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DISSERTATION

Gluteal Muscle Status and the Impact on Postoperative Joint Loading in Total Hip Arthroplasty Patients

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von

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1. Abstract (deutsch)

Einleitung: Die Belastung des Hüftgelenkes kann bis auf ein Vielfaches des Körpergewichtes ansteigen und dadurch die Lebensdauer sowohl des natürlichen Gelenkes als auch künstlicher Implantate negativ beeinflussen. Ziel dieser Arbeit ist es den Zusammenhang zwischen Art und Umfang der intraoperativen Muskelschädigung bzw. der daraus entstehenden muskulären Veränderungen auf die postoperativ (pOP) in vivo wirkenden Hüftkontaktkräfte zu untersuchen. Darüber hinaus wurde die Änderung der in vivo wirkenden Gelenkbelastung im Zeitraum 3-50 Monate, sowie die Änderungen der gelenküberspannenden Muskulatur bzw. Muskelverfettung dargestellt und quantifiziert. Unsere Hypothese war dabei, dass ein operationsbedingter Muskelschaden der Hüftmuskulatur direkt mit erhöhten in vivo Gelenkkontaktkräften korreliert.

Methoden: Zehn über einen transglutealen Zugang mit instrumentierter Hüftendoprothese versorgte Patienten wurden präoperativ, 3 und 50 Monate pOP untersucht. Für verschiedene Aktivitäten des täglichen Lebens (ADL) wurden die in vivo wirkenden Gelenkkräfte mit simultaner Ganganalyse gemessen. Prä- und postoperative axiale Becken/Bein CT Aufnahmen wurden für die Bestimmung der individuellen bilateralen Muskelvolumina und -verfettung der gelenkübergreifenden Muskeln verwendet. Totale und bereinigte Muskelvolumina (Totales Muskelvolumen -Muskelverfettung) wurden anschließend mit den Belastungen der während unterschiedlichen ADL gemessenen Gelenkbelastungen korreliert.

Ergebnisse: Die höchste Gelenkkontaktkraft wurde mit 418% Körpergewicht bei der Aktivität "Treppen steigen" gemessen. 3 Monate nach Hüfttotalendprothesenoperation konnte noch kein Einfluss des Muskelschadens des Gluteus medius (GMed) gezeigt werden, wohingegen ein vermindertes reines Muskelvolumen des Gluteus minimus (GMin) bereits mit erhöhten Gelenkkontaktkräften in allen getesteten ADL korrelierte (r_s= -0.67* - -0.94**). In den Messungen 50 Monate pOP konnte eine Effekt von verminderten reinen Muskelvolumina des ipsilateralen GMed und Gluteus maximus (GMax) auf erhöhte Gelenkkräfte im Gehen gezeigt werden (r_s=0.53, r_s=0.68*).

Schlussfolgerung: Natürliche Gelenke und Hüftendoprothesen müssen enormen Gelenkbelastungen während verschiedenen ADL standhalten. Unsere Ergebnisse unterstützen allgemein unsere Hypothese, dass eine stark verfettete Glutealmuskulatur zusammen mit einem verminderten bereinigten Muskelvolumen im Zusammenhang mit einer Erhöhung dieser Gelenkbelastungen steht.

2. Abstract (English)

Background: Hip joint loads can exceed many times our body weight (BW) and thus negatively influence the native hip joint as well as implant longevity in total hip arthroplasty (THA) patients. The objective of this study was to investigate the impact of intraoperative muscle damage on postoperative *in vivo* joint contact forces. In addition, longitudinal postoperative changes of the *in vivo* acting contact forces from 3 to 50 months and changes of the muscles acting over the hip joint were reported and quantified. Our hypothesis was that an approach-related damage to the periarticular hip muscles will be directly correlated to higher joint loads.

Methods: We examined ten patients with an instrumented implant using the direct lateral approach (DLA) at 0, 3 and 50 months after THA. *In vivo* joint load measurements with simultaneous gait analysis were performed for different activities of daily living (ADL). Pre- and postoperative transaxial pelvic / lower limb CT scans were used for analysis of individual changes in volume and fatty degeneration of the bilateral periarticular muscles. Finally, total muscle and lean muscle volumes (total muscle volume - fatty degeneration) were correlated with the peak values of the *in vivo* measured hip joint contact forces.

Results: Stair climbing produced the highest hip joint loading of all tested ADL with a maximum of 418% body weight (%BW). At 3 months after THA, the influence of a gluteus medius muscle (GMed) injury had not yet been evident, whereas we found a clear correlation of lower lean gluteus minimus muscle (GMin) volume with higher contact forces during all tested ADL (r_s =-0.67* - -0.94**). 50 months after THA, statistical analysis revealed lower lean volume of the ipsilateral GMed and gluteus maximus muscle (GMax) to have an effect on higher joint loads in walking (r_s =0.53, r_s =0.68*).

Conclusion: The native hip joint as well as artificial arthroplasties have to withstand high loading during daily activities. Our data generally support our hypothesis that an impaired periarticular musculature, especially the abductor muscles, contributes to an increase of these joint loads.

3. Introduction

3.1 Muscle damage in total hip arthroplasty

3.1.1 Indications for total hip arthroplasty

Osteoarthritis (OA) is among the leading causes of physical disability and impairment of quality of life in developed countries. It is characterised by the breakdown of cartilage between two articulating bones, causing deterioration and reactive inflammation of the synovial fluid. However, recent studies also found changes in the subchondral bone, surrounding ligaments and periarticular muscles to play a role in the pathogenesis ¹. Hence, OA can be defined as a multifactorial disease that affects the entire joint and whose etiology bridges biomechanics and biochemistry.

Epidemiological data shows OA to be the most common form of arthritis in Germany. Of all participants aged 18 to 79 years enrolled in the German Health Interview and Examination Survey for Adults (DEGS1) ² published in 2013, 20.2% indicated a physician-diagnosed OA. The most common sites of disease were found to be the knee joint with approximately 50%, followed by the hip with 26%. Further, percentages of OA diagnoses significantly increase in both male and female patients 50 years of age or older. Due to demographic changes and rising life expectancy, it is predicted to become the fourth most common disabling condition by 2020 ³.

Primarily conservative treatment, including analgesics and physical therapy, aims at reducing pain and improvement of joint functionality, although its efficacy remains a topic of discussion ⁴. THA is an effective treatment in patients with symptomatic disease in the hip where conservative treatment has failed. In THA, the hip joint is replaced entirely by an artificial prosthesis. The procedure is mostly utilised in symptomatic OA patients but it may also be used in treating patients with osteonecrosis (2%), developmental hip dysplasia (2%), rheumatoid arthritis (1%) or femoral neck fracture (2%) in an emergency setting ⁵. With 293 surgeries per 100 000 inhabitants, Germany has one of the highest THA case numbers worldwide, by far surpassing the EU27 average of 189 per 100 000 inhabitants. Only in Switzerland were there more THAs performed in 2014 according to latest statistics. In line with the general trend of rising demand in other OECD countries, the total number of THAs performed in German hospitals increased by 15% (+ 39 000) from 2006 to 2014 ⁶.

3.1.2 Periarticular outcome after total hip arthroplasty

The functional outcome after THA is influenced by the postoperative status of the stabilizing musculature. The hip joints are centres of a complex of muscles that not only act on the hip, but also on the knee joints. Figure 1 gives an overview of the hip joint and the periarticular muscles. These muscles can be grouped by their role in enabling the respective movements of the joint into flexors (sartorius and iliopsoas muscle), extensors (lower gluteus maximus muscle (IGMax)), adductors/external rotators (quadratus femoris muscle) and abductors (GMin, GMed, upper gluteus maximus muscle (uGMax), tensor fasciae latae (TFL)). The GMed further functions as the principal internal hip rotator ^{7,8}.

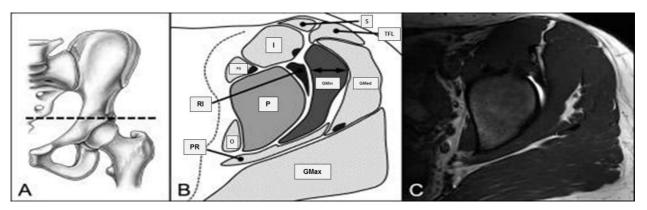


Figure 1: (A) Section at the level of the acetabular roof. (B, C) GMin = gluteus minimus, RI = rectus femoris, P = pelvis, GMax = gluteus maximus, GMed = gluteus medius, TFL = tensor fasciae latae, S = sartorius, PS = psoas, I = iliacus, O = obturator internus, PR = piriformis 9 .

Among the most common causes of damage to the gluteal muscles in particular are degenerative or traumatic rupture of tendon attachments, as well as iatrogenic surgical muscle injury during THA, a potential risk factor for hip dislocation ¹⁰. In addition to an approach-related muscle damage, surgical risks affecting the muscles or their attachments in THA include trochanteric fracture and nerve injury. Direct muscle injury and denervation often consecutively cause fatty degeneration and atrophy of the muscle bellies ^{11,12}. The degree of fat accumulation has been shown to partially determine the muscular function, although many of the molecular mechanisms remain unclear. The transcript factor PPARγ (peroxisome proliferator receptor gamma) was found to play a central role as it regulates lipid uptake and fatty acid synthesis in adipocytes ¹³. However, there are other soft tissue structures, such as ligaments and the joint capsule, surrounding the hip joint that ensure its integral function. These structures are entirely removed during THA and hence may change the post-surgery hip mechanics ¹⁴.

3.1.3 Surgical approaches in total hip arthroplasty

Analogous to other surgical procedures, a variety of different techniques and approaches exist that are commonly used in primary THA patients. The direct anterior (DAA), DLA and posterolateral (PLA) approaches are among the widely recognised standards in THA 15–17

latrogenic injury of the GMed caused by surgical incision is particularly common in the transgluteal DLA ¹⁸⁻²⁰. In this procedure, the acetabulum is exposed by releasing the GMed and GMin from their insertion site at the femur ²¹. While the advantage of this technique lies in preserving the posterior soft tissue, it can cause iatrogenic injury to the anterior part of the GMed. An impaired postoperative regeneration of the gluteal muscles can result in lateral trochanteric pain, gait alterations and a limited range of motion (ROM) ^{11,18,22,23}. Clinically, these patients often present with Trendelenburg limp, i.e. excessive contralateral pelvis drop combined with increased adduction in the hip during walking ²⁴. A review by Demos et al. ²⁵ in 2001 showed mild to severe limping in 11.6% of patients who were operated by the DLA. On the other hand, dislocation of the implant, another considerable risk after THA, was almost eliminated with this technique with only 0.4% of patients affected. This incidence rate of dislocation was shown to be much lower than in patients that have been operated using the posterior approach. The PLA spares the abductor muscles during surgical exposure of the acetabulum and was found to be the internationally most common approach for THA ¹⁹. Dislocation rates for the posterior approach vary from 1 to 5% in the literature ²⁶. An additional alternative approach is the DAA, which has recently increased in popularity. It was shown to result in faster postoperative rehabilitation of the patients while keeping the risk of dislocation at an equally low level ²⁷. In conclusion, each surgical approach has its merits and limitations, and the question of which technique is best for primary THA remains a topic of discussion. This is supported by Jolles et al. ²⁸ who concluded in their Cochrane review in 2014 that the quality and quantity of previous studies have not been sufficient to demonstrate that one approach is superior to others.

Moreover, von Roth et al. ²⁹ found that most primary THA patients are able to compensate for the iatrogenic muscle damage, as they showed no signs of gait impairment during clinical exam. However, this may change when a patient needs a revision surgery, which can result in additional muscle damage along with intensified fatty degeneration. Due to rising case numbers of primary and revision THAs, minimising the intraoperative muscle damage becomes even more important.

Thus, different minimally invasive surgery (MIS) approaches aimed at reducing surgical trauma of the soft tissue have been evaluated over the past decades ^{30,31}. Several studies reviewed the damage of the gluteal muscles in these less invasive and tissue-sparing techniques ^{20,32,33}. In a cadaver study, van Oldenrijk et al. ³² compared several techniques (MIS anterior, anterolateral, 2-incison, posterior) to the standard lateral transgluteal approach, finding only the MIS anterior approach to be superior as it preserved the GMed completely. Muller et al. ²⁰ also showed that damage to the GMed can be limited by using the anterolateral MIS technique rather than the modified direct lateral approach. Postoperative MRI scans in this study revealed a lower degree of fatty degeneration of the anterior third of the GMed at three and 12 postoperative months in patients operated using the MIS anterolateral approach. Additionally, the clinical outcome was improved in this group, showing a lower incidence of Trendelenburg limp at 12 months ^{20,34}. However, MIS approaches may lead to other intra- and postoperative problems such as difficulties in implant positioning and postoperative malposition ^{35–39}. A long-term observation even showed a substantial decrease in time regarding revision surgery in patients with THA using MIS ⁴⁰. Some studies also found indications of increased risk of wound infection, femoral fracture and nerve palsy ^{37,40}.

3.1.4 Assessment of surgical muscle injury

Patients that underwent hip replacement surgery generally show a postoperative improvement in joint mobility and quality of life, but there may also be negative consequences from THA as described before (see 3.1.3). By examining different indicators, several studies previously tried to determine surgical injury and the postoperative status of the hip muscles in THA patients.

Recent studies attempted to quantify direct muscle injury after orthopaedic surgery by measuring elevations in serum markers such as creatine kinase, creatine phosphokinase and serum myoglobin ^{41,42}. Although reproducible trends in serum enzyme levels were noted, the data did not show one particular surgical approach to be superior.

Another tool for assessment of the hip muscle status are clinical function tests. Gore et al. ⁴³ used these methods in 1986 to show that patients with revision surgery after THA needed significantly more assistive devices, walked slower and had a reduced ROM compared to primary replacements. More recent studies looked at spatiotemporal parameters in functional testing of THA patients, including step length and speed of gait ⁴⁴

A Trendelenburg gait pattern is one of the widely recognized standard signs of abductor muscle impairment of the lower limb. It describes a pelvis tilt above level in the unsupported stance phase of walking, as the gluteal muscles (GMed, GMin) cannot stabilise the pelvis on the load bearing side. An impaired gait pattern, such as the Trendelenburg limp, has also been related to higher in vivo joint contact forces ^{45,46}. Other standard tests for assessment of hip joint functionality include measurements of unlimited walking distance, Short Physical Performance Battery (SPPB), 6-minutes-walking test (6MWT), stair climb and the Timed Up and Go test (TUG) ^{47–49}. Most of these tests are also encompassed in the standard clinical scores that measure hip muscle function in daily medical practise (see 4.6) ^{50,51}.

Electrophysiological studies using electromyography (EMG) also allow assessment of postoperative muscle functionality. Baker et al. ²³ examined abductor function after THA, looking at gluteal denervation marked by spontaneous electrical activity that can be seen as fibrillation potentials. A study by Ramesh et al. ⁵² showed injury of the superior gluteal nerve in patients operated using the DLA leading to detectable electrophysiological muscle damage, as well as a positive Trendelenburg sign.

Finally, multiple studies evaluated postoperative changes in muscle volume of the periarticular hip and thigh muscles in OA and THA patients ^{53–58}. Several studies reported overall hip muscle atrophy in OA patients by comparing cross-sectional areas (CSA) of the affected side with the contralateral healthy hip ^{7,8,54–56}. Other longitudinal studies evaluated CSA in pre- and postoperative scans showing a significant increase of the thigh muscles (iliopsoas, quadratus femoris, adductors, hamstrings) ^{53,57}. However, no reports have shown a volume increase of the gluteal muscles, whereas Uemura et al. ⁵⁷ reported the thigh muscles, GMed and GMax to recover in volume after THA in a two-year follow-up. Although the literature remains contradictory, volume measurements using radiological scans remain a valid method in determining the status of the hip and thigh muscles.

The muscle status is further determined by atrophy and fatty degeneration ^{59–61}. Fatty degeneration is caused by muscle injury or iatrogenic surgical damage and defines the replacement of contractile muscle tissue with fat ³⁴. In rotator cuff of the shoulder, fatty degeneration has been shown to negatively influence the functional outcome and muscle strength after repair ⁶².

With a sensitivity of 89 to 100%, ultrasound was determined to be an accurate method of depicting fatty degeneration in superficial muscles of the rotator cuff (supra- and infraspinatus muscles) ⁶³. Garcia et al. ⁶⁴ found ultrasound to be moderately accurate when looking for tendon avulsion of the GMed in primary THA patients.

Over the past decade, MRI has become a standard tool for assessing traumatic tendon and muscle injuries in THA patients ^{11,34,65,66}. Teratani et al. ⁶⁵ looked for muscle strain injuries in THA using postoperative MRI, whereas other studies tried to detect abductor muscle avulsion from the greater trochanter ⁶⁶. Pfirrmann et al. ¹¹ not only used MRI to look for tendon defects of the GMed and GMin muscles, but also measured their degree of fatty degeneration in patients after lateral transgluteal THA. They found significantly higher defects in abductor tendons, fatty degeneration of the GMed and the posterior third of the GMin in symptomatic compared to asymptomatic THA patients. Similarly, data from 38 primary THA patients examined in a study by Müller et al. ⁶⁵ found tendon defects and fatty atrophy of the GMin in up to 65.8% of the subjects.

In addition to ultrasound and MRI, previous studies have proven computed tomography (CT) to be a valid method for assessing the periarticular hip muscle status and fat content ^{61,68–71}. Daguet et al. ⁷¹ used non-enhanced CT for evaluation of fatty degeneration in a healthy population finding an anteroposterior gradient from the hip flexors (mean 2%) to the extensors (mean 10%). Their results also suggest a higher fat content to be associated with greater age, higher body-mass index (BMI), lower physical activity, Trendelenburg limp, a lower performance in the Six-Meter Walk and the Repeated Chair Stand test.

3.2 Hip joint loading

3.2.1 Mechanics of the hip joint

Looking at the statics of the hip as a physical system, one finds different loads, which together with the lever arm of each individual muscle, determine moments that are responsible for the equilibrium of the pelvis. For a translational equilibrium, the combination of all acting forces needs to be zero in all axes $F_{x, y, z}$. Figure 2 shows the different axes of the femur in a coordinate system. Because of the offset and anteversion of the proximal femur, torque moments are also applied, hence, the sum of these moments must be zero for a rotational equilibrium. Hip movements are referred to as the movement of the femur in relation to the pelvis around the hip joint centre.

As a ball and socket joint the hip has a large ROM in all three planes. In a healthy subject, this allows abduction/adduction of 70°, flexion/extension of 130°/10° and 50° rotational movements.

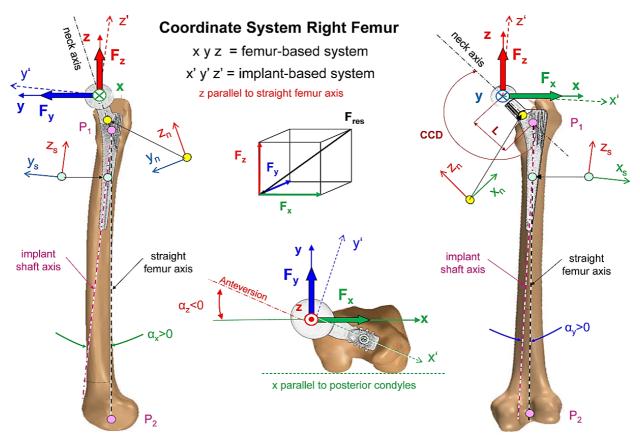


Figure 2: Coordinate system of right femur and implant. x, y, z = axes of femur coordinate system. x = parallel to posterior contour of condyles. P1 = intersection of neck axis and femoral midline. P2 = middle of intercondylar notch. z = straight femur axis between P1 und P2. Force components F_x , F_y , F_z act in directions x, y, z. The implant is turned clockwise by angles α_z , α_y and α_x around the femur axes z, y, x. α_z = anteversion of neck (negative). x', y', z' = axes of implant. x_n , x_n , z_n = coordinate system at distal end of implant neck. x_s , y_s , z_s = coordinate system of stem 80mm below head centre 72 .

During walking, the body temporarily comes into a one-legged-stance as the leading leg leaves the ground and steps forward. At this moment, the entire BW pulls the body downwards to lean over, however, the hip abductor muscles counterbalance this movement. Hence, the acting principle of the hip can be compared to a lever arm, marked by alternating loads and efforts. During standing, the BW acts on both hip joints, thus, in a perfectly balanced stance, each side would carry half the weight. However, our in vivo measurements of joint reaction forces showed an averaged maximum of 112%BW for two-legged-stance and 323%BW for one-legged-stance. Thus, the abductor muscles play a central role in pelvic stability and balance and become even more important in dynamic movements.

Gait analysis differentiates between the stance phase, when the foot is on the ground and its return during the swing phase. The abductors consequently have to balance the static leg as well as the forward movement of the other leg. A normalized gait cycle is pictured in figure 3. The force moment, determined by muscle force and arm, applied by the abductors is correspondingly greater during the stance than the support phase as figure 4 shows. However, even when no BW is applied, the hip is never totally unloaded, as swinging the leg forward requires muscles to control this motion.

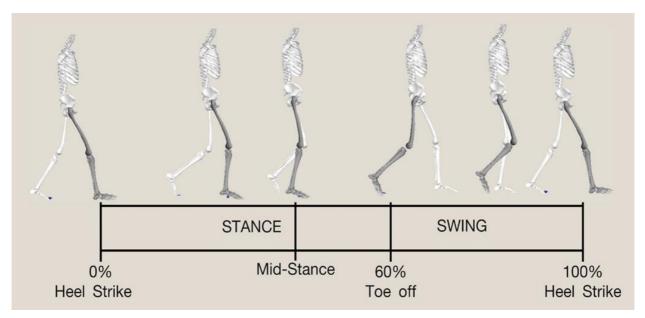


Figure 3: Normalised gait cycle of right limb with the stance phase ending at 60% with the toe off the ground and beginning of swing phase ⁷³.

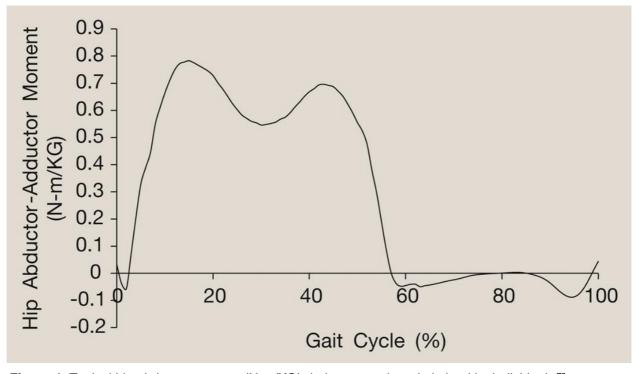


Figure 4: Typical hip abductor moment (N-m/KG) during one gait cycle in healthy individuals 73.

If the muscle arm length is changed by a pathology, the muscle force then has to change to achieve the same force moment. Patients with OA will thus try to reduce joint reaction forces by leaning towards the painful hip, so that the moment arm and force applied by the abductors are reduced. An alternative to reduce hip pain is to use a walking cane on the contralateral side, which also aims at decreasing the hip abductor forces. Clinically, impairment of the hip abductors often leads to the Trendelenburg gait pattern described in 3.1.4. The body will naturally try to compensate for unilateral weakness by changing the direction and transferring loads to other joints. By assisting with this load transfer, the knee was shown to be particularly at risk for injury in patient with diseased hip joints ^{74,75}.

3.2.2 Measurements of hip joint loads

Today, total hip replacement needs to meet patients' increasingly high expectations concerning implant longevity and postoperative quality of life ⁵. Consequently, innovations in implant design continuously aim to improve anatomic fit and material quality to ensure perfect function. Developing and testing new prostheses thus requires knowledge of the joint loading that will act in the postoperative setting. These joint loads can exceed our BW many times and are not only determined by the periarticular muscle status as described in 3.1, but the implant angle and lever arm have also been shown to play a role ^{76,77}.

Measuring joint contact forces is difficult by nature. Previous research in gait analysis mostly used computational muscle models to estimate resultant forces in the hip joint. Although some of the results of these studies are generally comparable with in vivo load measurements, they have often been shown to overestimate contact forces. Validation of these models against measurements obtained through instrumented prostheses remains rare ^{78–83}. In 1988, Davy et al. ⁸⁴ published the first in vivo measured contact forces, but their analysis was limited to only a few exercises. Bergmann et al. ⁴⁶ proceeded to use instrumented hip implants to measure hip contact and ground reaction forces with simultaneous gait pattern analysis. The data obtained with these implants enabled them to document the mechanical loading of the hip joint and the proximal femur. The averaged data showed hip joint loads to be up to 238%BW in level walking at 4 km/h and slightly lower loads in one-legged-stance. Stair climbing was found to produce the highest contact forces overall, with up to 251%BW in ascent and 260%BW when descending.

As the acting forces during other activities were significantly lower than the above, the authors argued that implants in development should be tested with loading conditions that are similar to those in walking and stair climbing ⁸⁵.

Since then, a much broader range of activities involving the hip joint has been measured using instrumented implants. Schwachmeyer et al. ⁸⁵ published data on loads in physiotherapeutic exercises, and Damm et al. ⁸⁶ examined conditions in walking with forearm crutches, both being relevant rehabilitative activities in the postoperative management of THA patients.

3.2.3 Muscle activity patterns in activities of daily living

The hip joint plays a central role in almost all activities humans perform during their daily life, such as the two-legged-stance, level walking, sitting down and standing up from a chair, and stair negotiation. He et al. ⁸⁶ used EMG data to analyse activity levels of different muscle groups of the lower limb involved in these movements. Looking at the hip joint, they found the periarticular muscles working in an agonist-antagonist way to enable full ROM as described in 3.2.1. However, normal gait was shown to only take the hip joint through a 40-50° rotation, 35° flexion and maximum 10° extension ⁸⁷. Extension is mainly actuated by the semitendinosus and the IGMax, whereas flexion is carried out by the TFL, rectus femoris and iliopsoas muscle. The GMed functions as the principal internal rotator of the hip. Results show that as the main flexor, the activity levels for the TFL are the highest while sitting down, during the swing phase of level walking (see figure 3) and during the lifting phase when climbing up stairs.

By contrast, the gluteal muscles and the semitendinosus reach the highest activity levels while standing up, during the support phase of walking and contact phase of stair climbing ^{76,86,88–91}. All these complex movements may become difficult to perform when muscle function is impaired by injury, age, disease or incomplete postoperative rehabilitation. Although other muscles may hypertrophy and compensate in these cases, there is little knowledge about how much weakness may be tolerated before a muscle decompensates in its function. Van der Krogt et al. ⁹⁰ developed a muscle-driven simulation to examine the extent of weakness muscles can be subjected to before walking is affected. Gait was found to be the most sensitive to weakness in hip abductors. For most muscles, normal gait was still possible when removing the muscle from the model, apart from the GMed. While level walking consists of the assimilation of numerous actors, the gluteal muscles were found to play the central role determining up to 95% of the joint loading.

When looking at the influence of the gluteal muscle status on joint contact forces, most studies correlate gait patterns and ground reaction forces, while the in vivo situation often remains unclear ⁹².

3.3 Aim and hypothesis

The aim of this study was to investigate the impact of the hip muscle status on postoperative in vivo hip joint loading in THA patients. Based on theoretical considerations and previous research, our hypothesis was that an impairment of the periarticular muscle function causes higher in vivo joint loads. We therefore investigated the status of the ipsi- and contralateral gluteal muscles and the TFL one day prior (0M), 3 (3M) and 50 months (50M) after THA surgery. We determined the hip muscle status by evaluating the degree of fatty degeneration and muscle volumes in pelvic CT scans. Further, we differentiated the muscle volumes into lean muscle and fat volume. As a primary endpoint, we assessed the correlation of the hip muscle status and hip joint loads. The resultant in vivo hip joint loads during different ADL were measured using standard motion and gait laboratory techniques. The secondary endpoints of joint functionality and pain were assessed by postoperative physical examination combined with standardised questionnaires including the Harris Hip Score (HHS), Visual Analog Scale (VAS), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and EuroQol-5D-3L (EQ-5D-3L). The in vivo data obtained in this study are unparalleled worldwide and the results may influence the development of future prosthetic hip implants and lead to an optimization of the joint biomechanics adapted to the surgically caused muscle injury. It may also help with postoperative rehabilitation and long-term clinical management of THA patients.

4. Materials and Methods

4.1 Study design

This multicentre, non-interventional study (DRKS-ID: DRKS00000563) was conducted at Julius Wolff Institut / Berlin Center for Regenerative Therapies and Charité Universitätsmedizin Berlin, Germany. Ethical approval from the Charité Ethics Commission (EA2/057/09) and informed written patient consent were obtained prior to data collection.

All THA surgeries were performed at Sana Kliniken Sommerfeld / Kremmen by one orthopaedic surgeon. Patient analyses were performed one day before the surgery, as well as at two additional time points: 3M and 50M post THA surgery. During each visit, study subjects received a pelvic \pm lower limb CT. Prior to the operation and at time point 50M, patients also received a physical examination by a board certified orthopaedic surgeon. Moreover, hip joint loads with synchronous gait analysis data were collected during all postoperative appointments. Surface EMG and clinical scores evaluating the patient's hip pain and overall functionality were only obtained at 50M postoperatively. Table 1 below summarises the exams and measurements that took place at the different time points throughout the study.

Table 1: Overview study design, indicative of exam taken place.

	0 months preoperative	3 months postoperatively	Average 50 months postoperatively
Physical exam	✓		√
CT pelvis +/- LE	✓	✓	✓
Gait analysis + in vivo load measurements		1	1
Surface EMG			✓
Clinical scores			✓

4.2 Patients

We examined ten (n=10) patients that underwent THA for primary arthritis of the hip. All study subjects received an instrumented cementless stem of the "Sportono" type, which is considered clinically to be one of the most successful types ⁹³. Two study subjects (H2, H5) were previously provided with a standard hip implant on the contralateral side, one of them (H5) needed two revision surgeries due to periprosthetic joint infections. Study subjects were recruited using the following criteria:

Inclusion criteria

- Age: minimum 50 years, maximum 65 years
- Need for conventional total hip prosthesis due to primary arthritis of the hip
- Commitment and motivation to participate in a long-term clinical study
- Informed written consent

Exclusion criteria

• Active implants (e.g. cardiac pacemakers)

4.3 The instrumented total hip arthroplasty

4.3.1 Implant design and instrumentation

The instrumented hip joint prosthesis that our study subjects received was designed to measure all three force components together with the three moment components acting between the femoral head and cup ⁹⁴. Figure 2 shows the resultant force F_{res} obtained by addition of the force vectors of F_x, F_y and F_z. Additionally, the implant also needed to meet several technical and clinical requirements, including biocompatible materials, hermetically sealed electronics and long-term power supply. Finally, function and fixation of a clinically proven prosthesis needed to be the basis when developing the instrumented implant.

The instrumented implant used in our study consisted of the "Cemented Tapered Wedge" (CTW) prosthesis (Merete Medical GmbH, Berlin, Germany) and an XPE inlay (Durasul, Zimmer GmbH, Winterthur, Switzerland) ⁹³. In short, the inductive power is supplied through a small coil and the deformation measurements are transmitted using telemetry. These signals and the subject's movements are recorded simultaneously on videotape.

The external equipment calculates the contact forces and displays real time loads. A detailed description of the implant mechanics has been published previously ^{93,95}.

4.3.2 Surgical technique and rehabilitation protocol

All patients were operated using the transgluteal DLA, a widely accepted technique as stated in 3.1.3. According to this procedure, the skin incision was made laterally along the greater trochanter (GT), before going through subcutaneous fat tissue to open the deep fascia lata. By incising the iliotibial band, the surgeon gained access to the gluteal muscles of which approximately 5 cm were detached from the GT at its anterior third. The resulting flap, consisting of the gluteal and vastus muscle, was lifted and the articular capsule, femoral head and neck resected. The acetabulum was removed and the prosthetic socket put in place. In the next step, the leg was externally rotated to a maximum extent in order to prepare the medullary cavity of the femur. The stem of the femoral head was put in place followed by repositioning of the leg. An intraarticular drain was placed and the gluteal muscle sutured along the incision line. Finally, the iliotibial tract and subcutaneous fat were readapted, the skin incision closed and covered with a sterile dressing.

All patients followed the same standardised postoperative rehabilitation protocol. During the first four weeks after surgery patients were seen on the third or fourth, 14th, 21st and 28th postoperative day (POD), undergoing in vivo measurements of the hip during different physiotherapeutic exercises (ROM, -stance, walking with forearm crutches). Patients were encouraged to further exercise independently at home and measurements were repeated at month six and one year follow up. Data obtained during these measurements have been published before ^{94,96}.

4.4 Assessment of periarticular muscle status

4.4.1 Radiological imaging

All study subjects received a preoperative CT scan of the pelvis \pm lower limb at the radiology department at Charité Universitätsmedizin Berlin Campus Virchow and Campus Mitte. The postoperative imaging was realised by pelvic and lower limb CT scans using helical CT (Toshiba Aquilion ONE software version V4.61GR004 and Aquilion 64 software version V3.30GR501, Tokyo, Japan; 120kV, 200mAs, FOV 40cm). Since the scans were obtained in two different radiology departments, we standardised all images by reconstructing them into sequences of 5mm slice thickness.

4.4.2 Muscle volumes

All scans obtained were imported into Osirix v.5.8.2 (Osirix Imaging Software, Geneva, Switzerland) before a transverse image series of each patient was selected for further analysis. The series were then loaded in the imaging software Amira (Visage Imaging, Berlin, Germany). CT-based muscle tissue measurements and three-dimensional reconstruction have been shown to be very accurate for diagnostics of the hip joint and its stabilizing musculature ^{69,97}.

To check for variation in patient body heights, muscle volumes of the ipsi- and contralateral gluteal muscles and TFL were measured between the anatomic landmarks of the fourth lumbar vertebra (L4) and the lesser trochanter (LT). In every fifth slice (5mm thickness), the muscles were manually outlined as shown in figure 5 and the intermediate surfaces completed using the interpolating function.

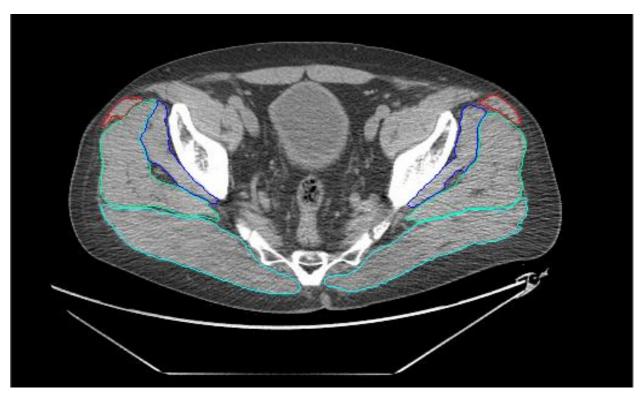


Figure 5: Preoperative transverse CT scan with manually outlined gluteal muscles and TFL on ipsi- and contralateral side. Blue = GMin, green = GMed, light blue = GMax, red=TFL.

When outlining the muscle cross-sections, we adjusted the threshold, which allowed us to differentiate muscle tissue from surrounding structures such as tendons, bones and fatty streaks. Then, three-dimensional reconstructions of the measured muscles were generated as shown in figure 6. Using the fat ratios measured as described in 4.4.3 below and the total muscle volumes, we calculated the fat and lean muscle volume of each muscle.

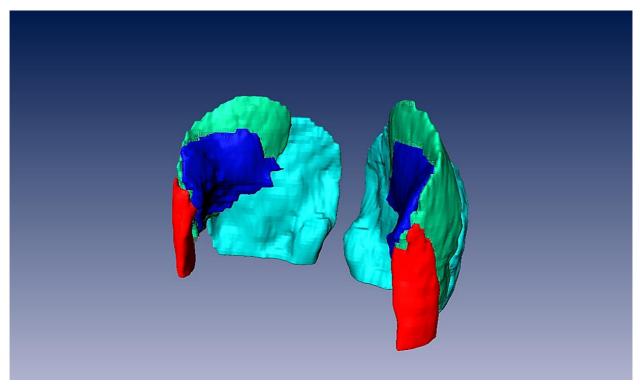


Figure 6: Three-dimensional reconstruction of volumes of gluteal muscles and TFL between L4 and the LT.

4.4.3 Fatty muscle degeneration

One of the radiologic characteristics of fat and muscle tissue is their variation in radiation attenuation that can be expressed in Hounsfield units (HU) ⁹⁸. Each pixel in a CT scan is assigned a Hounsfield number, which is a rescaled normalized function of the linear attenuation coefficient. The CT Hounsfield scale is calibrated such that the HU value for water is set to 0 HU and that for air is -1000 HU ⁹⁹. Thus, HUs allow for the quick differentiation between tissues in medical imaging.

The degree of fatty degeneration of the hip muscles determined in 3.1 was assessed using a modified approach described by Engelken et al. ^{29,100}. For the gluteal muscles, three consecutive slices were selected for analysis by going 30 mm cranial of the GT as a reproducible anatomic landmark. Since the TFL has its largest extent in a lower region, we measured its fatty degeneration in three consecutive slices (30 mm) inferior to the superior base of the GT.

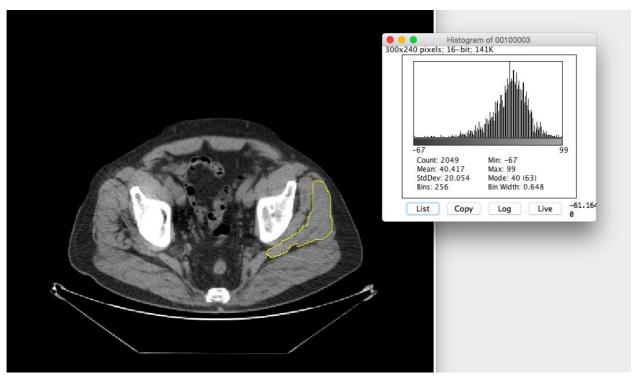


Figure 7: Transverse CT scan for assessment of fatty degeneration of left GMed. The histogram on the right shows the greyscale distribution of pixels.

Daguet et al. ⁷¹ previously measured hip muscle fat content using CT in healthy subjects. We used their classification system and cut-off values for our analysis. The psoas muscle was chosen as a reference point for muscle tissue and showed a mean density of 60 +/- 15 HUs. The mean of the subcutaneous fat tissue was -108 +/- 16 HUs. Pixels within two standard deviations of the reference, thus 30 and 90 HU, were defined as pure muscle. Analogously, pixels with a density of < - 75 HU were classified as pure fat. Between those boundaries, values of 29 to -5 HU were counted as 25% fat, -6 to -40 HU as 50% fat and -41 to -75 as 75% fat. The three consecutive slices were saved in a 16-bit format and loaded into ImageJ 1.44 (Wayne Rasband, National Institutes of Health, Bethesda, Maryland, USA) for further analysis.

When analysing the fatty degeneration of the muscles the transverse surfaces were analysed as one entity and not further divided. Using the histogram tool, the software calculated the distribution of grayscale pixels for the manually outlined muscle surfaces as shown in figure 7. Finally, the degree of fatty degeneration of a muscle was calculated using the following equation:

$$Fat \ ratio = \frac{pixels (fat)}{pixels (fat) + pixels (muscle)} \times 100$$

4.5 Gait analysis with in vivo load measurements

The in vivo joint loads of our patient collective were measured on the same days as the CT scans of the hip and lower extremities were obtained for assessment of the muscle status (see 4.4). At both, 3M and 50M, all patients were in good physical condition, allowing them to perform the exercises without any obvious limitations. Except for H5, who had had revision surgery of her contralateral THA, our subjects did not present with any obvious impairment of their gait patterns.

The instrumented implant used in our study is described in 4.3.1. For measurements in the gait laboratory, our patients were equipped with reflective skin markers and electrodes that followed a preset pattern of anatomic landmarks. Simultaneously acquired motion data, captured using a Vicon MX camera system (Oxford, UK) allowed for analysis of velocity of the segments and hip motion angles. We also obtained ground forces through AMTI force plates (Watertown, USA) in the floor and recorded lower extremity muscle activity using surface EMG. The external measurement system was described in detail elsewhere ^{95,101}. The combination of synchronous motion, muscle activation and force measurements is the basis of a model that calculates internal stress of the musculoskeletal system.

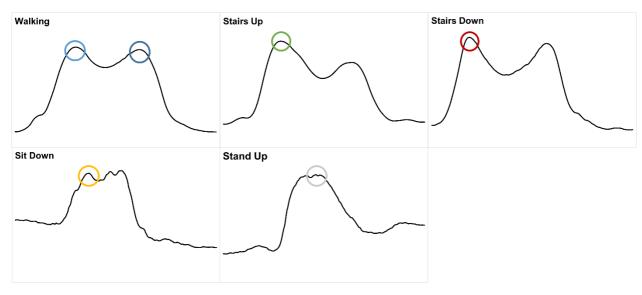
In individual measurements, all patients followed an investigation protocol that consisted of various exercises including the most frequent ADL. These were level walking at a self-selected speed, stair climbing without support, standing up and sitting down, squatting, jogging and standing in a one-legged-stance ⁷². In this report, we first analysed the activities of level walking, stair climbing, standing up and sitting down. All basic activities and conditions of our measurements are listed in table 2 below.

Table 2: Protocol activities at 3M and 50M postoperative measurements.

Activity	Measurement conditions
Walking	Level walking, Speed = 1.0-1.3 m/s; Average = 1.1 m/s
Stance	Shifting weight from both to one leg and back
Sit Down / Stand Up	Without support. Seat height = 45cm
Stairs Up / Stairs Down	Without support. Step height = 19.8cm, width = 26.3cm
Squat	Max. knee flexion
Jogging	1.9 – 2.8 m/s (7-10 km/h) on treadmill

Previous research found the gluteal muscles and TFL to play a major role in walking, hip abduction and posture balance ^{88–90}. Their activity during the ADL included in this study has equally been studied before and is shown in figure 8B ^{91,102,103}. Figure 8A shows the average load cycles of these activities and the investigated peak values. Data for standing up and sitting down was only obtained for six out of eight subjects at 3M. Analysis of joint loads from other activities, included in the investigation protocol but not in this report, will be a focus of our study group in the future.

(A)



(B)

ADL	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
Walking 1 Peak	+	+	+	+
Walking 2 Peak	+	+	-	-
Stairs up 1 Peak	+	+	+	+
Stairs Down 1 Peak	+	+	+	+
Sit Down Max	+	+	+	+
Stand up Max	+	+	+	+

Figure 8: (A) Average load patterns of in vivo measured hip joint contact forces during different ADL. Indicated are investigated peak values. (B) Activity pattern of gluteal muscles and TFL during ADL. + indicates the muscle to be active at investigated peak values.

All further analyses in this study are based on the resultant force (F_{res}), which results from the addition of the force vectors F_x , F_y and F_z described in 3.2.1 (see figure 2) ⁹⁴. The resultant forces used in our measurements have been converted from Newton (N) to %BW. The sum of the three moment vectors M_x , M_y and M_z equals the resultant friction moment M_{res} measured in newton meters (Nm). For the remainder of this study, a force refers to the peak value during the loading cycles shown in figure 8A, unless otherwise indicated. Thus, a "load" refers to the sum of all six components.

4.6 Clinical scores

We used the following standardised scores to assess the clinical outcome and disease-related quality of life: 1. HHS; 2. WOMAC; 3. EuroQol-5D-3L; 4. VAS Pain. Scores 1-3 consist of multiple choice questions asking the patient for the single most adequate answer. The HHS additionally includes the assessment of ROM of the hip joint during physical exam.

4.6.1 Harris Hip Score

The HHS ⁵⁰ questionnaire assesses joint pain and functionality of the hip using a scale ranging from 0 to a maximum of 100. Patients scoring above 90 are considered to have full function in their hip joints. Scores between 80 and 89 indicate a generally good functionality, whereas scores below 70 are consistent with a rather poor outcome. Answers to the following items are summed up to obtain the overall score:

То	tal Score	max. 100 pts
•	Maximal range of motion	max. 5 pts
•	Difference in leg length	max. 1 pts
•	Contractures	max. 3 pts
•	Limping	max. 11 pts
•	Hip joint pain	max. 44 pts
•	Ability to sit on chair	max. 5 pts
•	Distance walked	max. 11 pts
•	Walking support	max. 11 pts
•	Use of public transportation	max. 1 pts
•	Stair climbing	max. 4 pts
•	Activities - shoes/socks	max. 4 pts

4.6.2 Western Ontario and McMaster Universities Osteoarthritis Index

The WOMAC ⁵¹ is commonly used to evaluate the status of patients with cox- or gonarthrosis and exists in its German version for clinical use since 1996. Items are grouped and assess pain, rigidity and joint functionality. High scores after adding up all items indicate an impaired functionality. The subgroups contain the following items:

Pain (0-20 pts)

Functionality (0-68 pts)

•	Walking	max. 4 pts
•	Stair climb	max. 4 pts
•	At night	max. 4 pts
•	Sitting / lying down	max. 4 pts
•	Standing	max. 4 pts
Rigio	lity (0-8 pts)	
•	Mornings	max. 4 pts
•	Daytime	max. 4 pts

Stair climb max. 8 pts Get up max. 4 pts Standing max. 4 pts

 Bend forward 	max. 4 pts
 Level walking 	max. 4 pts
 Get into car 	max. 4 pts
 Grocery shopping 	max. 4 pts
 Put on socks 	max. 8 pts
 Get out of bed 	max. 4 pts
 Lying in bed 	max. 4 pts
 Get in/out bath tub 	max. 4 pts
 Prolonged sitting 	max. 4 pts
Sit on toilet	max. 4 pts
 Housekeeping activities 	max. 8 pts
Total Score	max 96 pts

4.6.3 Visual Analogue Scale Pain

The VAS Pain ^{104,105} aims at evaluating subjective pain sensation by asking the patient to indicate a point on a horizontal continuum line ranging from no pain at all to worst possible imaginable pain. The indicated intensity of pain is then quantified into a score between 0 (no pain) and 10 (worst pain the patient could imagine).

4.6.4 EuroQoI-5D-3L

The EuroQoI-5D-3L ^{106,107} questionnaire is a standardised tool for measurements of the generic health status. First developed in 1990, it is not disease-specific but widely accepted today, with numerous countries having developed their own value sets. The first part consists of a health state description including the following dimensions: mobility, self-care, usual activity, pain/discomfort and anxiety/depression. The EQ-5D 3 level version gives the patient three options to best describe each item. The second part consists of a visual analogue scale as described in 4.6.3.

4.7 Clinical assessment of function

At 50M, all study subjects received a clinical examination. The orthopaedic physical exam included both objective and subjective parameters to evaluate the status of a patient. With the neural-zero-method, the maximum ROM of the hip joint is tested in an objective way during flexion/extension, abduction/adduction and internal/external rotation.

Patients were further tested for pain above the GT, in the inguinal region when applying pressure and peripheral blood flow, motor and sensor neuropathy. Functional testing of the GMin and GMed was performed by looking for the Trendelenburg sign when the patients were asked to perform one-legged-stance or 10 meters of level walking ¹⁰⁸.

4.8 Statistical analysis

Statistical analysis was performed using SPSS Statistics (IBM, Version 22, NY, 2013). The volume and fat content of each hip muscle was reported as the mean and standard deviation. Due to the small subject number (n=10), we assumed and showed the samples to be non-parametrically distributed. The Mann-Whitney U test was used for independent inter-individual central tendencies. Intra-individual comparisons were evaluated using Wilcoxon's test for dependent and non-parametrical samples. Correlations between the volume and fat ratio of a muscle and the continuous variable in vivo joint load were analysed using of the Spearman rank test (r_s). A p-value of 0.05 (two sided) was considered significant.

5. Results

5.1 Patients

The demographic characteristics of the patients at OM, 3M and 5OM after THA are shown in table 3 below. At 5OM, only 9 patients were included as subject H1 dropped out of the study. The patient collective was predominantly male (male-female ratio = 8:2 at 3M, 7:2 at 5OM).

Table 3: Demographic characteristics of patient collective at time points 0M, 3M and 50M after THA. Indicated are average values \pm SD, N = number, BMI = body mass index.

	0 months preoperative (N=10)	3 months postoperative (N=10)	Average 50 months postoperative (N=9)
Age (years)	56.9 ±6.4	57.3 ±5.9	61.4 ±6.4
Sex			
female, N (%)	2 (20)	2(20)	2 (22.2)
male, N (%)	8 (80)	8(80)	7 (77.7)
Body height (cm)	174 ±1.0	174 ±1.0	174 ±6.0
Body weight (kg)	88.7 ±13.1	86.9 ±11.4	91.4 ±14.7
BMI (kg/m²)	29.4 ±4.7	28.8 ±4.3	30.3 ±4.6
Ethnic background			
Caucasian, N (%)	10 (100)	10 (100)	9 (100)

5.2 Status of periarticular hip muscles

The assessment of the degree of fatty degeneration of the hip muscles described in 4.4.3 allowed differentiation of the total muscle volume into its two components, lean muscle and fat volume. In order to illustrate the time course of postoperative recovery of the analysed muscles, the changes in different volumes are shown in tables 4 and 5 below.

Table 4: Ipsilateral total muscle, lean and fat volume. Volumes in [cm³], indicated are averages ±SD

	Ipsilateral	ОМ	3M	50M
Gluteus	Muscle volume	34 ±6.3	25 ±3.7	28 ±4.0
Minimus	Lean volume	30 ±7.4	21 ±4.4	23 ±3.3
	Fat volume	5 ±2.1	5 ±3.0	5 ±2.4
Gluteus	Muscle volume	119 ±15.5	125 ±16.1	129 ±21.4
Medius	Lean volume	101 ±14.9	104 ±19.0	107 ±16.2
	Fat volume	17 ±8.6	21 ±13.0	23 ±9.6
Gluteus	Muscle volume	260 ±38.3	252 ±40.0	278 ±49.3
Maximus	Lean volume	211 ±31.3	193 ±57.1	225 ±43.8
	Fat volume	49 ±20.2	52 ±22.6	53 ±17.5
Tensor	Muscle volume	26 ±6.7	29 ±6.1	31 ±12.5
Fasciae	Lean volume	21 ±6.4	27 ±6.2	28 ±11.2
Latae	Fat volume	5 ±3.4	2 ±1.4	4 ±2.0

Table 5: Contralateral total muscle, lean and fat volume. Volumes in [cm³], indicated are averages ±SD

	Contralateral	ОМ	3M	50M
Gluteus	Muscle volume	34 ±8.1	29 ±5.7	35 ±7.9
Minimus	Lean volume	30 ±10.1	26 ±7.6	31 ±9.4
	Fat volume	5 ±2.6	3 ±3.0	4 ±2.1
Gluteus	Muscle volume	130 ±23.9	131 ±18.5	132 ±24.7
Medius	Lean volume	112 ±26.5	114 ±29.4	112 ±28.4
	Fat volume	18 ±9.0	17 ±15.7	19 ±10.6
Gluteus	Muscle volume	288 ±54.4	283 ±45.6	288 ±59.7
Maximus	Lean volume	241 ±46.8	236 ±58.4	235 ±52.4
	Fat volume	47 ±16.8	48 ±26.0	53 ±16.5
Tensor	Muscle volume	28 ±10.0	30 ±8.4	28 ±10.0
Fasciae	Lean volume	23 ±9.5	27 ±8.7	24 ±9.1
Latae	Fat volume	4 ±2.3	3 ±1.4	5 ±3.3

5.2.1 Total muscle volume

The *preoperative* average muscle volume on the ipsilateral side was 34 ± 6.3 cm³ for the GMin, 119 ± 15.5 cm³ for the GMed, 260 ± 38.3 cm³ for the GMax and 26 ± 6.7 cm³ for the TFL. On the contralateral side, the *preoperative* muscle volume was 34 ± 8.1 cm³ for the GMin, 130 ± 23.9 cm³ for the GMed, 288 ± 54.4 cm³ for the GMax and 28 ± 10.0 cm³ for the TFL. Figure 9 shows the changes and variance in total muscle volume at *OM*, *3M* and *50M* for both the ipsi- and contralateral gluteal muscles and TFL.

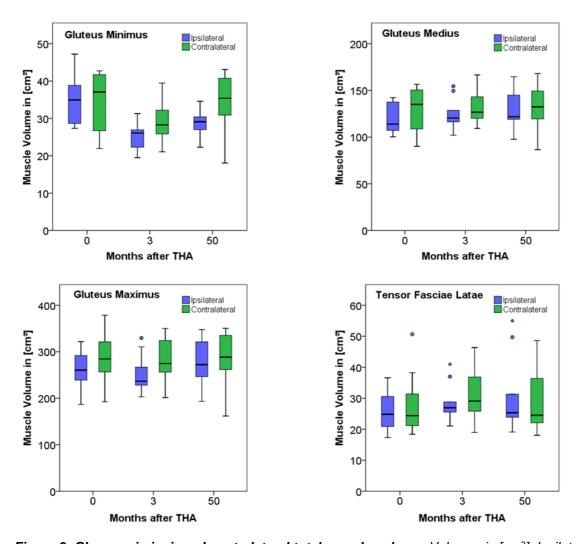


Figure 9: Changes in ipsi- and contralateral total muscle volume. Volumes in [cm³]. Ipsilateral = blue, contralateral = green.

Ipsilateral side

 $At\ 3M$, we noted no total muscle volume changes of the GMed (6 ±12.5%), the GMax (-2 ±9.8%) or the TFL (14 ±21.9%). The average -25 ±15.3% decrease of the ipsilateral GMin was statistically significant (p=0.005). $At\ 50M$ the ipsilateral GMed and GMax did not change in total muscle volume (7 ±9.7%, 6 ±8.4% respectively). The GMin significantly decreased in volume by -18 ±10.8% (p=0.008), whereas the TFL had increased by 15 ±18.5% (p=0.015). The intra-individual differences in total muscle volume during the postoperative course of 3M-50M did not show statistical significances, except for the ipsilateral GMax which increased by 9 ±8.1% (p=0.011). Inter-individual differences of total muscle volumes between 0M-3M (p=0.001) and 0M-50M (p=0.034) were only significant for the ipsilateral GMin. The individual changes and trendlines in total muscle volume for the ipsilateral side are given in figure 10 and table 6 below.

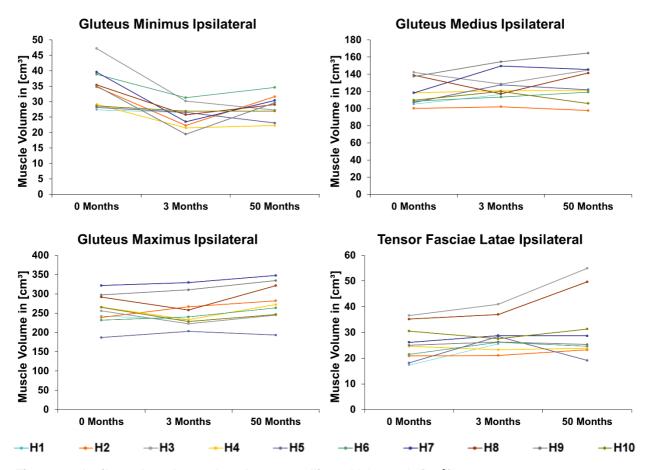


Figure 10: Ipsilateral total muscle volume trendlines. Volumes in [cm³].

Table 6: Individual total muscle volume changes of the ipsilateral muscles. Changes in [%], p-values calculated using Wilcoxon's test, significance level ** = 0.01, * = 0.05, SD = standard deviation, NA = not available.

	<u>Ipsilateral</u>	H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)	P- value
	GMin	-3	-36	-36	-26	-6	-20	-41	-27	-45	-6	-25 (15.3)	0.005**
Σ	GMed	11	2	-10	2	-19	4	26	-16	12	9	6 (12.5)	0.203
0-3M	GMax	-4	12	-13	-12	9	4	2	-12	4	-14	-2 (9.8)	0.333
	TFL	48	1	12	-6	56	22	10	5	5	-10	14 (21.9)	0.059
	GMin	NA	-9	-42	-23	-18	-11	-23	-18	-15	-6	-18 (10.8)	0.008**
0-50M	GMed	NA	-3	2	2	14	10	23	2	20	-4	7 (9.7)	0.058
0-5	GMax	NA	18	-4	3	3	14	8	10	12	-7	6 (8.4)	0.066
	TFL	NA	11	50	-3	5	15	10	41	1	3	15 (18.5)	0.015**
	GMin	NA	42	-10	4	-13	11	29	13	52	0	14 (22.6)	0.110
∑	GMed	NA	-4	13	0	-4	5	-3	21	6	-12	2 (9.9)	0.441
3-50M	GMax	NA	6	10	17	-5	10	6	25	8	8	9 (8.1)	0.011*
	TFL	NA	10	34	3	-33	-6	0	34	-4	14	6 (20.8)	0.374

Contralateral side

At 3M, we noted no total muscle volume changes of the GMed (2 $\pm 9.8\%$), the GMax (-1 $\pm 12.3\%$) or the TFL (13 $\pm 21.8\%$). The average -14 $\pm 11.3\%$ decrease of the contralateral GMin was statistically significant (p=0.009). At 50M, all contralateral muscles failed to show total muscle volume changes compared to 0M (GMin -3 $\pm 11.5\%$, GMed -1 $\pm 6.4\%$, GMax -1 $\pm 10.8\%$, TFL 3 $\pm 9.2\%$). The differences in total muscle volume between 3M-50M were not significant, although the 15 $\pm 20.3\%$ increase of the GMin indicated a trend (p=0.051). Inter-individual differences in total muscle volume between the time points 0M, 3M and 50M did not show statistical significance. Individual changes and trendlines in total muscle volume for the contralateral side are shown in figure 11 and table 7.

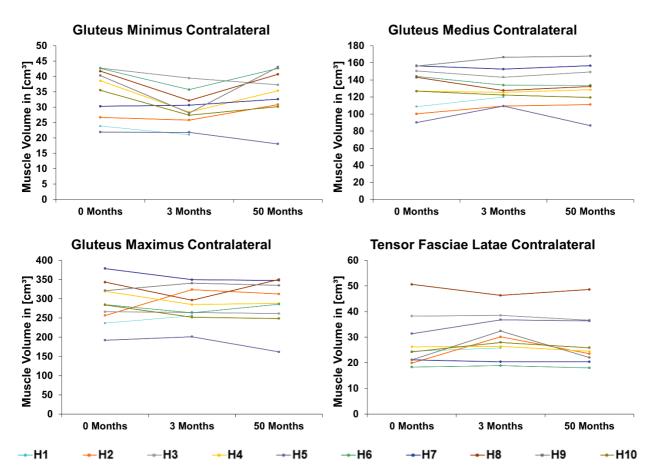


Figure 11: Contralateral total muscle volume trendlines. Volumes in [cm³].

Table 7: Individual total muscle volume changes of the contralateral muscles. Changes in [%], p-values calculated using Wilcoxon's test, significance level ** = 0.01, SD = standard deviation, NA = not available.

	<u>Contra-</u> <u>lateral</u>	H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)	P- value
0-3M	GMin	-12	-3	-8	-26	0	-16	1	-23	-30	-23	-14 (11.3)	0.009**
	GMed	10	9	-5	-1	21	-7	-3	-11	7	-4	2 (9.8)	0.799
	GMax	8	26	-1	-11	5	-7	-8	-14	6	-11	-1 (12.3)	0.386
	TFL	5	51	1	1	17	3	-3	-8	53	15	13 (21.8)	0.093
0-50M	GMin	NA	16	-13	-8	-18	0	8	-2	7	-15	-3 (11.5)	0.327
	GMed	NA	11	-1	1	-4	-7	0	-7	8	-6	-1 (6.4)	0.859
	GMax	NA	22	-2	-10	-16	0	-8	2	4	-6	-1 (10.8)	0.515
	TFL	NA	18	-4	-7	16	-2	-3	-4	4	7	3 (9.2)	0.767
3-50M	GMin	NA	19	-6	25	-17	19	6	27	53	10	15 (20.3)	0.051
	GMed	NA	2	4	2	-21	0	3	4	1	-2	-1 (7.8)	0.314
	GMax	NA	-3	-1	1	-20	8	-1	18	-2	-1	0 (10.1)	0.678
	TFL	NA	-22	-5	-7	-1	-5	0	5	-32	-7	-8 (11.6)	0.066

5.2.2 Lean muscle volume

For the following, lean muscle volume is defined as the difference of total muscle volume minus intramuscular fat volume, calculated using the fat ratio of each muscle. The average *preoperative* lean muscle volume on the ipsilateral side was 30 ±7.4cm³ for the GMin, 101 ±14.9cm³ for the GMed, 211 ±31.3cm³ for the GMax and 21 ±6.4cm³ for the TFL. On the contralateral side, the *preoperative* lean muscle volume was 30 ±10.1cm³ for the GMin, 112 ±26.5cm³ for the GMed, 241 ±46.8cm³ for the GMax and 23 ±9.5cm³ for the TFL. Figure 12 shows the changes in lean muscle volume at *OM*, *3M* and *50M* for both the ipsi- and contralateral gluteal muscles and TFL.

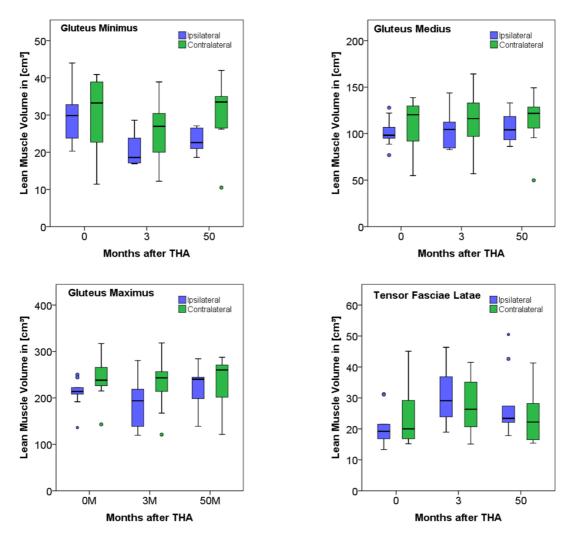


Figure 12: Changes in ipsi- and contralateral lean muscle volume. Volumes in [cm³]. Ipsilateral = blue, contralateral = green.

Ipsilateral side

At 3M, we noted no volume changes of the GMed (3 \pm 15.1%) and the Gmax (-9 \pm 21.8%). We found an average -28 \pm 14.4% decrease of the ipsilateral GMin (p=0.008) and 34 \pm 31.2% increase of the TFL (p=0.013) to be significant. At 50M, the ipsilateral GMed and GMax showed no changes in lean muscle volume (6 \pm 15.0%, 7 \pm 11.7%, respectively). The GMin had significantly decreased in lean volume by -21 \pm 17.1% (p=0.008), while the TFL significantly increased by 31 \pm 21.7% (p=0.008). The intra-individual differences in lean muscle volume in the course of 3M-50M did not reach statistical significance, however, the inter-individual differences of the ipsilateral GMin lean muscle volume between 0M-3M (p=0.006) and 0M-50M (p=0.034) were found to be significant. The individual changes and trendlines in lean muscle volume for the ipsilateral side are shown in figure 13 and table 8 below.

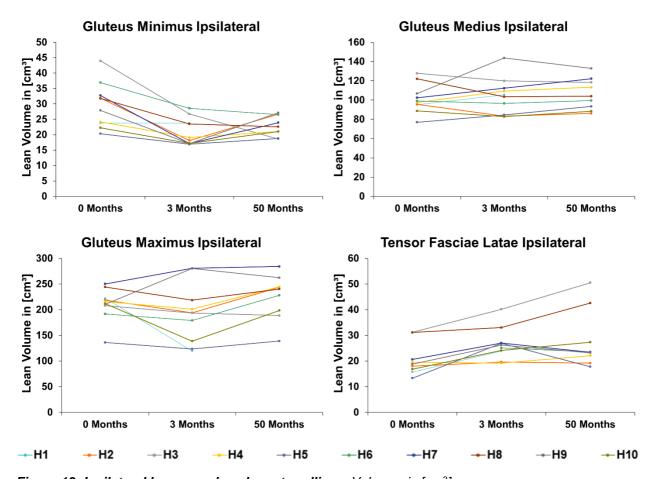


Figure 13: Ipsilateral lean muscle volume trendlines. Volumes in [cm³].

Table 8: Individual lean muscle volume changes of the ipsilateral muscles. Changes in [%], p-values calculated using Wilcoxon's test, significance level ** = 0.01, SD = standard deviation, NA = not available.

	<u>Ipsilateral</u>	H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)	P- value
	GMin	0	-43	-39	-21	-17	-23	-48	-26	-39	-23	-28 (14.4)	0.008**
Σ	GMed	11	-13	-6	12	10	-3	10	-15	35	-7	3 (15.1)	0.721
0-3M	GMax	-46	-11	-7	-7	-9	-7	12	-10	33	-35	-9 (21.8)	0.203
	TFL	52	9	29	-2	102	NA	31	6	39	43	34 (31.2)	0.013**
	GMin	NA	-16	-58	-13	-7	-28	-27	-29	-3	-6	-21 (17.1)	0.008**
MO	GMed	NA	-10	-7	16	21	0	19	-15	25	0	6 (15.0)	0.374
0-50M	GMax	NA	12	-9	13	2	19	14	-2	24	-6	7 (11.7)	0.110
	TFL	NA	6	62	13	33	NA	14	37	23	63	31 (21.7)	0.008**
	GMin	NA	47	-30	10	11	-7	40	-4	58	22	16 (28.5)	0.213
MO	GMed	NA	4	-1	4	10	3	9	1	-7	7	3 (5.4)	0.173
3-50M	GMax	NA	26	-3	21	12	27	1	10	-6	43	15 (16.1)	0.051
	TFL	NA	-2	26	15	-34	-6	-13	29	-12	13	2 (20.6)	0.213

At 3M, we noted no volume changes of the GMin (-10 \pm 16.6%), the GMed (3 \pm 14.7%), the GMax (-2 \pm 17.0%) or the TFL (20 \pm 31.8%). At 50M, all contralateral muscles did not change in lean volume compared to 0M (GMin -1 \pm 14.3%; GMed -2 \pm 11.8%; GMax -4 \pm 11.6%; TFL 2 \pm 12.4%). From 3M-50M, the differences in lean muscle volume on the contralateral side were only significant for the GMin (16 \pm 20.8%, p=0.038). Inter-individual differences in lean muscle volume at 0M, 3M and 50M did no show statistical significance. Individual changes and trendlines in lean muscle volume for the contralateral side are shown in figure 14 and table 9.

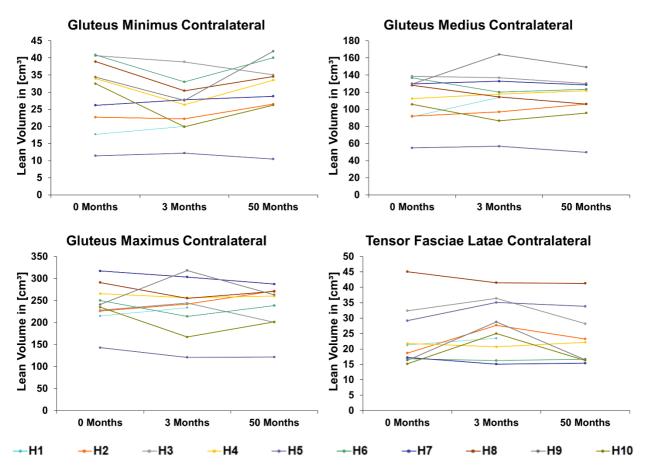


Figure 14: Contralateral lean muscle volume trendlines. Volumes in [cm³].

Table 9: Individual lean muscle volume changes of the contralateral muscles. Changes in [%], p-values calculated using Wilcoxon's test, significance level * = 0.05, SD = standard deviation, NA = not available.

	Contra- lateral	H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)	P- value
	GMin	13	-2	-4	-23	7	-19	6	-22	-20	-39	-10 (16.6)	0.074
Σ	GMed	25	5	-1	5	4	-12	2	-11	27	-18	3 (14.7)	0.575
0-3M	GMax	9	7	7	-3	-15	-14	-4	-12	32	-29	-2 (17.0)	0.575
	TFL	10	48	12	-5	20	-3	-12	-8	76	65	20 (31.8)	0.093
	GMin	NA	17	-14	-1	-8	-2	10	-11	12	-19	-1 (14.3)	0.594
Σo	GMed	NA	15	-6	8	-9	-10	-1	-17	15	-10	-2 (11.8)	0.678
0-50M	GMax	NA	20	-12	-2	-15	-5	-9	-7	9	-14	-4 (11.6)	0.314
	TFL	NA	24	-13	2	16	-1	-11	-8	1	7	2 (12.4)	0.722
	GMin	NA	19	-10	27	-14	21	4	14	52	32	16 (20.8)	0.038*
MO	GMed	NA	9	-5	3	-12	3	-3	-7	-9	11	-1 (8.1)	0.594
3-50M	GMax	NA	12	-18	1	0	11	-5	6	-17	21	1 (13.1)	0.859
	TFL	NA	-16	-23	7	-4	3	2	0	-43	-35	-12 (18.0)	0.139

5.2.3 Intramuscular fat

The *preoperative* average fat volume on the ipsilateral side was 5 \pm 2.1 cm³ for the GMin, 17 \pm 8.6 cm³ for the GMed, 49 \pm 20.2 cm³ for the GMax and 5 \pm 3.4 cm³ for the TFL. On the contralateral side, the *preoperative* fat volume was 5 \pm 2.6 cm³ for the GMin, 18 \pm 9.0 cm³ for the GMed, 47 \pm 16.8 cm³ for the GMax and 4 \pm 2.3 cm³ for the TFL. Figure 15 shows the change in fat volume at *OM*, *3M* and *50M* for both the ipsi- and contralateral gluteal muscles and TFL.

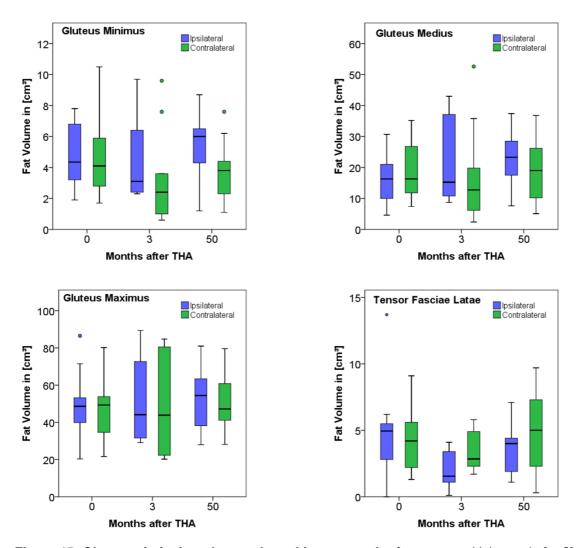


Figure 15: Changes in ipsi- and contralateral intramuscular fat content. Volumes in [cm³]. Ipsilateral = blue, contralateral = green.

Ipsilateral side

At 3M, we noted no fat volume changes of the GMin (-2 ±42.7%), GMed (48 ±112.0%) or GMax (31 ±94.3). The average -52 ±36.8% decrease of the ipsilateral TFL fat volume was found to be statistically significant (p=0.021). At 50M, all ipsilateral muscles failed to show changes in fat volume (GMin 50 ±129.9, GMed 48 ±72.8%, GMax 10 ±42.8%, TFL -17 ±54.4%). The intra-individual differences in fat volume in the course of 3M-50M did not show statistical significance, whereas inter-individual differences in fat volume between 0M-3M were significant for the TFL (p=0.015). The individual changes and trendlines in fat volume for the ipsilateral side are shown in figure 16 and table 10 below.

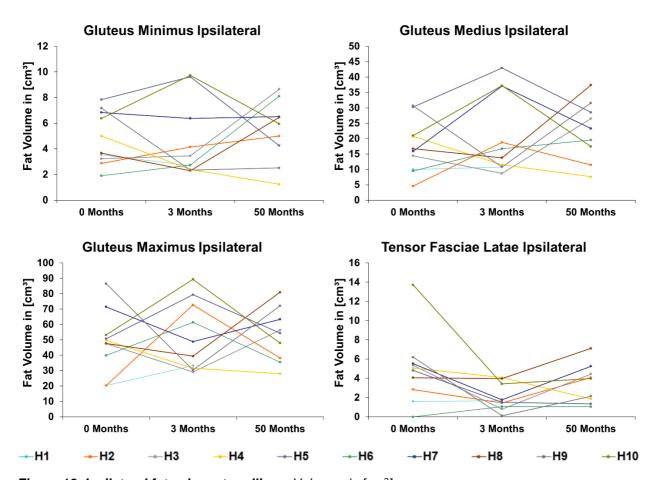


Figure 16: Ipsilateral fat volume trendlines. Volumes in [cm³].

Table 10: Individual fat volume changes of the ipsilateral muscles. Changes in [%], p-values calculated using Wilcoxon's test, significance level * = 0.05, SD = standard deviation, NA = not available.

	<u>Ipsilateral</u>	H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)	P- value
	GMin	-24	44	7	-52	23	43	-7	-37	-67	53	-2 (42.7)	0.838
Σ	GMed	8	311	-40	-45	42	77	133	-18	-65	77	48 (112.0)	0.386
0-3M	GMax	63	258	-39	-36	56	54	-32	-17	-65	68	31 (94.3)	0.721
	TFL	3	-49	-85	-20	-68	NA	-68	-2	-98	-75	-52 (36.8)	0.021*
	GMin	NA	74	168	-75	-46	325	-5	76	-65	-7	50 (129.9)	0.859
0-50M	GMed	NA	150	84	-63	-6	107	46	124	3	-17	48 (72.8)	0.260
0-5	GMax	NA	88	18	-44	7	-11	-11	70	-17	-10	10 (42.8)	0.953
	TFL	NA	44	-17	-64	-72	NA	-5	75	-66	-71	-17 (54.4)	0.214
	GMin	NA	21	151	-48	-56	196	2	181	7	-39	46 (101.4)	0.515
M	GMed	NA	-39	206	-34	-34	17	-37	172	193	-53	43 (112.0)	0.859
3-50M	GMax	NA	-47	94	-12	-31	-42	30	106	137	-46	21 (73.4)	0.859
	TFL	NA	183	462	-55	-12	0	197	79	1871	16	304 (608.3)	0.069

At 3M, we noted no volume changes of the GMin (-18 \pm 72.9%), the GMed (-3 \pm 62.4%), the GMax (14 \pm 73.8%) or TFL (1 \pm 55.2%). At 50M, all contralateral muscles showed no changes in fat volume compared to 0M (GMin 4 \pm 59.7%, GMed 8 \pm 44.3%, GMax 11 \pm 35.9%, TFL 1 \pm 39.1%). From 3M-50M neither intra- nor inter-individual differences in fat volume showed statistical significance. Individual changes and trendlines in fat volume for the contralateral side are shown in figure 17 and table 11.

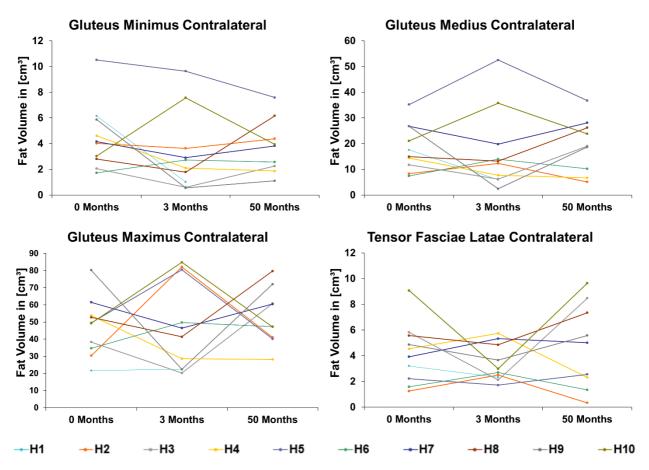


Figure 17: Contralateral fat volume trendlines. Volumes in [cm³].

Table 11: Individual fat volume changes of the contralateral muscles. Changes in [%], p-values calculated using Wilcoxon's test, SD = standard deviation, NA = not available.

	Contra-	H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average	P-
	<u>lateral</u>	nic	HZK	HJL	ПФС	HJL	HOK	пи	HOL	ПЭС	HIOK	(SD)	value
	GMin	-83	-10	-70	-55	-8	57	-30	-36	-91	149	-18 (72.9)	0.103
Σ	GMed	-66	48	-47	-46	49	88	-26	-12	-91	70	-3 (62.4)	0.646
0-3M	GMax	3	171	-47	-47	63	44	-25	-22	-72	72	14 (73.8)	0.959
	TFL	-27	99	-63	27	-23	71	36	-13	-25	-67	1 (55.2)	0,760
	GMin	NA	9	10	-60	-28	48	-8	120	-81	30	4 (59.7)	0.812
Σ	GMed	NA	-38	62	-53	4	38	5	75	-30	13	8 (44.3)	0.767
0-50M	GMax	NA	35	59	-48	-19	37	-2	51	-10	-4	11 (35.9)	0.594
	TFL	NA	-73	46	-49	15	-14	28	32	15	6	1 (39.1)	0.314
	GMin	NA	21	269	-11	-21	-6	32	245	102	-48	65 (117.0)	0.594
∑	GMed	NA	-58	206	-13	-30	-27	42	98	664	-33	94 (229.5)	0.678
3-50M	GMax	NA	-50	201	-2	-50	-5	30	93	223	-44	44 (105.7)	0.859
	TFL	NA	-86	299	-60	49	-50	-6	51	52	223	52 (130.1)	0.441

5.2.4 Fatty degeneration

The *preoperative* degree of fatty degeneration on the ipsilateral side was 15 \pm 7.4% for the GMin, 15 \pm 7.1% for the GMed, 19 \pm 6.7% for the GMax and 21 \pm 10.8% for the TFL. On the contralateral side, the average *preoperative* fat ratio was 16 \pm 13.1% for the GMin, 15 \pm 9.6% for the GMed, 16 \pm 5.5% for the GMax and 16 \pm 9.2% for the TFL. Figure 18 shows the changes in fat ratio at *OM*, *3M* and *50M* for both the ipsi- and contralateral gluteal muscles and TFL.

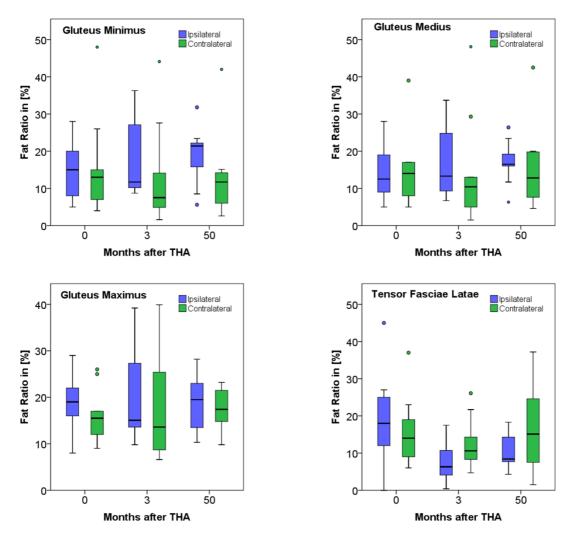


Figure 18: Changes in ipsi- and contralateral fat ratio. Ratios in [%]. Ipsilateral = blue, contralateral = green.

Ipsilateral side

At 3M, we noted no changes in fat ratio for the GMin (32 \pm 56.8%), the GMed (36 \pm 96.4%) or the GMax (31 \pm 80.8%). The average -57 \pm 32.1% decrease of the ipsilateral TFL was found to be significant (p=0.017). At 50M, the ipsilateral GMin (90 \pm 166.6%), GMed (37 \pm 69.8%) and GMax (2 \pm 34.9%) showed no changes of the fat ratio. However, the decrease of the TFL fat ratio by -36 \pm 41.1% (p=0.086) indicated a trend. The intraindividual differences in fat ratio in the course of 3M-50M did not show statistical significance. Inter-individual differences in fat ratio between 0M-3M were only significant for the ipsilateral TFL (p=0.013) but also showed a trend from 3M-50M (p=0.055). The individual changes and trendlines of the ipsilateral side are shown in figure 19 and table 12 below.

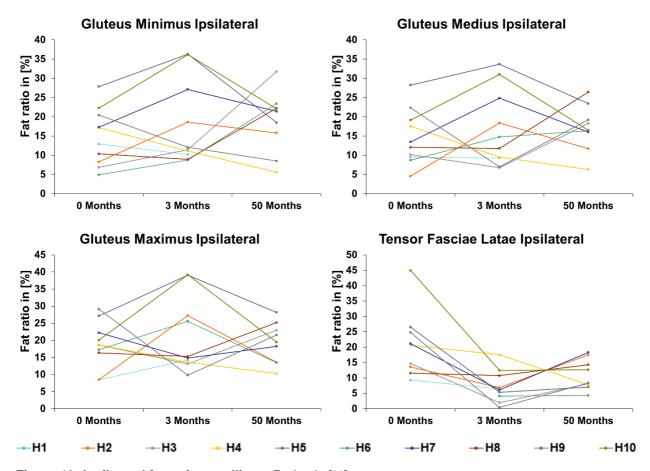


Figure 19: Ipsilateral fat ratio trendlines. Ratios in [%].

Table 12: Individual fat ratio changes of the ipsilateral muscles. Changes in [%], p-values calculated using Wilcoxon's test, significance level * = 0.05, SD = standard deviation, NA = not available.

	<u>Ipsilateral</u>	H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)	P- value
	GMin	-22	133	63	-35	30	75	59	-11	-40	64	32 (56.8)	0.169
Σ	GMed	3	268	-33	-47	20	64	91	-2	-68	63	36 (96.4)	0.445
0-3M	GMax	78	203	-31	-29	45	50	-33	-5	-66	96	31 (80.8)	0.475
	TFL	-28	-51	-87	-17	-80	NA	-71	-11	-98	-72	-57 (32.1)	0.017*
	GMin	NA	97	354	-67	-34	368	26	122	-58	0	90 (166.6)	0.374
∑	GMed	NA	134	83	-65	-16	82	23	120	-13	-13	37 (69.8)	0.374
0-50M	GMax	NA	50	21	-46	4	-21	-17	58	-26	-3	2 (34.9)	0.953
	TFL	NA	25	-46	-63	-74	NA	-13	19	-66	-72	-36 (41.1)	0.086
	GMin	NA	-15	178	-50	-49	168	-21	149	-30	-39	32 (100.3)	0.859
Σ	GMed	NA	-36	171	-34	-31	11	-36	125	175	-47	33 (95.3)	0.953
3-50M	GMax	NA	-50	76	-24	-28	-47	23	65	120	-50	9 (64.1)	0.374
	TFL	NA	156	319	-56	31	6	198	33	1949	2	293 (631.9)	0.066

At 3M, we noted no fat ratio changes of the GMin (-5 \pm 89.8%), the GMed (-3 \pm 64.1%), the GMax (13 \pm 63.1%) or the TFL (-9 \pm 47.1%). At 50M, all contralateral muscles showed no changes in fat ratio compared to 0M (GMin 7 \pm 59.8%, GMed 13 \pm 50.8%, GMax 9 \pm 38.4%, TFL -1 \pm 40.8%). Between timepoints 3M-50M neither the intra- nor interindividual differences in fat ratio reached statistical significance. Individual changes and trendlines of fat ratios on the contralateral side are shown in figure 20 and table 13.

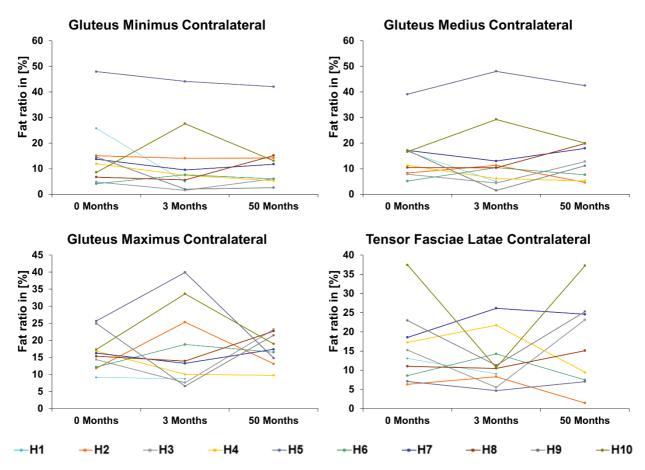


Figure 20: Contralateral fat ratio trendlines. Ratios in [%].

Table 13: Individual fat ratio changes of the contralateral muscles. Changes in [%], p-values calculated using Wilcoxon's test, SD = standard deviation, NA = not available.

	Contra- lateral	H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)	P- value
	GMin	-81	-6	-69	-38	-8	91	-32	-21	-87	206	-5 (89.8)	0.139
Σ	GMed	-71	41	-46	-44	23	108	-24	4	-91	72	-3 (64.1)	0.799
0-3M	GMax	-3	111	-46	-41	54	57	-17	-7	-74	98	13 (63.1)	0.878
	TFL	-31	38	-63	28	-33	59	38	-5	-51	-71	-9 (47.1)	0.475
	GMin	NA	-5	21	-56	-12	51	-16	116	-83	45	7 (59.8)	0.594
Σ	GMed	NA	-42	59	-53	9	53	6	98	-34	17	13 (50.8)	0.678
0-50M	GMax	NA	9	66	-43	-43	38	9	52	-14	11	9 (38.4)	0.678
	TFL	NA	-76	54	-44	0	-17	29	37	10	1	-1 (40.8)	0.575
	GMin	NA	1	290	-29	-5	-21	24	173	32	-53	46 (112.3)	0.859
Σo	GMed	NA	-59	193	-15	-12	-27	38	91	658	-32	93 (225.8)	0.678
3-50M	GMax	NA	-48	205	-3	-63	-12	31	-63	228	-44	40 (107.9)	0.953
	TFL	NA	-83	319	-57	51	-48	-6	44	124	249	66 (139.9)	0.441

5.3 In vivo hip joint contact forces

Measurements of the resulting joint loads at *3M* and *50M* after THA showed high interindividual and activity-related differences. For the activities standing up and sitting down data was only available for six subjects at *3M*. Figure 21 shows the inter-individual differences in investigated peak values of in vivo measured joint loads in the hip during walking, sitting down, standing up and stair climbing.

At 3M, the overall highest loads were measured in stair descent with an average load of 281 \pm 62%BW at the 1st Peak. On the other hand, sitting down showed the lowest loads with an average of 169 \pm 64%BW. With a 418%BW load in stair descent, patient H5 reached the highest single peak force among all measured activities. At 50M, the overall highest loads were measured for stair descent with an average 336 \pm 35%BW at the 1st Peak. In line with the data from 3M, sitting down was found to produce the lowest loads with an average of 195 \pm 92%BW. The highest single peak force was measured during stair descent with H4 reaching 409%BW.

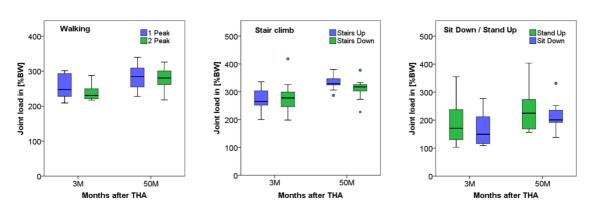


Figure 21: Peak forces of in vivo measured hip joint loads in different ADL. Loads in [%BW].

5.3.1 Level walking

Level walking at 3M produced contact forces with an average of $255 \pm 33\%$ BW at the 1st Peak and $238 \pm 24\%$ BW at the 2nd Peak, whereas forces at 50M reached slightly higher average loads of $282 \pm 35\%$ BW and $277 \pm 37\%$ BW, respectively. Inter-individual differences between 3M-50M were shown to be significant for the 2nd Peak (p=0.027). Further, we found intra-individual differences in contact forces to be significant for both the 1st and 2nd Peak between 3M-50M (p=0.038, p=0.015). Individual load cycles of level walking at 3M and 50M are shown in figure 22 and table 14 below.

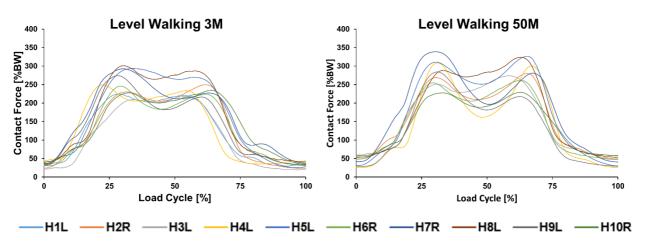


Figure 22: Individual contact forces and load cycles during level walking. Loads in [%BW].

Table 14: Individual contact forces and load cycles during level walking. Loads in [%BW (N)], SD =standard deviation, NA =not available, P =Peak.

		H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)
	Walking	225	230	209	249	294	246	293	301	275	228	255 (33)
5	1 P	[1679]	[1808]	[1841]	[1950]	[1530]	[2044]	[2634]	[2346]	[3044]	[2197]	[2209(429)]
3M	Walking	221	250	217	234	270	224	228	288	217	235	238 (24)
	2 P	[1666]	[1959]	[1915]	[1829]	[2326]	[1860]	[2045]	[2241]	[2408]	[2260]	[2051(246)]
	Walking	NA	269	251	309	311	255	339	288	284	228	282 (35)
Σ	1 P	INA	[2225]	[2055]	[2493]	[2370]	[2084]	[2911]	[2680]	[3505]	[2234]	[2506(467)]
50M	Walking	NA	280	274	301	326	261	281	324	218	229	277 (37)
	2 P	INA	[2318]	[2244]	[2425]	[2487]	[2138]	[2413]	[3012]	[2685]	[2248]	[2441(267)]

5.3.2 Stair climbing

At 3M, stair ascent and descent produced higher 1st Peak loads than level walking with an average load of 267 \pm 42%BW and 281 \pm 62%BW. At 50M, the average joint load at the 1st Peak of stair ascent (333 \pm 28%BW) and descent (336 \pm 35%BW) were the highest among all exercises included in the protocol. H4 reached the highest overall peak value of 409%BW in stair descent. Inter- and intra-individual differences between 3M-50M loads were significant for the 1st Peak in stair ascent (p=0.003, p=0.008). 3M and 50M individual load cycles of each activity are shown in figure 23 and table 15 below.

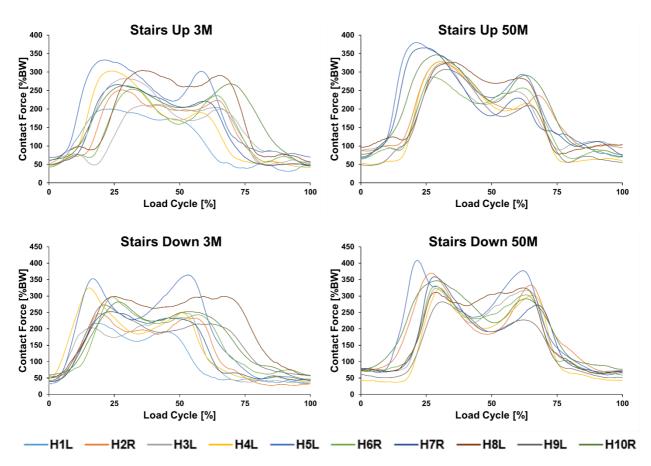


Figure 23: Individual contact forces and load cycles during stair climb. Loads in [%BW].

Table 15: Individual contact forces and load cycles during stair climb. Loads in [%BW (N)], $SD = standard\ deviation$, $NA = not\ available$, P = Peak.

		H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)
	Stairs Up	200	252	212	303	336	254	266	304	283	263	267 (42)
	1 P	[1509]	[1976]	[1871]	[2373]	[2896]	[2111]	[2395]	[2372]	[3135]	[2535]	[2317(480)]
	Stairs Up	172	224	204	190	324	237	222	291	200	268	233 (48)
_	2 P	[1294]	[1756]	[1799]	[1491]	[2794]	[1970]	[1994]	[2269]	[2218]	[2386]	[1997(442)]
3⊠	Stairs Down	217	246	198	325	418	298	253	299	273	282	281 (62)
	1 P	[1635]	[1933]	[1745]	[2548]	[3604]	[2477]	[2272]	[2328]	[3029]	[2722]	[2429(598)]
	Stairs Down	192	233	250	249	388	243	233	300	218	253	256 (54)
	2 P	[1450]	[1827]	[2202]	[1947]	[3344]	[2020]	[2099]	[2338]	[2394]	[2437]	[2206(498)]
	Stairs Up	NA	329	325	329	380	287	366	327	306	347	333 (28)
	1 P	INA	[2718]	[2658]	[2653]	[2898]	[2348]	[3139]	[3043]	[3773]	[3402]	[2959(436)]
	Stairs Up	NA	237	248	215	294	258	230	284	209	292	252 (32)
Σ	2 P	INA	[1959]	[2029]	[1739]	[2246]	[2110]	[1974]	[2644]	[2574]	[2860]	[2237(374)]
50M	Stairs Down	NA	324	324	409	331	359	312	283	345	336	336 (35)
	1 P	INA	[3062]	[2656]	[2619]	[3117]	[2707]	[3081]	[2899]	[3484]	[3383]	[3001(309)]
	Stairs Down	NA	333	317	302	377	304	273	326	227	324	309 (42)
	2 P	INA	[2757]	[2599]	[2441]	[2879]	[2484]	[2341]	[3028]	[2802]	[3180]	[2723(281)]

5.3.3 Sit down / Stand up

Compared to other ADL, the peak loads in sitting down (169 \pm 64%BW) and standing up (195 \pm 192%BW) at 3M were markedly lower. Also at 50M, joint loads in sitting down (211 \pm 59%BW) and standing up (248 \pm 100%BW) were the lowest among all activities, while the latter showed the highest inter-individual difference, with patient H5 reaching a maximum of 404%BW compared to H3 of 157%BW. Inter- and intra-individual differences in maximum loads sit down and stand up were not significant. 3M and 50M individual load cycles of each activity are shown in figure 24 and table 16 below.

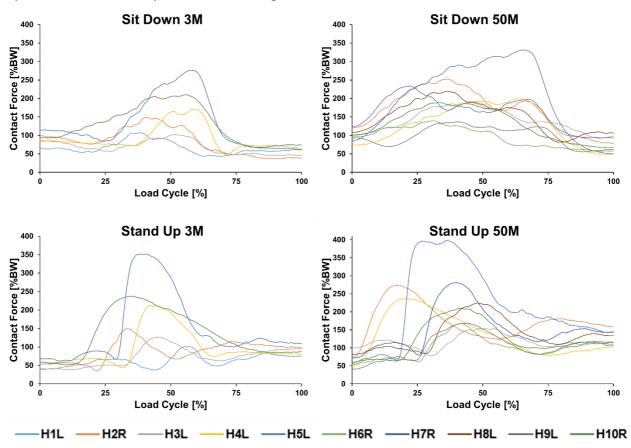


Figure 24: Individual contact forces and load cycles during sit down / stand up. Loads in [%BW].

Table 16: Individual contact forces and load cycles during sit down / stand up. Loads in [%BW (N)], SD = standard deviation, NA = not available.

		H1L	H2R	H3L	H4L	H5L	H6R	H7R	H8L	H9L	H10R	Average (SD)
	Sit Down	109	154	116	145	277	NIA	NIA	NIA	NIA	212	169 (64)
5	Max	[819]	[1208]	[1004]	[1158]	[2387]	NA	NA	NA	NA	[2044]	[819(628)]
3M	Stand Up	103	151	130	192	355	NA	NA	NA	NA	238	195 (92)
	Max	[776]	[1183]	[1127]	[1158]	[2387]	INA	INA	INA	INA	[2291]	[1487(677)]
	Sit Down	NA	253	191	201	332	140	235	220	138	192	211 (59)
Σ	Max	INA	[2090]	[1568]	[1621]	[2530]	[1144]	[2017]	[2049]	[1703]	[1879]	[1844(394)]
50M	Stand Up	NA	274	157	237	404	168	281	225	169	210	248 (100)
	Max	INA	[2265]	[1283]	[1909]	[3080]	[1376]	[2414]	[2089]	[2078]	[2059]	[1983(733)]

5.4 Impact of muscle status on in vivo hip loads

5.4.1 Correlation between total muscle volume and in vivo contact forces

Ipsilateral side

At 3M, only the muscle volume of the ipsilateral GMed ($r_s=0.67^*$) was found to be significantly correlated with the 1st Peak contact forces in level walking, although it also showed an effect in stair ascent ($r_s=0.60$). All calculated correlations of the ipsilateral total muscle volume and contact forces at 3M are shown in table 17 and figure 25 below.

Table 17: Correlation of ipsilateral total muscle volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level * = 0.05, P = Peak.

<u> </u>	<u>lpsilateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r _S = -0.25 (0.49)	rs = 0.67* (0.033)	r s = 0.35 (0.33)	r _s = 0.46 (0.19)
	Walking 2 P	r s = -0.19 (0.60)	r s = 0.49 (0.15)	r s = 0.12 (0.75)	r s = 0.41 (0.24)
3⊠	Stairs Up 1 P	r s = -0.33 (0.35)	rs = 0.60 (0.07)	$\Gamma_S = 0.14 (0.70)$	r s = 0.16 (0.65)
<u></u>	Stairs Down 1 P	r s = -0.14 (0.70)	r s = 0.36 (0.31)	r s = -0.12 (0.75)	r s = 0.02 (0.96)
	Sit Down Max	r s = -0.09 (0.87)	r s = 0.09 (0.87)	r s = -0.31 (0.54)	r s = 0.09 (0.87)
	Stand Up Max	$r_s = -0.03 (0.96)$	r s = 0.26 (0.63)	l 's = -0.37 (0.47)	r s = 0.14 (0.79)

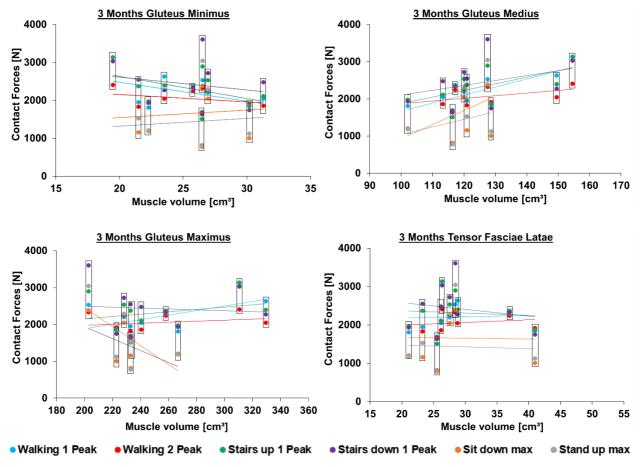


Figure 25: Correlation of ipsilateral total muscle volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

At 50M, the muscle volume of the ipsilateral GMax ($r_s=0.72^*$) was found to correlate with 1st Peak contact forces in walking, while the GMed was also shown to have an effect ($r_s=0.58$). All calculated correlations of the ipsilateral total muscle volume and contact forces at 50M are shown in table 18 and figure 26 below.

Table 18: Correlation of ipsilateral total muscle volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level * = 0.05, P = Peak.

	<u>psilateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r _S = - 0.10 (0.80)	r _S = 0.58 (0.10)	r _S = 0.72* (0.029)	r _S = -0.03 (0.93)
	Walking 2 P	r _S = -0.32 (0.41)	r _S = 0.45 (0.22)	r _S = 0.42 (0.27)	r s = -0.12 (0.77)
20M	Stairs Up 1 P	r s = -0.05 (0.90)	$r_s = 0.42 (0.27)$	r s = 0.42 (0.27)	r _S = 0.27 (0.49)
20	Stairs Down 1 P	$\Gamma_{S} = 0.08 (0.83)$	r _S = 0.18 (0.64)	r _S = 0.18 (0.64)	r _S = -0.10 (0.80)
	Sit Down Max	r s = -0.12 (0.77)	r _S = -0.12 (0.77)	r s = 0.08 (0.83)	r s = -0.37 (0.33)
	Stand Up Max	r s = 0.03 (0.93)	r s = 0.08 (0.83)	r s = 0.28 (0.46)	r s = -0.45 (0.22)

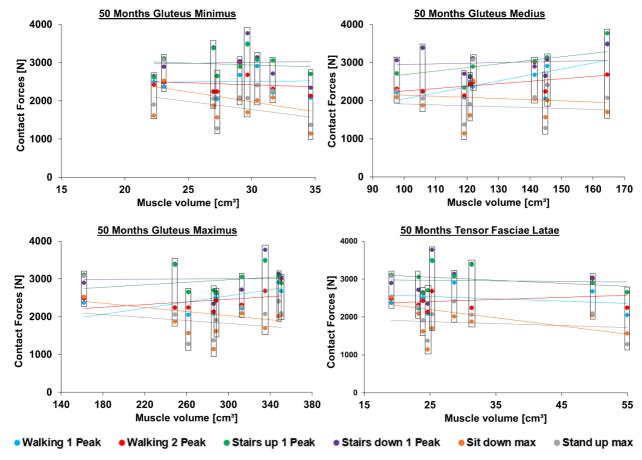


Figure 26: Correlation of ipsilateral total muscle volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

At 3M, total muscle volumes on the contralateral side did not show significant correlations with the investigated peak forces, although the GMed and TFL volumes indicated to have an effect in walking (r_s =0.54, r_s =0.50). All calculated correlations of the contralateral lean volume and contact forces at 3M are shown in table 19 and figure 27 below.

Table 19: Correlation of contralateral total muscle volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, P = Peak.

C	<u>ontralateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r s = 0.15 (0.68)	rs = 0.54 (0.11)	r s = 0.30 (0.41)	r _S = 0.15 (0.68)
	Walking 2 P	r s = -0.12 (0.75)	r _S = 0.18 (0.63)	r _S = 0.10 (0.78)	rs = 0.50 (0.14)
3⊠	Stairs Up 1 P	r _S = -0.14 (0.70)	r _S = 0.25 (0.49)	$r_S = 0.08 (0.83)$	$r_S = 0.13 (0.73)$
<u></u>	Stairs Down 1 P	r s = -0.14 (0.70)	r s = 0.06 (0.88)	r s = -0.21 (0.56)	r s = 0.14 (0.70)
	Sit Down Max	$\Gamma_{S} = -0.09 (0.87)$	r _S = -0.43 (0.40)	r _S = -0.43 (0.40)	$r_S = 0.37 (0.47)$
	Stand Up Max	r s = 0.03 (0.96)	r s = -0.20 (0.70)	r s = -0.49 (0.33)	r _S = 0.26 (0.62)

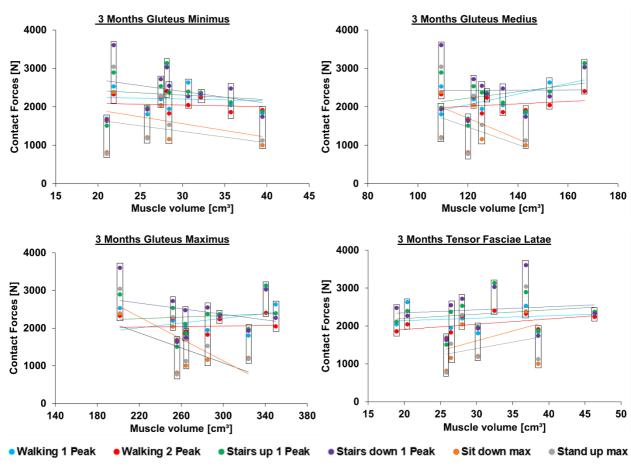


Figure 27: Correlation of contralateral total muscle volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

At 50M, we found a higher total muscle volume of the contralateral GMin and GMed to have an effect on lower contact forces in sitting down (r_s =-0.63, r_s =-0.57) as well as for the GMin in standing up (r_s =-0.52). Statistical analysis further revealed the GMax total muscle volume to have an effect on walking 1st Peak (r_s =0.62). All calculated correlations of the contralateral total muscle volume and contact forces at *50M* are shown in table 20 and figure 28 below.

Table 20: Correlation of contralateral total muscle volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, P = Peak.

Co	ontralateral	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r _S = 0.18 (0.64)	r _S = 0.35 (0.36)	r _S = 0.62 (0.08)	r _S = -0.13 (0.73)
	Walking 2 P	r _S = 0.08 (0.83)	r _S = 0.00 (1.00)	r _S = 0.48 (0.19)	r _S = 0.33 (0.38)
Σ	Stairs Up 1 P	$r_S = -0.08 (0.83)$	$\Gamma_{S} = 0.23 (0.55)$	r _S = 0.27 (0.49)	$r_{s} = 0.07 (0.87)$
20M	Stairs Down 1 P	r _S = -0.22 (0.58)	r _S = 0.02 (0.97)	r _S = -0.03 (0.93)	r s = -0.15 (0.70)
	Sit Down Max	r _S = -0.63 (0.07)	rs = -0.57 (0.11)	r s = 0.10 (0.80)	r s = 0.32 (0.41)
	Stand Up Max	r _S = -0.52 (0.15)	r _S = -0.33 (0.38)	$r_{s} = 0.22 (0.58)$	r s = 0.00 (1.00)

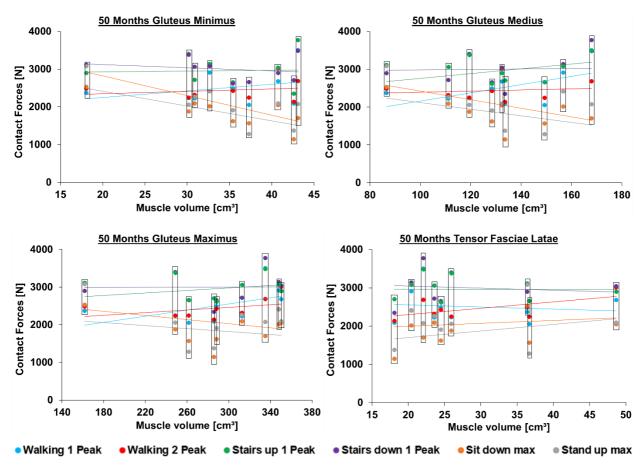


Figure 28: Correlation of contralateral total muscle volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

5.4.2 Correlation between lean muscle volume and in vivo contact forces

Ipsilateral side

At 3M, the lean muscle volume, which is defined as the total muscle volume minus total fat volume, of the ipsilateral GMin was found to be significantly correlated with lower in vivo joint contact forces in all ADL but stair descent (r_s =-0.67* - -0.89**). Further, a lower GMax lean volume was shown to have an effect on increased contact forces in sitting down (r_s =-0.71). All calculated correlations of the ipsilateral lean muscle volume and contact forces at 3M are shown in table 21 and figure 29 below.

Table 21: Correlation of ipsilateral lean muscle volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level ** = 0.01, * = 0.05, P = Peak.

<u> </u>	<u>Ipsilateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	rs = -0.67* (0.035)	r s = 0.24 (0.51)	r s = 0.30 (0.41)	r s = 0.47 (0.17)
	Walking 2 P	rs = -0.75** (0.013)	r _S = -0.08 (0.83)	f s = -0.02 (0.96)	r s = 0.41 (0.24)
38	Stairs Up 1 P	$\Gamma_{\rm S}$ = -0.82** (0.004)	$r_s = 0.02 (0.96)$	$\Gamma_{S} = 0.07 (0.86)$	r _S = 0.10 (0.78)
ਲ	Stairs Down 1 P	r s = -0.61 (0.06)	r _S = -0.18 (0.63)	f s = -0.24 (0.51)	r _S = -0.04 (0.91)
	Sit Down Max	$\Gamma_{\rm S}$ = -0.94** (0.005)	r _S = -0.66 (0.16)	r _S = -0.71 (0.11)	r _S = -0.14 (0.79)
	Stand Up Max	rs = -0.89** (0.019)	r _S = -0.49 (0.33)	r s = -0.60 (0.21)	r s = 0.09 (0.87)

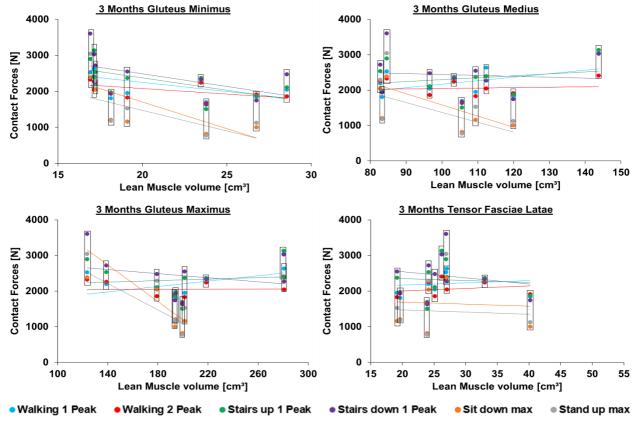


Figure 29: Correlation of ipsilateral lean muscle volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

At 50M, only higher lean volume of the ipsilateral GMax was correlated with lower loads in level walking 1^{st} Peak (r_s =0.68*), while the GMed lean volume was also shown to have an effect (r_s =0.53). All calculated correlations of the ipsilateral lean muscle volume and contact forces at *50M* are shown in table 22 and figure 30 below.

Table 22: Correlation of ipsilateral lean muscle volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level * = 0.05, P = Peak.

	<u>lpsilateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r s = 0.36 (0.31)	rs = 0.53 (0.14)	rs = 0.68* (0.042)	r _S = -0.20 (0.61)
	Walking 2 P	r _S = 0.14 (0.72)	r _S = 0.28 (0.46)	r _S = 0.32 (0.41)	$\Gamma_{S} = 0.21 \ (0.59)$
Σ	Stairs Up 1 P	r _S = 0.25 (0.52)	r _S = 0.23 (0.55)	r s = 0.28 (0.46)	r s = -0.09 (0.83)
20M	Stairs Down 1 P	$\Gamma_{S} = 0.34 (0.37)$	$r_S = -0.03 (0.93)$	r _S = 0.08 (0.83)	r _S = -0.37 (0.32)
	Sit Down Max	r _S = 0.02 (0.97)	r s = -0.42 (0.27)	r s = -0.05 (0.89)	r _S = -0.23 (0.56)
	Stand Up Max	r _S = 0.19 (0.62)	r _S = -0.18 (0.64)	r _S = 0.18 (0.64)	r _S = -0.56 (0.11)

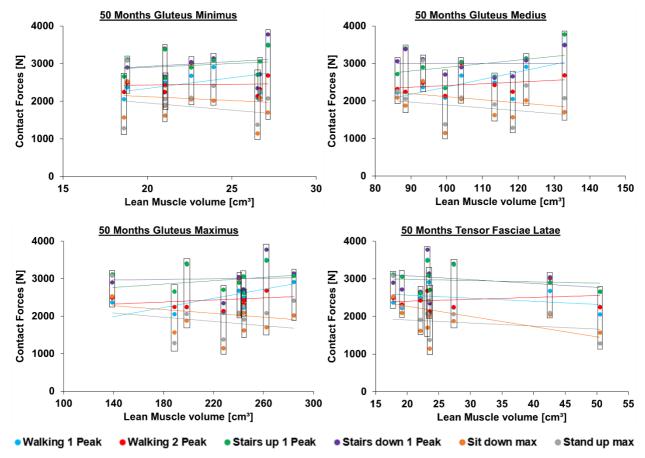


Figure 30: Correlation of ipsilateral lean muscle volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

At 3M, a higher lean muscle volume of the contralateral GMed (r_s =-0.83*) was correlated with lower joint loads in sitting down. The GMed also showed an effect on loads in standing up and the GMax in sitting down (r_s =-0.71, r_s =-0.60 respectively). All calculated correlations of the contralateral lean muscle volume and contact forces at 3M are shown in table 23 and figure 31 below.

Table 23: Correlation of contralateral lean muscle volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level * = 0.05, P = Peak.

Co	ontralateral	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r _S = 0.03 (0.93)	r _S = 0.25 (0.49)	r _S = 0.32 (0.37)	r _S = 0.07 (0.86)
	Walking 2 P	r s = -0.24 (0.51)	r _S = -0.08 (0.83)	r s = 0.04 (0.91)	r s = 0.46 (0.19)
3⊠	Stairs Up 1 P	r _S = -0.33 (0.35)	r _S = -0.02 (0.96)	$r_S = 0.14 (0.70)$	$\mathbf{r}_{S} = 0.03 \ (0.93)$
ਲ	Stairs Down 1 P	r _S = -0.37 (0.29)	r _S = -0.18 (0.63)	r s = -0.13 (0.73)	r _S = 0.09 (0.80)
	Sit Down Max	r _S = -0.66 (0.16)	$\Gamma_{\rm S} = -0.83^* (0.04)$	$\Gamma_{\rm S}$ = -0.60 (0.21)	$\mathbf{f}_{S} = 0.26 \ (0.62)$
	Stand Up Max	r _S = 0.60 (0.21)	rs = -0.71 (0.11)	r s = -0.49 (0.33)	r _S = 0.09 (0.87)

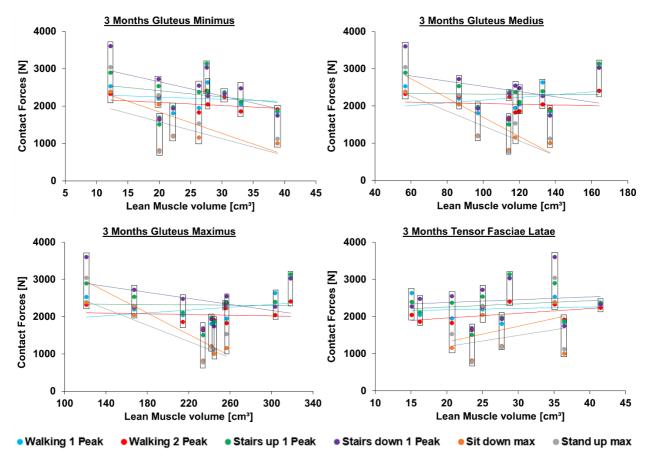


Figure 31: Correlation of contralateral lean muscle volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

At 50M, a higher lean volume of the GMin (r_s =-0.72*) was shown to be correlated with lower contact forces in sitting down. The TFL lean volume further showed an effect on contact forces in walking 2nd Peak (r_s =0.61), as well as the GMin in standing up (r_s =-0.60) and the GMed in sitting down (r_s =-0.65). All calculated correlations of the contralateral lean muscle volume and contact forces at *50M* are shown in table 24 and figure 32 below.

Table 24: Correlation of contralateral lean muscle volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level * = 0.05, P = Peak.

Co	ontralateral	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r _S = 0.08 (0.83)	r _S = 0.20 (0.61)	r _S = 0.52 (0.15)	r s = -0.17 (0.66)
	Walking 2 P	r s = -0.03 (0.93)	r s = -0.08 (0.83)	r _S = 0.28 (0.46)	rs = 0.61 (0.09)
20M	Stairs Up 1 P	r _S = -0.13 (0.73)	$\Gamma_{S} = 0.03 (0.93)$	r _S = 0.25 (0.52)	r _S = -0.20 (0.61)
20	Stairs Down 1 P	r _S = -0.25 (0.52)	r _S = -0.15 (0.70)	r _S = 0.05 (0.89)	r _S = -0.29 (0.45)
	Sit Down Max	r _S = -0.72* (0.030)	rs = -0.65 (0.06)	r s = 0.22 (0.58)	r s = 0.48 (0.19)
	Stand Up Max	rs = -0.60 (0.09)	r _S = -0.45 (0.22)	r _S = 0.35 (0.36)	r _S = 0.24 (0.54)

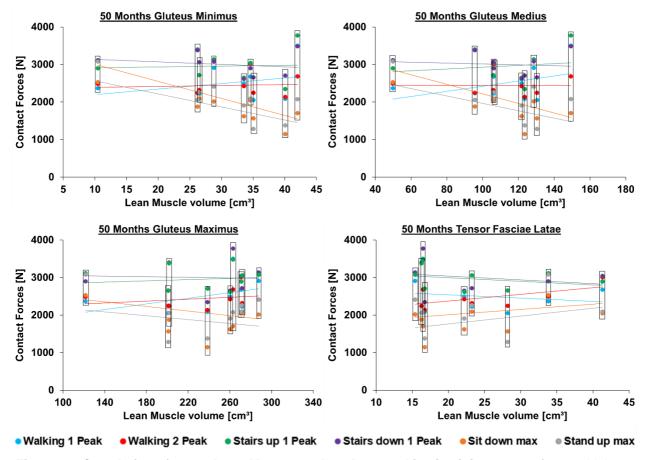


Figure 32: Correlation of contralateral lean muscle volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

5.4.3 Correlation between intramuscular fat and in vivo contact forces

Ipsilateral side

At 3M, a lower total fat volume of the GMed was correlated with lower contact forces in sitting down (r_s =0.94*) and standing up (r_s =0.87*). A high GMed fat volume further showed an effect on increased contact forces in stair negotiation (r_s =0.52-0.53), as well as the GMin and GMax in sitting down and standing up (r_s =0.60-0.77). All calculated correlations of the ipsilateral fat volume and contact forces at 3M are shown in table 25 and figure 33 below.

Table 25: Correlation of ipsilateral fat volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level * = 0.05, P = Peak.

	<u>lpsilateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r _S = 0.02 (0.96)	r s = 0.41 (0.24)	r s = 0.10 (0.78)	r s = -0.04 (0.91)
	Walking 2 P	r s = 0.21 (0.56)	r s = 0.48 (0.16)	$r_s = 0.30 (0.41)$	r s = -0.19 (0.60)
3⊠	Stairs Up 1 P	r s = 0.18 (0.63)	rs = 0.53 (0.12)	r s = 0.26 (0.47)	$r_s = 0.06 (0.88)$
<u></u>	Stairs Down 1 P	$r_s = 0.13 (0.73)$	rs = 0.52 (0.13)	$r_s = 0.33 (0.35)$	r s = 0.04 (0.91)
	Sit Down Max	ľs = 0.77 (0.07)	$r_S = 0.94* (0.005)$	ľs = 0.77 (0.07)	r s = 0.09 (0.87)
	Stand Up Max	r _S =0.60 (0.21)	ľ _S =0.87* (0.019)	$\Gamma_{\rm S} = 0.66 \ (0.16)$	r _S = 0.31 (0.54)

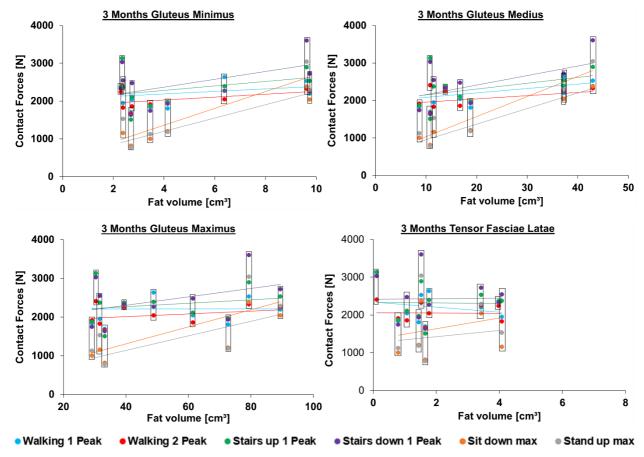


Figure 33: Correlation of ipsilateral fat volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

At 50M, a higher fat volume of the ipsilateral GMax was only correlated with higher contact forces in stair ascent (r_s =0.68*). However, all gluteal muscles were found to have an effect on loads in walking 2nd Peak (r_s =-0.57-0.57), as well as the GMin and GMax for walking 1st Peak (r_s =-0.53, r_s =0.53 respectively). All calculated correlations of the ipsilateral fat volume and contact forces at *50M* are shown in table 26 and figure 34 below.

Table 26: Correlation of ipsilateral fat volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level * = 0.05, P = Peak.

	<u>Ipsilateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	rs = -0.53 (0.15)	r s = 0.38 (0.31)	rs = 0.53 (0.14)	r s = 0.22 (0.58)
	Walking 2 P	rs = -0.57 (0.11)	r _S = 0.55 (0.13)	rs = 0.57 (0.11)	r s = 0.23 (0.55)
20M	Stairs Up 1 P	r _S = -0.24 (0.53)	r _S = 0.45 (0.22)	r _S = 0.68* (0.042)	r _S = 0.38 (0.31)
20	Stairs Down 1 P	r _S = -0.30 (0.43)	r s = 0.35 (0.36)	f s = 0.43 (0.24)	r _S = -0.02 (0.97)
	Sit Down Max	r _S = -0.33 (0.39)	$\Gamma_{S} = 0.22 (0.58)$	$r_S = 0.30 (0.43)$	r _S = 0.28 (0.46)
	Stand Up Max	r _s = -0.35 (0.35)	r _S = 0.25 (0.52)	r _s = 0.33 (0.38)	r s = 0.18 (0.64)

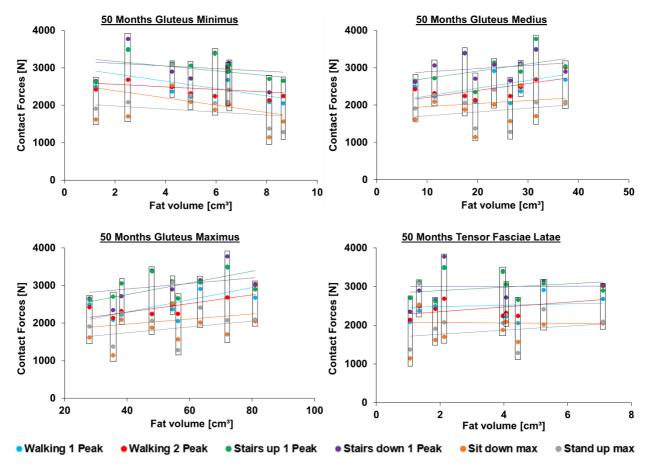


Figure 34: Correlation of ipsilateral fat volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

At 3M, higher fat volumes of the contralateral GMin and GMed were correlated with higher contact forces in sitting down ($r_s=0.94^{**}$, $r_s=1.00^{**}$) and standing up ($r_s=0.89^{*}$, $r_s=0.94^{**}$). The GMax fat volume was also found to have an effect on increased joint contact forces ($r_s=0.77$). All calculated correlations of the contralateral fat volume and contact forces at 3M are shown in table 27 and figure 35 below.

Table 27: Correlation of contralateral fat volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level ** = 0.01, * = 0.05, P = Peak.

<u>C</u>	<u>ontralateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	$r_S = 0.09 (0.80)$	r _S = 0.33 (0.35)	r _S = 0.18 (0.63)	r _S = 0.37 (0.29)
	Walking 2 P	r s = 0.22 (0.53)	$r_s = 0.33 (0.35)$	r s = 0.37 (0.29)	r s = 0.01 (0.99)
5	Stairs Up 1 P	r s = 0.29 (0.43)	$\Gamma_S = 0.37 (0.29)$	$\Gamma_{S} = 0.36 (0.31)$	$r_s = 0.32 (0.37)$
38	Stairs Down 1 P	$r_s = 0.35 (0.33)$	$\mathbf{f}_{S} = 0.41 \ (0.24)$	$\Gamma_S = 0.42 (0.23)$	r s = 0.16 (0.65)
	Sit Down Max	rs = 0.94** (0.01)	rs = 1.00** (0.00)	$\Gamma_{\rm S} = 0.77 (0.07)$	r s = -0.09 (0.87)
	Stand Up Max	r _S =0.89* (0.02)	$\Gamma_{\rm S} = 0.94^{**} (0.005)$	$\Gamma_{S} = 0.66 (0.16)$	$\mathbf{r}_{S} = 0.03 (0.96)$

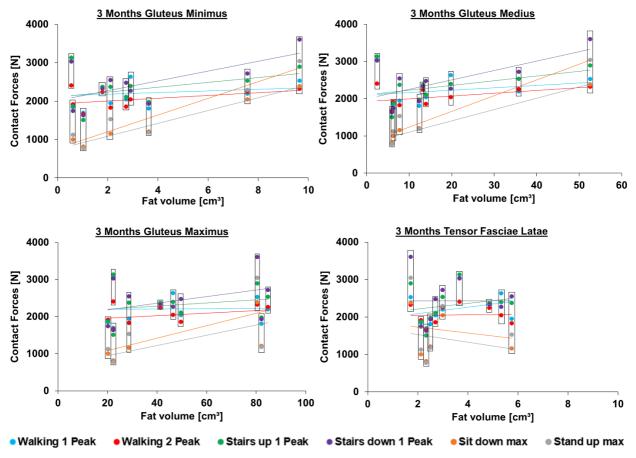


Figure 35: Correlation of contralateral fat volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

At 50M, only higher fat volumes of the contralateral GMin correlated with higher contact forces in sitting down (r_s =0.80**). Further, the contralateral GMin and GMed fat volumes were shown to have an effect on loads in standing up (r_s =0.65, r_s =0.50 respectively). The TFL was found to only have an effect on loads in stair ascent (r_s =0.57). All calculated correlations of the contralateral fat volume and contact forces at *50M* are shown in table 28 and figure 36 below.

Table 28: Correlation of contralateral fat volume and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level ** = 0.01, P = Peak.

Co	ontralateral	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r _S = -0.12 (0.77)	r s = 0.32 (0.41)	r _S = 0.27 (0.49)	r _S = 0.12 (0.77)
	Walking 2 P	r s = 0.18 (0.64)	r _S = 0.33 (0.38)	r s = 0.22 (0.58)	r s = 0.10 (0.79)
20M	Stairs Up 1 P	$r_S = 0.08 (0.83)$	$\Gamma_{S} = 0.47 (0.21)$	$\Gamma_{S} = 0.42 (0.27)$	$\Gamma_{\rm S} = 0.57 (0.11)$
20	Stairs Down 1 P	r _S = 0.20 (0.61)	r _S = 0.40 (0.29)	r _S = 0.17 (0.69)	r _S = 0.28 (0.46)
	Sit Down Max	rs = 0.80** (0.010)	r s = 0.43 (0.24)	r _S = -0.17 (0.69)	r _S = -0.10 (0.80)
	Stand Up Max	rs = 0.65 (0.06)	r _S = 0.50 (0.17)	r _S = -0.13 (0.73)	r _S = -0.22 (0.58)

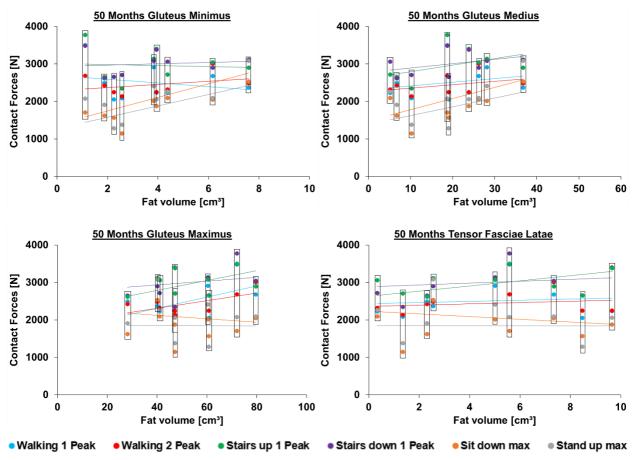


Figure 36: Correlation of contralateral fat volume and in vivo joint contact forces. Volumes in [cm³], loads in [N]. Each block represents one patient, each colour an activity.

5.4.4 Correlation between fat ratio and in vivo contact forces

Ipsilateral side

Analogous to the fat volume, higher fat ratio (total area of fat divided by total area of fat plus total area of muscle) of all ipsilateral gluteal muscles at 3M correlated with increased contact forces in sitting down ($r_s=0.84^*-0.94^{**}$) as well as for the GMin and GMed in standing up ($r_s=0.84^*$, $r_s=0.89^*$ respectively). However, the GMax fat ratio was also shown to have an effect on loads in standing up ($r_s=0.75$). Further, a higher fat ratio of all muscles but the GMin was correlated with increased contact forces at walking 2^{nd} Peak ($r_s=0.65^*-0.71^*$). All calculated correlations of the ipsilateral fat ratio and contact forces at 3M are shown in table 29 and figure 37 below.

Table 29: Correlation of ipsilateral fat ratio and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level ** = 0.01, * = 0.05, P = Peak.

	psilateral	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r s = 0.03 (0.93)	r _S = 0.31 (0.39)	r s = 0.14 (0.70)	r s = 0.09 (0.80)
	Walking 2 P	$r_s = 0.20 (0.58)$	rs = 0.71* (0.022)	rs = 0.73* (0.018)	$\Gamma_{S} = 0.65^{*} (0.042)$
38	Stairs Up 1 P	r s = 0.20 (0.59)	$r_s = 0.32 (0.37)$	$\Gamma_S = 0.18 (0.63)$	r s = 0.21 (0.58)
<u></u>	Stairs Down 1 P	$r_s = 0.05 (0.89)$	f s = 0.43 (0.21)	$r_s = 0.39 (0.27)$	r s = 0.33 (0.34)
	Sit Down Max	rs = 0.93** (0.008)	rs = 0.94** (0.005)	rs = 0.84* (0.036)	r s = 0.14 (0.79)
	Stand Up Max	rs = 0.84* (0.036)	rs = 0.89* (0.019)	$\Gamma_S = 0.75 (0.08)$	r s = 0.26 (0.62)

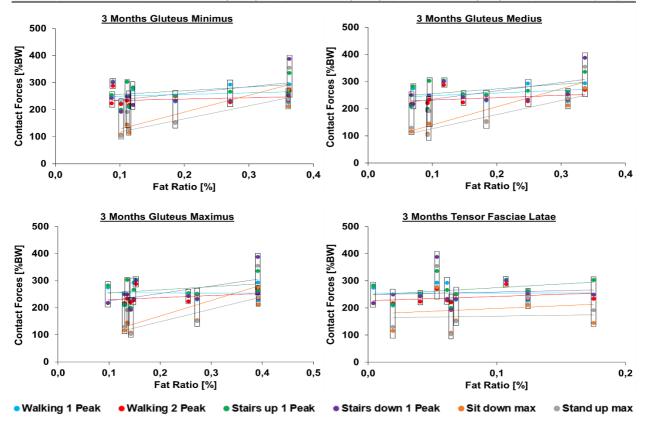


Figure 37: Correlation of ipsilateral fat ratio and in vivo joint contact forces. Ratios in [%], loads in [%BW]. Each block represents one patient, each colour an activity.

However, at 50M, the only effect found was that of an increased ipsilateral GMin and TFL fat ratio on higher contact forces in sitting down (r_s=0.64). All calculated correlations of the ipsilateral fat ratio and contact forces at 50M are shown in table 30 and figure 38 below.

Table 30: Correlation of ipsilateral fat ratio and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, P = Peak.

	<u>lpsilateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r _S = -0.48 (0.19)	r _S = -0.02 (0.97)	r _S = 0.08 (0.85)	r _S = 0.15 (0.70)
	Walking 2 P	$\Gamma_{S} = -0.12 (0.77)$	r _S = 0.12 (0.77)	$\Gamma_{S} = 0.25 (0.52)$	$r_S = 0.00 (1.00)$
50M	Stairs Up 1 P	r s = -0.32 (0.41)	r s = -0.10 (0.80)	r s = 0.15 (0.70)	r _S = 0.27 (0.49)
20	Stairs Down 1 P	r s = 0.20 (0.61)	r s = 0.30 (0.43)	r s = 0.40 (0.28)	r s = -0.03 (0.93)
	Sit Down Max	rs = 0.64 (0.07)	r s = 0.09 (0.81)	r _S = 0.19 (0.62)	rs = 0.64 (0.06)
	Stand Up Max	r s = -0.23 (0.55)	r s = -0.07 (0.87)	r s = 0.15 (0.70)	r s = 0.33 (0.38)

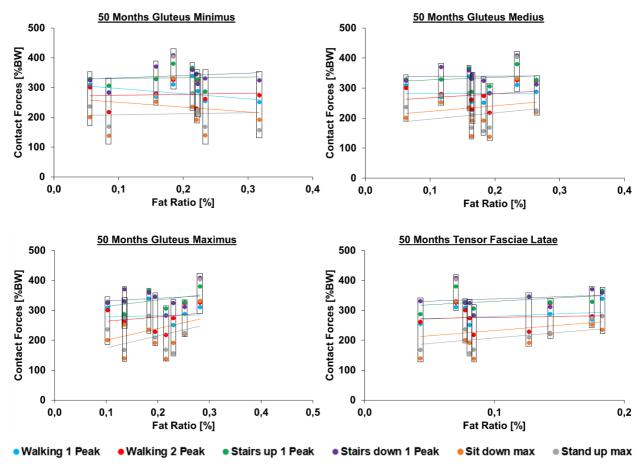


Figure 38: Correlation of ipsilateral fat ratio and in vivo joint contact forces. Ratios in [%], loads in [%BW]. Each block represents one patient, each colour an activity.

Analogous to the fat volume, at 3M, higher fat ratios of all contralateral gluteal muscles were correlated with higher contact forces in sitting down (r_s =0.94**) and standing up (r_s =0.89*). A higher fat ratio of all gluteal muscles also correlated significantly with increased forces in walking 2nd Peak (r_s =0.70*-0.79**). All calculated correlations of the contralateral fat ratio and contact forces at 3M are shown in table 31 and figure 39 below.

Table 31: Correlation of contralateral fat ratio and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level ** = 0.01, * = 0.05, P = Peak.

	<u>Contralateral</u>	Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
	Walking 1 P	r _S = 0.21 (0.56)	r _S = 0.34 (0.34)	r s = 0.25 (0.49)	r _S = 0.24 (0.51)
	Walking 2 P	$\Gamma_{\rm S} = 0.70^* \ (0.025)$	$\Gamma_{\rm S} = 0.75^* (0.013)$	r _S = 0.79** (0.006)	r _S = -0.22 (0.53)
Σ	Stairs Up 1 P	r s = 0.27 (0.45)	r s = 0.35 (0.32)	r s = 0.30 (0.41)	r s = 0.15 (0.68)
<u></u>	Stairs Down 1 P	r s = 0.43 (0.21)	r s = 0.44 (0.21)	r s = 0.50 (0.14)	r s = 0.18 (0.63)
	Sit Down Max	$\Gamma_{\rm S} = 0.94^{**} (0.005)$	$\Gamma_{\rm S} = 0.94^{**} (0.005)$	$\Gamma_{\rm S} = 0.94^{**} (0.005)$	r _S = -0.26 (0.62)
	Stand Up Max	r _S = 0.89* (0.019)	$\Gamma_{\rm S} = 0.89^* \ (0.019)$	r _S = 0.89* (0.019)	r s = -0.09 (0.87)

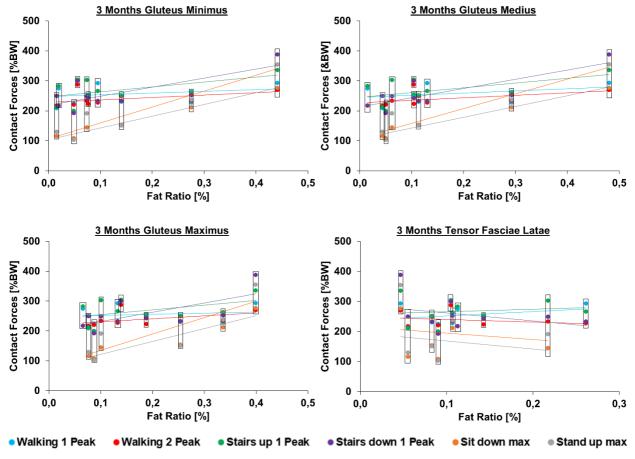


Figure 39: Correlation of contralateral fat ratio and in vivo joint contact forces. Ratios in [%], loads in [%BW]. Each block represents one patient, each colour an activity.

At 50M, higher fat ratios of the contralateral GMin were shown to have an effect or correlated with higher contact forces in all ADL but sitting down (r_s =0.57-0.88**). Further, effects were shown for GMed and GMax fat ratios on increased forces in stair ascent (r_s =0.52) and sitting down (r_s =0.60). A lower contralateral TFL fat ratio also showed an effect on decreased contact forces in stair descent (r_s =-0.57). All calculated correlations of the contralateral fat volume and contact forces at *50M* are shown in table 32 and figure 40 below.

Table 32: Correlation of contralateral fat ratio and in vivo joint contact forces. r_s (p-values) calculated using Spearman's rank correlation, significance level ** = 0.01, P = Peak.

Contralateral		Gluteus Minimus	Gluteus Medius	Gluteus Maximus	TFL
20M	Walking 1 P	r _S = 0.17 (0.67)	r _S = 0.13 (0.73)	r _s = -0.37 (0.33)	r _S = -0.23 (0.55)
	Walking 2 P	r _S = 0.62 (0.08)	$\Gamma_{S} = 0.27 (0.49)$	r _S = -0.33 (0.38)	r _S = -0.55 (0.13)
	Stairs Up 1 P	rs = 0.57 (0.11)	r _S = 0.52 (0.15)	r _S = -0.38 (0.31)	r _S = -0.03 (0.93)
	Stairs Down 1 P	r _S = 0.88** (0.002)	$ _S = 0.33 \ (0.38)$	r _S = -0.15 (0.70)	$\Gamma_{\rm S}$ = -0.57 (0.11)
	Sit Down Max	r s = 0.24 (0.53)	f _S = 0.13 (0.75)	rs = 0.60 (0.09)	r s = 0.26 (0.50)
	Stand Up Max	rs = 0.80** (0.010)	f _S = 0.25 (0.52)	r s = -0.48 (0.21)	r s = -0.53 (0.14)

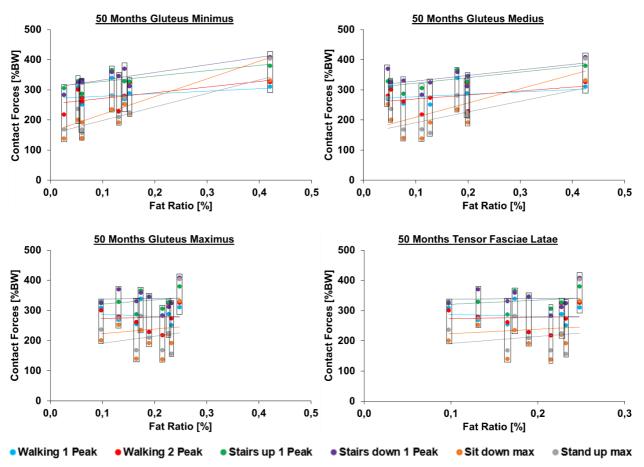


Figure 40: Correlation of contralateral fat ratio and in vivo joint contact forces. Ratios in [%], loads in [%BW]. Each block represents one patient, each colour an activity.

5.5 Clinical scores and examination

5.5.1 Harris Hip Score

With an average of 92 (5.5) points, all nine patients reached a good to very good score, indicating a satisfactory long-term outcome at *50M* post THA. Six patients reached >90 points, they are hence expected to have full function of their hip joint. The other three patients scored lower because of joint pain and decreased ROM.

5.5.2 Western Ontario and McMaster Universities Osteoarthritis Index

In line with the results above, all patient scores (mean 91 (5.7)) remained under the first percentile, indicating that there was almost no disease activity postoperatively. Patient H5 was found to have the lowest score (80) thus worst functionality of her hip joint.

5.5.3 Visual Analogue Scale Pain

The mean for the VAS Pain was 0.56. Seven out of nine patients indicated to have no pain at all in the operated hip joint on the day of examination at *50M*. Only two patients ranked their pain at 2/10 and 3/10 respectively, which may be evaluated as transitory, as these two patients did not report any general pain in the other questionnaires.

5.5.4 EuroQuol-5D-3L

The mean value for the EuroQuol-5D-3L in our patient collective was 0.95. Seven out of nine patients reached the maximum score of 1.0, indicating an excellent generic health status. Only three patients scored lower (0.788-0.887), although these results still indicate a satisfactory health status.

5.6 Summary main results

Muscle status

Total muscle volume

At 3M, we only found the change in total muscle volume of the ipsilateral GMin to be significant (-25 \pm 15.3%, p=0.005). Also at 50M, the GMin (-18 \pm 10.8%, p=0.008) as well as the TFL (15 \pm 18.5%, p=0.015) showed significant changes in total muscle volume. From 3M-50M, only the ipsilateral GMax significantly changed in total muscle volume (9 \pm 8.1%, p=0.011). On the contralateral side, only GMin total muscle volume change after 3M was significant (-14 \pm 11.3%, p=0.009).

Lean muscle volume

At both, 3M and 50M, the ipsilateral GMin (-28 ±14.4%, p=0.008; -21 ±17.1%, p=0.008) and TFL (34 ±31.2%, p=0.013; 31 ±21.7%, p=0.008) showed a significant change in lean muscle volume. On the contralateral side, only the GMin was found to significantly change in lean muscle volume from 3M-50M (16 ±20.8%, p=0.038).

Intramuscular fat content

Only the change of fat volume of the ipsilateral TFL after 3M showed statistical significance (-52 ±36.8%, p=0.021). Further, analogous to the fat volume, the change in fat ratio of the ipsilateral TFL at 3M was shown to be significant (-57 ±32.1%, p=0.017).

In vivo hip joint contact forces

At both *3M* and *50M*, the highest joint loads were reached during stair descent (average 281%BW and 336%BW), whereas sitting down produced the lowest in vivo loading (average 169%BW and 211%BW).

Impact of muscle status on in vivo hip loads

At 3M, only the total muscle volume of the ipsilateral GMed correlated with the in vivo measured joint loads in walking 1st Peak ($r_s=0.67^*$). However, at 50M, we found the total muscle volume of the ipsilateral GMax to correlate with increased joint loads in walking 1st Peak ($r_s=0.72^*$).

Further, a lower ipsilateral lean muscle volume at 3M correlated with increased loads in all ADL but stair descent (r_s =-0.67* - -0.94**). At 50M, only the ipsilateral GMax lean muscle volume was shown to be significantly correlated with loads in walking 1st Peak (r_s =0.68*).

On the contralateral side, a low GMed lean volume at 3M was correlated with increased loads in sitting down ($r_s=-0.72^*$), however, at 50M, this correlation was only shown for the GMin lean muscle volume ($r_s=-0.72^*$).

At 3M, an increase in ipsilateral intramuscular fat volume of the GMed was found to correlate with higher hip joint loads in sitting down (r_s =0.94**) and standing up (r_s =0.87*). This correlation was also shown for the contralateral GMed (r_s =1.00**, r_s =0.94**) and GMin (r_s =0.94**, r_s =0.89*). However, these effects were less evident in the long-term follow-up after 50M.

Finally, a high ipsilateral fat ratio at 3M was correlated with increased joint loads in walking 2^{nd} Peak (GMed r_s =0.71*, GMax r_s =0.73*, TFL r_s =0.65*), sitting down (GMin r_s =0.93**, GMed r_s =0.94**, GMax r_s =0.84*) and standing up (GMin r_s =0.84*, GMed r_s =0.89**). Moreover, a high contralateral fat ratio at 3M was correlated with increased joint loads in walking 2^{nd} Peak (GMin r_s =0.70*, GMed r_s =0.75*, GMax r_s =0.79**), sitting down (GMin r_s =0.94**, GMed r_s =0.94**, GMax r_s =0.94**) and standing up (GMin r_s =0.89*, GMed r_s =0.89*, GMax r_s =0.89*). At s=0.89*, GMax s=0.89*, GMax s=0.89*) and standing up (s=0.80**).

6. Discussion

To the best of our knowledge, this study is the first to correlate the periarticular muscle status with in vivo measured hip joint contact forces. Our hypothesis that an impairment of the gluteal and TFL muscles, determined by fatty degeneration, is correlated with higher contact forces - can be generally supported by our results. Contrary to our theoretical considerations, the total muscle volume was shown not to be a reliable indicator for the in vivo measured contact forces, neither in the short- nor in the long-term postoperative follow-up. We found the lean muscle volume and fat ratio of the gluteal muscles to be correlated with the joint loads during different ADL, while this effect was greater at 3 than at 50 months after THA surgery. This effect was mainly seen for the bilateral GMin and GMed in standing up, sitting down and stair climbing. Further, the TFL, despite hypertrophic reaction postoperatively, did not significantly influence the in vivo measured contact forces in our study.

6.1 Patients

Our patient collective was markedly younger than the average primary THA patient in other studies ^{29,109}. Since our objective was to measure physically demanding exercises in our gait analyses using the instrumented implant, we included rather younger and active subjects in our study. Further, the average body height (mean 174cm) together with the BMI (mean 29.4 to 30.3) of our subjects was higher than in other investigations ^{71,109}. As the BMI has previously been shown to be associated with greater fat content of the hip muscles, this may have influenced our findings regarding the hip muscle morphology ⁷¹.

6.2 Periarticular hip muscle status

There is a lack of comprehensive information on the preoperative muscle status in patients with OA of the hip, although this information is required to properly evaluate the effects of THA on the pelvic musculature. Several studies reported the hip and thigh muscles to atrophy in patients with arthritis of the hip ^{7,8,54,56,109}. Arokoski et al. ⁵⁴ reported younger OA patients (aged 47 to 64 years) to suffer from significant muscle weakness and atrophy of the flexors, lower ab- and adductors, however, they did not proceed to assess postoperative changes in muscular force or volume. Hence, the objective of a study by Rasch et al. ¹⁰⁹ was to measure a complete preoperative set of periarticular hip muscle function in OA patients that could be used as baseline data.

They found the hip extension, flexion, ab- and adduction strength of the OA-diseased joint to be reduced by 11 to 29% compared to the healthy contralateral limb. Surprisingly, the CSA of all major muscles functioning around the hip but the abductors was reduced (11 to 19%). Similarly, the radiological density (RD) was reduced by 5 to 15 HUs in all muscle groups but the hip flexors. Further, Grimaldi et al. ⁸ suggest that the GMed on the OA-affected side is rather predisposed to hypertrophy in earlier stages before atrophying in later stages of joint pathology. However, single CSA measurements are unlikely to be as reflective of a muscle's morphology as a measurement of total muscle volume. Moreover, it is reported in the literature that aged and inactivated muscles are subject to an increased fat infiltration⁷¹, hence measurements of the mere CSA of a muscle supposedly overestimate its contractile muscle mass. In line with previous investigations ^{29,71,109} we therefore differentiated between total and lean muscle volume by determining fat ratios of the individual muscles.

6.2.1 Muscle volumes

We found the ipsi- and contralateral GMin to significantly decrease in muscle volume over the first 3 months after surgery. The volume decrease on the operated side was equally significant in the long-term course of 50 months compared to the preoperative state. A decrease of the GMin muscle volume can be seen as a direct effect of THA surgery. Similar findings have previously been described in the literature and are further supported by our data ^{53,55,57}. Concurrently with the GMin volume decline, we found a bilateral hypertrophy of the TFL muscle that showed on the operated side a trend at 3 months and was significant at 50 months after THA. Hypertrophy of the ipsilateral TFL has been described as a benign reaction after THA in several studies 110,111 and is supposed to be a compensatory mechanism for an approach-related impaired abductor muscle function after THA surgery. Sutter et al. 111 found the TFL muscle in patients with an abductor tendon tear on the damage side to hypertrophy compared to the TFL of the healthy limb. Our patients did not suffer from a tendon tear per se, but since all patients were operated using the DLA, their gluteal muscles were inevitably damaged. It is further known that muscular weakness in the immediate postoperative period on the ipsilateral side persists for up to six weeks and thus provides, next to the surgical iatrogenic muscle damage, another explanation for morphologic changes of the GMin ¹¹². Our data complements previous findings on TFL hypertrophy as a compensation strategy for gluteal muscle impairment.

No long-term changes of the contralateral TFL muscle, as shown in our 50M data, is also consistent with previous observations ⁷. The volume decrease of the contralateral GMin was only significant in the short-term follow up and may be explained in several ways. First, impaired mobility after a surgical intervention such as THA may play an important role in muscular atrophy due to inactivity. Even after successful THA and rehabilitation, patients may remain relatively inactive. A study by Suetta et al. 111 showed that aged and inactivated muscles are at great risk for muscular atrophy and thus may partially explain our findings on the non-operated side. Second, changes in hip and gait kinematics leading to unloading of the previously high loaded contralateral side after THA may explain the GMin volume loss in the short-term postoperative course. As previously described, patients with OA present alterations in gait patterns to avoid pain on weightbearing structures, that subsequently influence joint moments on the contralateral side ¹¹³. Although the literature is not unanimous on the time period that preoperative gait adaptions persist after THA, one could argue that after successful THA, the biomechanics of the hip shift back to normal and the loading on the contralateral side decreases together with the muscle volume 114.

As THA alleviates pain and generally increases the patients' activity levels, one would expect the muscular strength of hip and thigh muscles to recover in the long term. We found a postoperative volume increase of the ipsilateral GMed in the short and long-term follow up. These findings are consistent with a study by Uemura et al. ⁵⁸ who reported a significant increase in CSA by 11% of the GMed on the operated side more than two years after THA. In contrast, Rasch et al. ⁵⁵ showed the GMed and GMin to slightly decrease in volume in a six month and two year postoperative follow up. However, these data are not directly comparable, as they measured the CSA of the abductors grouped together, providing a global measure, hence, the GMin may have dominated the volume loss over the GMed. The contralateral GMed showed a stable muscle volume over the 50 months following surgery, which is also in line with previous research ⁵⁵. There have been very few quantitative analyses of muscle volume changes of the hip and thigh muscles after THA and a clear trend has not yet been established in the literature.

Finally, the GMax on the operated side significantly increased in the postoperative course of 50 months, suggesting that it could fully recover from a possibly impaired preoperative state. These findings on the ipsilateral side, as well as the GMax of the non-operated limb that did not show volume changes, are consistent with the literature ⁵⁵.

6.2.2 Fatty degeneration

It has been shown that fatty infiltration is a common muscular response to degenerative or traumatic tendon rupture as well as iatrogenic muscle injury during THA ^{10,34}. Our patients were operated using the transgluteal DLA, in which the anterior part of the GMed is split and detached from the greater trochanter, causing imminent muscle damage. We therefore hypothesized the ipsilateral GMin and GMed to be subject to higher fatty degeneration and consequently lower RD than non-affected muscles. A study by Goodpaster et al. ⁷⁰ found CT to be a valid method with low methodological error to assess muscular RD. They reported that each percent increase in tissue fat corresponded to a density reduction of 0.75 to 1 HU. A previous study by Daguet et al. ⁷¹ used CT scans to evaluate the variability of fat content of the hip muscles and their impact on physical performance in a healthy control population. They reported a general anteroposterior gradient with a mean of 2% in the hip flexors, 6% in the abductors to 10% in the hip extensors. Further, the fat content was found to increase with age, BMI and lower physical activity.

In their preoperative measurements of OA hip patients, Rasch et al. ¹⁰⁹ found a marked decline of RD in most of the periarticular muscles except hip flexors (5 to 15 HUs) on the diseased side relative to the healthy limb, indicating a significant infiltration with fat. With similar fat ratios of the abductors (mean 15 to 16%) and elevated bilateral fat content of the GMax (mean 16 to 19%), our data on preoperative fatty infiltration generally supports prior findings reported in the literature. Significant preoperative inter-individual differences in the fat content of our patients may be explained by differences in age, BMI and level of physical activity as reported before ⁷¹. Unfortunately, there is no study that measured fatty degeneration of the TFL as an individual muscle, thus there is no data available for comparison.

In the postoperative course of 3 months, our analyses of fatty degeneration showed high inter-individual differences on the ipsilateral side. These findings may be explained in two ways. First, preoperative fat ratios between our study subjects already showed marked differences, one could thus expect these variances to persist postoperatively. On the contralateral side, the fat ratio of the abductors and TFL moderately decreased in the short-term course after THA. This decrease and the significant decline in RD of the ipsilateral TFL over 3 and 50 months could be explained by the aforementioned compensatory mechanism for impaired muscle strength of the ipsilateral abductors.

Consistent with observations from Rasch et al. ⁵⁵ who reported the mean RD of all ipsilateral periarticular muscles to be reduced at the six month follow up, we noted an increase of fat ratio in all gluteal muscles at 3 months. If our 3-month data is comparable to measurements at six postoperative months may remain a topic of discussion.

Second, the increase in fat content in the long-term follow up persisted, notably for the ipsilateral abductors but also for the GMax. These findings are equally in line with previously published data ^{29,55,71} reporting a global increase of fatty degeneration after THA. The moderate increase in fat ratio on the contralateral side after 50 months postoperatively is most likely due to the physiological decline of muscle strength with age and BMI.

In conclusion, the most striking finding of our analyses was that the marked preoperative atrophy, characterised by muscle volume and fatty degeneration, of the analysed hip muscles persisted until the long-term follow up at 50 months, but some muscles (ipsilateral GMax) fully recovered. Being a more reliable indicator than the total muscle volume, the significant reduction in RD indicates a substantial net loss in contractile muscle tissue. Only the ipsilateral GMax seemed to have the potential to recover over time: here our findings are in line with previous reports that all hip muscles but the GMax do not recover at the same rate as muscles of the calf and thigh after THA ⁵⁵. Hence, this study further supports prior findings in that fat infiltration is a strong negative predictor of muscle recovery ⁶².

The impaired long-term recovery of the healthy limb may be explained by relatively stagnant activity levels of the patients even after successful joint replacement. Alternatively, one can argue that the healthy side is overloaded during preoperative years, as the patient tries to alleviate pain by shifting its weight to avoid excessive impact on the diseased side. Hence, this behavior could be seen as preoperatively adopted strategies that persist in the postoperative setting. The aforementioned would argue against extensive conservative management of OA but for earlier operative treatments.

6.3 Hip joint loading

Previous research has shown THA patients to improve postoperatively in performing different ADL ^{115–117}, while some activities such as chair rising and sitting remain challenging ^{115,118}. Due to a low number of studies, many long-term effects of THA on gait and ADL are not yet accurately known. Moreover, outcomes after THA are commonly assessed using clinical scores, most of them being based on subjective measurements (see 4.6). Hence, for a comprehensive and objective evaluation of the hip function after surgery, there is a need for quantitative measurements such as gait analysis ¹¹⁹. Measurements of in vivo contact forces in the hip, however, remain the exception in studies of gait alterations after hip replacement surgery ⁴⁶. Hip contact forces measured in vivo were first obtained by Rydell (1966) ¹²⁰, Davy et al. (1988) ⁸⁴ and Kotzar et al. (1991) ¹²¹, however, these reports are limited to short-term data of only two patients and do not include detailed gait data. Comparable standardised loads acting in hip implants have been published previously by our study group ⁷².

Walking has been studied most extensively among all ADL. In general, gait kinematics are supposed to improve after successful THA, although it was found not to attain normal levels in the long term ^{114,122}. A meta-analysis by Ewen et al. ¹²³ revealed significant reductions in walking velocity, sagittal hip ROM and peak hip abduction moments on the operated side. It has been shown that most of these changes in hip kinematics are related to abnormal joint loading, which in return may imperil fixation of the prosthesis or cause debilitative effects on other joints ^{124,125}. Measuring joint loads is difficult by nature, while previous joint loading data are generally based on musculoskeletal simulations, in vivo measurements are scarce in the literature. Our measurements showed a notable variance in individual magnitudes of F_{res} during level walking, whereas the load cycles all showed a double-peak pattern, with the first peak being slightly higher than the second one. The significant intra-individual differences in the postoperative course from 3 to 50 months may have several explanations. First, an age-related physiological decline in strength of the hip muscles could explain the general increase in contact forces that could be found among all study subjects. Another explanation for higher contact forces in the long-term follow up could be the previously mentioned compensatory mechanism of the impaired abductors by other hip muscles. A study by Bergmann et al. 85 showed these muscles to unfavourably adjust their lever arm acting at the hip joint, which may cause the contact forces to increase.

To this day, research into ADL other than level walking has been scarce in THA patients, but force moments in stair climb were generally similar or lower than in level walking 115-^{118,126,127}. However, these observations are not supported by our data, as average loads at 3 and 50 months exceeded those obtained in level walking. Moreover, patient H5 reached the highest overall peak value of 418%BW during stair descent. Previous measurements of kinetics in stair ascent reported the peak hip abduction moment in THA patients to be lower or similar to matched controls, whereas the adduction moment was similar among all studies 115,128,129. Also peak internal rotations moments and total hip power generation was shown to be lower than in controls 115,128-130. As expected, the operated side showed lower internal peak hip rotation moments than the healthy limb ¹³¹. The decline in the abduction moment that takes place in the frontal plane (see Trendelenburg gait) could hence be explained by a persistent muscle weakness that THA patients acquired in preoperative years or by the iatrogenic muscle injury inherent to surgical THA procedures such as the DLA (see 3.1.3). Surprisingly, studies that looked at patients operated using an abductor sparing technique also reported a reduced hip abduction moment ²⁸. The lower peak internal rotation moment might be associated with injury to the anterior GMed and GMin, as both can also function as internal rotators. In stair descent, differences with controls were even less apparent as the peak hip internal rotation, ab- and adduction moments were found to be similar to healthy subjects ^{128–130}. Moreover, the stance duration on the operated side was shown to be shorter than that on the healthy limb ¹³¹. Gait kinematics have been obtained from our patients during the postoperative gait laboratory measurements and will be a focus in future reports of our study group.

Hip joint loads in double-legged activities (chair rising and sitting) have previously been reported to be markedly lower than in single-legged exercises (level walking, stair negotiation) ⁷². Investigations of standing up and sitting down, although considered to be among the most common ADL, are rare to find in the literature, but their performance is described to be generally asymmetric in THA patients ¹¹⁶. At both follow ups, we found loads to be lower than in the other ADL, while differences in the postoperative course were insignificant. This may be explained by the minimally impaired function of the ipsilateral GMax, together with the vastus muscle, being primarily responsible for this movement.

6.4 Impact of muscle status on in vivo joint contact forces

To the best of our knowledge, the present investigation is the first to examine the impact of the periarticular hip muscle status on in vivo joint contact forces. Based on previous research ⁸⁵ and theoretical considerations, we hypothesized that a muscle impairment would be associated with increased joint loads. As a consequence, we would expect a high lean muscle volume and low fat ratio, together with the interaction and balance of the activated muscles, to correspond with lower contact forces.

We found a surprisingly weak correlation of total muscle volume and joint loads at both the short- and long-term measurements taken in the postoperative course. The volume of the ipsilateral GMed correlated negatively with 1st Peak forces only in level walking, however, we equally noted this effect for the GMed and GMax over the 50 months course after surgery. These findings further support the assumption that total muscle volume overestimates the contractile muscle mass and therefore is not a valid indicator of in vivo contact forces. We found the lean muscle volumes to be a better indicator, since in the GMax it was shown to be associated with higher joint loads in sitting on a chair at 3 months and walking at 50 months, which is consistent with previous reports of the GMax to play a major role in these exercises ¹³². Moreover, lower lean muscle volume of the ipsilateral GMin was found to be correlated with higher force peaks in all tested ADL at 3 months, which further supports our hypothesis that more contractile muscle tissue corresponds with lower joint loading. Our second hypothesis that higher fat infiltration of the gluteal muscles would be associated with increased joint loads can be further supported by our findings. Daguet et al. 71 reported fatty muscle degeneration to cause gait impairments, whereas changed gait patterns were found to be associated with higher in vivo contact forces 45,46,94. Previous research of the shoulder musculature indicated a decline in muscle force due to fat infiltrated stiff muscles attended by a substantial loss in contractility ¹³³. Our data further supports these observations, since higher fat ratios were found to generally correlate with increased in vivo joint contact forces. Thus, the strongest correlation of fat ratio, in line with total fat volume, and joint loading was found for all gluteal muscles during chair rising and sitting, as well as walking for all muscles but the GMin 3 months after THA surgery. Interestingly, this impact could not be reproduced in the long-term follow up data, in which only the fat ratio of the GMin showed a weak effect. This could be explained by the decrease of the GMed and GMax fat ratio we found in half of the patients in the postoperative course of 3 months to 50 months.

One hypothesis is that there exists a cut-off point in fat ratio of the gluteal muscles before the joint load becomes affected. Other ADL (level walking, stair negotiation) produced notably higher contact forces, hence the lack of correlation between muscular degeneration of the gluteal muscles and joint loads may be explained by the compensatory strategy of other muscles, which have not been included in our analysis, taking over parts of the required joint moment.

Long-term kinetic differences between the ipsi- and contralateral limb in THA patients is an interesting field of study, as it allows identification of inter-limb strategies to compensate for impaired muscle function and biomechanics. Compared to healthy controls, Foucher et al. 125 observed significantly increased hip abduction and internal rotation moments on the non-operated side in THA patients. Furthermore, McCrory et al. ¹²⁴ previously showed a potential harm for prosthesis longevity in adopting asymmetric gait patterns with associated higher joint loading. By shifting loads, these strategies were reported to have debilitating effects on adjacent joints of the lower limb, notably the knee joint ¹²⁵. Interestingly, we found a higher muscle volume of the contralateral GMin and GMed to have an effect on lower peak forces in chair sitting and raising 50 months after THA. Although we would have expected this compensation for other ADL that produce higher contact forces, this might be identified as a compensatory mechanism of the abductors of the healthy limb. Even stronger correlations were shown for the lean muscle volume of the contralateral GMed and GMax at 3 months, which could be indicative of a short-term compensation, whereas long term the contralateral abductors play a more important role. The most striking finding was a decreased fat ratio of all contralateral gluteal muscles to be associated with lower peak forces sitting down, standing up and level waking 3 months postoperatively. These effects were again found to shift to the GMin only in the long-term follow up for the activities of stair climbing and sitting down, which is more consistent with the initially described activity pattern of the GMin (see 4.5). In conclusion, biomechanically speaking, severe unilateral OA of the hip can be seen as a bilateral disease extending down the kinetic chain of the lower limb, while these abnormal biomechanics were shown not to recuperate after THA ¹²⁵. The findings on the contralateral side call for further investigations into gait re-training and rehabilitative measurements to re-establish a symmetric gait pattern. Hence, strengthening of the contralateral abductor muscles should be recommended when first clinical signs or subjective complaints become symptomatic in hip OA patients.

6.5 Clinical scores

Since clinical scores were only obtained in the postoperative setting, we can unfortunately not compare values in order to assess the evolution of symptoms and joint functionality in our study subjects longitudinally. However, Rasch et al. ¹⁰⁹ determined in their preoperative study the HHS, EQ-5D and VAS in 22 patients with unilateral OA. Although the patients included were on average older (mean 67 years) than in our study and predominantly female, the values obtained in this study were similar to those in other studies and could be used as baseline data for comparison: mean EQ-5D score was 0.44, HHS 51.6 and VAS 5.2. In their follow up assessment two years after THA, all scores significantly improved to 0.85, 86.2 and 0.05 respectively. Our results showed a mean score of 0.95 for the EQ-5D, 92 for the HHS and 0.56 for the VAS, being consistent with previous reports on significant improvement of postoperative joint functionality and quality of life ^{55,114}. Findings for the WOMAC are in accord with the other scores, while our patients even reached a mean postoperative score that was above a healthy reference group reported in a study by Nilsdotter et al. ¹³⁴.

6.6 Clinical implications

Due to the small number of studies, the relationship between hip abductor weakness and joint loading as well as many long-term effects of THA on gait and ADL are not yet fully known. Our results suggest that the TFL muscle compensates in the short and long term for the loss in muscle volume and strength of the abductors, which is in line with previous research reporting that other hip muscles to take over ⁴⁵. Grimaldi et al. ⁸ however, propose that this hypertrophy of superficial abductors reflects a weakness in the deeper abductors and thus question the current clinical rationale for generalised hip abductor strengthening.

We only found a weak correlation of total muscle volume and in vivo contact forces, whereas lean muscle volume and fat ratio were shown to have a stronger impact. Further, Daguet et al.⁷¹ have previously reported the fat ratio to be a good predictor of hip muscle function and clinical outcomes. Our results further support their findings, as we found the aforementioned to have an effect on the in vivo measured loads and derive the conclusion that the fat ratio is a valuable indicator of hip joint loading. Therefore, further research should take the muscle status into consideration when aiming at optimising the postoperative joint biomechanics and long-term clinical management of THA patients.

The GMin was previously presumed to play only a minor role in pelvic stability ⁹⁰, however, we found the bilateral loss of contractile muscle tissue of the GMin to be correlated with higher joint loads in walking, chair sitting and rising 3 months after THA. As higher loads favour OA progression ^{7,8,135} and can have debilitating effects on neighbouring joints. Muscle strengthening of deeper abductors should be focused on pre- and postoperative THA patient management ⁵⁴. These findings would also argue to promote MIS and tissue-sparing surgical approaches in THA to prevent extensive muscle damage of the deep abductors.

There is, however, a scarcity in the literature on the activity pattern of the GMin alone, as it is often looked at as a functional unit together with the GMed. To our knowledge, there is only one study from Semciw et al. ¹⁰³ that investigated GMin activity limited to level walking using fine wire intramuscular EMG. Hence, the GMin may not be activated in all measured ADL and the question whether all gluteal muscles are active at both force peaks remains open. The GMax, however, was reported to be equally active at heel strike to help absorb ground reaction forces causing lateral pelvic drop and flexion moments at the hip and knee ¹³⁶. The TFL was shown to work against gravity in the swing phase of the gait cycle rather than be active in heel strike ⁹¹. Besides the muscle force, lever arm functioning of the hip muscles and implantation angles of the prosthesis have been identified to contribute to in vivo contact forces ⁴⁵. Although not directly comparable to the joint contact force, the ground reaction forces have been shown to depend 50 to 90% of muscule force and therefore play a major role in determining the joint loading ^{76,77,88}. There are no established benchmarks for gait mechanics after THA, whereas

abnormalities may be a barrier to full restoration of physical function ^{113,122}. Differences in recovery after THA have been explained by varying strengths of the severed muscles and subsequent compensation mechanisms of the pelvis after each type of surgery. Kiss et al. ¹³⁷ directly compared gait parameters of patients that underwent THA using the DLA and anterolateral approach (ALA) during the first postoperative year. They could support their hypotheses that the recovery period for the ALA patients was shorter than in those operated using the DLA, and that the two approaches would lead to different gait characteristics, as they affect different structures around the hip. The patients operated using the DLA, which affects mainly the gluteal muscles, were found to have a persistent reduction of ROM compared to healthy controls one year after surgery.

Our long-term data support these findings as well as the observation by Beaulieu et al. ¹¹³ that this is primarily compensated by the non-affected hip. They further confirmed that patients operated by the DLA did not reach normal gait mechanics and explained this by postoperatively adopted pain-avoidance strategies. These strategies were reported to result either from pain one year after surgery or non-recovery of proprioception of the transected gluteal muscles. In accord with our findings, two major conclusions can thus be drawn. Firstly, all patients operated by the DLA experience limitations in ROM and joint loading that are addressed by compensatory strategies. Secondly, the postoperative gait mechanics and joint ROM are significantly influenced by the surgical approach. Hence, improving gait mechanics may be one way to improve overall clinical and functional outcomes.

6.7 Limitations

The present study is subject to several limitations. The main limitation is the relatively small subject number of ten (n=10) at 3 months and nine (n=9) at 50 months, since patient H1 dropped out after the short-term follow up. Reaching statistically significant results given the small number of patients with an instrumented hip implant is difficult. However, our study recently received ethics and insurance approval for another ten years, indicating that our implants do not raise any concerns and that they are just as safe as a standard hip implant for the patients. The rather small patient collective in this study however allowed a close monitoring of each subject together with continuous gait laboratory measurements and follow ups. The most recent measurement at an average of 50 months after THA surgery is one of the incontestable strengths of this study. Second, this study assessed only the status of the TFL and gluteal muscles. Although we investigated the muscle status bilaterally, the impact of other muscles acting over the hip joint was not addressed in our study. Previous research suggests to differentiate between an anterior, middle and posterior part of the GMed when assessing the fatty degeneration ²⁹, however we based our analysis on the GMed as one functional entity. Similarly, Grimaldi et al. ⁷ proposed to assess the GMax as two functionally separate entities, an

upper (uGMax) and lower (IGMax) part. Whereas the uGMax was shown to act as a hip

abductor that remains rather unaffected in THA patients, the IGMax allows hip extension,

internal rotation anteriorly, external rotation posteriorly and is often subject to local

atrophy. Flack et al. ¹³⁸ propose to equally divide the GMed and GMin into compartments

with differential activation. In this study, we looked at each muscle as one functional entity.

Thirdly, MRI has been reported to be the best radiological technique to image soft tissue ^{11,66,139,140}, however, CT has been shown to be an equally valid method for assessment of muscular RD ⁶¹. Due to the inductive character of the instrumented implants used in our study, we obtained CT scans for a comparable assessment of the muscle status. In addition, inconsistent criteria for the upper and lower HU cut-offs used to characterise muscle radiation attenuation have been reported in the literature, which in turn limits comparison between different investigations of muscular RD ⁹⁸.

Fourthly, in vivo joint loads and clinical scores assessing overall joint functionality were only obtained in the postoperative setting. We thus cannot compare our results to either preoperative scores or joint loads acting in the hip. Further, data at 3 months is also limited for some activities as this study protocol was started only after some patients had already been to the gait laboratory for measurements. Therefore, data for sitting down and standing up is only available for six out of ten patients at 3 months after surgery.

Fifthly, we did not correct our measurements for inter-individual differences of our patients in age, sex or BMI. Engelken et al. ¹⁰⁰ found significant variances in fat ratios in THA patients of different sex and level of physical activity. Further, by investigating healthy control subjects Daguet et al. ⁷¹ showed the fat content of a muscle to increase with age and a higher BMI. This assumption may have influenced our analysis.

Finally, although the TFL and gluteal muscles have previously been shown to play a role in stance support, gait and the other ADL, we only investigated moments and force peaks throughout the load cycles ^{88–90}. Although unlikely, the possibility remains that the hip muscles reach their highest activity levels at other times than the moments we chose for analysis. In this case, the moment of the maximum joint load would differ from the peak contraction of the muscle. Analysis of EMG data of the lower limb simultaneously recorded to our ADL measurements will help to elucidate the peak contraction pattern of the analysed muscles.

6.8 Outlook on further research

The objective of this study was to investigate the impact of the hip muscle status on in vivo hip joint loads. In doing so, we identified several areas related to this question that should be addressed in future research projects.

Firstly, we used total muscle volumes for our analysis although the gluteal muscles have been shown to be anatomically divided into different entities ¹⁴¹, that show different activity patterns in ADL ^{7,8,90}. Moreover, the anterior part of the GMed needs to be incised in the DLA, causing direct trauma and differentiating it from its posterior segments ³⁴. Consequently, a more detailed investigation of the influence of different anatomic gluteal muscle zones on the in vivo contact forces would help to further understand mechanisms of action. Although we investigated the gluteal and TFL muscles bilaterally, our analysis was limited to only four out of numerous muscles acting over the hip. A more comprehensive investigation could help to elucidate the effect of THA on other hip muscles and their impact on in vivo measured joint contact forces.

Second, as mentioned previously not all of the investigated muscles were reported to be active in every moment of the gait cycle (see fig.3) ^{86,91,103}. As we only compared the muscle status with the 1st and 2nd force peaks there remains the possibility of stronger correlations with other moments, in which the muscle may reach maximum activation.

Third, we based our analysis on the resulting force F_{res} , which is the sum of the force vectors F_x , F_y , F_z acting on the hip joint (see 3.2.1). However, we did not include other forces such as torsion and friction moments (M_{res}), which have been shown to endanger prosthesis fixation and consecutive implant failure due to cup loosening 72 . In addition to the contact forces, friction also affects the joint load within the femoral component and thus should be focused on in future studies to get a comprehensive understanding of all force moments acting in the hip joint.

Finally, we included surface EMG of the lower limbs in our measurements taken 50 months after THA surgery. Analysis of these data is about to be initiated in our working group and will yield further understanding of muscle activity patterns in a comprehensive set of ADL included in our gait analysis protocol. As a surrogate for muscle force, these electromyographic data, next to the in vivo measured contact forces, will be helpful in further validating musculoskeletal models of the lower limb ¹⁴².

Index of Abbreviations

ADL Aktivitäten des täglichen Lebens

ADL Activities of daily living
ALA Anterolateral approach

BMI Body mass index

BW Body weight

CSA Cross-sectional area

CT Computed tomography

DAA Direct anterior approach

DEGS1 German Health Interview and Examination Survey for Adults

DLA Direct lateral approach

EMG Electromyography

EQ-5D-3L EuroQuol-5D-3L

Fig. Figure

Fres Resulting force

GMax Gluteus maximus

GMax Gluteus maximus muscle

GMed Gluteus medius

GMed Gluteus medius muscle

GMin Gluteus minimus

GMin Gluteus minimus muscle

GT Greater trochanter

HHS Harris Hip Score

LT Lesser trochanter

L4 Fourth lumbar vertebrae

MIS Minimally invasive surgery

MRI Magnetic resonance imaging

N Newton

N Number

NA Not available

Nm Newton meter

OA Osteoarthritis

PLA Posterolateral approach

POD Postoperative day

pOP Postoperative

PPAR_γ Peroxisomal proliferator-activated receptor gamma

RD Radio density

ROM Range of motion

SD Standard deviation

SPPB Short Physical Performance Battery

Tab. Table

TFL Tensor fasciae latae

THA Total hip arthroplasty

TUG Timed Up and Go test

VAS Visual Analog Scale

WOMAC Western Ontario and McMaster Universities Osteoarthritis Index

0M One day before THA

3M 3 months after THA

6MWT 6-minutes-walking test

50M 50 months after THA

%BW Percentage body weight

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Affidavit

"I, Sophie Charlotte Brackertz certify under penalty of perjury by my own signature that I

have submitted the thesis on the topic "Gluteal Muscle Status and the Impact on

Postoperative Joint Loading in Total Hip Arthroplasty Patients". I wrote this thesis

independently and without assistance from third parties, I used no other aids than the

listed sources and resources.

All points based literally or in spirit on publications or presentations of other authors are,

as such, in proper citations (see "uniform requirements for manuscripts (URM)" the

ICMJE www.icmje.org) indicated. The sections on methodology (in particular practical

work, laboratory requirements, statistical processing) and results (in particular images,

graphics and tables) correspond to the URM (s.o) and are answered by me. My interest

in any publications to this dissertation correspond to those that are specified in the

following joint declaration with the responsible person and supervisor. All publications

resulting from this thesis and which I am author correspond to the URM (see above) and

I am solely responsible.

The importance of this affidavit and the criminal consequences of a false affidavit (section

156,161 of the Criminal Code) are known to me and I understand the rights and

responsibilities stated therein.

Date

Signature

95

Declaration of any eventual publications

Sophie Charlotte Brackertz had the following share in the following publications:

Publication 1: T.Winkler, J.Zonneveld, S.Brackertz, F.Streitparth, P.Damm, Gluteal muscle damage leads to higher in vivo hip joint loads 3 months after total hip arthroplasty, PLoS ONE, submitted 10/2017

Contribution in detail: analysis and processing of data, drafting the publication

Publication 2: T.Winkler, S.Brackertz, F.Streitparth, P.Damm, Muscle atrophyrelated increased joint loading persists four years after total hip arthroplasty (working title), PLoS ONE, 2017

Contribution in detail: conception, data collection, analysis and processing of data, drafting the publication

ignature, date and stamp of the supervising University teacher
ignature of the doctoral candidate

Curriculum Vitae

"Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht."

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