstring lengthening surgery had shorter psoas muscles, despite the fact that their hamstrings were not short preoperatively [31]. The article suggests that due to the larger moment arm of the hamstrings at the hip joint compared to the knee joint, increased anterior pelvic tilt can be the main problem leading to crouch gait [31].

1.4.3 Gait scores

Gait scores provide an objective assessment of overall gait improvement by generating a single number that represents the deviation from the normal gait. The Gillette Gait Index (GGI) is reported as the most commonly cited method [37] that uses 16 independent gait features obtained from gait analysis and generated a single number while considering the interdependency between the gait features. Those 16 gait features are reported as: "*time to foot off as a percent of the total gait cycle time, walking speed normalized by leg length, cadence, mean pelvic tilt, pelvic range of motion in the sagittal plane, mean pelvic rotation, minimum hip flexion, total range of hip flexion-extension, peak abduction in swing, mean hip rotation in stance, knee flexion at initial contact, time to peak knee flexion, total range of knee flexion-extension, peak dorsiflexion in stance, peak dorsiflexion in swing and mean foot progression angle in stance*" [36].

Although the GGI is commonly accepted as representative, several limitations are also reported including the unclarity of the physical meaning of the gait features and impractical usage [37].

The Gait Deviation Index (GDI) is proposed to eliminate these limitations [37]. The GDI computes the score from 15 gait features that are reconstructed from 9 joint angles obtained from gait analysis. The joint angles are pelvic tilt, pelvis obliquity, pelvis rotation, hip flexion/extension, hip abduction/adduction, hip rotation, knee flexion/extension, ankle flexion/extension and foot progression [37]. The GDI calculated unilaterally and requires multiple control subjects/sides. Since the GDI is computed by extracting the z-score of the natural logarithm of the Euclidean distance between subject and the control data, higher GDI's are closer to the normative gait, where lower GDI's have higher deviation from the normative gait. Schwartz et al. also provided an excel file in the electronic addendum for GDI calculation [37].

1.5 Rationale

With the enhancement of the musculoskeletal modeling, retrospective studies reported that there are numerous cases where the CP patient underwent hamstring lengthening surgery whose hamstrings were not short or slow pre-operatively and still benefitted from the surgery [e.g., 30]. Therefore, this thesis was designed to assess the MTU length changes of the target and non-target muscles to investigate their contribution to the gait improvement, objectively.

The target muscle group in remedial surgery i.e., the hamstrings, are biarticular muscles that manipulate hip and knee angle during gait. Due to that, the gait improvement of the CP patients was conceptualized to be investigated separately for the knee and hip joints. A gait score is intended to represent the overall gait for completeness.

1.6 Aim of the Thesis

The aim of the thesis is to investigate if there is a gait improvement after surgery in CP patients who does not have short or slow hamstrings, by computing their gait improvement parameters and assessing the mechanism of that. Specifically, the following hypothesis were tested:

i. The knee joint movement of the patients during gait is improved post-operatively.

ii. The hip joint movement of the patients during gait is deteriorated post-operatively.

iii. The GDI of the patients increased post-operatively.

iv. The MTU lengths of the target muscles (i.e. hamstrings) do not increase post-operatively.

v. Psoas MTU lengths of the patients are shorter than those of typically developing (TD), pre-operatively.

2. METHODS

2.1 Subjects

A total of eight limbs of surgically treated CP patients (3 male, 1 female) were studied. All patients underwent bilateral hamstring lengthening surgery, and only one of them also had bilateral gastrocnemius lengthening surgery. The mean age of the patients at the time of surgery was 12.75 years with standard deviation 1.71 years. For all patients, kinematic gait analysis data 12 months pre-, and 12 months post-hamstring lengthening surgery were available. The patients had not undergone any other intervention (botulinum toxin A injections etc.) between the pre- and post-gait analyses.

Kinematic gait analysis data of the seven typically developing (TD) children were used as normative data. The mean age of the TD participants was 8.14 years with standard deviation 1.77 years. Both limbs of the TD participants were included in the study, yielding in total normative data of fourteen limbs.

2.2 Gait Analysis

Gait analysis data were collected from Istanbul University Orthopedics & Traumatology Department Gait Analysis Laboratory Database, by retrospective search. Kinematic gait analysis data was obtained from ELITE2002 motion capture system (BTS Bioengineering, Milan, Italy) that included six infrared cameras and twenty-two retro-reflective markers. The markers were placed according to Helen Hayes Marker Placement Protocol [40], with three on the trunk, three on the pelvis and the rest on the legs (see Figure 2.1).

- Markers on the trunk were placed at the acromions bilaterally and the seventh cervical vertebra (C7).
- Markers on the pelvis were placed at the anterior superior iliac spines (ASIS) bilaterally and the second sacral vertebra, sacrum.
- Markers on the leg were placed bilaterally at the greater trochanter, lateral of the femoral wand, the lateral femoral epicondyle, the fibular head, lateral of the tibial wand, the lateral malleolus, the fifth metatarsal head and the heel.

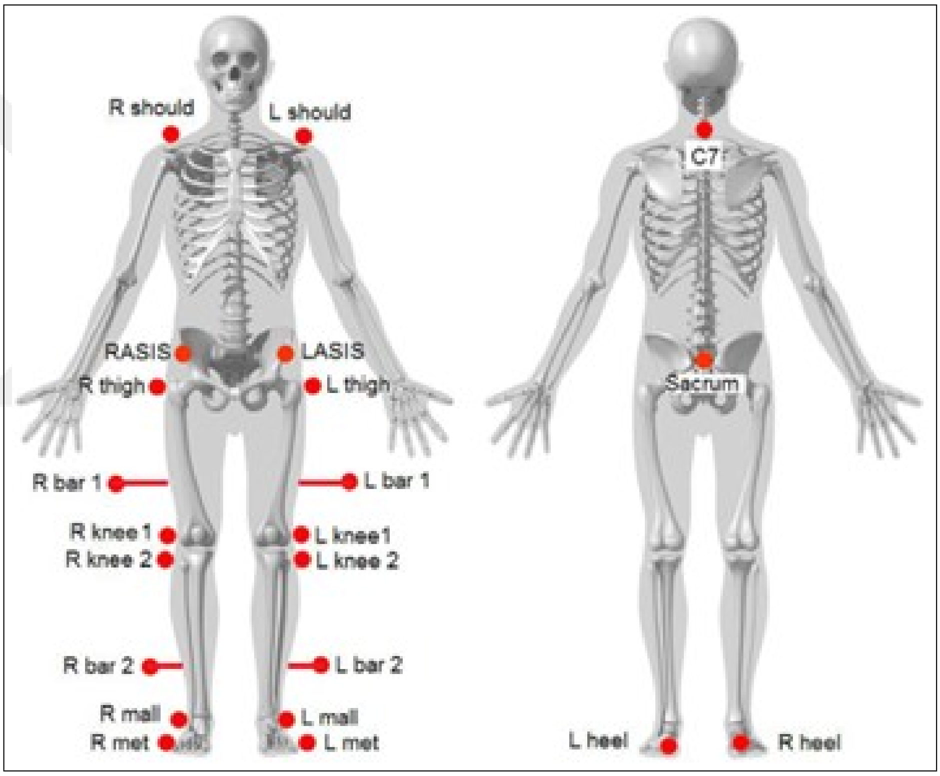


Figure 2.1: Placement of the twenty-two retro-reflective markers [41].

Prior to walking (kinetic) trials, a static trial was conducted. In the static trial the participants were requested to stand at the upright position for 5 seconds while all the markers were visible to the cameras. After the static trial, heel markers were removed.

In the kinetic trials, participants were requested to walk along the 5m-isle with self-selected speed. Ideally, kinetic trials should be repeated for at least three times to be able to detect unusual patterns of gait that might be caused by the experiment environment.

Taking that into account and to avoid any loss of data due to missing markers or incomplete gait cycles, kinetic trials were repeated 5-10 times.

To be able to obtain useable gait analysis data, the recordings must contain at least one complete gait cycle (stride) for each of the legs. One gait cycle is defined by the two successive contacts of the same (ipsilateral) foot, which represents the 0% and the 100% of the gait cycle, respectively. A gait cycle is divided into two phases by the toe-off event of the opposite (contralateral) foot and each phase is divided into several periods (see Figure 2.2) [43]. For this study, "initial contact" event and "terminal stance" periods have particular importance since CP patients experience the maximum resistance to knee extension at these points of the gait.

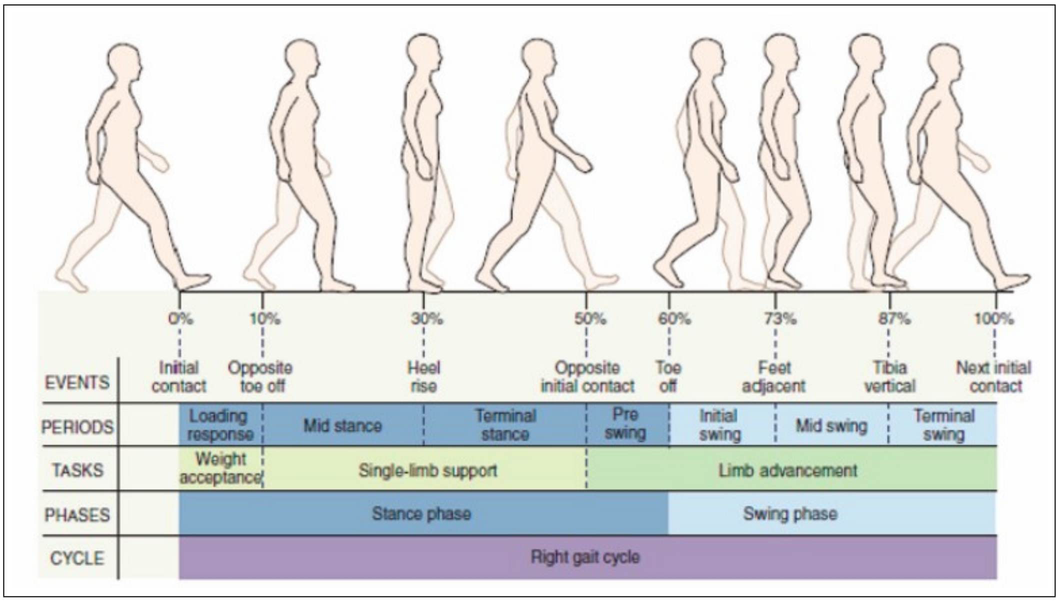


Figure 2.2: Phases of gait cycle for right leg [42].

2.3 Musculoskeletal Modeling

2.3.1 OpenSim

Muscle tendon unit (MTU) lengths for a gait cycle of each subject were computed with OpenSim software (OpenSim 4.0) [44][45]. OpenSim is an open-source platform that enables researchers to create their own musculoskeletal models or utilize already existing models in the Musculoskeletal Models library. OpenSim provides the users two simulation options.

i. Inverse problem simulation enables researchers compute kinetic and kinematic variables of joints and muscles from experimental movement data.

ii. Forward problem simulations allow users to generate motion based on certain objectives.

In this thesis, inverse problem simulations were used.

2.3.1.1 Data Preparation. Marker trajectories of each trial (static and kinetic) were gathered from interface of the motion capture system in .C3D format. With Mokka [46] software, C3D files were converted into .TRC format which is the type of file that can be used as input in the OpenSim. Before converting the trials into .TRC format, the time points where one or more markers were missed were clipped and gait cycles for each leg were determined.

2.3.1.2 Generic Model Properties. In the OpenSim simulations a generic model "Gait_2392" was used. "Gait_2392" is a 3D 23 degree of freedom human musculoskeletal model that represents the torso and the lower extremities. The model consists of 76 muscles which are modelled with 92 muscle-tendon actuators. Each muscle-tendon unit is modelled as a line and constraint by its origin and insertion points and wrapping points are also appointed to accurately represent the pathways of the muscles.

The default version of the "Gait_2392" is modelled as 75.16 kg and 1.80 m tall and in accordance with the experimental data that is collected by John et al [47]. Twenty-two virtual markers were placed to the subject's anatomical landmarks in accordance with the Helen Hayes protocol for following application.

In the Gait_2392 psoas muscle is modelled with fixed origin to the pelvis to neglect its influence on the trunk position and used only as the indicator for the hip flexion/extension movement [31].

2.3.1.3 Scaling Tool. Scaling step is the initial step should be done prior to muscle-tendon unit (MTU) length calculations. Its aim is to scale the generic model (Gait_2392) based on the data obtained during the static trials. Each body segment on the musculoskeletal model is defined with two virtual markers and the dimensions of the body segments are adjusted based on the scale factors. OpenSim provides users two types of scale factor calculations which can be chosen separately for each body segment. Measurement-based scaling calculates the scaling factor as the ratio between virtual and experimental data.

Virtual distance is measured as the distance between two virtual markers that defines the body segment at the model's default position. On the other hand, the distance between experimental markers computed per each frame then averaged along the duration of the static trial. In the manual scaling users can enter the scaling factor of each segment as they desire. In this study I used measurement-based scaling.

Masses of each segment also scaled based on the body mass of the subject and the scaling factors. As an output scaling tool provides the scaled version of the generic model with new set of virtual markers positioned as much as close to the positions in the static trial and removes the excessive marker that will not be used in the kinetic trials (heel markers). Maximum and the round mean square error between virtual and experimental markers are also computed by the scaling tool and they should not exceed 0.05 and 0.03 respectively.

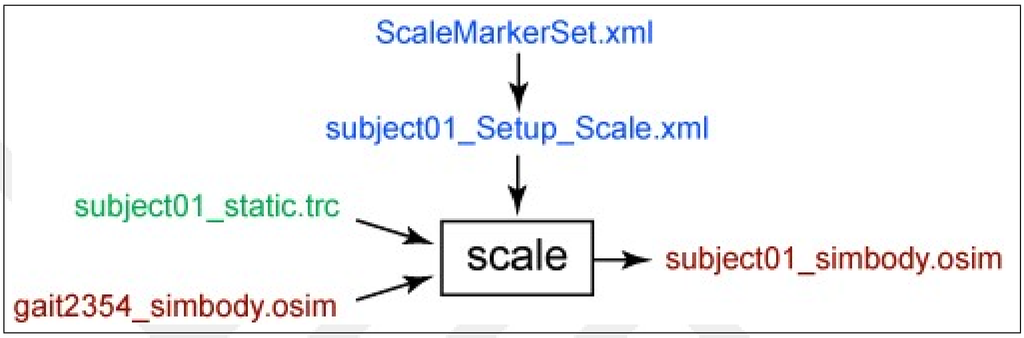


Figure 2.3: Schema of the inputs and the outputs of the scaling tool [48].
Note: Green .trc file represents the experimental data, marker locations of the subject during static trial.Red .osim files are the musculoskeletal model, input is the default version whereas output is the scaled version.Blue .xml files are the setting files, ScaleMarkerSet.xml contains the location information of the virtual markers and the subject01_Setup_Scale.xml is the operational file of the scaling tool.

2.3.1.4 Inverse Kinematics Tool. The inverse kinematic tool generates the motion of the musculoskeletal model by using the experimental marker locations obtained from motion capture system. Joint angles of the musculoskeletal model are computed by solving the weighted least square problem. Different weight values are appointed for each marker based on their reliability during the gait analysis. For example, markers that are located on the bony landmarks have higher weight ie. higher reliability than the markers located on the bars of the body segments. The error between experimental and the virtual markers placed after scaling step minimized further for markers with higher weights.

The inverse kinematics tool uses the scaled version of the model, marker location information of the kinetic trials and the setup file as inputs and generates a motion file for the output.

After motion file is generated, MTU lengths of desired muscles or angles of the desired joints can be plotted and exported for the duration of the trial.

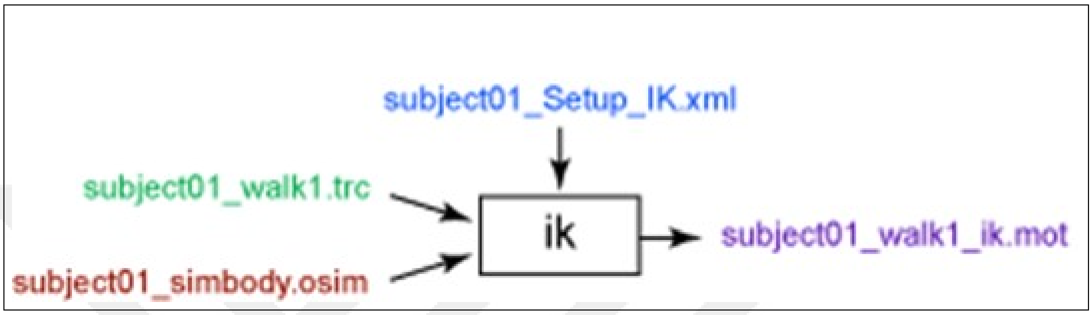


Figure 2.4: Schema of the inputs and the outputs of the inverse kinematic tool [49]. **Note:** Green .trc file represents the experimental data, marker locations of the subject during kinetic trial. Red .osim file is scaled version of the musculoskeletal model. Blue .xml files is the operational file of the inverse kinematic tool.

2.3.2 MTU Length and Velocity Calculations

One representative gait cycle was chosen for each limb and MTU lengths and lengthening velocities were computed for that gait cycle [30][38]. The representative gait cycle is determined based on the maximum peak hamstring MTU length achieved by the limb. Semimembranosus was selected to represent the hamstrings. Although both semimembranosus and semitendinosus are knee flexors, semimembranosus has shorter muscle fibers compared to semitendinosus [39]. By choosing the semimembranosus as representative of hamstring, we intent to avoid the limiting effects of longer muscle fibers in contracture [20]. To eliminate the subjects' anthropometric differences MTU lengths were normalized to their segment lengths. Semimembranosus was normalized with the femur length and the length of the femur was calculated by placing two virtual markers at the greater trochanter and the mid-point of the epicondyles on the scaled musculoskeletal model.

Psoas was normalized to the distance between anterior superior iliac spine (ASIS) markers. Although this distance was not in line with the pathway of psoas, it is chosen since scaling tool uses this distance to scale the pelvic bone.

Each gait cycle consisted different amounts of data-points due to the difference in the durations. All MTU length to time curves converted into 101 data-points to represents each percentile of the gait cycle. "imresize" function of the MATLAB was used to convert MTU length curves into 101 data-points while keeping the shape of the curve still.

MTU elongation velocities were computed by the first derivative of the normalized and resized MTU lengths with respect to time. To eliminate the noise caused by the derivation process, a zero-phase digital filter (2nd-order Butterworth, MATLAB) was applied with cut-off frequency 8Hz [30][38].

2.4 Gait Improvement Parameters

2.4.1 Knee Angle in sagittal plane

The knee angles of the subjects (CP and TD) in the sagittal plane i.e., knee flexion/extension angles for a gait are obtained from the interface of the motion capture system. Each data set comprises a hundred knee angle for a gait and these data sets are converted into 101 data-points to represent each percentile of the gait cycle. The conversion is done by the "imresize" function of the MATLAB.

2.4.2 Hip Angle in sagittal plane

Similar to the knee angles, the hip angles of the subjects also are obtained from motion capture system and converted to 101 data-points to represent the 1% of the corresponding gait cycles.

2.4.3 Gait Scores

In the present study the Gait Deviation Index (GDI) is used as a gait score. The Excel file provided by Schwartz et al. [37]. The Excel file was already consisting of 166 control data sets however, control data sets were replaced with the TD data set of the current study. The required 9 joint angles for each 2% of the gait cycle were provided by converting the joint angle data sets into 51 data-point sets by "imresize" function of the MATLAB to match the each 2% of the gait cycle. Once the TD joint angles were placed as control data sets, the GDI of the patients were calculated individually by adding their 51 data-points joint angles to the excel file.

2.5 The Statistical Analyses

2.5.1 Subject Validation

The "shortness" and the "slowness" decisions of the muscles were made by comparing each patient's MTU length and elongation velocity curves with the mean TD MTU length and velocity curves, in accordance with the previous studies in the literature [30][34][38]. If the MTU lengths or velocities of a patient was below the mean minus two standard deviation (SD) of the peak TD value at any time of the gait cycle, then that patient does not belong to the normative values obtained from TD,$\alpha = 0.05$. When a muscles MTU length or velocity i.e., lengthening velocity is below the mean minus 2 SD that muscle appointed as "short" or "slow" respectively and if not, they appointed as "not short" or "not slow".

2.5.2 Pre- and post-operative comparison of CP patients

We checked the normality of the data sets by Shapiro-Wilk normality test. The mean pre- and post-operative joint angles and MTU lengths for a gait cycle and gait scores were compared by Student's t-paired test or Wilcoxon signed-rank test based on the normality of the data. If a main effect was detected, then Student's t-paired test or Wilcoxon signed-rank test was applied to every 1% of the gait cycle to locate where the local effects were. For local effects, pre- and post-operative angle, or length values for each 1% GC time-points per patient compared pairwise. Differences considered significant when $p<0.05$.

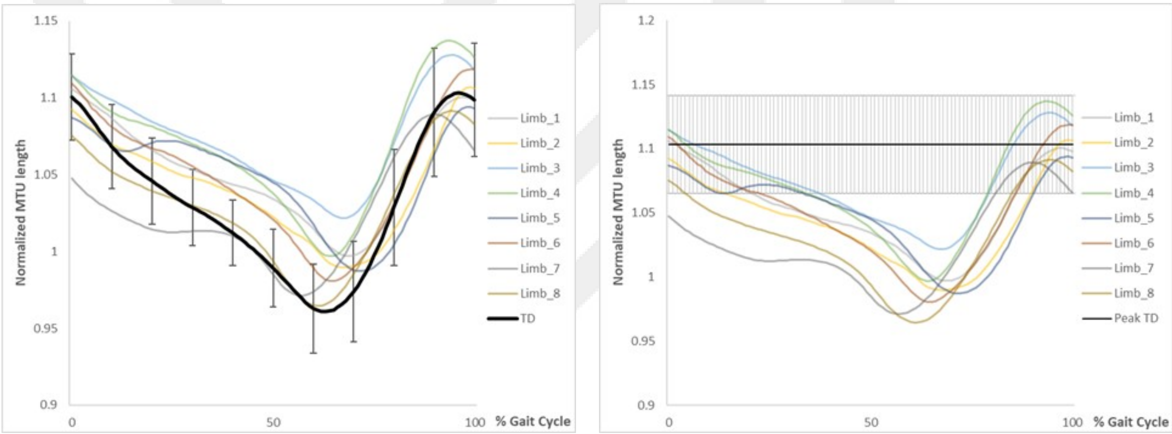
2.5.3 Correlation Analyses

The correlation analyses were conducted to investigate that if the changes in the MTU lengths of the mentioned muscles had significant relation with the knee and the hip angles in the sagittal plane at the initial contact phase of the gait cycle and/or the gait scores. The normality of the data sets was tested by the Shapiro-Wilk normality test. The Pearson product-moment correlation or Spearman's rank correlation was computed based on the normality of the data sets.

3. RESULTS

3.1 Subject Validation

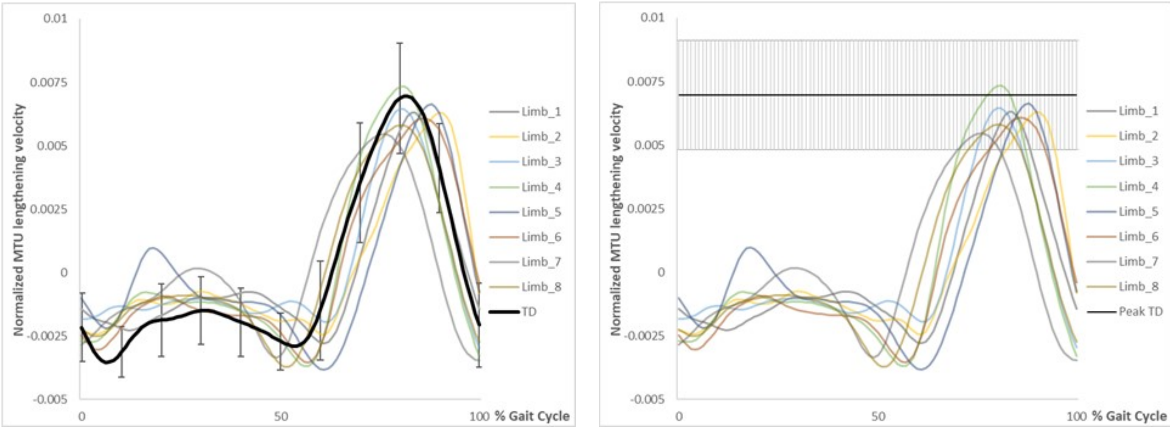
Figure 3.1.a. and b. show that all patients' pre-operative semimembranosus MTU lengths for a gait cycle were not below the mean minus 2SD of the peak semimembranosus MTU lengths of TD in at least one time-point. Therefore, semimembranosus muscles of all patients were classified as "not short".



(a) (b)

Figure 3.1: Pre-operative normalized semimembranosus MTU length of participants for a gait cycle a. compared to mean length of TD with 2 SD. b. compared to peak of the mean MTU length of TD participants.

Figure 3.2.a and b. show that pre-operative semimembranosus MTU velocity of all patients were not below more than 2 SD of the peak mean velocity of the TD participants in at least one time point of a gait cycle. Consequently, the semimembranosus muscles of the patients were classified as "not slow".



(a) (b)

Figure 3.2: Pre-operative normalized semimembranosus MTU lengthening velocity of participants for a gait cycle a. compared to mean lengthening velocity of TD with 2 SD b. compared to peak of the mean MTU lengthening velocity of TD participants.

3.2 Gait Improvement Parameters

3.2.1 Knee Angle in sagittal plane

The pre- and post-operative mean knee angles per gait cycle were not normally distributed. Statistical analysis revealed significant main effect ($p<0.001$) and local effects. Significant local effects were detected at the 0-3%, 28-43% and 95-100% of GC, $p<0.05$.

At the same time points, which correspond to 0% and 100% of the gait cycle pre-operative mean knee angles exceeded the mean knee angle of TD more than 2 SD. Figure 3.3 shows that after surgery, mean knee angles at those time points decreased between the 2 SD range.

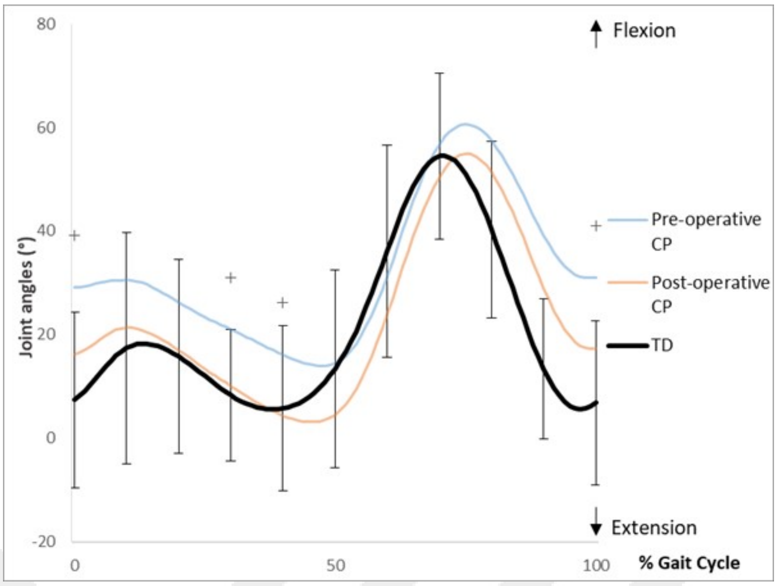


Figure 3.3: Pre-operative and post-operative mean knee angles of the patients with CP compared to TD for a gait cycle. (+) signs indicate the points where there is a significant local effect between pre- and post-operative knee angles $p<0.05$.

This result confirms the first hypothesis and demonstrates that CP patients with "not short" and "not slow" hamstrings, showed significant improvement in the knee angle, especially at the initial contact phase of the gait, which CP patients often experience as a consequence of excessive knee flexion.

3.2.2 Hip Angle in sagittal plane

Figure 3.4 shows that neither pre-operative nor post-operative mean hip angle-GC curves exceed that for TD±2SD. Normality of the pre- and post-operative hip angles per GC both failed. The statistical analysis showed significant main effect ($p<0.001$), but no local effects.

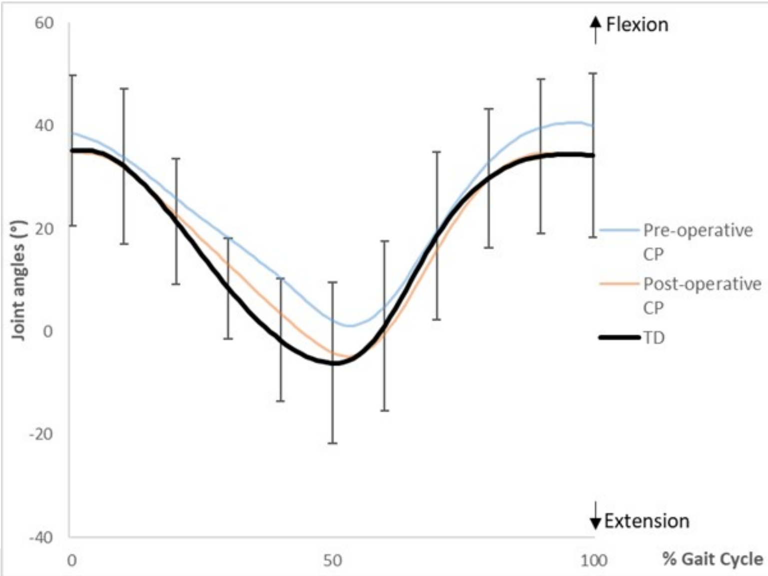


Figure 3.4: Pre-operative and post-operative mean hip angles of the patients compared to TD for a gait cycle.

These results reject the second hypothesis.

3.2.3 Gait Score

Table 3.2.3 shows the GDI calculated per each limb studied, pre- vs. post-operatively. The GDI's of each CP patient were calculated using the excel file provided by Schwartz et al. [37]. Instead of using the existing control data, joint angles of the TD participants were used.

Table 3.1: The Gait Deviation Index (GDI) of each subject, pre- and post-operatively.

	Limb_1	Limb_2	Limb_3	Limb_4	Limb_5	Limb_6	Limb_7	Limb_8
Pre-operative	76.1	61.8	72.5	78.1	77.5	82.4	84.8	77.6
Post-operative	71.3	75.9	93.4	89.4	75.1	75.4	86.0	90.0

The pre- and the post-operative GDI data were normally distributed. No significant difference was detected between them.

This result rejects the third hypothesis.

3.3 MTU Length Change of Hamstrings

The pre- and the post-operative SM MTU length curves failed normality test. The statistical analysis revealed significant main effect ($p<0.001$), yet no local effects.

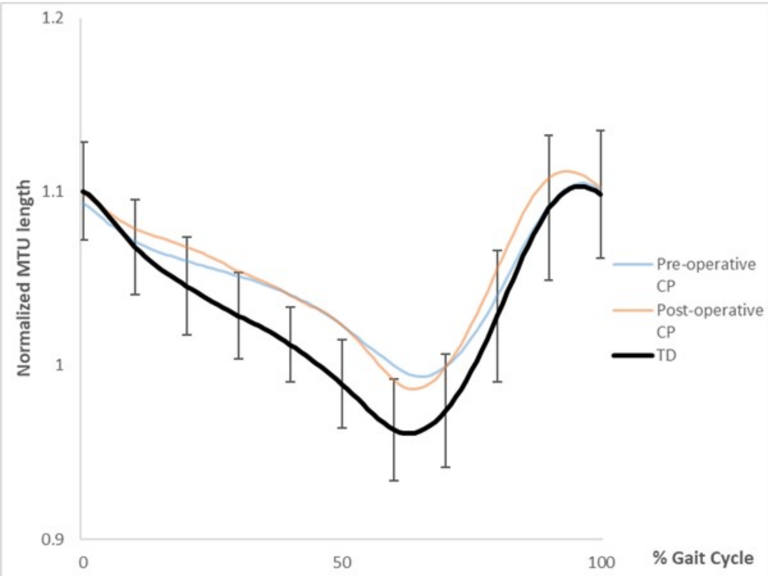


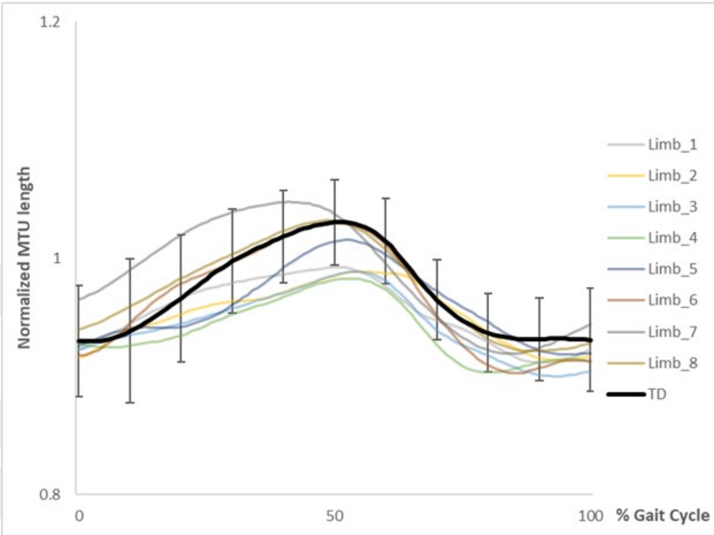
Figure 3.5: Pre-operative and post-operative mean normalized MTU lengths of semimembranosus of the CP patients compared to TD for a gait cycle.

Compared to TD, pre- and post-operative SM MTU lengths mostly were within the range of 2SD from the mean MTU lengths of TD. Especially, at the initial contact (0% GC), where CP patients experience excessive resistance to knee extension, normalized hamstring MTU lengths pre- and post-operatively were not significantly different than the TD MTU lengths. This result confirms the fourth hypothesis.

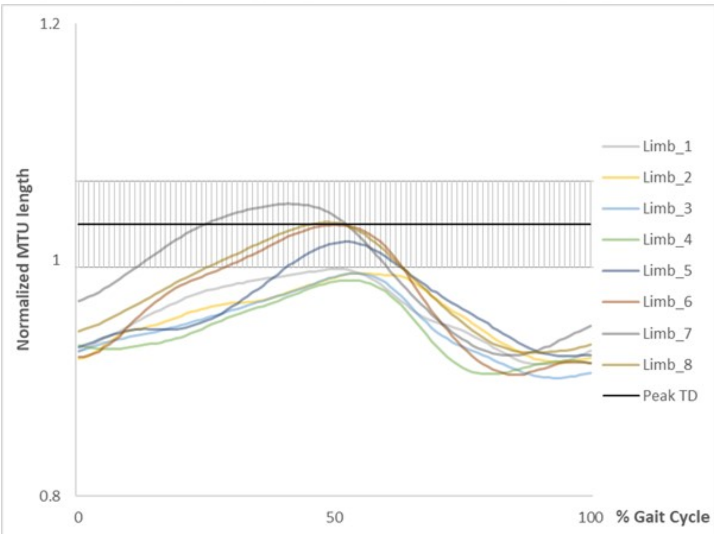
3.4 Psoas

3.4.1 Pre-operative MTU lengths

Figure 3.6 a. and b. show pre-operative psoas MTU lengths of CP patients.



(a)



(b)

Figure 3.6: Pre-operative normalized psoas MTU length of CP patients for a gait cycle compared to a. mean length of TD with 2SD b.peak of the mean MTU legth of TD participants.

Pre-operative psoas MTU lengths of CP patients were mostly within the range of normative data. Yet, peak MTU lengths of limb_1, limb_2, limb_3 and limb_4 were below more than 2 SD from the peak MTU length of TD and classified as "short", whereas psoas lengths of limb_5, limb_6, limb_7 and limb_8 were classified as "not short".

These results partially rejects the fifth hypothesis.

3.4.2 MTU length change

Figure 3.7 shows the mean of the pre- and the post-operative psoas MTU lengths of the CP compared to mean psoas MTU length of TD.

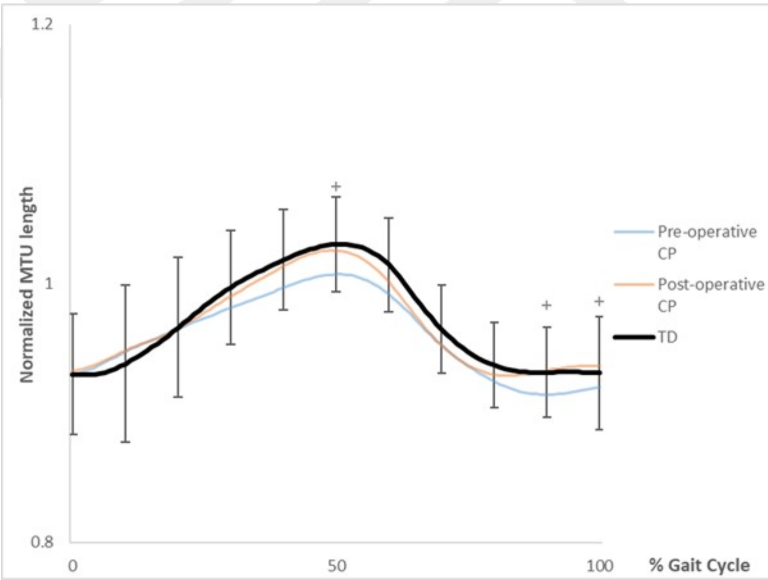


Figure 3.7: Pre-operative and post-operative mean MTU lengths of psoas of the CP patients compared to TD for a gait cycle. (+) signs indicate the point where there is a significant local effect between pre- and post-operative psoas lengths, $p<0.05$.

Both curves failed the normality test. The statistical analysis revealed significant main effect($p<0.001$) and local effects. The local effects were detected at the 41-52% and 87-100% of GC, $p<0.05$.

Even though the surgical intervention did not target the psoas, Figure 3.7 shows a significant impact of surgery on the psoas. These significant changes occurred at the terminal stance and terminal swing phases of the gait which corresponds to the peak extension and flexion of the hip, respectively.

These results suggest that even though the difference at the hip angle is not statistically significant, those changes have significant impact on the MTU lengths of the muscles crossing the hip joint.

3.5 Correlation Analyses

Table 3.2: Gait improvement parameters per subject

Subjects	Knee angle at initial contact (0% Gait cycle)	Hip angle at initial contact (0% Gait cycle)	Gait Score
Limb_1	-30.712°	-18.506°	-4.8
Limb_2	-23.844°	-13.031°	14.1
Limb_3	15.665°	10.670°	20.9
Limb_4	-2.953°	6.597°	11.2
Limb_5	-20.650°	-5.814°	-2.3
Limb_6	-13.115°	-0.734°	-7.0
Limb_7	-12.146°	-2.789°	1.3
Limb_8	-15.666°	-5.900°	12.4

Each column represents the difference between the pre- and post-operative data.

Table 3.3: Normalized MTU length changes at initial contact (0% gait cycle) per subject

Subjects	Semimembranosus	Psoas
Limb_1	-0.005	0.015
Limb_2	0.016	-0.006
Limb_3	-0.031	0.024
Limb_4	-0.018	0.009
Limb_5	0.020	-0.010
Limb_6	0.022	-0.016
Limb_7	0.029	0.003
Limb_8	0.012	0.007

Each column represents the difference between the pre- and post-operative data.

Table 3.4: Pearson product-moment correlations

	Knee Angle	Hip Angle	GDI	Semimembranosus MTU length	Psoas MTU length
Knee Angle	1	.947**	.615	-.621	.479
Hip Angle	.947**	1	.458	-.480	.260
GDI	.615	.458	1	-.571	.547
Semimembranosus MTU length	-.621	-.480	-.571	1	-.805*
Psoas MTU length	.479	.260	.547	-.805*	1

** Correlations with $p<0.001$

* Correlations with $p<0.05$

Significant correlations were shown only between knee and hip angle change at the initial contact and the MTU length changes of SM and Ps.

Statistical analysis revealed that there is a strong positive correlation between the knee and hip angle changes. Considering the decreasing trend in the knee angle changes e.i., a shift to more extended positions at the initial contact, resulted in a shift in the hip towards more extended positions.

Similarly, a strong negative correlation was also detected between SM MTU lengths and the Ps MTU lengths, which indicates that an increase in SM MTU length induced a decrease in Ps MTU lengths.

4. Discussion & Conclusion

4.1 Recent Study

CP results in various symptoms that affect PNS adversely in different levels and severity. The complexity of the pathology cause difficulties in the treatment strategies. Understanding the working mechanism behind the pathology is crucial to better the treatment.

Muscle lengthening surgery is a common method to correct the muscle shortness leads to crouched gait, CP patients often suffer. Yet the presumption of the shortness usually fails for the patients with crouched gait. These results indicate that there are different pathologies beside the shortness causing the gait impairment and these pathologies may be overlooked although they have a major impact. To search for this overlooked mechanism, this thesis focused on a certain group of patients who underwent hamstring lengthening surgery with not short and not slow hamstring muscles pre-operatively.

Eight patients were included in the study. Pre- and post-operative joint angles and MTU lengths were calculated with a musculoskeletal model. Kinematic gait analysis data modelled by OpenSim allow us to investigate the changes in the limbs of the patients as close as experienced in daily life.

Subject validation was initial for the study. Pre-operative hamstring MTU lengths and lengthening velocities were compared to the TD to demonstrate that all CP patients in the study had not short and slow hamstrings. Later, the success of the lengthening surgery assessed by first three hypotheses. The post-operative knee angles during the gait is the most commonly used success indicator.

The decreased knee angle in sagittal plane at the initial contact shows the gait improvement by decreasing the excessive resistance to the knee extension. The unchanged hip angle in sagittal plane during the gait also supports the gait improvement after the surgery. Despite the positive results in the knee and hip angle, the unchanged GDI scores suggest that the improvement in the two of the joints are not sufficient or accompanied by deterioration in different joints or planes. Although there is a significant improvement at the knee flexion/extension angle, it failed to improve the total gait of the patients.

Since the recovery in the knee angle is evident, the MTU lengths of the target muscles i.e., semimembranosus was calculated to investigate the reasoning behind it. No significant difference were detected as expected and suggested by Salami et al. [34]. These findings indicated that the improvement in the knee angle did not originate from the increase in the MTU length of the target muscles of the lengthening surgery. The psoas MTU lengths of the patients were also studied, since a study conducted by Delp et al. suggested that CP patients who does not suffer from short hamstrings and still benefitted from hamstring lengthening surgery often had shorter psoas MTU lengths compared to TD [31]. In accordance with that study, the half of the patients had shorter psoas MTU lengths pre-operatively. The post-operative analysis of the psoas muscle showed that there was a significant increase in the psoas MTU length although the muscle was not surgically intervened. This outcome also showed that a significant increase in the psoas MTU length does not cause a significant increase in the posterior pelvic tilt during the gait. However, a significant increase in the MTU length of the psoas muscle which is a hip flexor can indicate the opposite behavior of the hamstrings as hip extensors.

The significant strong negative correlation between semimembranosus and psoas MTU length change (ρ=-.805) also supports the previous interaction. Additionally, the positive strong correlation between the knee and hip angle change in initial contact (ρ=.947) revealed that increased knee extension caused hip extension although the difference cannot be stated as significant.

When all outcomes are combined, the only physically possible explanation is that the hamstrings of the CP patients were not elongated after the surgery but shifted isometrically towards the knee allowing an increased knee extension at the initial contact. This result can be achieved by the release of the overly tight epimuscular structures during the surgery or remodeling of them during the healing period. The abnormal cross-linking of the collagen fibers causes stiffness in the connective tissue [11], this abnormality may lead to joint contracture through EMFT. The CP patients suffering from crouched gait with not short or slow hamstrings can be experiencing stiffness in the epimuscular structures that leads their hamstrings to operate at more proximal positions whereas they should operate at more distal positions.

4.1.1 Limitations

Due to the intricate mechanism of the human motion, coarse classification is required to obtain a meaningful data. Since CP lead to variety of gait pathologies and in various degrees only patients with similar diagnosis can be grouped. On the other hand, single event multilevel surgeries allow patients to undergo several interventions at the same time. However multilevel surgeries makes it hard to assess single interventions outcome.

Because of these constraints, small number of patients were involved in the study. Increased numbers of patients would have led stronger statistical analyses. The required number of patients were calculated as 28 patients in the proposal.

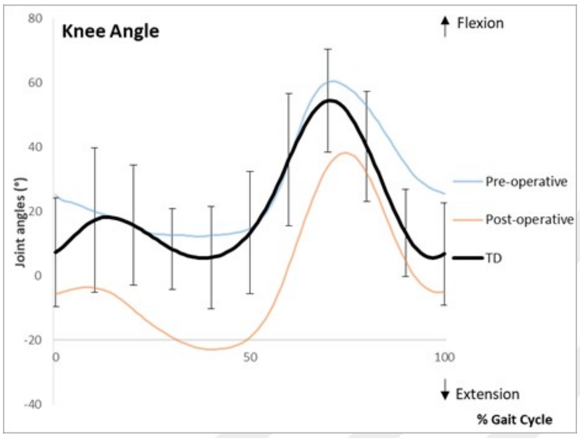
Secondly, the ground reaction force data during the gait analyses were not available in the database. Yet previous studies indicated that muscle lengthening surgery affect force exertion significantly [19][27]. The changes in the force exertion should be studied to better understand the mechanism behind the recovery. Although the musculoskeletal model OpenSim allows to approximate the force exertion in the single muscle during the gait, it does not take account of epimuscular connections thus does not separate the changes in the MFT and EMFT.

4.1.2 Future Studies

In the future studies the number of patients should be increased to conduct statistically powerful analyses. Also, the increased number of patients will allow sub-grouping based on the pre-operative psoas MTU lengths to further investigate its contribution in the pathology. The ground reaction force data during the gait must be included to study to investigate its contribution to the gait improvement.

APPENDIX A. PRE- AND POST-OPERATIVE JOINT ANGLES AND MTU LENGTHS PER LIMB

A.1 Limb_1



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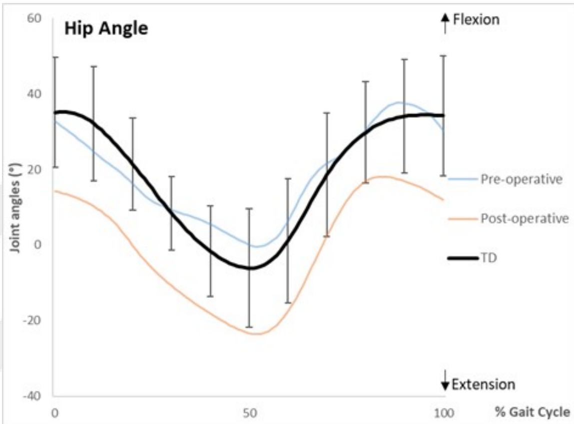

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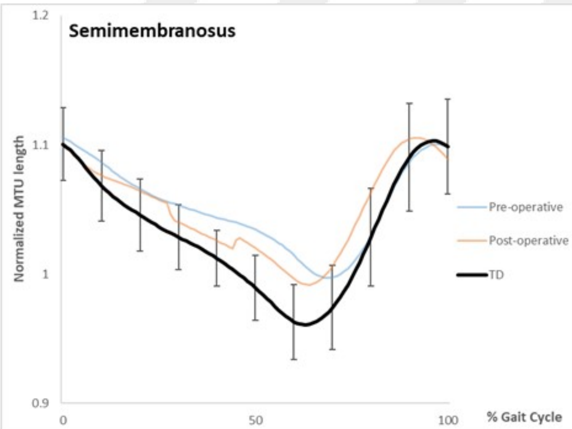

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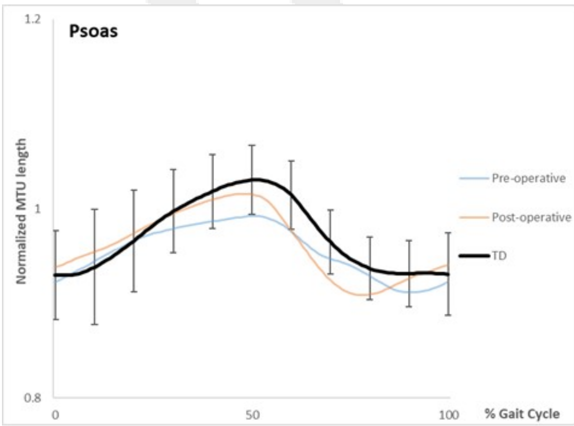
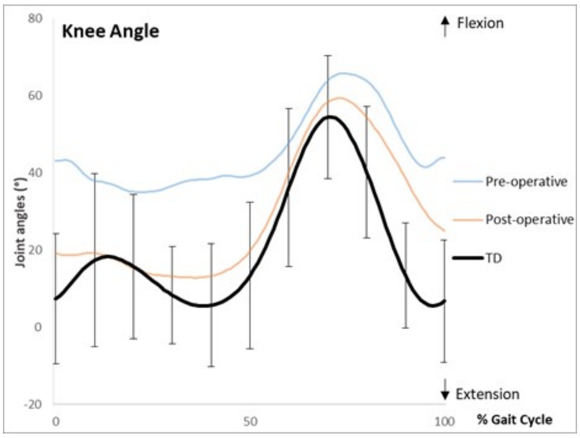


(d)

Figure A.1: Pre-operative and post-operative a. knee angles b. hip angles c. Semimembranosus MTU length d. Psoas MTU length of the Limb_1 compared to TD for a gait cycle.

A.2 Limb_2



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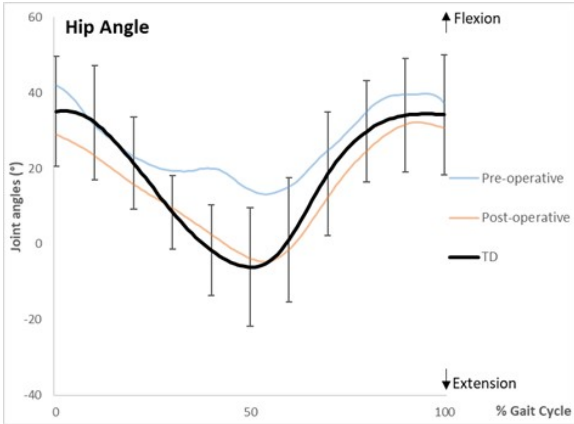

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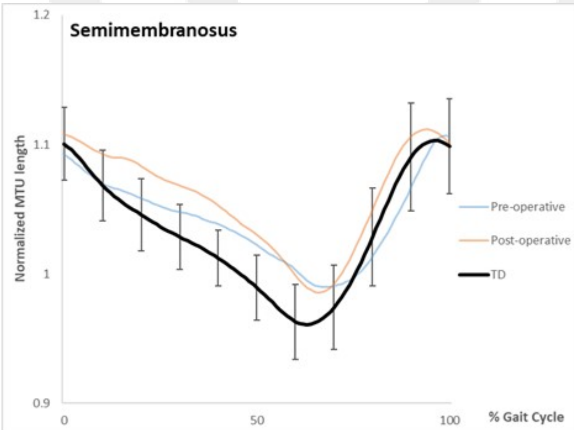

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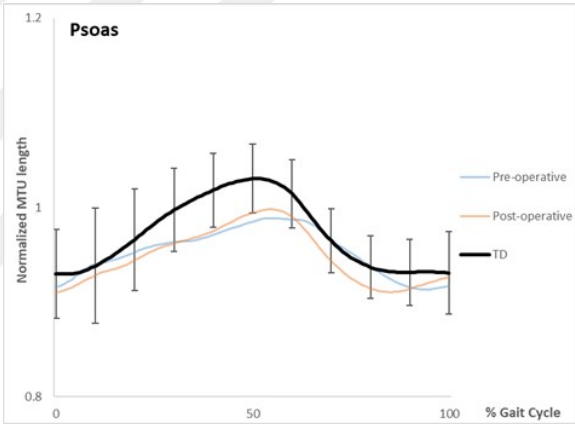
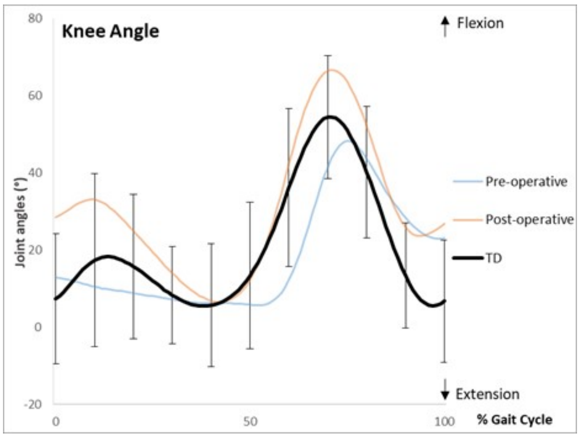


(d)

Figure A.2: Pre-operative and post-operative a. knee angles b. hip angles c. Semimembranosus MTU length d. Psoas MTU length of the Limb_2 compared to TD for a gait cycle.

A.3 Limb_3



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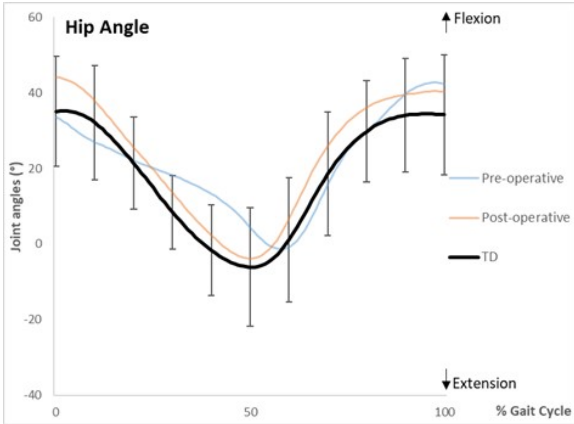

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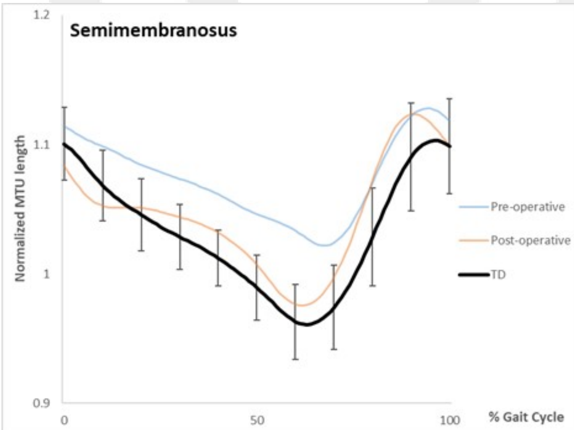

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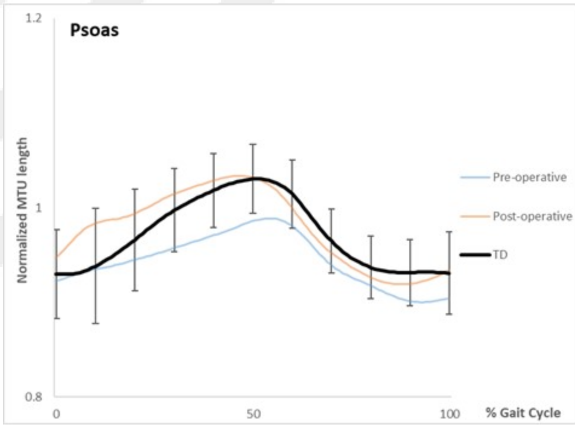
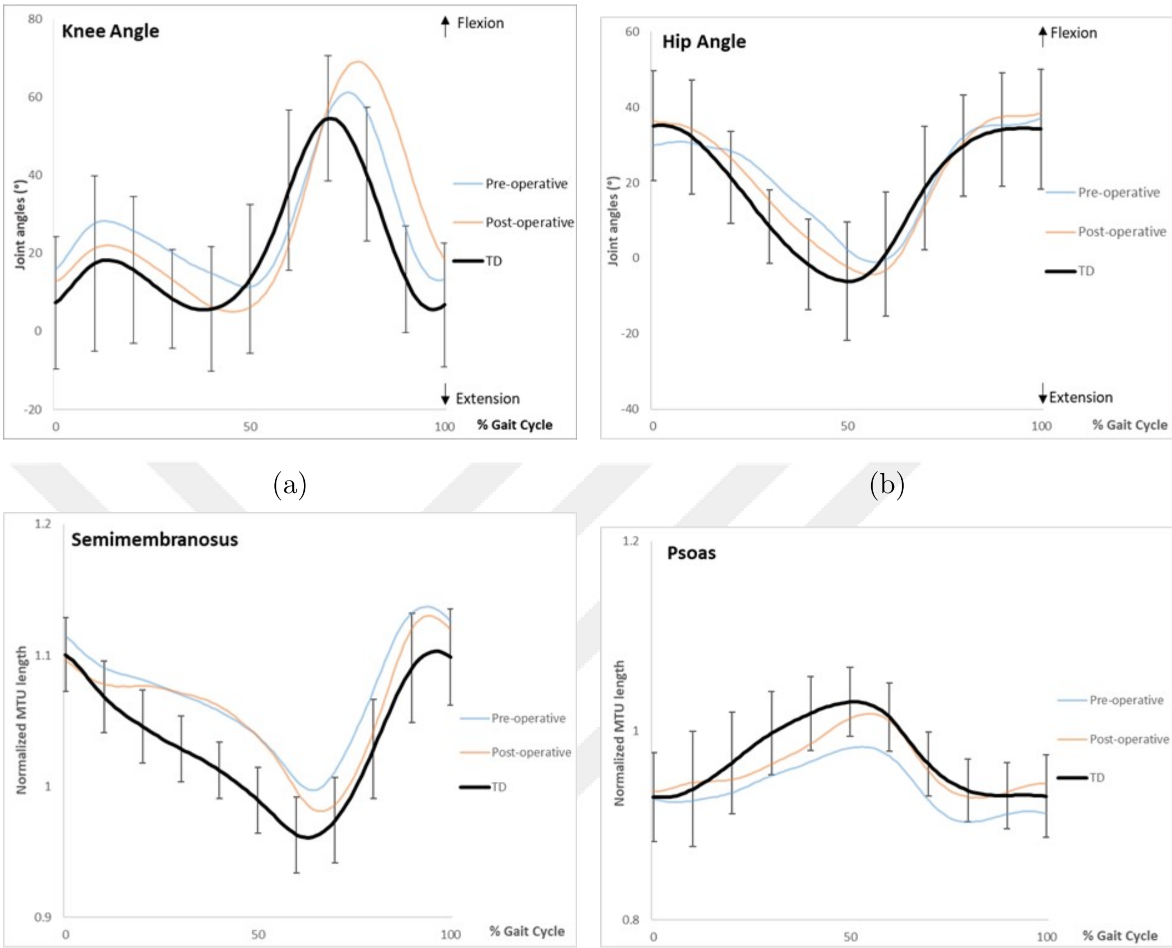


(d)

Figure A.3: Pre-operative and post-operative a. knee angles b. hip angles c. Semimembranosus MTU length d. Psoas MTU length of the Limb_3 compared to TD for a gait cycle.

A.4 Limb_4

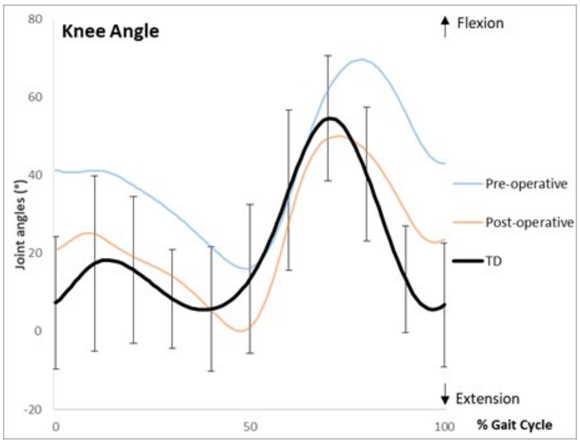


(a) (b)

(c) (d)

Figure A.4: Pre-operative and post-operative a. knee angles b. hip angles c. Semimembranosus MTU length d. Psoas MTU length of the Limb_4 compared to TD for a gait cycle.

A.5 Limb_5



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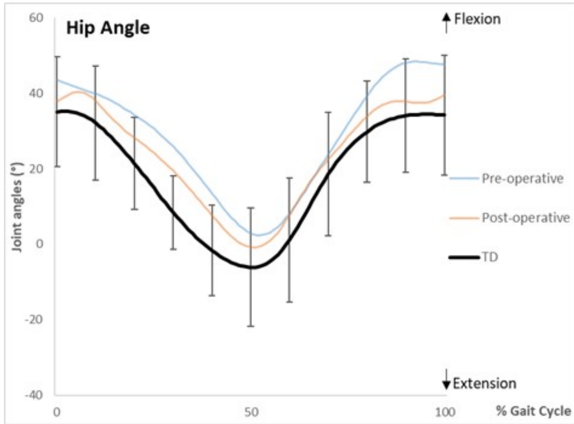

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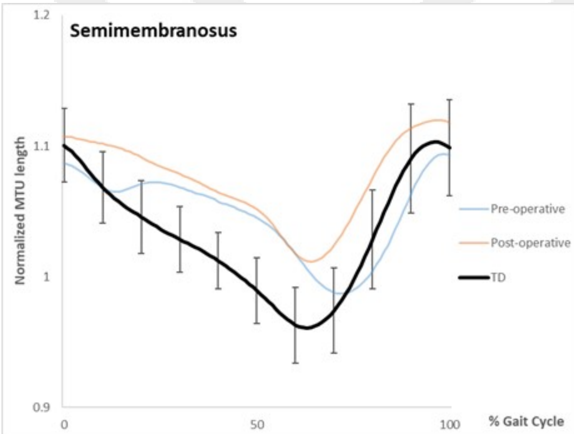

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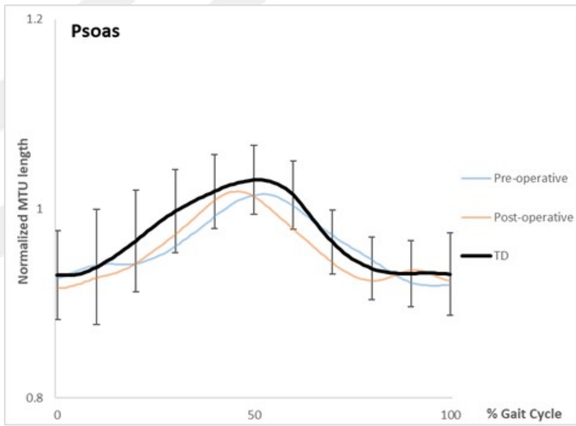

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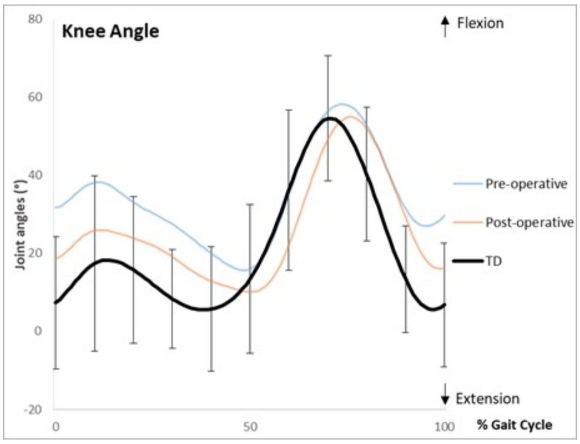
Figure A.5: Pre-operative and post-operative a. knee angles b. hip angles c. Semimembranosus MTU length d. Psoas MTU length of the Limb_5 compared to TD for a gait cycle.

A.6 Limb_6



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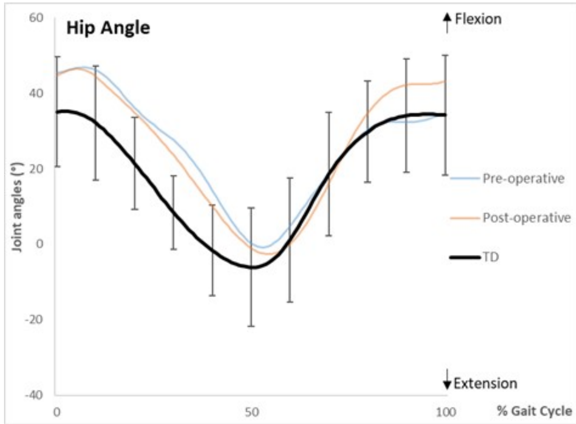

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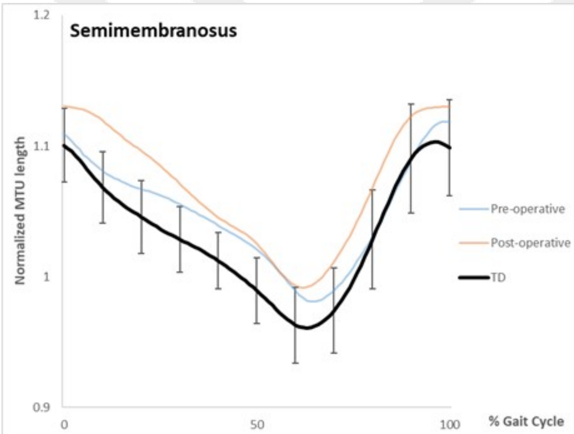

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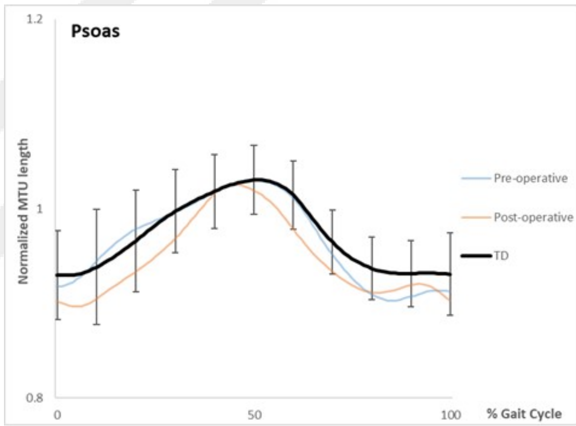

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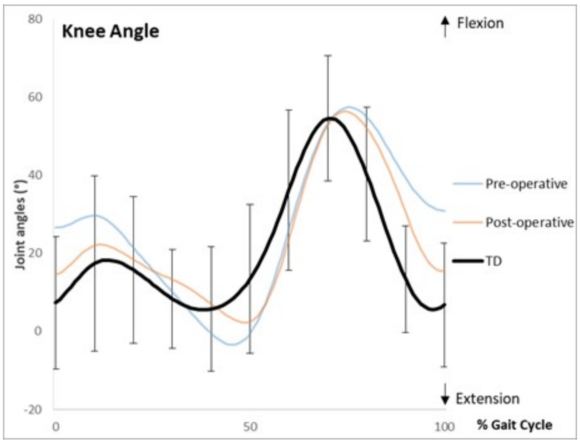
Figure A.6: Pre-operative and post-operative a. knee angles b. hip angles c. Semimembranosus MTU length d. Psoas MTU length of the Limb_6 compared to TD for a gait cycle.

A.7 Limb_7



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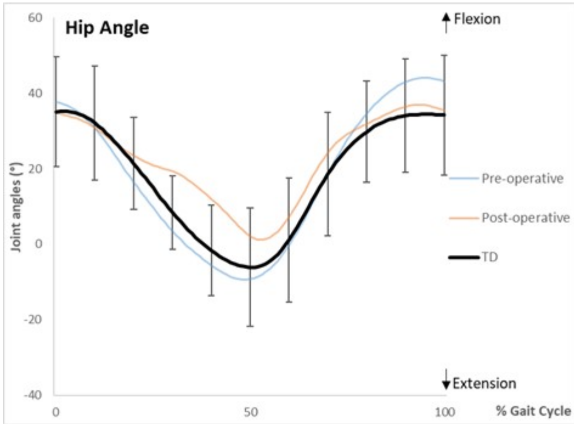

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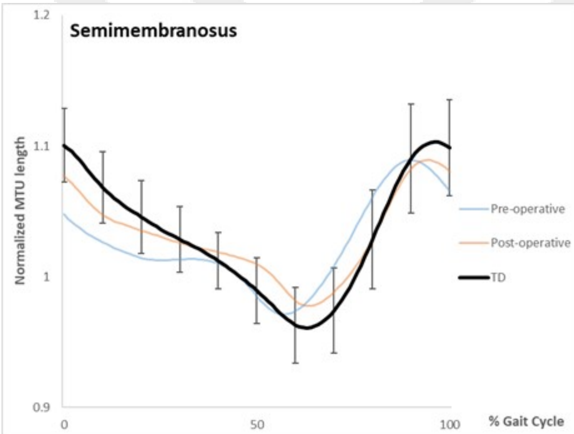

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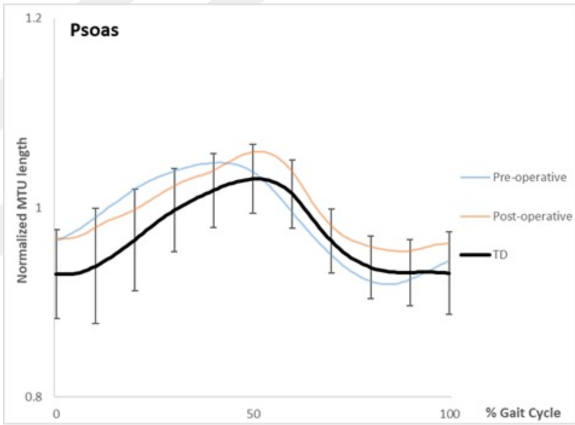
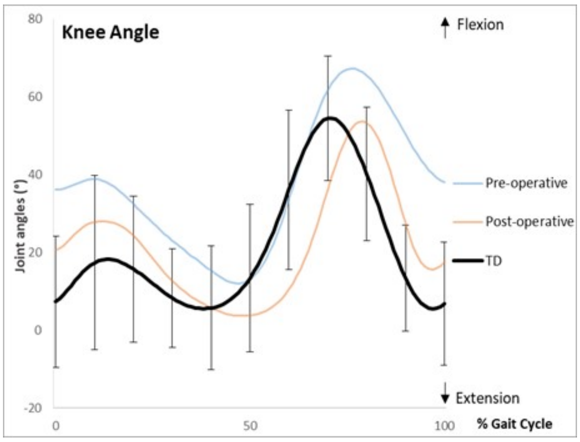


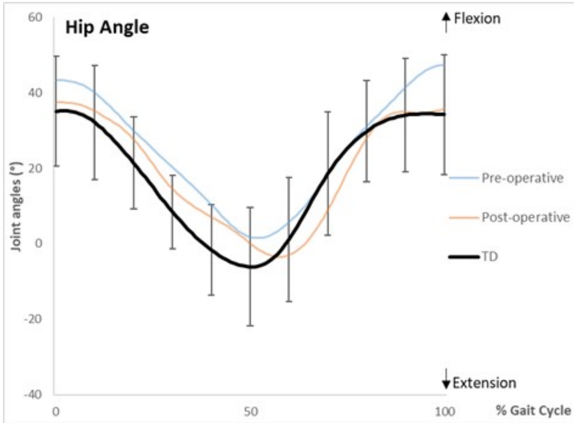
(d)

Figure A.7: Pre-operative and post-operative a. knee angles b. hip angles c. Semimembranosus MTU length d. Psoas MTU length of the Limb_7 compared to TD for a gait cycle.

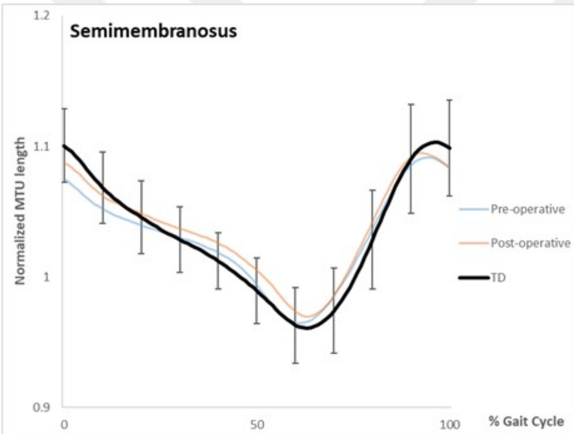
A.8 Limb_8



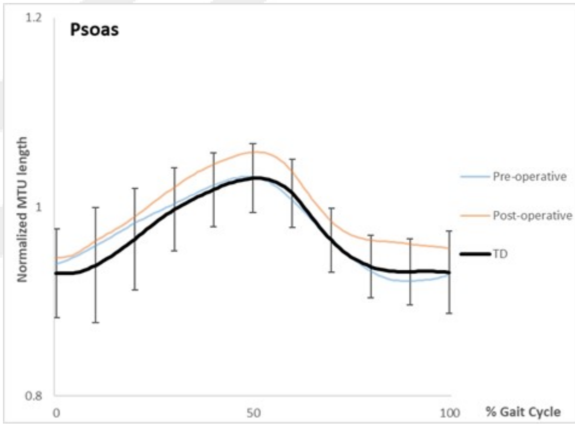
(a)



(b)



(c)



(d)

Figure A.8: Pre-operative and post-operative a. knee angles b. hip angles c. Semimembranosus MTU length d. Psoas MTU length of the Limb_8 compared to TD for a gait cycle.

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