BIOMECHANICS OF THE TIBIOFEMORAL JOINT IN RELATION TO THE MECHANICAL FACTORS ASSOCIATED WITH OSTEOARTHRITIS OF THE KNEE

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Contents

SUMMARY

In this study the kinematics and kinetics of weight bearing knee activities were examined in the context of the mechanical factors related to the risk of osteoarthritis (OA) in the tibiofemoral joint. Activities requiring deep knee bending and high physical loading are predisposing factors to OA. As cartilage has a limited potential to remodel and adapt to loading changes, it is stipulated that changes in kinematics and kinetics can especially raise the risk factor for OA, as regions of cartilage not prepared to deal with these different loading patterns might be involved. Some of the unknowns investigated, for the purpose of the present study on tibiofemoral joint biomechanics and the mechanical factors associated with OA, involved:

1. The forces and stresses in weight bearing knee flexion activities.
2. The role of the anterior-cruciate-ligament (ACL) in weight bearing knee activities such as stairclimbing.
3. The mechanical and morphological properties of the articular cartilage, including that beneath the meniscus.

In the present study both in-vivo and in-vitro investigations were carried out. Motion analysis of subjects performing activities of daily living (walking, stair climbing, and deep flexion squat) were studied. Kinematics, forces and moments were derived. A comparative study was also performed of ACL deficient subjects during stair climbing. The in-vitro aspect looked at mechanical and morphological

properties of articular cartilage and the contact stresses that arise when the joint was loaded in walking and deep knee flexion.

The results from the study showed that the peak moments in the tibiofemoral joint in stairclimbing were three times larger than in level walking, and in deep flexion they were about two and a half times larger. The peak forces in the tibiofemoral joint during level walking reached about 3 times body weight, similar to those reported in previous studies. In stairclimbing, relative to the global reference, peak vertical forces reached five times bodyweight, while significant peak horizontal reaction forces were about five times larger than in level walking. In deep knee flexion peak horizontal reaction forces on average were about two to three times larger. From the in-vitro study, the peak contact stresses in deep flexion were found to be about 80% larger than that in level walking. Contact areas at peak pressure were low at about 1 to 2cm^2. In stairclimbing, anterior cruciate ligament deficiency resulted in a gait adaptation to try to reduce the amount of net quadriceps moment, suggesting altered tibiofemoral kinematics. Such altered kinematics is especially relevant as it was found that peak contact forces in stairclimbing reached 5 times body weight. Finally, compared to the articular cartilage not covered by the meniscus, the articular cartilage of the region beneath the meniscus in the tibial plateau was significantly stiffer, thinner and had less dense subchondral bone.

The findings from the present study contribute to the explanations for two criteria on the mechanisms that can raise the risk for cartilage failure. One is the risk from significantly increased loads with reduced contact area, and the other, from a pathomechanical change that would result in some inadequacy in joint weight-bearing. This change could be due to altered joint mechanics or changes in the material properties of the supporting structures.

The weight-bearing capabilities of the joint structures are generally expected to be adequate to withstand the loads from activities of daily living without damage. However with abnormal loading patterns from joint instability, excessive stresses from significantly reduced contact area and the engagement of cartilage with significantly different material properties, the ability of the joint to weight-bear safely is compromised.

LIST OF RELEVANT PUBLICATIONS

Published

1. Thambyah A. *A hypothesis matrix for studying biomechanical factors associated with the initiation and progression of posttraumatic osteoarthritis.* **Med Hypotheses.** 2005;64(6):1157-61.

2. Thambyah A, Goh JC, De SD. *Contact stresses in the knee joint in deep flexion.* **Med Eng Phys.** 2005 May;27(4):329-35.

3. Thambyah A, Thiagarajan P, Goh Cho Hong J. *Knee joint moments during stair climbing of patients with anterior cruciate ligament deficiency.* **Clin Biomechanics** (Bristol, Avon). 2004 Jun;19(5):489-96.

4. Satku K, Kumar VP, Chong SM, Thambyah A. *The natural history of spontaneous osteonecrosis of the medial tibial plateau.* **J Bone Joint Surg Br.** 2003 Sep;85(7):983-8.

5. Thambyah A, Pereira BP, Wyss UP. *Estimation of bone-on-bone contact forces in the tibiofemoral joint in walking.* **KNEE** (in press)

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6. Thambyah A, Nather A, J Goh. *Mechanical properties of the articular cartilage covered by the meniscus.* American Journal of Sports Medicine.

Conferences

1. Thambyah A, Nather A, Goh J. *Mechanical properties of the articular cartilage covered by the meniscus.* (Accepted) In Trans. of **51st Annual**

Meeting of the Orthopaedic Research Society February 20 - 23, 2005, Washington, D.C..

2. Thambyah,A; Ang, KC; Padmanaban, R, Thiagarajan P. *Tibiofemoral contact point in the weight-bearing ACL deficient knee*. In Trans. of **51st Annual Meeting of the Orthopaedic Research Society** February 20 - 23, 2005, Washington, D.C.

3. Thambyah A and Pereira BP. *Tibiofemoral joint forces in walking and deep flexion.* (Accepted) In Trans. of **51st Annual Meeting of the Orthopaedic Research Society** February 20 - 23, 2005, Washington, D.C.

4. Thambyah A. *Mechanical properties of the articular cartilage beneath the meniscus.* In CD-ROM Proceedings of the **European Society of Biomechanics**, July 4-7 2004, Holland.

5. Thambyah A, Goh J, Das De S. *Are the articular contact stresses in the knee joint during deep flexion critical ?*. In CD-ROM Proceedings of the **International Society of Biomechanics**, July 2003, Dunedin, New Zealand.

6. Thambyah A, Goh JCH, Bose K. *Contact stresses in the knee joint during walking and squatting.* (short article) in CD-ROM Proceedings of the **World Congress on Medical Physics and Biomedical Engineering**, July 23-28 2000 (USA)

7. Thambyah A, Goh J, Das De S. *Are the articular contact stresses in the knee joint during deep flexion critical ?*. In CD-ROM Proceedings of the **World Congress on Biomechanics**, August 4-9 2002, Calgary, Canada.

8. Thambyah A. *Mechanical properties of the articular cartilage beneath the meniscus.* In CD-ROM Proceedings of the **International Conference on Biological and Medical Engineering**, Dec 4-7 2002, Singapore.

AWARDS

1. **Best Clinical Science (poster) Award *(1st Prize).*** *Contact stresses in the knee during walking and squatting*. NUH Faculty of Medicine 3rd Scientific Meeting, August 1999, National University of Singapore, Singapore.

2. **Young Investigator Award (*certificate of nomination)*** *Biomechanical study on tibiofemoral contact stresses.* 10th International Conference on Biomedical Engineering, December 2000.

3. **Albert Trillat Young Investigator's Award. (*Winner).*** *Mechanical properties of the articular cartilage covered by the meniscus.* From International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine, ISAKOS 2005, Florida.

CHAPTER ONE: Introduction

Several elements provide the integrated approach to the investigation of tibiofemoral joint mechanics in relation to osteoarthritis. For the present study these 'ingredients' principally involved anatomical, mechanical and physiological studies motivated by, and guided in relevance to, the clinical problem of osteoarthritis. The tibiofemoral models chosen for the present study were: deep flexion and anterior cruciate ligament deficiency.

Both deep flexion activity and anterior cruciate ligament deficiency are associated with a higher incidence of tibiofemoral osteoarthritis [Zhang Y et al. 2004, Jomha NM et al.1999]. In both deep flexion activity and anterior cruciate ligament deficiency tibiofemoral kinematics have been shown to involve the posterior periphery of the tibial plateau [Logan M and Williams A et al 2004, Scarvell J et al 2004, Logan M and Dunstan E et al 2004, Spanu CE and Hefzy MS 2003, Hefzy MS et al 1998]. Clinically such abnormal kinematics correlate with osteoarthritic wear patterns in the anterior cruciate ligament deficient knees [Daniel DM et al 1994, Johma NM et al. 1999]; and patterns of medial and lateral cartilage wear are hypothesized to be influenced by weight-bearing flexion, [Weidow et al 2002] where the tibia rotates internally and the posterior lateral aspect of the tibia plateau is engaged [Hill PF et al 2000]. The posterior aspect of the tibial plateau involves articular cartilage covered (protected) by the meniscus. Few

studies have investigated the properties of the cartilage in this region with many biomechanical analyses assuming uniform properties throughout the plateau. The concern is that the strength of cartilage in these areas may be overestimated, such that the effects of physiological loading become underestimated. A previous study has investigated the regions covered by the meniscus in a quadruped model (Appleyard RC et al 2003) showing thicker and softer cartilage at the periphery. The role of topographical variations of articular cartilage mechanical properties in relation to the mechanical factors involved in the initiation and progression of osteoarthritis needs to be elucidated. It is envisaged that with this information on the material and morphological properties in the joint, biomechanical models would benefit in their study of tibiofemoral mechanics together with appropriate input on the intra-articular loads and stresses.

Subsequently accurate tibiofemoral loads and stresses are important to determine. Previous studies on loads in the anterior cruciate ligament deficient knee in walking have shown a gait adaptation in joint moments quantifiable via motion analysis [Berchuck M et al 1990]. In deep knee flexion, the joint moments have been found to be significantly larger than in walking [Nagura T et al 2002]. Much work has been done to study the biomechanics of the tibiofemoral joint. The main endeavour has been to measure joint kinematics and kinetics. Both in-vivo and in-vitro methods for investigating joint mechanics have

been employed. In-vivo kinematics of the tibiofemoral joint has involved motion analysis using optoelectronic systems, X-rays [Komistek RD and Dennis DA 2003], and MRI [Scarvell J et al 2004, Hill PF et al 2000] . In-vitro analyses have largely been performed to include more detailed investigations on joint loads or contact forces and stresses. In-vivo tibiofemoral contact forces are difficult to measure because the joint is encapsulated, articulating and difficult to access. Even in the unlikely scenario where one is able to access the living joint to measure forces, sensors have to be rugged, fast and accurate to capture forces in dynamic activities. Many studies therefore resort to modeling the joint mathematically and then calculating the forces [Paul JP 1976, Morrison JB 1970, Hattin HC et al 1989, Seireg A and Arvikar RJ 1973, Abdel-Rahman E and Hefzy MS 1993], or simulating articular joint mechanisms in-vitro and using sensors to measure the forces. [Fujie H et al 1995, Markolf KL et al 1990]. Previous studies show peak contact forces to be as high as three times body weight during walking [Morrison JB 1970, Schipplein OD and Andriacchi TP 1991], but these 'bone-on-bone' forces have been less studied for deep flexion.

Stresses consequently are more difficult to determine as the measurement of contact area is also necessary. Previously earlier work done to measure area used static techniques of pressure sensitive film [Fukubayashi T and Kurosawa H 1980] or miniature piezoresistive transducers [Brown TD and Shaw DT 1984]. More dynamic systems have evolved [Manouel M et al 1992] and recently the

use of thin film electronic sensors have become acceptable for deriving pressure directly in the joint [Harris ML et al 1999, Wilson DR et al 2003, McKinley TO et al 2004]. The stresses have been determined for the tibiofemoral joint in loading simulating a weight-bearing stance and found to be about 3MPa on average, reaching peaks of up to 8MPa [Brown and Shaw 1984]. There have however been no studies reporting the contact stresses in deep knee flexion.

Contact stresses are important to determine in order to study more appropriately the failure mechanism of articular cartilage. With the knowledge of physiological stresses and stress to failure, a safety factor may be derived that is useful to form the basis for the criteria for cartilage damage to occur. Shear appears to be a leading cause of cartilage failure [Flachsmann ER et al 1995, Broom ND et al 1996] but since cartilage deforms in all axes, a more relevant mechanism of deformation that has been noted and occurs during joint motion is called 'ploughing' [Mow VC et al 1993, Mow VC et al 1992]. In this, cartilage is loaded, such that together with a direct compression into the cartilage, there is force acting somewhat tangential to the cartilage surface. The end result is a ploughing-like motion that occurs. This essentially is a combination of compression, tension and shear. Shear stress is more difficult to derive than compressive stress, but if 'ploughing' is the preceding mechanism involved in cartilage failure, then the study of the compressive stresses will be a useful endeavour to ultimately contribute to the larger model incorporating shear stress

analyses, a methodology that has been employed before [Atkinson TS et al 1998].

The principle aim of the present study was to establish a system of approach to study the biomechanics of the tibiofemoral joint in relations to the factors associated with osteoarthritis. This approach was proposed to be aligned with current recommendations on the proposed framework for investigating the pathomechanics of osteoarthritis at the knee which would ultimately be based on an analysis of studies describing assays of biomarkers, cartilage morphology, and human function (gait analysis) [Andriacchi TP et al 2004].

Thus the focus of the present study was to develop the systems for obtaining data on tibiofemoral joint forces and stresses, as well as relevant mechanical and morphological properties of the weight bearing structures. In particular the following were investigated:

1. The forces and stresses in weight bearing knee flexion activities.
2. The role of the ACL in weight bearing knee activities such as stairclimbing.
3. The mechanical and morphological properties of the articular cartilage, including that beneath the meniscus.

From this the possibility of damage from the unique joint mechanics to deep flexion and anterior cruciate ligament deficiency was discussed in the context of factors related to the risk of osteoarthritis in the tibiofemoral joint.

CHAPTER TWO: Literature Review

2.1 Biomechanics of the tibiofemoral joint

In this section the relationships and influences of the anatomy and design of the human knee joint, to kinematics, contact stresses, and the mechanical limits of the supporting structures are presented.

2.1.1 Design of the joint

The components of the tibiofemoral knee joint can be divided into the tibio-femoral articulation, cruciates and collateral ligaments, menisci and capsular structures. In the tibiofemoral joint the articulation is between the distal end of the femur and the proximal end of the tibia. The medial femoral condyle is larger and more symmetrical than the lateral femoral condyle. The long axis of the lateral condyle is slightly longer than the long axis of the medial condyle and is placed in a more sagittal plane. Also the width of the lateral femoral condyle is slightly larger than the medial femoral condyle at the centre of intercondylar notch [Williams P.L. 1995]. The contact area of the medial plateau is said to be 50% larger than that of the lateral tibial plateau and the articular cartilage of the medial tibial plateau is thicker than that of the lateral tibial plateau. This is relevant because of the larger loads in the medial compartment [Kettlekemp DB

1972]. The lack of conformity between the femoral and tibial articulation is augmented by the presence of menisci, which serve as a shock absorber and cushions the load sustained during normal activities. The menisci rest on the articular surface supported by the subchondral plate. Each meniscus covers approximately the peripheral two-thirds of the articular surface of the tibia. The medial menisci are semilunar in shape and the lateral menisci nearly circular. The lateral menisci transmit 75% and the medial meniscus 50% of the load [Walker PS 1975].

The anterior and posterior cruciate ligaments are the prime stabilisers of the knee in resisting anterior and posterior translation, respectively [Noyes FR 1980]. The collateral ligaments, menisci and the capsule provide additional restraint to the anterior and posterior movement of the knee, as well as to rotation. The anatomy of the cruciates and the collateral ligaments has been well described in the literature [Arnoczky SP 1983, Jakob and Staubli HU 1992]. The articular surfaces hold the two bones apart and resist interpenetration by transmitting compressive stresses across their surfaces, whereas the ligaments hold the two bones together and resist distraction by transmitting tensile stresses along the line of their fibres. The ligaments often act together in limiting motion, sometimes creating primary and secondary ligamentous restraints. These are well described in the literature [Butler DL 1978, Daniel DM 1990].

2.1.2 Tibiofemoral Joint Kinematics & Physiological Loads during Activities of Daily Living (ADL)

Kinematics describes the general motion of a body in space in terms of its relative position at any one time. It is the study of positions, angles, velocities and accelerations of body segments and joints during motion. The motion can be described as one or all of three translations and three rotations, and in the knee joint, the combination of translations and rotations describes the degrees of freedom the joint has. The tibiofemoral joint is capable of all three translations and rotations [FIGURE 2.1]. If one considers the tibia moving freely relatively to the femur, the tibia is able to translate in anterior-posterior, medial-lateral and proximal-distal directions. The tibia can also rotate in flexion-extension, varus-valgus, and internal-external directions. These six degrees of freedom that the tibiofemoral joint can undergo are crucial to its function as a flexible and effective weight-bearing joint. The normal range of motion [FIGURE 2.2] has been studied extensively over the years, with numerous methods used to determine displacement and rotation in these six degrees of freedom. Below is a brief note of these normal ranges (in parentheses).

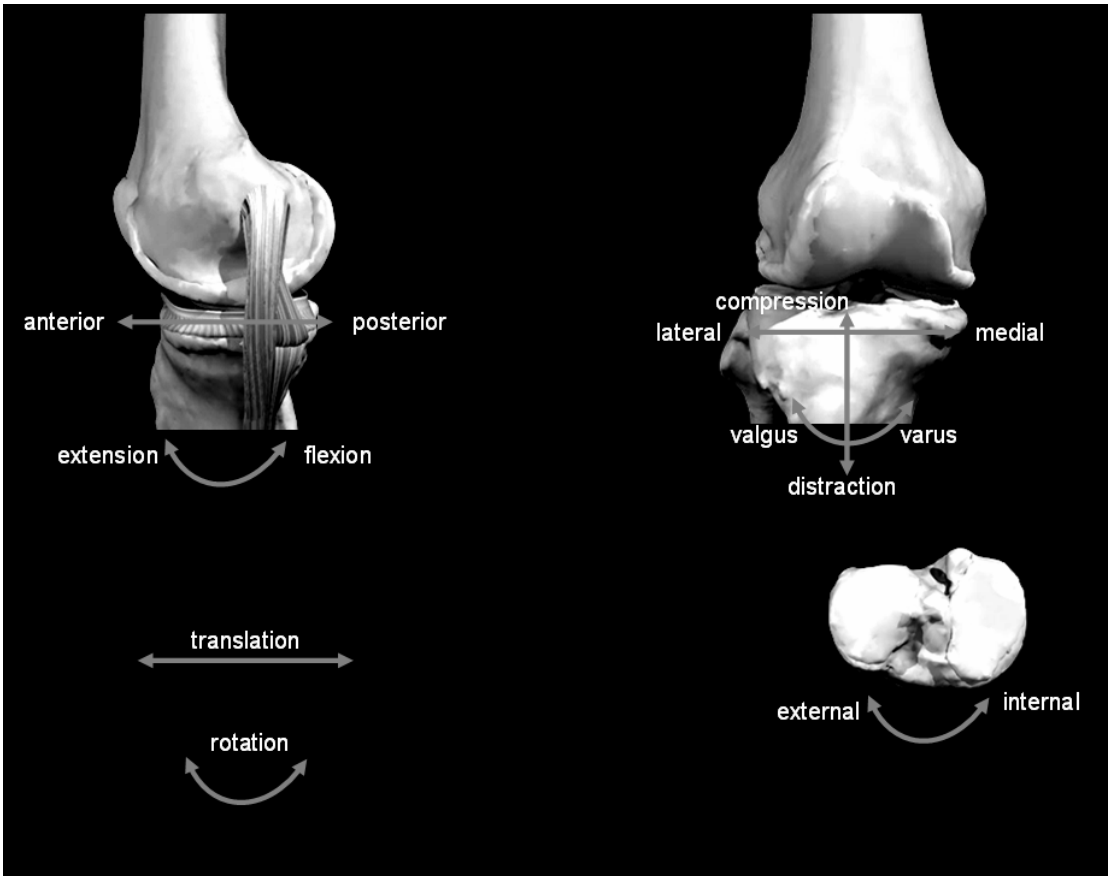


FIGURE 2.1 Three translations and three rotations are possible in the knee joint. With the tibia moving about the femur, these motions are illustrated here. The top left view is in the sagittal plane, the top right is in the coronal plane and the bottom right shows a transverse section through the tibiofemoral joint. (pictures from anatomytv.com)

A). Flexion-extension rotation (flex 120º-150º / 0º / ext 5º-10º) : Most of the motion in the knee occurs in this plane where flexion-extension takes place. Many of the previous studies have been concerned with studying knee joint kinematics in this plane, as it involves the largest range of motion and the moment generated from the body's largest muscle, the quadriceps. In level walking the normal range of motion in the sagittal plane has been recorded to be up to about 25º in stance phase and 50º in swing [Nadeau S et al 2003]. In

stairclimbing it was found to be as much as 75º in initial foot contact and 100º in swing [Nadeau S et al 2003]. Deep flexion activity studied in subjects performing squats showed that knee angles reached peaks of up to 160º [Nagura T et al 2002].

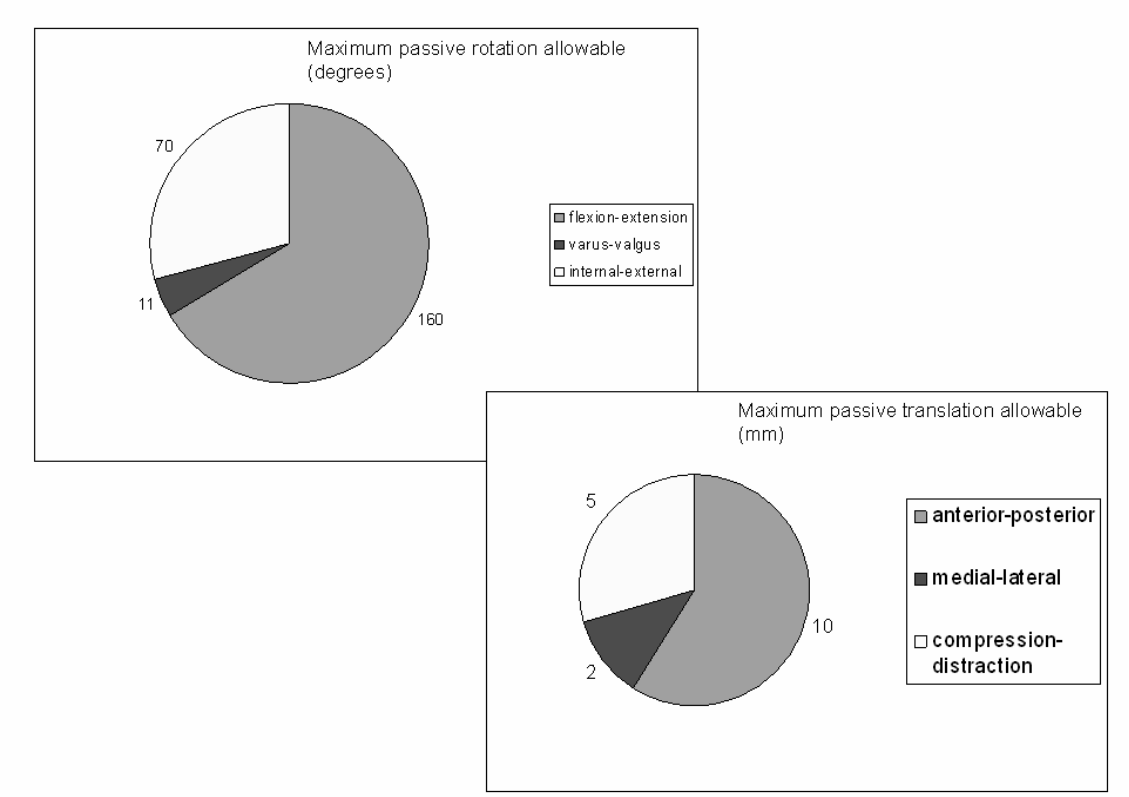


FIGURE 2.2 The maximum range of motion in each plane for the normal knee is compared here. (Chart and compilation by Thambyah A.)

In-vivo studies using MRI found that flexion is accompanied by a shift in the tibiofemoral contact point such that there was a backward movement of the medial femoral condyle of 4 mm and backward movement laterally by 15mm. [Karrholm J et al 2000, Nakagawa S et al 2000, Hill PF et al 2000, Iwaki H et al 2000]. Other studies on tibiofemoral kinematics using videofluoroscopy found

that during gait, the lateral condyle experienced 4.3 mm of average motion posteriorly, whereas in comparison, during deep flexion activities, subjects experienced 12.7 mm of lateral condyle motion [Komistek RD and Dennis DA 2003].

B). Anterior-posterior translation (5mm to 10mm): The primary restraints for this motion are the ligamentous bundles of the anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL). While the ACL limits anterior tibial translation, the PCL limits posterior translation. The anterior-medial bundle of the ACL is taut in flexion, and this creates some internal rotation. The allowable AP translation typically ranges from 5 to 10mm. This produces enough laxity in these directions to facilitate optimum tibiofemoral contact and load bearing between the cartilage and ligaments, to reduce shear effects. Measurement of translation of the tibia with respect to the femur, or anterior-posterior (AP) translation, is influenced by the position of the knee at the time of measurement. Flexion-extension and internal-external rotation can affect the degree of AP translation allowed by the restraints of the knee. The femur of the normal knee contacts the tibia anterior to the tibial midpoint in the sagittal plane in full extension, and translates posteriorly during flexion [Dennis DA 1996].

C). Varus-valgus rotation (Abduction/adduction): No active varus-valgus rotation is possible. However the joint is not fused, and the deformation allowable in the

collateral ligaments gives the joint some degree of freedom in this plane for rotation. In full knee extension however the motion in the frontal plane is essentially not possible. Passive abduction and adduction increases with knee flexion (up to 30º knee flexion), reaching a maximum of only a few degrees. In walking, maximal adduction is observed as the knee is flexed during the swing phase, with maximum abduction at heel strike when the knee is in extension [Kettelkamp 1970]. The range from adduction to abduction was observed to be on average 11º in total. In stairclimbing, with larger knee flexion angles and loading, the knee varus angle was about 5° (corresponding to a maximum knee internal valgus moment) and was significantly greater than that in level walking, where it was about 2.5° [Yu B et al 1997].

D). Medial-lateral translation (1 to 2mm) : In the knee, pure medial-lateral translation is relatively small at 1mm to 2 mm. Besides the congruity of the tibiofemoral joint, the cruciate ligaments, and to a certain extent the menisci, the primary restraints for this motion are the collateral ligaments, which are tough and taut across the tibiofemoral joint.

E). Internal-external rotation (*at 90º flexion* up to 45º external and 30º internal): Relative rotation of the tibia and femur about its longitudinal axis can only be performed with the knee flexed. With the knee in full extension, rotation is almost completely restricted by the interlocking of the femoral and tibial

condyles, which occurs mainly because the medial femoral condyle is longer than the lateral condyle. The range of rotation increases as the knee is flexed, reaching a maximum at 90º of flexion; with the knee in this position, external rotation ranges from 0º to approximately 45º and internal rotation ranges from 0º to approximately 30º. Beyond 90º of flexion, the range of internal and external rotation decreases, primarily because the soft tissues restrict rotation. In walking, external rotation begins during knee extension in stance phase, reaching a peak at the end of the swing phase just before heel strike. Internal rotation was mainly confined to that during flexion in swing phase. The total range of rotation in walking was found to be 8.6º [Levens 1948] to 13.3º [Kettlekamp 1970].

F). Compression-distraction translation (2 to 5mm) : A subtle yet important degree of freedom in the knee joint is the translation along the proximal-distal axis. The translation in this axis includes both the amount of space between the tibia and femur when the knee is allowed to hang free, as well as the allowable deformation in the cartilage. In compression-distraction testing, displacements can range from 2mm to 5mm, from the effects of the meniscus (compression) to reduce impact between the tibia and femur, and the minimal yet significant compliance of the collaterals (distraction) to prevent excessive build –up of loads while restraining the joint.

The limits of motion in these six degrees of freedom are defined by constraints from neuro-muscular control, proprioception, ligamentous restraints, cartilaginous cushions and bearings against bone. The range of motion for the healthy human adult knee is generally consistent, such that its kinematics is fairly well defined in terms of the six degrees of freedom - a reproducible pattern of gait occurs for each person, with insignificant variations occurring between individuals. While there are such degrees of freedom, the primary motion is really in flexion and extension, with the other motions coupling to facilitate optimum balance in weight-bearing within the joint. Therefore, the motion in the sagittal plane is beyond that of a simple hinge joint. The complexities involve the coupling motion in the other axes.

The kinematics of the tibiofemoral joint as discussed in the earlier section involves the study of motion between the tibia and femur bones. Kinetics of the tibiofemoral joint looks at the forces and energy that is involved in either maintaining static equilibrium or initiating dynamic activity for the joint. In the knee joint the loading is as much as three times body weight during walking [Morrison JB 1970]. Calculated forces in the medial and lateral compartments indicate relatively more loading in the medial compartment [Schipplein OD et al 1991]. The design of the tibiofemoral joint is such that the relatively more concave medial plateau provides more congruency for contact with the femoral condyle, and the lateral plateau being convex provides some freedom for condylar mobility over the plateau. Determination of the tibiofemoral contact

area is significant in evaluating the weight bearing capacity of the joint. For example, the average area of contact on the medial plateau is 1.6 times greater than the area on the lateral plateau [Kettlekamp 1972]. Therefore it is easy to deduce that even though forces in the medial compartment may be larger than in the lateral, the contact stresses may not be different in the two compartments if there is more distribution of forces in the medial compartment due the increased area of contact. These forces are cushioned and accommodated largely by the meniscus and articular cartilage. The distribution of the forces over the area of contact (mainly involving cartilage in the healthy joint) determines the stresses that result. Some of the stresses calculated in previous studies are shown (Table 2.1). Contact areas in the tibiofemoral joint were found to be in the range 20.13cm^2 to 11.60cm^2 [Maquet PG et al 1975] for intact menisci, and 12cm^2 to 6cm^2 with the menisci removed. *With three times bodyweight loading of approximately 2100N for a 70kg person, the stresses can be calculated to range between 1MPa to 2MPa with menisci and up to 5MPa with the menisci removed.* Contact stresses are also affected by joint malalignment. A varus malalignment of 30 degrees at the proximal third of the tibia was found to increase medial compartment contact pressures by 101% and decrease the lateral compartment contact pressure by 89% [McKellop et al 1991]. Like any multi-support weight bearing structure, the location of the center of gravity will determine the distribution of the forces. With malalignment, and in this case varus deformity, the center of gravity shifts more medially, and so does the

center of maximal joint pressure, with even a likelihood of separation of the lateral tibiofemoral joint and "condylar lift-off" [Noyes FR 1992] during maximum weightbearing in walking.

TABLE 2.1 Some previously derived contact stress measured in the knee are shown here.

Author	Year	Specimen	Joint	Joint studied	Loading	contact area	mean contact stress	peak contact stress
Kurosawa et al	1980	human cadaver	tibiofemoral	tibia	1500N	14.1cm2		
Brown and Shaw	1984	human cadaver	tibiofemoral	femur	3000N		2.6MPa	8MPa
Luepongsak et al	1997	human in-vivo	hip	femoral head	BodyWeight (BW)			4 to 6 MPa
Luepongsak et al	1997	human in-vivo	hip	femoral head	BW plus 11.8kg load			13.7MPa
Herberhold et al	1999	human cadaver	patellofemoral	patella	1.5BW		3.6MPa	

It was found that varus knee malalignment was a contributory cause to OA from the effects of obesity [Sharma L et al [2000]. Increased dynamic loads on the medial compartment as a result of varus malalignment in OA [Baliunas AJ et al 2002, Prodomos CC et al 1985] aggravates the problem of excessive loading, and presents the question of whether the malalignment precedes or follows the onset of the disease. In any case many studies on OA wear patterns indicate a higher incidence of degenerative changes in the medial compartment compared to the lateral [Weidow J et al 2002]. Another study on Chinese subjects relating the activity of squatting with tibiofemoral OA [Zhang Y et al 2004] also found a significantly higher incidence of medial compartment OA compared with lateral. Incidentally, Chinese subjects were found to have significantly more varus mal-

alignment of the lower extremity compared with westerners [Tang WM et al 2000] and also for studies on Asians specifically [Zhang et al 2001] it was estimated that the prevalence of radiographic and symptomatic knee OA in a population–based sample of elderly subjects in China were higher than that reported in the Framingham OA study which looked at a primarily Caucasian population.

2.1.3 Structure and Function of Cartilage in the Knee

The articular surface of the distal femur, the articular surface on the posterior aspect of the patella and the articular surfaces on the tibial plateau are covered by a variety of hyaline cartilage termed articular hyaline cartilage. Articular hyaline cartilage offers a firm, smooth and relatively friction-free surface facilitating joint movements. The thickness of articular hyaline cartilage in the knee is not uniform but varies from 3mm to 7mm. Articular hyaline cartilage possesses a degree of compressibility and elasticity. These features enable the articular surfaces to dissipate laterally the vertical compressive forces to which the knee joint is subjected during weight transmission. Articular hyaline cartilage does not usually ossify. Instead the surface of articular hyaline cartilage is lubricated by synovial fluid secreted by the synovial membrane lining the inner surface of the joint capsule. However, the articular cartilage itself is not covered by synovial membrane. As with hyaline cartilage in extraarticular sites, the substance of articular hyaline cartilage is made up of cells termed chondroblasts and chondrocytes, and an intercellular matrix elaborated by the chondrocytes. The intercellular matrix is biochemically complex, and is composed of various proteins including different types of collagen, a variety of cell adhesion molecules and glycosaminoglycans, and lipids. The glycosaminoglycans are arranged systematically about a core protein to form complex hydrophilic molecules termed proteoglycans.

The proteoglycans are chiefly responsible for the impressive viscoelastic biomechanical properties of articular cartilage. Healthy articular hyaline cartilage in the young individual has a pale and glistening appearance, and a firm and smooth texture. With age degenerative changes begin to appear, and cartilage loses its smooth and glistening character. At the histological level, articular hyaline cartilage is seen to be made up of four layers or zones on the basis of differences in cellular morphology, cellular density as well as differences in the composition of extracellular matrix.

Of the four layers, the most superficial layer faces the joint cavity, and the deepest layer is apposed to, and fused with, the subchondral bone. From superficial to deep, these layers (FIGURE 2.3) are named as follows:

i) Tangential stratum (Zone 1)

ii) Transitional stratum (Zone 2)

iii) Radiate stratum (Zone 3)

iv) Calcified stratum (Zone 4)

The region between Zone 3 and Zone 4 is called the tidemark and is readily discernible in young cartilage. The progressive ossification of Zone 4, which accompanies aging, results in the blurring of the tidemark. Articular hyaline cartilage is devoid of innervation and lymphatic vessels. Except for the presence

of a few blood vessels in Zone 4, articular hyaline cartilage is also normally devoid of vascularity, and is believed to derive its nutrition mainly by diffusion from synovial fluid and from the vascular plexus in synovial membrane.

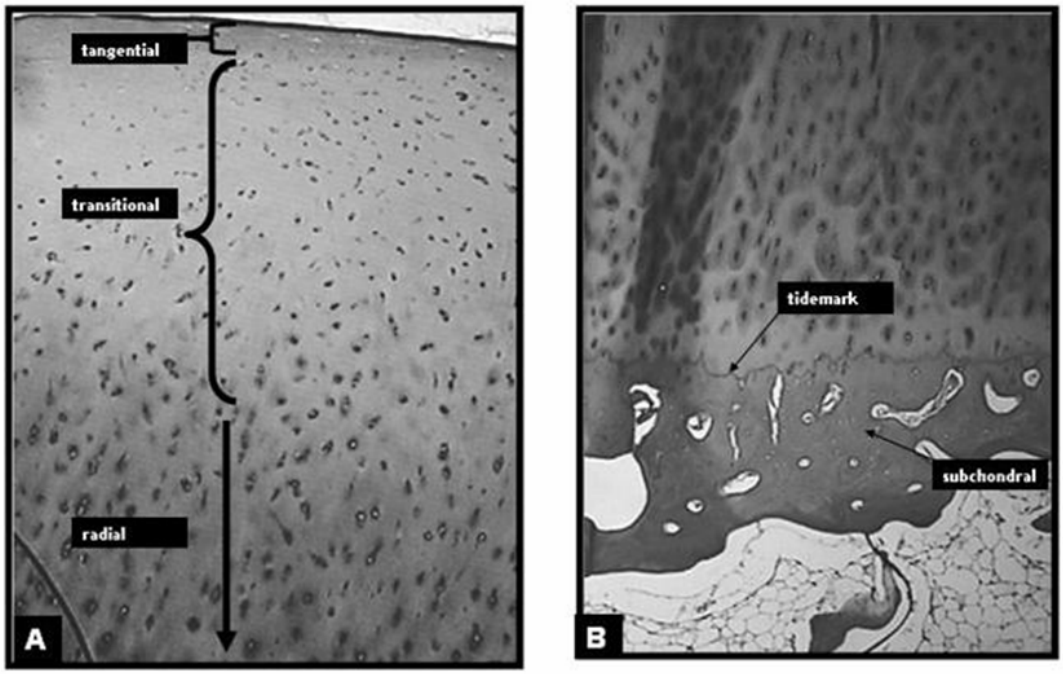


FIGURE 2.3 showing the typical zones identifiable in normal articular cartilage (via Haemotoxyline and Eosin staining) for A). the superficial cartilage and B) the deeper subchondral region. (Source: Thambyah A.)

The 3 main functions of the articular cartilage are listed as follows:

1. Acts as covering to protect the underlying bone from abrasive damage.
2. Distribution of forces over the boney ends.
3. Provides joint lubrication.

From these functions, it is clear to realize the important biomechanical role the cartilage plays in protecting and lubricating the joint. The make up of cartilage consisting of proteoglycans and collagen is used to explain its mechanical properties. Collagen is strong in tension. The proteoglycans provide an internal network that meshes to resist compressive loads. Turgidity of the cartilage from its water content is also effective in providing a cushioning effect, making the tissue less compliant and compressible.

2.1.4 Mechanical Properties of Articular Cartilage

Joint cartilage is a soft tissue with a compressive modulus of less than 1.5MPa, a shear modulus of less than 0.5MPa and a Poisson's ratio modelled from 0 to 0.42 [Mow VC et al 1993, Mow VC et al 1989, Athanasiou KA et al 1991]. In terms of ultimate load, the strength of cartilage is limited in withstanding impact. Some of its mechanical properties have been determined in previous studies [Table 2.2]. Cartilage explants under cyclic loads showed visible damage occurring between 20MPa to 50MPa, and subtle damage was seen to be initiated as low as 5MPa to 10MPa [Farquhar et al 1996]. In impact loading, the stresses found to cause fissures and laceration in articular cartilage have been estimated to be about 25MPa [Repo and Finlay, 1977; Torzilli PA et al, 1999, Haut RC 1989]. The limits for articular cartilage damage are inexact and still provide much of the motivation for contact stress studies of articular cartilage. What kinds of stresses are involved and how does the cartilage react to these forces? Some work has

been done to determine the physiological loads experienced by the knee joint in terms of the stresses acting on the articular cartilage [Table 2.1]. The physiological loading of the cartilage is important to determine, as 'ideal' loading lies within a relatively small window, such that too much or too little stress can be detrimental [FIGURE 2.4]. Accurate and functionally relevant intra articular contact stresses in the natural knee joint is difficult to determine, and there are no known published data on the stresses that result in the tibiofemoral knee joint during activities of daily living such as walking and squatting. The knee joint reaction forces from walking have been estimated to be as high as 3 to 5 times bodyweight [Morrison JB 1970, Kuster MS et al 1997]. This duly raises concern when strength studies of cartilage explants have shown that damage occurs with as low as 5 to 10MPa of cyclic stress [Farquhar T et al. 1996]. Furthermore, given the evidence that osteoarthritis and cartilage damage can occur in the knee as a result of frequent or high contact stresses [Farquhar T et al 1996, Dekel S et al 1978], the relevance in measuring these stresses becomes especially significant for population groups where cultural and social habits commonly include high weight-bearing daily activities of deep flexion such as squatting and kneeling. The role of the meniscus, cartilage and soft tissue to neutralise high stresses becomes increasingly diminished in larger flexion angles, where the tibiofemoral contact is largely reduced [Hefzy MS et al 1998]. Studies of deep flexion biomechanics in the past have been largely focused on the patellofemoral joint [Hungerford DS and Barry M 1979, Haut RC 1989, Koh TJ et

al 1992, Singerman R et al 1999], looking at forces and stresses in this joint and their impact on cartilage. The possibility of failure in the tibiofemoral articular cartilage from any likelihood of high stresses in deep flexion has not been investigated.

TABLE 2.2 Some properties of articular cartilage as reported by previous authors. The column on physiological stresses shows the contact stresses as measured during daily activities such as walking and going up stairs.

Study	Ultimate stress (MPa)*	Compressive Modulus (MPa)	Aggregate Modulus (Ha)	Instantaneous Modulus (MPa)	Physiological stresses (MPa)
Repo RU and Finlay JB 1977	>25				
Torzilli PA et al 1999	>25				
Afoke NYP et al 1987					5 to 10 (hip)
von Eisenhart R et al 1999					5 to 8 (hip)
Oloyede A and Broom N 1996	> 20				
Farquhar T et al 1996	> 20				
Clements KM et al 2001	>6†				
Korhonen RK et al 2002			0.66	0.8	
Franz T et al 2001				3 to 4	
Jurvelin JS et al 2003			0.85		
Shepard DE and Seedhom BB 2001		4.4 to 27			
Jurvelin JS		2 to 15			
Falcovitz YH 2001 (ORS)			1.27		
Ipavec M et al 1996					0.8 to 2.6 (hip)

* reference includes cartilage that experiences functional failure, metabolic inhibition, cell death, fissure and lacerations

† decrease in cell viability

An important property of cartilage not shown in the table above is its low coefficient of friction. The coefficient of friction in animal joint cartilage is found to be as low as 0.002, and when the cartilage fluid content is greatly diminished, the figure is as high as 0.35 [Mow VC et al 1993, McCutchen CW 1962]. In general, though, fully hydrated healthy cartilage tends to have a coefficient of 0.01. Compare this with the coefficient of friction of some common materials

such as ice on ice, which is 0.1, and ultra-high molecular weight polyethylene on cobalt chrome alloy, at 0.05. The low coefficient of friction in cartilage essentially allows for less resistance in shear and hence prevents damage to the soft tissue of the cartilage while the joint is locked for optimum balance, support and locomotion. A higher coefficient of friction would result in larger reaction forces for a given load, and would promote wear. Therefore maintaining this low friction condition is crucial to the protection and effective service of the joint. The stresses in the joint are affected by the coefficient of friction, and interestingly, the degree of dynamic activity in turn also affects the coefficient of friction. The kinetic coefficient of friction, derived from dynamic studies of cyclic loading, is higher than the static coefficient as discussed so far [Mow VC et al 1993, McCutchen CW 1962]. That is to say, with cyclic loading the coefficient increases; this inevitably results in larger reaction forces, higher stresses and increased propensity to wear. The reason for this is related to the fact that cartilage contains fluid that is not entirely static, and which is allowed to flow in and out of the material. The rate of expunging and replacement of this fluid would greatly determine the coefficient of friction and therefore remains dependent on the kind of cyclic loading and its duration. The difficulty in predicting and modelling this phenomenon is largely due to the viscoelastic behaviour of articular cartilage, where mechanical properties of the material can be influenced by variation in loading and strain rates. While cartilage can deform in all axes, one important mechanism of deformation that has been noted and

occurs during joint motion is called 'ploughing' [Mow VC et al 1993, Mow VC et al 1992]. In this, cartilage is loaded, such that together with a direct compression into the cartilage, there is force acting somewhat tangential to the cartilage surface. The end result is that a ploughing-like motion occurs. This essentially is a combination of compression, tension and shear. The force acting downwards compresses; and the force pushing the cartilage laterally creates both tension and shear. Increased ploughing results from larger loading rates, and this promotes interstitial fluid flow. This in turn causes a build-up of drag forces due to the limited permeability of the cartilage pore-network, and the viscoelastic effect. The fluid in the cartilage as a result becomes more pressurized and this provides load support. The ploughing effect and the internal dissipation of fluid also give rise to ploughing friction, which results in larger reaction forces and stresses to maintain load. The ploughing friction is again influenced by strain and loading rates, and therefore it is difficult to predict accurately what limits exist before cartilage fails from this action.

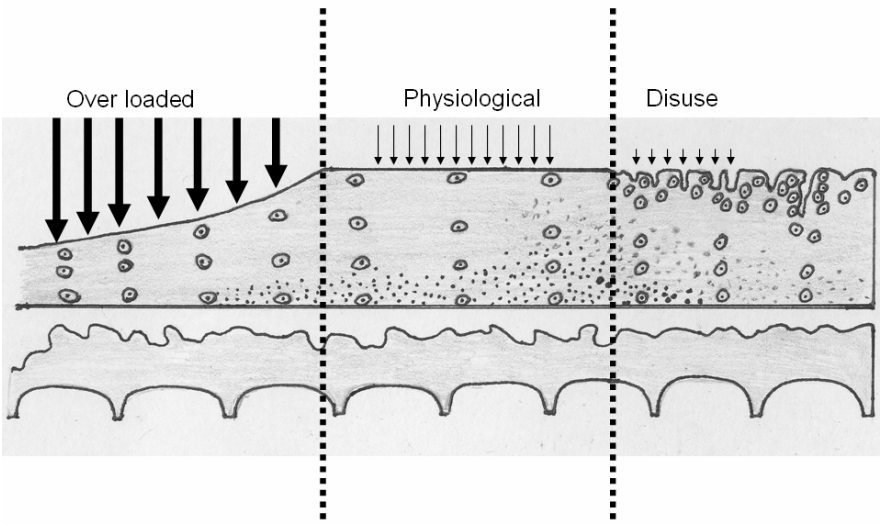


FIGURE 2.4 Articular cartilage subject to load is sensitive to magnitude. High loads cause pressure necrosis and ulceration and low loads or disuse cause chondromalacia which can lead to fibrillation. (Re-drawn from Basic Orthopaedic Biomechanics, 1997)

2.1.5 Topograhical Variations in Cartilage Properties and their Significance to Tibiofemoral Joint Biomechanics

Tibiofemoral joint kinematics and loading are especially relevant given previous reports of topographical variation in the mechanical properties of articular cartilage [Jurvelin JS 2000, Lyyra T et al 1999, Athanasiou 1991]. The articular cartilage and subchondral bone appear to have adapted in order to best withstand the variations in loading [Armstrong SJ et al 1995, Appleyard RC et al 2003]. These findings bear relevance especially to the aging knee, where mechanical properties of the structures are likely to be altered [Hudelmaier M et al 2001], or the pathological knee, where for example the combined deficiency of the anterior cruciate ligament and the meniscus would be indicative of a

tibiofemoral contact that engaged the articular cartilage that previously was covered by the meniscus. In view of this pathomechanical abnormality, there has been little or no discerning study performed on the mechanical properties of, for instance, the normal articular cartilage beneath the meniscus. Biomechanical models to study knee joint kinematics and kinetics, especially those requiring the input of consequential and relevant material properties may benefit from realistic information pertaining to topographical variation of cartilage properties.

An alteration in the joint anatomy or external conditions, due to disease, wear, injury, or excessive and strenuous activities, can lead to modifications in the sum of forces and the area of contact. Stresses are directly proportional to force, and inversely to area of contact. These stresses are important to consider, as they are crucial for determining the *service* weightbearing performance of the supporting structures. In typical engineering design the factor of safety is determined from obtaining a ratio on the ultimate stress of a material or structure and its service load, or the load that the material or structure will be experiencing on a daily basis. Likewise, for the biological joint, a similar ratio is useful to understand the influence of daily physiological loads and the ultimate strength of the joint structures.

These supporting structures consist of entire musculoskeletal components, of muscle, tendon, bone, ligament and cartilage. The muscle as an actuator is used extensively to provide force to either balance-off excessive forces, or to initiate

motion. Tendons function as 'tension cables' to effectively transfer muscle forces to bones, which then provide leverage for the body to control motion. In between these moving bones are tough stabilizers (ligaments) that are constraints to motion. Therefore when large forces are involved these stabilizers provide the defined and mechanically-acceptable working range for the bones to articulate without becoming dislodged from the joint. At the joint, the reaction forces are cushioned by fibrous cartilage, as well as the smooth articular (hyaline) cartilage. When loaded, the water-filled healthy articular cartilage provides a key role in lubricating the joint via facilitating the flow of fluid into the joint space, through its permeable membrane. This reduces friction and shear forces and keeps the joint reaction forces as minimal as possible. In osteoarthritis, it is this articular cartilage that deteriorates, and if not stopped, can lead to the progression of the disease and its manifestations.

2.1.6 Summary

The more relevant points from the text of this review (Section 2.1) are highlighted as follows:

1) Most of the motion in the knee joint occurs in the plane where flexion extension takes place.
2) The anterior cruciate ligament is the prime stabiliser of the knee in resisting anterior translation.
3) In the knee joint the loading is as much as three times body weight during walking.
4) Contact areas in the tibiofemoral joint were found to be in the range 20.13cm^2 to 11.60cm^2 in the neutral position.
5) The contact area of the medial plateau is said to be 50% larger than that of the lateral tibial plateau.
6) The articular cartilage of the medial tibial plateau is thicker than that of the lateral tibial plateau.
7) Deep flexion results in a shift in the tibiofemoral contact point such that there is a backward movement of the medial femoral condyle of 4 mm and backward movement laterally by 15mm.

8) Topographical variation in properties exists in articular cartilage, and the articular cartilage and subchondral bone appear to have adapted in order to best withstand the variations in loading.
9) Articular hyaline cartilage possesses a degree of compressibility and elasticity. These features enable the articular surfaces to dissipate laterally the vertical compressive forces to which the knee joint is subjected during weight transmission.
10) Cartilage explants under cyclic loads showed visible damage occurring between 20MPa to 50MPa, and subtle damage was seen to be initiated at as low as 5MPa to 10MPa. In impact loading, the stresses found to cause fissures and laceration in articular cartilage have been estimated to be about 25MPa.

2.2 The rationale for a biomechanics approach to investigating the causes and risks of knee osteoarthritis

The primary cause of osteoarthritis (OA) remains vague. Some of the earlier hypotheses and experimental work on the mechanisms involved in the initiation of osteoarthritis come from Radin EL and co-workers, where the fundamental emphasis has been that the cause of OA is due to an "*imbalance between the mechanical stress and the integrity of the tissues"* in absorbing the loads [Radin EL 1987]. Bone proliferation in the subchondral area in the cortical envelope of bone just below cartilage (eburnation) or at the margins of the bone (osteophytes), and radiographic joint space narrowing are hallmarks of OA [Kellgren JH and Lawrence JS 1957, Felson DT and Neogi T 2004]. The clinically useful definition of OA is "the symptomatic loss of significant articular cartilage in a habitual load bearing area of a joint associated with subchondral sclerosis and osteophyte formation" [Radin EL 1995]. OA may be a result of tissue injury, damage, or degeneration in relation to mechanical factors, as evidenced by clinical and animal studies of alterations in the mechanical environment of the joint caused by trauma, joint instability, disuse, or obesity [Guilak F et al 2004]. The term posttraumatic arthritis [Guilak F et al 2004, Buckwalter JA et al 2004] has also been used to distinguish OA as a disease commonly initiated by damage or injury in the joint.

The evidence that injury or damage produces a significantly higher likelihood for the development of OA is confirmed in prospective studies, where it was reported that this likelihood could be enhanced by as much as 7 times [Wilder FV et al 2002]. However there are hardly any studies that show the relative change, if any, in the rapidity of the onset of OA as a result of injury or the type of injury. A prospective study of over 1000 subjects aged about 22 years old and followed-up for over 30 years show that for subjects entering the study without joint injury, the incidence of OA after 30 years was 6%, while for those entering the study with a prior knee injury the incidence increased to 14% by the same time, with clear OA signs manifesting itself earlier for many [Gelber AC et al 2000]. However, not much more was reported on the type of injury sustained, or the length of time before OA signs were observed. In another report it was found that osteonecrosis in the medial tibial plateau presents a significantly high risk for the development of OA in the tibia; this occurred rapidly within a period of one year for many of the subjects studied [Satku K et al 2003]. Like its cause, the exact initial onset of OA is difficult to determine and remains vague. Spotting any initial signs is limited to current clinical features mainly of radiographic changes that look for osteophytes and/or joint space narrowing [Satku K et al 2003]. From a study of patients with unicompartmental OA, it was shown during intraoperative treatment that the apparently unaffected cartilage was mechanically inferior to normal cartilage, even although clinically, radiologically and morphologically it appeared to be sound [Obeid EM et al 1994]. Even in the

event that direct visualization of the joint is possible, for example via arthroscopy, there is also no guarantee that the initiation of degenerative changes may be ascertained. Animal studies have shown that macroscopic assessments are insensitive to articular cartilage softening, suggesting that arthroscopic assessments of cartilage status might also perform poorly [Oakley SP et al 2004]. This is also indicative that the actual start of the degenerative process, and the time when symptoms first appear, are likely to be different. In a recent review, the pathogenesis and epidemiology of OA were discussed as risk factors for OA and the *symptoms* of OA [Felson DT 2004], the initiation of OA being distinguished from the initiation of symptomatic OA. Symptoms usually present themselves at a later stage after the onset of OA. This is largely due to the reliance on pain as the initial symptom. Cartilage with no nerve endings is usually wornout and it is the bone's pain fibres, the synovium or other structures that need to be involved before pain is felt. Evidence of this has been reported in previous studies [Conaghan PG et al 2004, Hill CL et al 2001, Felson DT et al 2001]. Factors that are known to result in symptoms or the progression of OA are obtained from clinical observation of patients. These are, for example, bone marrow edema, synovitis, and joint effusion [Felson DT 2004]. Bone marrow edema lesions in the subarticular bone in patients with knee osteoarthritis identify knees at high risk for radiographic progression [Felson DT et al 2003], and its relation to progression is explained in part by its association with limb alignment.

The initiation of OA and the progression of OA are two processes that may require two different approaches for understanding. In this section the current theories on how OA may be initiated and progressed are described in relation to the different injury and damage modes. The development of OA is discussed as being initiated or propagated via one of several ways. These are based on theories on how cartilage damage may be initiated and propagated from I. subchondral bone changes [Radin EL and Rose RM 1986] II. microdamage in the subchondral plate and calcified cartilage that leads to enchondral ossification [Burr DB and Radin EL 2003] ,and III. altered mechanics that cause a shift in contact to cartilage that is not conditioned to high loads [Andriacchi TP et al 2004]. The common feature is that OA is a consequence of injurious activities acting on a vulnerable joint [Felson DT 2004] and leading to cartilage degeneration as the major clinical sign [Radin EL 1995].

2.2.1 Theories on the initiation and development of OA

The subchondral bone is considered a major part of the impact-absorbing structures in the joint, with the basic premise that articular cartilage has significantly less impact-absorbing function [Radin EL and Paul IL 1971]. It was proposed that if a 'stiffness variation' in the underlying subchondral layer existed it would affect the way the contact stresses were distributed in the composite of cartilage and bone, causing the damping or attenuation of forces to vary

accordingly. It was stipulated that changes in bone densities along the subchondral layer, which were determined by either the loading history or degree of bone remodeling occurring in that area, would be able to cause such a stiffness variation. The consequent development of stress risers and excessive shear were thought to be able to reach peaks sufficient to cause damage in the articular cartilage [Radin EL and Rose RM 1986]. Bone remodeling from microfracture was suggested as the key method of causing these acute stress risers, proposed as an important initiator of articular cartilage fibrillation in the early phases of osteoarthritis [Radin EL et al 1972, Radin EL et al 1973]. In patients, the microfractures were mainly found to occur beneath the deepest layers of the articular cartilage [Fazzalari NL et al 1998, Fazzalari NL et al 2002, Mori S et al 1993, Sokoloff L 1993]. Earlier work on cadaver studies showed a significant increase in trabecular microfracture in the proximal tibias of knees with early OA, compared to those without [Radin EL et al 1970]. How these microfractures arose was difficult to ascertain. Experiments conducted on animals showed that with repetitive impulse loading microfractures do occur, and also confirmed subchondral bone stiffening as a result of these microfractures healing with callus formation [Farkas T et al 1987]. Microfractures were present in the early stages of OA [Radin EL et al 1970] but hardly in the late stages, as was reported in studies of specimens obtained from joint replacement surgery [Fazzalari NL et al 1987, Koszyca B et al 1989, Grynpas MD et al 1991, Li B and Aspden RM 1997]. The reason for the reduced incidence of microfractures in the

later stages of OA was largely explained as increased trabecular thickening and strengthened subchondral architecture as OA progressed. Consequently, the increased subchondral bone strength was thought to either initiate or progress the OA by causing excessive stresses to develop in the over-laying articular cartilage when loaded. This has been the hypothesis of the earlier literature for a large part of the last thirty years, until recently [Burr DB and Radin EL 2003].

Instead of an excessive stress causing cartilage damage and initiating OA, investigators believe that the microfractures and remodeling triggers an ossification process that advances the tidemark, thereby thinning the cartilage [Burr DB and Radin EL 2003]. This thinning of the cartilage also resulted from an increase in shear stresses at the base of the over-laying articular cartilage that eventually lead to loss of more cartilage by this positive feedback mechanism [Burr DB and Radin EL 2003, Anderson DD et al 1993]. This reasoning arose mainly from the inability over the years to produce proof that the strengthened subchondral structure leads to a significant increase in the stresses in the over-laying articular cartilage, let alone that it leads to the development of OA [Burr DB and Radin EL 2003, Burr DB and Schaffler MB 1997].

Therefore, recently, the thoughts on the intitiation and progression of OA have been described as follows (quote): *Failure to properly absorb impact leads to microdamage in the subchondral plate and calcified cartilage. (It is believed) that*

this action causes the secondary center of ossification at the tidemark to advance by enchondral ossification, leading to thickening of the mineralized tissues and thinning of the overlying hyaline articular cartilage. Microcracks will cause the initiation of targeted remodeling, accounting for the increased turnover and reduced material density of the subchondral plate. The resultant thinning of the articular cartilage might lead to initiation of further microdamage in bone and cartilage through a positive feedback mechanism, which can ultimately lead to complete loss of the articular cartilage. In this view, the mechanical overload that initiates microdamage of the subchondral bone provokes a biological response that potentiates the progression of articular cartilage damage in OA. [Burr DB and Radin EL 2003]. A summary of this theory is interpreted and schematically described (Figure 2.5) in an 'OA cycle' showing the initiation process and cycle of progression affected by certain biomechanical events and biological responses. The focus is therefore drawn to the process of enchondral ossification and the region close to the tidemark. The advancement of the tidemark and consequent thinning of the articular cartilage becomes an important mechanism to investigate in determining the mechanical causes of the progression of OA. Duplication of the tidemark is cited as evidence of this advancement [Dequeker J et al 1997]. Current explanations for the biological responses that lead to the physical manifestation of thinning cartilage, mainly involve one or both of the following views: that it is either linked to an increased vascularisation or altered osteoblasts in the subchondral bone. The increased vascularity from passages

formed via the microcracks, conduits extending from the subchondral bone to the articular cartilage [Farkas T et al 1987], is a probable reason for cartilage depletion. Healthy articular chondrocytes mainly live in an avascular surrounding or conditions with low oxygen supply deriving nutrition primarily from the synovial fluid [Krane SM and Goldring MB 1990]. With a disruption in this environment, such as that of increased vascularity, the oxygen tension in the synovial fluid is subject to fluctuation, and subsequently partial oxygen pressure variations [Blake DR et al 1989, Henrotin YE et al 2003]. In response to partial oxygen pressure (pO_2) variations, and other factors such as mechanical stress, and immunomodulatory and inflammatory mediators, chondrocytes produce abnormal levels of reactive oxygen species that are generally produced by immune cells to assume host defense [Tiku ML et al 1990, Henrotin Y et al 1993, Hayashi T et al 1997, Fermor B et al 2001]. The literature shows that reactive oxygen species are deleterious agents involved in cartilage degeneration [Henrotin YE et al 2003] and this suggests a mechanism by which increased vascularisation can cause cartilage degeneration, and lead to OA.

Another explanation for the thinning of the articular cartilage comes from the suggestion that there is an alteration in the osteoblasts in the subchondral layer that affects the metabolism of the chondrocytes [Massicotte F et al 2002, Westacott CI et al 1997]. The evidence for this comes mainly from observations made when osteoblasts taken from the subchondral region of OA bone are co-

cultured with healthy normal articular cartilage, and compared with co-cultures using osteoblasts taken from normal bone. Increased glycosaminoglycan release was observed in the co-culture using osteoblasts taken from OA bone compared with the other group [Westacott CI et al 1997] indicating a breakdown in the cartilage matrix. The clinical inference is that if bone cells from OA patients can influence cartilage metabolism, then this might explain why increased subchondral bone activity can predict cartilage loss [Westacott CI et al 1997].

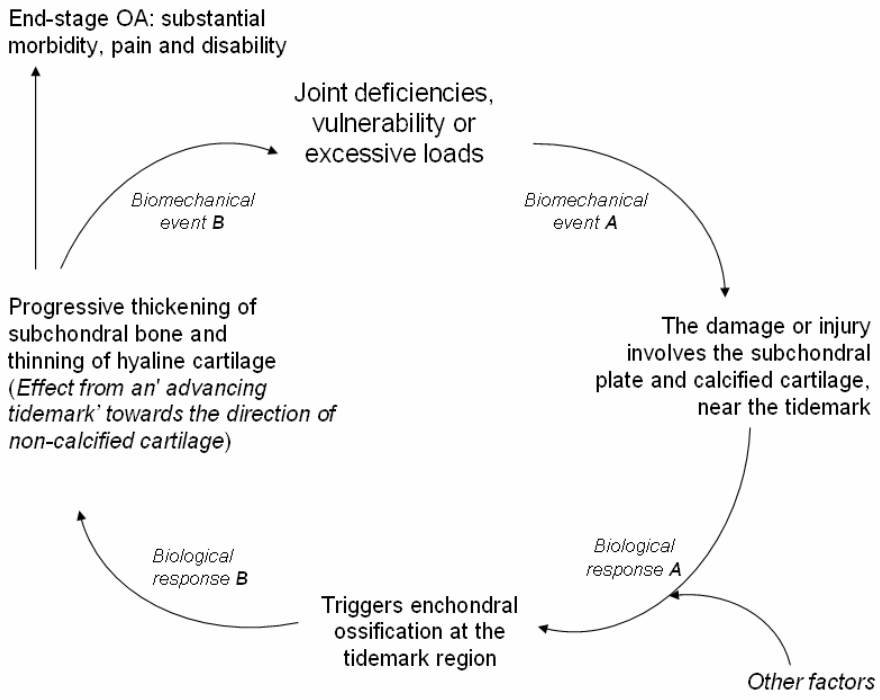


Figure 2.5 a schematic of the theories on the initiation and development of osteoarthritis in relation to a posttraumatic event (Burr DB and Radin EL 2003, Dequeker J. et al 1997) is shown. Both biomechanical and biological factors are involved in the cycle of OA progression. Biomechanical event A refers to mechanical factors that cause damage or injury to the subchondral plate and calcified cartilage near the tidemark. Biomechanical event B refers to changes in material properties as a result of tissue remodeling.

2.2.2 Joint injury, tissue damage and the biomechanical factors of OA

In relation to joint injury or tissue damage, besides being involved in determining the likelihood of whether OA develops or not, and the rapidity in which it progresses, mechanical factors also determine the type of the damage that occurs in the joint. From a review of models of cartilage failure mechanism from impact loads [Wilson W et al 2003, Atkinson TS et al 1998], load-induced articular cartilage damage has been characterized as either type (1)—damage without disruption of the underlying bone or calcified cartilage layer—or type (2), subchondral fracture with or without damage to the overlying cartilage. The damage characterized here is that from blunt impact tests simulating trauma. It was found that the key predictor of a fissure was shear stress, rather than impact force or energy. Shear stresses are difficult to obtain directly and in the previous study [Atkinson et al., 1998] a numerical analysis was used to derive these stresses from input of vertical forces. Shear stresses of 5.5 MPa was associated with 50% probability of fissure while at 10MPa the probability was 100%. Furthermore differences in damage mechanisms may also be due to the type of loading and the age of the joint. It was found that cell death in mature cartilage explants occurred after 6 hours of continuous repetitive load at 1MPa and only in the superficial tangential zone [Lucchinetti E et al 2002]. Another study found that a relatively small magnitude load of 1000 psi after up to 250 cycles was shown to have a generalized overall effect beginning with surface

abrasion of the cartilage, followed by primary fissuring, secondary fissuring and finally fragmentation after 8000 cycles [Zimmerman NB et al 1988]. In fast high-strain-rate shearing, mature tissue delaminates within a well-defined tidemark region whilst the immature tissue fractures through the subchondral bone into which fingers of articular cartilage penetrate [Broom ND et al 1996]. This is attributed to the junction between the compliant articular cartilage and the rigid bone. This junction represents an abrupt change in mechanical properties and is a region of potential weakness in the joint system [Flachsmann ER et al 1995]. For clinical application, categories of injury in relation to the type of joint damage described above are useful to derive. For example cell or matrix, chondral and osteochondral injuries all have different repair responses and are categorised accordingly [Buckwalter JA 2002]. The clinical response, repair response and potential for healing are thus influenced by this initial categorisation of the injury or damage and are believed to affect the probability of whether OA develops or not [Buckwalter JA 2002].

2.2.3 Risk factors for OA

As the causes are yet to be defined, the term 'risk factors' are commonly used to try to describe the epidemiology of OA. It is important to distinguish between 'risk' and 'cause' as one refers to a '*hazard that present a danger or probability of the unwanted event occurring*' and the other '*that that produces an effect, result or consequence*'. Attempts to learn more about the epidemiology of knee OA

have been performed extensively, especially via the 'Framingham Study' [McAlindon TE et al 1999 Am J Med]. These studies are noted in its choice of words in describing some of the probable causes of knee OA or more appropriately, its 'risk factors' [Felson DT et al 1997]. The associated mechanical risk factors most markedly have been heavy physical activity, injury, malalignment and obesity [Felson DT et al 1997, Cooper C et al 2000, Jurmain RD 1977, Anderson and Felson 1988, Sharma L 2000, Kettlekamp DB 1988]. Heavy physical activity, but not moderate or light activities, was found to be an important risk factor for knee OA in the elderly [McAlindon TE et al 1999]. "Heavy" activities ranged from lifting or carrying objects greater than five pounds, mowing with a non-power mower, gardening with heavy tools, shoveling, digging, chopping wood, brisk cycling, and other strenuous sports or recreation. 'Functional stress' [Jurmain RD 1977] could also be considered heavy physical activity, especially where occupational or even culturally-patterned behaviour involving repeated loading in the joint in extreme orientations, such as squatting and kneeling, may constitute 'heavy' activity. This is further illustrated in the studies looking at heavy physical workload showing that excessive squatting and kneeling are important risk factors to knee OA [Manninen P 2002, Coggon D 2000]. With strong evidence for an occupational hazard of knee OA resulting from prolonged kneeling and squatting, one approach to reducing this risk may lie in the avoidance of obesity in people who perform this sort of work [Coggon D 2000].

Obesity is most strongly linked to knee OA and is a risk for both the development and progression of the condition [Felson DT 1992, Anderson JJ 1988, Ledingham J 1995, Dougados M 1992]. Increased loads in the joint that cause the cartilage to be overloaded is associated with degenerative OA [Frost H 1994, Radin EL 1991]. The increased joint loading from obesity makes this a clearly biomechanical problem, where the concern that excessive stresses in the joint from being over-weight may be further elevated with accompanying malalignment. It was found that varus knee malalignment was a contributory cause to the effects of obesity [Sharma L et al [2000]. Increased dynamic loads on the medial compartment as a result of varus malalignment in OA [Baliunas AJ et al 2002, Prodomos CC et al 1985] aggravates the problem of excessive loading, and presents the question of whether the malalignment precedes or follows the onset of the disease. Chinese subjects were found to have significantly more varus mal-alignment of the lower extremity compared with westerners [Tang WM et al 2000] and coincidentally for studies on Asians specifically [Zhang et al 2001] it was estimated that the prevalence of radiographic and symptomatic knee OA in a population–based sample of elderly subjects in China were higher than that reported in the Framingham OA study which looked at a primarily Caucasian population.

The risk factors mentioned in this review are clear indication of the significant effects of mechanical factors in the consequential development of knee OA. It would not be correct to assign these mechanical risk factors as the cause of knee OA as little is known on what exactly is the sequence of events that follow when such risk is present. The relationship between abnormal joint loading and the epidemiology of knee OA remains merely suggestive. The paper by Sharma L et al [2001] summarises succinctly what the factors in osteoarthritis are most likely to consist of. Basically it consists of two broad classifications defining extrinsic factors and intrinsic factors. In extrinsic factors, the risk of knee OA arising from physical activity and injury are catergorised. Intrinsic factors cover risks from malalignment, muscle strength, varus-valgus laxity, anterior-posterior laxity, proprioception, congenital abnormalities and meniscectomy. Physical activity (excessive) is classified as an extrinsic factor for knee OA [Sharma L 2001]. This specifically refers to frequent or repetitive joint loading that may be excessive enough to cause injury. Activities such as squatting and kneeling, although common enough, when done repetitively have been shown to be associated with the risk of knee OA [Framingham study]. Heavy physical activity is an important risk factor for the development of knee osteoarthritis in the elderly, especially among obese individuals. [McAlindon TE 1999]. Some of these activities that pose as risks include physical demands from frequent knee bending [Felson DT 1991] or squatting [Coggon D 2000]. The damage from these activities may be significant enough to cause structural failure and lead to the onset of knee OA. However this cause and effect has not been shown or proven.

Another extrinsic factor for knee OA [Sharma L et al 2001] is *injury*. It is a common cause of premature OA in the young [Kannus P 1989, Lane NE 1993]. These injuries that result in knee OA include ligamentous and cartilagenous injuries that if not leading to premature OA, may then lead to OA in later life [Gelber AC 2000]. Studies have shown that the anterior cruciate ligament deficient knee joint of young active adults often tend to develop osteoarthritis of the joint with both conservative and surgical management [Noyes 1983, Casteleyn PP 1999]. In fact the relationship is so powerful that the current most popular method to create a model for osteoarthritis in animals for research involves the sectioning of the anterior cruciate ligament [Brandt 1991a, 1991b, Suter 1998, Setton 1999]. However the joint mechanics is still unclear with considerable speculation that OA may be initiated following ACL transection because of an overloading of specific regions of the joint, either because of the altered contact mechanics or the disrupted joint stability [Wu 2000]. Extrinsic factors are dependent on an external environmental input that results in compromise of the natural physiological load expectation or capability of the joint. It is at the least therefore a mechanical consideration that has impetus for further biomechanical analyses.

Intrinsic factors of knee OA are mal-alignment of the limb, abnormal muscle strength, joint laxity and meniscectomy [Sharma L et al 2001]. Mal-alignment of the lower extremity results in abnormal load distribution across the joints and

eventually contributes to cartilage wear and degenerative arthropathy or osteoarthritis [Radin EL et al 1991]. With varus knee mal-alignment, the association between the abnormal mechanical axis and the breakdown of cartilage followed by degenerative osteoarthritis [Hernborg JS et al 1997, Kettlekamp DB et al 1988] indicates the possibility of achieving a predictive formula to describe the critical varus knee deformity that could result in osteoarthritis. Recent findings show that Chinese subjects have significantly more varus alignment of the lower extremity compared with westerners [Tang WM et al 2000]. Given also the co-incidence of varus knee deformity and knee osteoarthritis [Hoaglund FT et al 1973] and the extreme variations in racial rates on the prevalence of knee osteoarthritis [Zhang Y et al 2001] pointing to a significantly higher incidence among the Chinese, it becomes relevant to understand the relationship between varus knee deformity and the consequential onset of osteoarthritis, in particular for our Asian populations.

Muscle strength and in particular, quadriceps weakness has been found to be associated with the risk of incidence of knee OA [Slemenda C 1998, Slemenda C 1997, Brandt KD 1999, Hunter DJ 2002]. Coincidentally, quadriceps weakness is also seen in anterior cruciate deficient patients [Hole CD 2000, St Clair Gibson A 2000], an injury that tends to lead to knee OA [Noyes 1983, Casteleyn PP 1999]. The kinematic changes that result from anterior cruciate deficiency are seen in the patients' adaptation in dynamic activity such that there tends to exist a

quadriceps avoidance [Berchuck M et al 1990] or at least a reduced quadriceps activity [Timoney JM 1993, Rudolph KS 2001]. Knee effusion is also found to induce quadriceps avoidance [Torry MR 2000] and is associated with joint space narrowing [Ledingham J 1995]. The alteration in joint kinematics as a result of quadriceps weakness or avoidance is therefore worth considering in terms of any accompanying alteration in the tibiofemoral joint contact that results. A change in joint contact may cause undue stress to be borne upon cartilage that is otherwise not used to the magnitude and frequency of loading it is being subjected to. However there is little in the literature to prove this point or otherwise.

Another intrinsic factor of knee OA is joint laxity. Joint laxity is widely used as a method to induce osteoarthritis in animal models [Brandt 1991a, 1991b, Suter 1998, Setton 1999, Pond MJ 1973]. This point was raised in the introduction of the paper by Sharma L et al [1999] looking at laxity in healthy and osteoarthritic knees. The authors [Sharma et al 1999] also listed other evidence to show that laxity may contribute to the development of knee OA. These were the clinical-based studies that suggested the association between generalised joint hypermobility syndrome and OA [Bridges AJ et al 1992, Bird HA et al 1978], that report that laxity is associated with changes in joint motion and suboptimal distribution of larger forces over the articular cartilage [Woo SL-Y 1995, Buckwalter JA 1995], and the finding that with aging, both a decline in the

material properties of knee ligaments [Woo SL et al 1990, Noyes FR et al 1976, Woo SL et al 1991] and the increase in the incidence of OA are likely to occur. The paper by Sharma et al [1999] then went on to describe their study looking at varus-valgus and anterior-posterior laxity in older patients with and without knee OA, compared with younger controls. It was found that there was greater varus-valgus laxity in the uninvolved knees of OA patients versus older control knees and an age-related increase in varus-valgus laxity. This, the authors said, supports the concept that some portion of the increased laxity of OA may predate disease. Also, loss of cartilage/bone height is associated with greater varus-valgus laxity, raising the possibility that varus-valgus laxity may increase the risk of knee OA and cyclically contribute to progression.

Meniscectomy is associated with long-term symptoms and functional limitations. In such patients those who developed severe radiographic OA experienced more symptoms and functional limitations [Roos EM et al 2001]. In 53 patients with meniscectomy consenting to bilateral radiography of the knee, the incidence of narrowing of the articular cartilage in the operated knee increased significantly between the reviews over 30 years. [McNicholas MJ 2000]. Experimentally in rabbit knees with the meniscus removed, more cartilage changes were seen at the joint surface area of contact on radiographs than in the sham-operated knees [Messner K 2001]. While it is quite evident that the absence of the meniscus does have a direct effect on articular cartilage loading, it remains

unclear of the co-effects of other factors such as ligamentous instability [Kurosawa H et al. 1976], obesity [Coggon et al 2001], and the level of physical activity. It was reported previously that outcome after meniscectomy is influenced by the quality and the frequency of postoperative athletic activity [Hoshikawa Y et al 1983].

2.2.4 The Biomechanics Approach

The knowledge of risk factors is thus limited in that the primary cause of OA still remains vague. The solution to understanding the cause of osteoarthritis must therefore involve both biological and mechanical investigations [Burr and Radin 2003] and this will probably involve relating the mechanical risk factors as well. The clinically useful definition of OA is "the symptomatic loss of significant articular cartilage in a habitual load bearing area of a joint associated with subchondral sclerosis and osteophyte formation" [Radin EL 1995]. This therefore creates enough impetus to focus the biomechanical analysis to understanding several related areas that include factors that cause or lead-to cartilage damage and degeneration. The common feature in both, mechanical causes and risk factors associated with OA, involves some form of biomechanical event that affects the composite of articular cartilage and bone at the joint.

In a recent review, a framework was proposed for the pathomechanics of OA at the knee [Andriacchi TP et al 2004]. It was suggested that this framework for

the study of knee OA be used to investigate the Initiation Phase and the Progression Phase of knee OA. The Initiation Phase is associated with kinematic changes that shift load bearing to infrequently loaded regions of the cartilage that cannot accommodate the loads, while the Progression Phase is defined following cartilage breakdown [Andriacchi TP et al 2004]. From a biomechanical standpoint this framework therefore includes describing variations in functional mechanics, levels of function, contact mechanics, joint laxity, cartilage mechanical properties and morphology, and mechanobiology (Figure 2.6) [Andriacchi TP et al 2004].

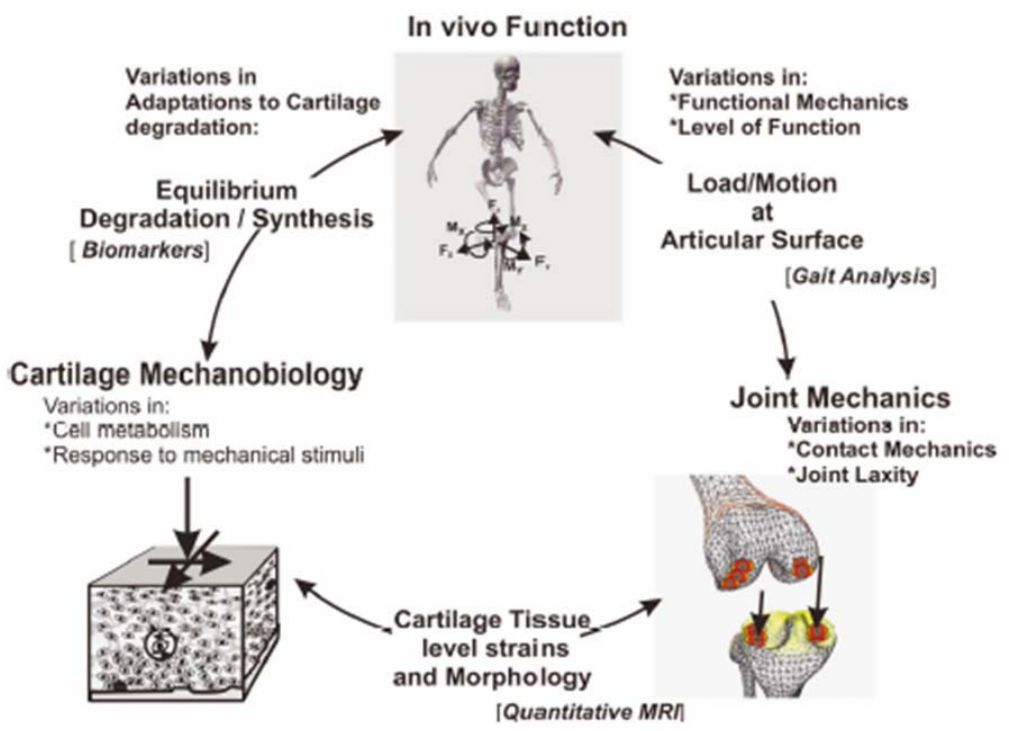


FIGURE 2.6 Understanding the in vivo response of articular cartilage to its physical environment requires an integrated view of the problem that considers functional, anatomical, and biological interactions. Gait analysis, quantitative MRI, and assays of biomarkers provide a basis for understanding the interaction between the various pathways that lead to the initiation and progression of OA. (From Andriacchi TP et al 2004, Reprinted with the permission of the Biomedical Engineering Society.)

The central focus will then be to understand the in-vivo response of articular cartilage to its environment, linking directly to the clinically-useful definition of osteoarthritis ("the symptomatic loss of significant articular cartilage in a habitual load bearing area of a joint associated with subchondral sclerosis and osteophyte formation" [Radin EL 1995]) for which the mechanical factors will need to be defined. Ultimately the useful parameter to derive will be some form of critical factor or a 'safety factor' for articular cartilage with regard to the various risk factors associated, both intrinsic and extrinsic. One way a safety factor may be estimated is from deriving the ratio of the ultimate stress for the material in question and 'service' stress. In terms of the biomechanical model, ultimate stress would be the stress that would initiate or cause the progression of cartilage wear and degeneration, while the service stress would refer to the physiological loading from the activities performed. These stresses will have to be derived from several different approaches, some involving in-vivo investigations and others in-vitro (Figure 2.7).

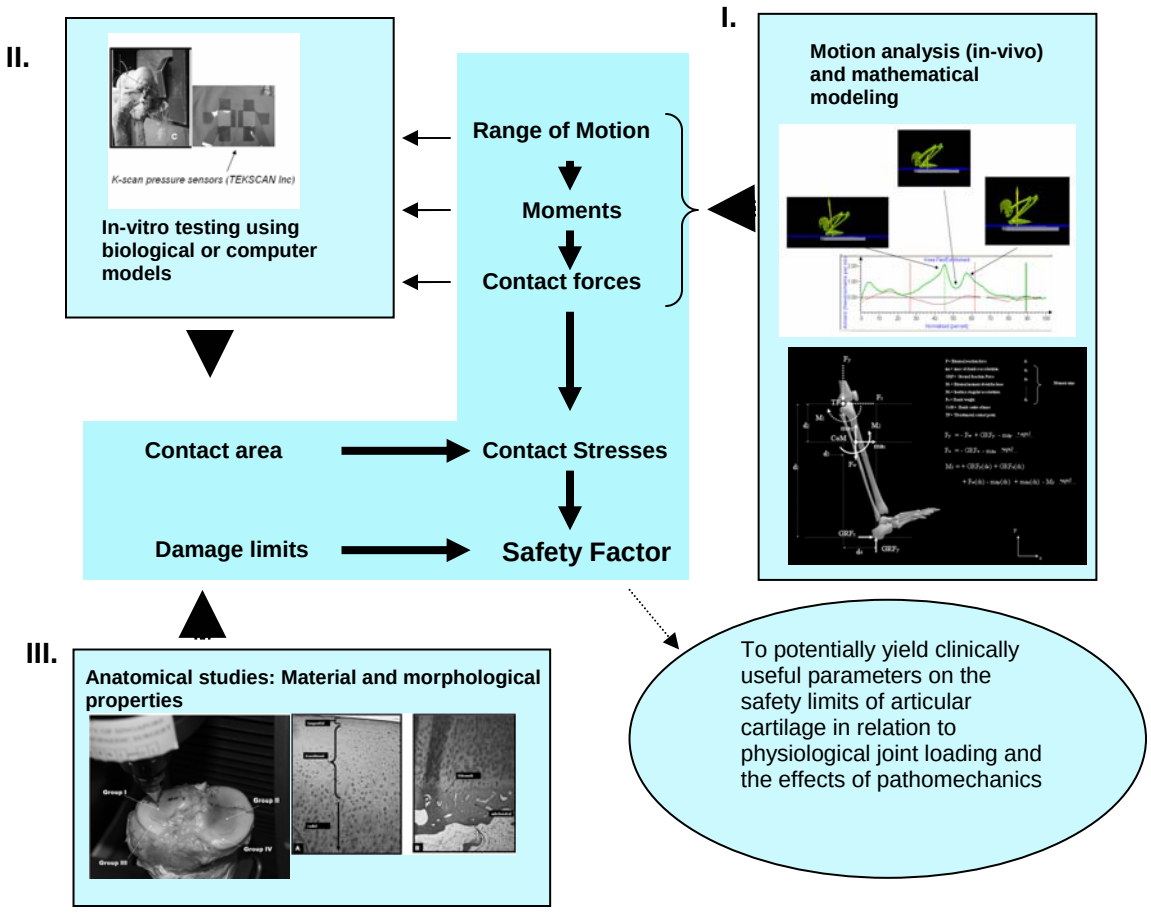


Figure 2.7 showing the several different approaches to solving the biomechanical question in the study of knee OA; involves both in-vivo and in-vitro investigations. First I). In-vivo motion analyses studies yield the input that allow the derivation of kinematics, moments and forces that is used in, II). In-vitro analyses where contact area is measured directly (by using thin film sensors for example). Contact stresses can then be derived and together with (III) information for material properties in the joint, a concept of safety factor is derived. The goal of this workflow is to have in place a viable system for quantifying the relationship between physiological joint loading, material properties and the factor of safety.

In discussing the critical stresses in the joint and its relation to the damage limits of articular cartilage, it will be useful to discern differences between light-repetitive and impact loading. Heavy repeated forces applied to the joints can cause degenerative changes that can be documented radiographically [Allan DA 1998]. Also, as shown by the reports from the Framingham study where frequent deep knee flexion from daily activity has been linked to a higher incidence of knee OA, repetitive actions that do not necessarily equate to large loads in the joint may eventually have some link to the consequential development and progression of OA. The actual mechanism of failure from repetitive strain or a large traumatic impact load is bound to be different. Because of several factors including viscoelastic effects, it is not as simple to assume that the relationship between repetitive loading and impact loading in cartilage follows typical relationships seen in engineered materials and described in fatigue (SN) curves depicting ultimate stress versus number of cycles (Figure 2.8). If however cartilage does follow a general principle where its factor of safety as a weight bearing material may vary with the number of cycles, strain rate and amount of load applied, then a suitable 'SN' relationship could conceivably be derived for cartilage. Such curves would probably be useful to study the influence of number of cycles, strain rate and the amount of load applied on the type of cartilage damage that results.

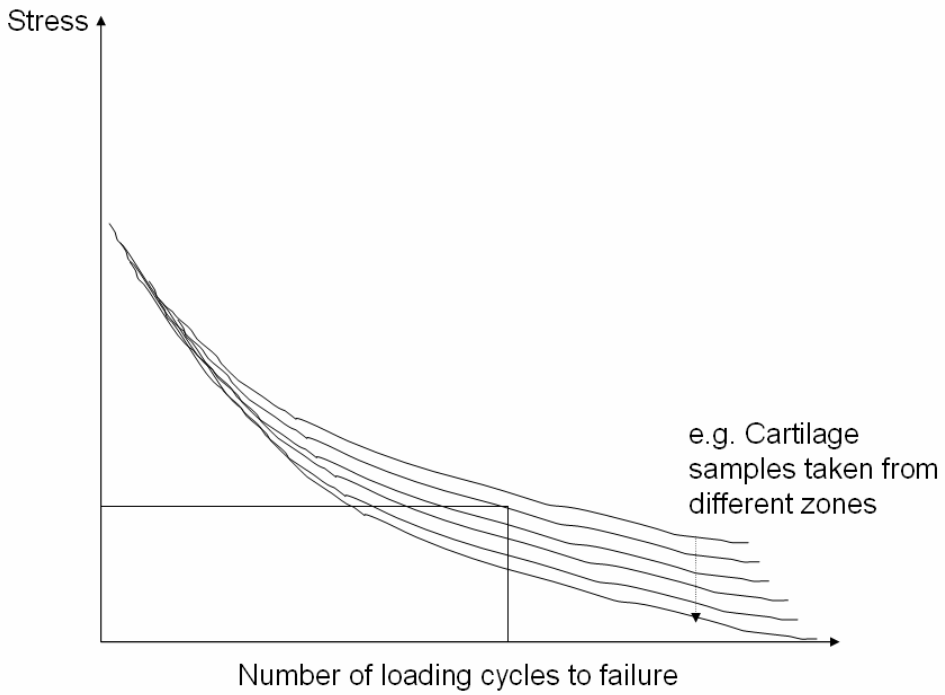


Figure 2.8 Repetitive load applied over many cycles may not cause failure initially but could reach some point where the next cycle could cause failure. The 'SN' curves here show how one perspective on the relationship between repetitive loading, impact load and failure. The example here hypothesises that cartilage from different zones will exhibit different responses to repetitive loading with different failure time points.

2.2.5. Summary

The causes and risks of knee osteoarthritis have been presented in the review in this section (Section 2.2) with an emphasis on the role of mechanical factors. Based on the review, the following conclusions are made:

1) There is a considerable role of extrinsic and intrinsic factors that affect the kinematic and kinetic intra-articular joint reactions, such that alterations in the normal physiological stresses becomes the most likely initiator of a series of events that has bearing on the biological, mechanical and chemical balance of the relevant musculoskeletal tissues.
2) The imbalance from these extrinsic and intrinsic factors include mechanical overload which results in microfracture and remodelling, and if in the region of the subchondral bone closest to the deeper layers of the articular cartilage, cause the triggering of enchondral ossification, tidemark advancement and cartilage thinning.
3) The progressive thinning of articular cartilage is due to one or all of the following factors:
    a) Increased stress from the underlying ossification and advancing tidemark.
    b) Alteration in the partial pressure of oxygen leading to cartilage matrix degradation.
    c) Altered osteoblasts from the remodelling areas of the subchondral bone that affect cartilage metabolism.

The role of mechanical factors continues from the initiation of the OA, through to development and progression of the condition. While other ('non-mechanical') factors involved will require their own unique interpretation, and ultimately be integrated to solve the unknowns in OA, the current interest in the mechanical factors should therefore focus on developing more knowledge of the stresses involved in reaching the various critical points or limits that have been described in this review. OA is likened to the failure of a system, and the limits that have to be reached before failure occurs should be ascertained in solving the design problem, one of the limits being the critical stresses that initiate the series of events, be they mechanical or biological, that initiate the degenerative process in the articulating joint. Critical stresses would refer to those from intra-articular joint reactions in relation to specific material properties of the supporting tissues. The biomechanics challenge is to determine these parameters with the specific aim of contributing new and useful knowledge to the larger effort of an integrated approach to resolving the unknowns of OA. The assumptions that provide the basis to the conjectural relationship between critical stresses and osteoarthritis can hopefully be elucidated in the process.

2.3 Excessive loading, joint vulnerability and the risk of cartilage damage.

From the literature review in the earlier section (2.2), it has been shown that extrinsic and intrinsic factors are involved in raising the risk for the development of knee OA. In this section of the review, some of these factors are discussed specifically with the aim of showing the relationship to altered mechanics and the risk of cartilage damage as an initial step prior to the onset of OA. The relevance of studying the models of deep flexion and anterior cruciate ligament deficiency are also presented.

2.3.1 Deep Flexion Activity and the Prevalence of Knee OA

The higher incidence of knee osteoarthritis in Asian populations where deep flexion activity is common, together with information from epidemiological studies conducted in non-Asian populations [Hart DJ and Spector TD 1993, Anderson JJ and Felson DT 1988, Cooper C et al 1994], make it meaningful to investigate further the cause-and-effect relationship of high stresses in the knee joint and the incidence of knee osteoarthritis from frequent deep flexion activity. Also evidence shows that the tibiofemoral compartments are commonly involved in knee osteoarthritis where clinical observation indicates that the medial side is the compartment most frequently affected [Windsor RE and Insall JN 1994,

Dieppe P and Lim K 1998]. Varus-knee deformities are commonly associated with medial side OA. Recent findings show that Chinese subjects have significantly more varus alignment of the lower extremity compared with Westerners [Tang WM et al 2000]. The concurrence of varus knee deformity and knee osteoarthritis [Hoaglund FT et al 1973] and the influence of race on the prevalence of knee osteoarthritis [Zhang Y et al 2001, Yoshida S et al 2002] pointing to a significantly higher incidence of knee oasteoarthritis among the Chinese and Japanese, raises some questions. This makes it relevant to further understand the relationship between knee joint mechanics and activity, and the consequential onset of osteoarthritis, in particular for our Asian populations. Mechanical factors for knee osteoarthritis in relation to differences that exist between Asian and Western populations groups should not be ignored. In particular there is more frequent deep flexion activity among Asian populations, which remains a significant difference observed when compared with Western populations [Mulholland SJ and Wyss UP 2001, Kurosaka M et al 2002]. The previous studies, conducted on Western population groups, show that physical factors such as excess weight [Hart DJ and Spector TD 1993], knee bending demands in the work place [Anderson JJ and Felson DT 1988] and squatting [Cooper C et al 1994] are positive factors that correlate significantly to the incidence of osteoarthritis of the knee.

The relevance of squatting to tibiofemoral osteoarthritis should not be understated, as it has been found that prolonged squatting is a strong risk factor for tibiofemoral knee OA and accounts for the relatively higher prevalence of tibiofemoral OA in Chinese subjects in China compared to White subjects in the United States [Zhang Y et al 2004]. Squatting has been found to generate larger external flexion moments about the knee than routine ambulatory activities, and the peak moments were generated between 90º and 150º of flexion [Nagura T et al 2002]. With such large moments about the knee and at such deep flexion angles, the joint contact forces and stresses that result in the tibiofemoral joint becomes an important consideration.

Accurate and functionally relevant intra articular contact stresses in the natural knee joint are difficult to determine, and there are no known published data on the stresses that result in the tibiofemoral knee joint in walking and squatting. The knee joint reaction forces from walking have been estimated to be as high as 3 to 5 times bodyweight [Morrison JB 1970, Kuster MS et al 1997]. This duly raises concern when strength studies of cartilage explants have shown that damage occurs with as low as 5 to 10MPa of cyclic stress [Farquhar T et al 1996]. Furthermore, given the evidence that osteoarthritis and cartilage damage can occur in the knee as a result of frequent or high contact stresses [Farquhar T et al 1996, Dekel S and Weissman SL 1978], the relevance in measuring these stresses becomes especially significant for population groups where cultural and

social habits commonly include high weight-bearing daily activities of deep flexion such as squatting and kneeling. The role of the meniscus, cartilage and soft tissue to neutralise high stresses becomes increasingly diminished in larger flexion angles where the tibiofemoral contact is largely reduced [Hefzy MS et al 1998]. Studies of deep flexion biomechanics in the past have been largely focused on the patellofemoral joint [Hungerford DS and Barry M 1979, Haut RC 1989, Koh TJ et al 1992, Singerman R et al 1999], looking at forces and stresses in this joint and its impact on cartilage. The possibility of failure in the tibiofemoral articular cartilage from high stresses in deep flexion, perhaps a cause for the development of knee osteoarthritis in these compartments, has not been investigated.

2.3.2 Altered kinematics in Anterior cruciate ligament deficiency

The anterior cruciate ligament is the predominant restraint to anterior tibial displacement and deficiency of this primary restraint has been reported to result in larger than normal anterior tibial translation, even during weight bearing [Dejour H et al, 1994]. Adaptations to anterior cruciate ligament deficiency include increased hamstring activity to maintain stability and to provide anterior tibial restraint [Aune AK et al, 1995; Bagger J et al, 1992] , and diminished quadriceps activity to reduce the demand on the anterior cruciate ligament [Berchuck M et al, 1990; Bulgheroni P et al, 1997]. In particular, Berchuck (1990) reported that during level walking, most patients with a deficient anterior

cruciate ligament had a quadriceps avoidance gait pattern, which was represented by the absence of net external flexion moments during level walking for the anterior cruciate ligament deficient knee. Without external flexion moments, patients with a deficient anterior cruciate ligament avoid internal extension moments caused by quadriceps muscles contraction, thereby reducing tension in the patellar ligament and consequently resulting in a decreased anterior drawer force on the tibia. This reduces the need for the anterior cruciate ligament to provide restraint to anterior tibial displacement.

Most studies examining anterior cruciate ligament deficient gait have focused on level walking [Berchuck M et al, 1990; Bulgheroni P et al, 1997] . However, it has been found that stair climbing produces a 12% to 25% increase in loading in the knee [Morrison JB, 1969; Paul and McGrouther, 1975] and, subsequently, a larger range of external moments [Andriacchi TP et al, 1980; Kowalk DL et al, 1996; Yu B et al, 1997; Costigan PA et al 2002]. This increased loading on the knee should be of concern to those involved in knee rehabilitation and injury prevention, because of the relationship between abnormal loading and cartilage damage [Gillquist and Messner , 1999; Setton LA et al, 1994]. To the patient with anterior cruciate ligament deficiency, abnormal knee loading is an additional concern, given reports pertaining to early onset of arthritis and meniscus damage as a result of an untreated or conservatively treated anterior cruciate ligament injury [Finsterbush A et al, 1990; Roos H et al, 1995; Rosenberg and Sherman,

1992]. Understanding the gait adaptations displayed by patients with anterior cruciate ligament deficiency during stair climbing is a useful way to assess the patient's ability to manage more extensive weight bearing activities. The relationship of injury to the potential for the onset of OA can possibly be made clear by evaluating the vulnerability of the injured joint.

2.3.3 The significance of anterior cruciate ligament deficiency with accompanying meniscal deficiency

Meniscal injury and damage is frequently associated with anterior cruciate ligament deficiency [Aagaard H and Verdonk R 1999]. In a cruciate ligament *and* meniscus deficient knee joint, the kinematics is altered with a subsequent weight-bearing tibiofemoral engagement of articular cartilage beneath the meniscus being a highly-likely, yet abnormal situation [Levy IM et al 1982, Levy IM et al 1989, Thompson WO and Fu FH 1993, Allen CR et al 2000, Brandsson S et al 2001, Papageorgiou CD et al 2001]. Prospective studies on patients showed via magnetic resonance imaging that the presence of meniscal and anterior cruciate ligament tears was associated with more rapid cartilage loss [Biswal S et al 2002]. The importance of the meniscus in covering the articular cartilage had been shown in animal studies [Aagaard H et al 2003, Szomor ZL et al 2000] where groups treated with a sham operation had no cartilage damage, while groups with meniscectomy resulted in significant macroscopic and microscopic damage to the articular cartilage in the medial compartment [Szomor ZL et al

2000]. In a study of the degenerative lesions in the articular cartilage after meniscectomy in dogs [Berjon JJ et al 1991], it was found that lesions proved to be more intense at the tibial plateau compared to the femoral condyle. The impact of an absent meniscus becomes more significant when the anterior cruciate ligament is absent [Schmitz MA et al 1996]. The role of the anterior cruciate ligament in maintaining stability and the forces acting on the meniscus is evident, as previous studies [DeHaven KE et al 1995] in the assessment of long-term survival rates of repaired menisci showed that significant increases in re-tear rates were encountered in unstable knees (anterior cruciate ligament deficient). The combined effect of instability from anterior cruciate ligament and meniscus deficiencies had been found to most likely lead to the development of knee arthrosis [Hazel WA et al 1993, Gillquist J and Messner K 1999]. In advanced osteoarthritis, anterior cruciate ligament integrity strongly influences the articular wear patterns [Harman MK et al 1998]. The anterior cruciate ligament deficient wear patterns showed a wear mechanism that was consistent with the posterior femoral subluxation and posterior tibiofemoral contact [Harman MK et al 1998]. The combined deficiency of the anterior cruciate ligament and the meniscus would thus be indicative of a tibiofemoral contact that engaged the articular cartilage that previously was covered by the meniscus. In view of this pathomechanical abnormality, there has been little or no discerning study performed on the mechanical properties of normal articular cartilage beneath the meniscus. Biomechanical models to study knee joint kinematics and

kinetics, especially those requiring the input of consequential and relevant material properties, may benefit from information pertaining to topographical variation of cartilage properties.

2.3.4 Summary

From this section (Section 2.3) some of the unknowns believed to be worth pursuing for the purpose of the present study on tibiofemoral knee joint biomechanics and the mechanical factors associated with knee OA were discussed. In particular the following are in need for more investigation:

1. The forces and stresses in the tibiofemoral joint in flexion activities, especially deep flexion.
2. The role of the anterior cruciate ligament in weight bearing knee activities such as stairclimbing.
3. The mechanical and morphological properties of the articular cartilage, including that beneath the meniscus, this in relation to deep flexion activity and anterior cruciate ligament deficiency.

CHAPTER 3: Preamble

The motivation for this study is based on the interest to explore the mechanical factors associated with tibiofemoral knee osteoarthritis (Figure 2.9 and 2.10). In the earlier chapter the literature review indicated several mechanical factors that are listed in relation to risks of knee osteoarthritis. It was shown in the review that mechanical factors may be related to damage or injury of the joint directly, or in terms of risks factors that include pathomechanical effects or certain activities which may predispose to injury or damage. Also altered tibiofemoral joint mechanics is believed to raise the risk for damage or injury, as regions of cartilage and bone not prepared to deal with different loading patterns might be involved.

In view of this, the focus of this study on the biomechanics of the tibiofemoral joint in relation to the factors associated with osteoarthritis is to investigate certain parameters that may reveal more of the relationship between joint vulnerability, excess loading and the probability of injury or damage. The end point would be to compare the findings from this study and present an understanding of weight-bearing knee activity in relation to the possible initiation of damage and injury and the subsequent onset of osteoarthritis.

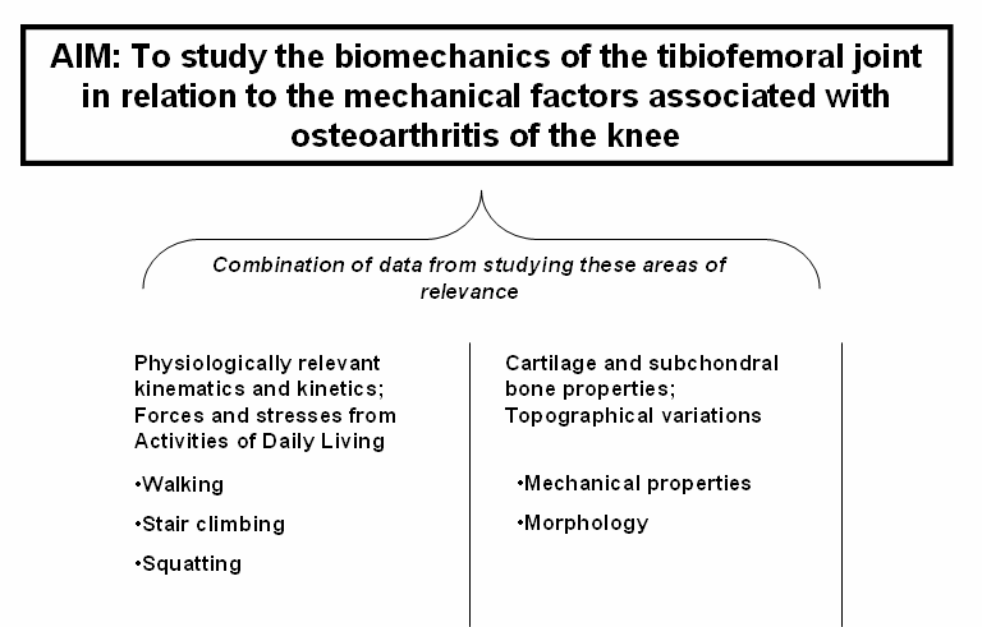


Figure 2.9 Overview of the focus of the present study.

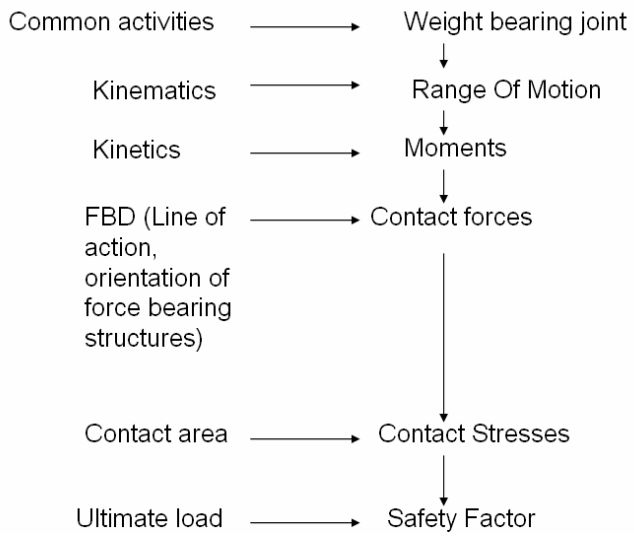


Figure 2.10 The approach used in the present study is illustrated here. Range of motion is obtained for the weight bearing joint from kinematic studies. Moments can then be obtained with additional input from kinetic data. With free body diagrams, force analyses allows for calculation of contact forces. Knowledge of contact area together with contact forces allows physiological stresses to be calculated. These stresses compared with ultimate stress that can cause damage or injury allows for a derivation of some safety factor or index to relate the type of activity to the risk of damage.

3.1 HYPOTHESIS

Altered tibiofemoral joint mechanics is believed to raise the risk for damage or injury, as regions of cartilage and bone not prepared to deal with different loading patterns might be involved. To investigate this a generalised *null* hypothesis is derived : that the weight-bearing capability of the joint structures will be adequate to withstand the loads from activities of daily living without damage, with no difference between normal and abnormal loading patterns.

3.2 AIMS

The specific aims of the present study are to:

i. quantify the forces and stresses that arise in the tibiofemoral joint during activities of daily living (the activities studied are level walking, stairclimbing and deep flexion)
ii. determine the mechanical properties of articular cartilage and subchondral bone in relation to topographical variation
iii. infer the factor of safety of the articular cartilage in negotiating the loads from activities of daily living
iv. deduce a criterion, if any, for predicting cartilage damage from activities in daily living for the tibiofemoral joint.

CHAPTER FOUR: Materials and Methods

4.1 Description of subjects and specimens

This study involved I). gait analysis, II). in-vitro biomechanical testing and III). morphological investigation via histological methods. Data from a total of 20 healthy subjects were used for the gait studies. A total of 12 cadaver joints were used for the in-vitro biomechanical tests. Twelve specimens constituted the histological investigation. The following describes the cohort in more detail.

I). The gait data of four healthy normal volunteers was used in the tibiofemoral contact force calculation model for walking and squatting. All were male. Average age was 21.5 years (Standard Deviation, 1.7 years). Height and mass were 167.0 cm (SD[1], 4.0 cm) and 60.0 kg (SD, 12.0 kg). Testing of the model to calculate (bone-on-bone) tibiofemoral contact force was performed by including the use of an existing data-set obtained from the CGA Normative Gait Database website (http://guardian.curtin.edu.au/cga/data/) where the gait data of 10 young adults compiled by the Hong Kong Polytechnic University were uploaded in the public domain. Six subjects participated in the stair ascent study and consisted of six healthy men ranging in age from 20 years to 29 years; mean

[1] Standard Deviation

height and mass of 169.6 cm (SD, 3.3 cm) and 59.1 kg (SD, 5.2 kg), respectively.

II). Five knees were used for the in-vitro biomechanical study of deep flexion contact stress. These knees were only examined during the test when the knee was exposed for the insertion of the sensors. The knees that were not healthy were not used and left for another unrelated study.

III). For the investigation on cartilage mechanical and morphological properties seven knees were used. The specimens came from a population of male cadavers whose ages ranged from 62 to 70 years old. All the cadaver specimens were obtained from bodies that had been donated to scientific and medical research, under administrative control of the Health Science Authority of Singapore. Careful gross examination was performed to exclude knees that had obvious injury or damage to the articular cartilage.

4.2 Description of patients

A comparative study was also performed of anterior-cruciate-ligament (ACL) deficient subjects during stair climbing and this involved nine men between the ages of 20 and 29 years with mean height and mass of 174.0 cm (SD, 5.3 cm) and 70.0 kg (SD, 5.9 kg), respectively, with unilateral, arthroscopically determined, isolated complete anterior cruciate ligament tears were selected for this study. There was no meniscal damage in these patients. As these data were collected before current implemented guidelines on patient consent and participation, the conventional method at that time (before 2001) was used. The first step was a call for volunteers, following which a meeting between the participating surgeon and patient was arranged. This mainly involved educating the patient on the potential risks of involvement in the study if any and describing in detail the purpose, method and proposed use of the results of this study. Patient assessment was performed by one surgeon and all patients had positive Lachman, anterior drawer, and pivot shift tests. The range of knee flexion-extension motion was normal in all patients (range, 0^0 – 150^0), and no patient had any evidence of other lower limb abnormalities, apart from a torn anterior cruciate ligament. The KT 1000 arthrometer (MEDmetric) mean difference in excursion between knees was 8.3 mm (SD, 0.7 mm; range, 7 - 9.5 mm) at manual maximum testing. Any difference in excursion greater than 3 mm between left and right knees was taken as an indication of anterior-posterior

laxity in the affected knee. All gait analyses were performed at a mean of 8.5 months (range, 7 - 10 months) after the original anterior cruciate ligament injury. After arthroscopic assessment of their injury, all patients underwent approximately 6 weeks of physiotherapy under the supervision of a sports therapist. The physiotherapy program consisted of regular cryotherapy, range-of-motion exercises, and muscle strengthening exercises. The patients were instructed to perform their own exercises, once they achieved full painless range of motion. The gait analyses of these patients were performed after the physical therapy regime and 6 to 8 weeks after the arthroscopy. All patients were regular and problem-free stair users in their daily activity.

4.3 Description of the Activities of Daily Living (ADL) studied

The three activities selected for this study were level walking, stairclimbing and deep flexion. Level walking refers to walking in a straight-line path on level ground. Stairclimbing involved the ascent of a special design staircase consisting of three steps. Deep flexion was studied while performing a squat. These three activities are to represent those of moderate to relatively demanding activity. A force platform was used in all three activities to study weight-bearing during the stance phase when the foot is in contact with the ground. Typical events in level walking were initial foot contact, double limb support, single limb support and foot-off. For stairclimbing initial foot contact refers to the first time the foot contacts the force platform that was embedded in the second step in the staircase (Figure 4.1), and toe-off the time when the foot leaves it.

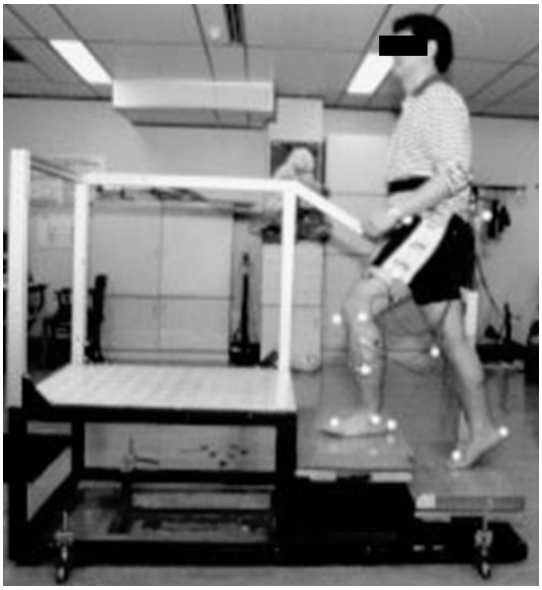


FIGURE 4.1 Subject walking up the staircase fitted with the forceplate.

In deep flexion the subject walks toward the force platform, and initial foot contact is the moment the foot contacts the force platform. The sequence then covers the time the subject takes to squat, and finally foot-off is when the foot begins to push off the force platform just before the subject walks away. For the stairclimbing study the subjects consisted of six healthy men ranging in age from 20 years to 29 years; mean height and mass of 169.6 cm (SD, 3.3 cm) and 59.1 kg (SD, 5.2 kg), respectively. Examined by an orthopaedic surgeon, control subjects had no symptoms or disease affecting their locomotion system, as confirmed by radiographs. Furthermore, the control subjects were found to be healthy on clinical examination. There was no significant difference in the mean excursion between knees of the control subjects during manual maximum testing using the KT 1000 arthrometer. For the deep flexion study, four healthy volunteers with no known knee pathology were used to perform the squats (FIGURE 4.2). Details of the protocol are described further in the up coming sections of this chapter.

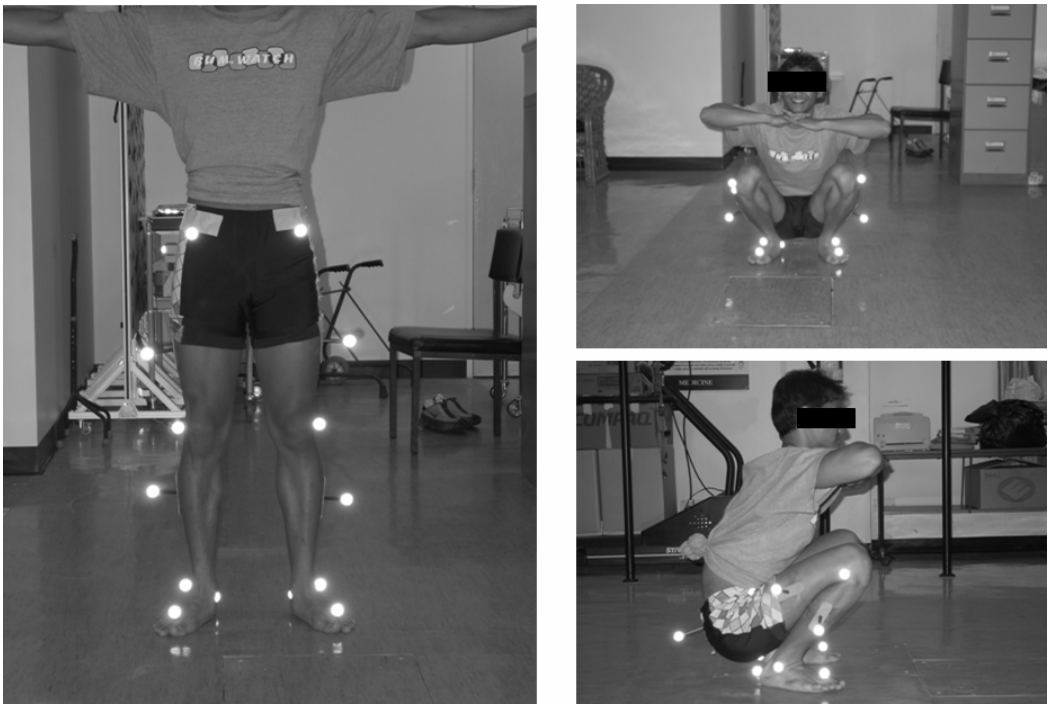


FIGURE 4.2 The normal healthy male volunteer shown here with retroreflective markers placed on specific anatomic sites for motion capture and gait analysis of walking and squatting.

4.4 Measurement of joint range of motion, external forces and moments

4.4.1 3D Motion Analysis System

Each subject was fitted with 17 skin markers, following a standard gait analysis protocol [Kadaba MP et al 1989, Goh JCH *et al*, 1993]. These markers were placed according to convention on selected anatomical features of each subject's right and left sides, namely on the anterosuperior iliac spine, greater trochanter, tibial tuberosity, fibula head, lateral malleolus, fifth metatarsal base, midheel,

calcaneous, and posterior pelvis. Stride characteristics and kinematic data were obtained from a five camera VICON motion analysis system (Oxford Metrics Limited, Oxford, United Kingdom). A Kistler force platform (Kistler Instrumentee AG, Winterthur, Schweiz, Switzerland) was used to obtain ground reaction forces at foot to ground contact. ADTECH Motion Analysis Software System (AMASS, Adtech, Adelphi,MD USA) and VICON Clinical Manager Software (Oxford Metrics Limited) were used in processing and analysis of the gait data. POLYGON software (Oxford Metrics Limited, Oxford, United Kingdom) was also used to study the deep flexion activity. To calculate the net external moments acting on the joint, the mathematical equations are essentially derived from balancing forces and moments about specific assumed joint centres calculated from intersegment motion measured form gait analysis [Kadaba MP et al 1989, Andriacchi TP et al 1997] A schematic of the model, as used in previous studies, is shown (Figure 4.4)

4.4.2 Protocol for the Stairclimbing Study and Staircase Design

Each subject was asked to walk up a custom set of stairs at a self-selected pace, with each step 155 mm high, 400 mm deep and 600 mm wide (FIGURES 4.1 and 4.3). The height of the stairs was designed to be similar to those found in most buildings in Singapore and is also within published ergonomic recommendations [Irvine CH *et al*, 1990]. A calibrated force platform was fitted into Step 2 to

capture (50 Hz) steady state ground reaction forces during stair ascent. The position of the force plate in the staircase was identified by placing a marker at each corner of the force plate during calibration. This was to ensure that the moments calculated were accurate.

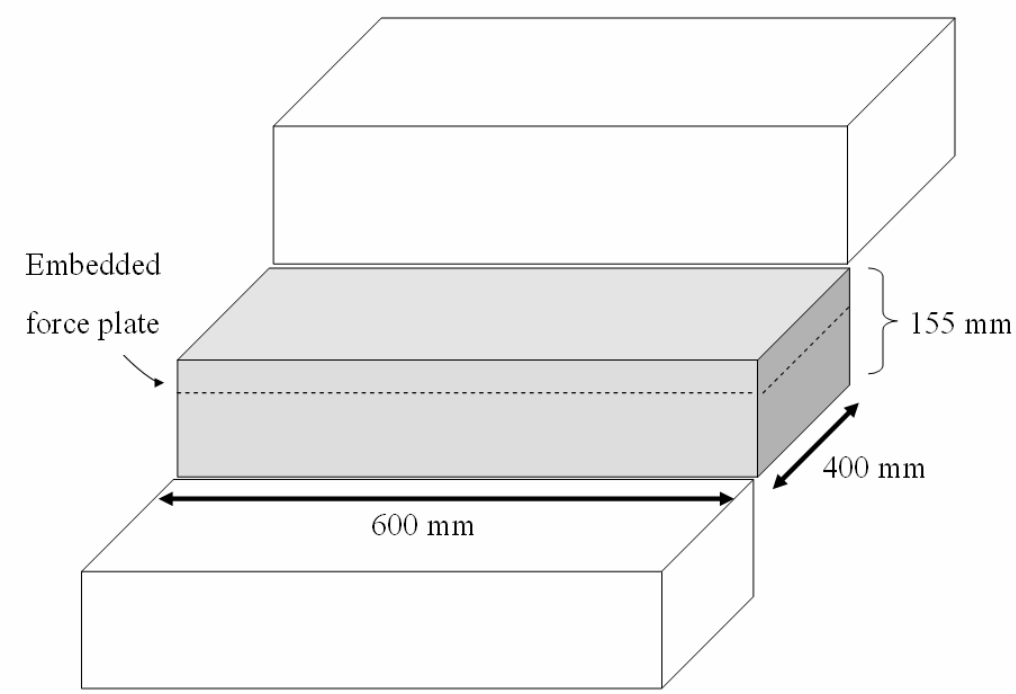


FIGURE 4.3 Schematic of the custom staircase showing where the force plate was embedded in the second step to facilitate direct foot contact with the plate during stair ascent. The heights shown here are the same for three steps.

The centre of pressure was located easily as the subject's foot directly contacted the force plate. Control subjects and patients walked barefoot, and ascended the stairs several times until they were comfortable with the exercise so that force plate data for the subjects' left and right limbs could be obtained efficiently. Three trials were collected for each subject for averaging. The kinematic data were captured (50 Hz) only during stair ascent. All subjects were observed for

characteristics such as the use of the handrail, reciprocating step clearance, and pain during ascent. Pain measurement was not scaled, but depended simply on the subject giving feedback on whether the exercise was causing discomfort or not.

4.4.3 Protocol for the Deep Flexion Activity

The subjects were made to perform three walking trials and three squatting trials. The squat involved approaching the force platform, squatting down on the platform, then getting up and moving away. Only one foot was in contact with the force platform. Arms were folded and elbows made to face the front. Motion and kinetic data was captured for the entire sequence. The motion data were from markers and modelling using the standard marker-model protocol described earlier. In the deep flexion exercise the subject was fitted with the same protocol of markers and motion was captured with the subject going into squat and rising from it. While performing the squat exercise the subject had both feet on the ground and with one foot on the force plate to record ground reaction forces for the moment calculations.

4.5 Estimation of Bone-On-Bone Contact Forces in the Tibiofemoral Joint

In-vivo tibiofemoral contact forces are difficult to measure because the joint is encapsulated, articulating and difficult to access. Even in the unlikely scenario where one is able to access the joint, sensors that measure forces have to be rugged, fast and accurate to capture forces in dynamic activities. Many studies therefore resort to modeling the joint mathematically and then calculating the forces [Paul JP 1976, Morrison JB 1970, Hattin HC et al 1989, Seireg A and Arvikar RJ 1973, Abdel-Rahman E and Hefzy MS 1993], or simulating articular joint mechanisms in-vitro using sensors to measure the forces. [Fujie H et al 1995, Markolf KL et al 1990] Here a method is described to obtain bone-on-bone contact forces from gait analysis data.

4.5.1 Introduction to the method

The first step would be to model the knee joint to obtain a typical free-body-diagram and then have the forces calculated thereafter. As with any free-body-diagram, external forces and moments acting on the system will need to be known, as well as the dimensions and geometrical layout of the interconnecting rigid links. Morrison [1970] used gait data of human subjects and the morphometric data of one human cadaver to construct the free body diagram and calculate the bone-on-bone forces. The gait data provides information on the

joint segment orientations as well as external forces and moments acting about the joint. The cadaver study reveals the anatomical details and relevant geometries necessary to complete the free-body-diagram of the joint; and this includes the moment arms of weight-bearing tendons and ligaments and the tibiofemoral contact point, all of which are involved in providing equilibrium to the joint in response to the external forces and moments acting on it.

The accuracy and reliability of gait analysis for a particular subject has been discussed in great detail with the conclusion that the joint angles and moments are acceptable for use in a standard fashion. [Chambers HG and Sutherland DH 2002, Sutherland DH 2002, Harris GF and Wertsch JJ 1994, Kadaba MP et al 1989] However, the validity of bone-on-bone contact forces remains vague, and one of the limiting factors is that the line of action and moment arms of the major force-bearing structures crossing the human knee joint of the subject is not known. These parameters may be obtained from means such as radiography [Nisell R et al 1986, Nisell R 1985, Kellis E and Baltzopoulos V 1999, Costigan PA et al 1992, Li J et al 1993] and magnetic resonance imaging [Spoor CW and van Leeuwen JL 1992, Wretenberg P et al 1996, Arnold AS et al 2000], but it becomes obvious that medical imaging involves processes that are costly and has its own inherent limitations. As an alternative, the lines of action and moment arms of the major force-bearing structures crossing the human knee joint have been estimated based on cadaver studies (Herzog W and Read LJ 1993) and

verified in experimental models [Lu TW and O'Connor JJ 1996]. The result is a series of relationships for the lines of action and moment arms of the major force-bearing structures, with respect to the flexion angle of the knee. The idea to combine the gait analysis data, together with the lines of action and moment arms of the major force-bearing structures crossing the human knee joint from the study of Herzog and Read [1993] to estimate tibiofemoral contact forces, therefore becomes an attractive proposition. This method is not new, as Zheng et al. [1998] combined the data from these two sources to calculate tibiofemoral contact forces. However, the potential efficiency of this methodology, especially for a quick and simple way to analyze many subjects, may have not been highlighted enough in the previous study because of the emphasis of the use of additional inputs, for example optimal muscle-length relationships [Zheng N et al 1998]. While it is important to consider the role of muscle inputs, the straightforwardness of this model in remaining such, via adopting a basic methodology as used by Morrison, [1970] where a closed quasistatic system of balancing external forces and moments with internal stabilizing structures to calculate tibiofemoral joint forces is an attractive option.

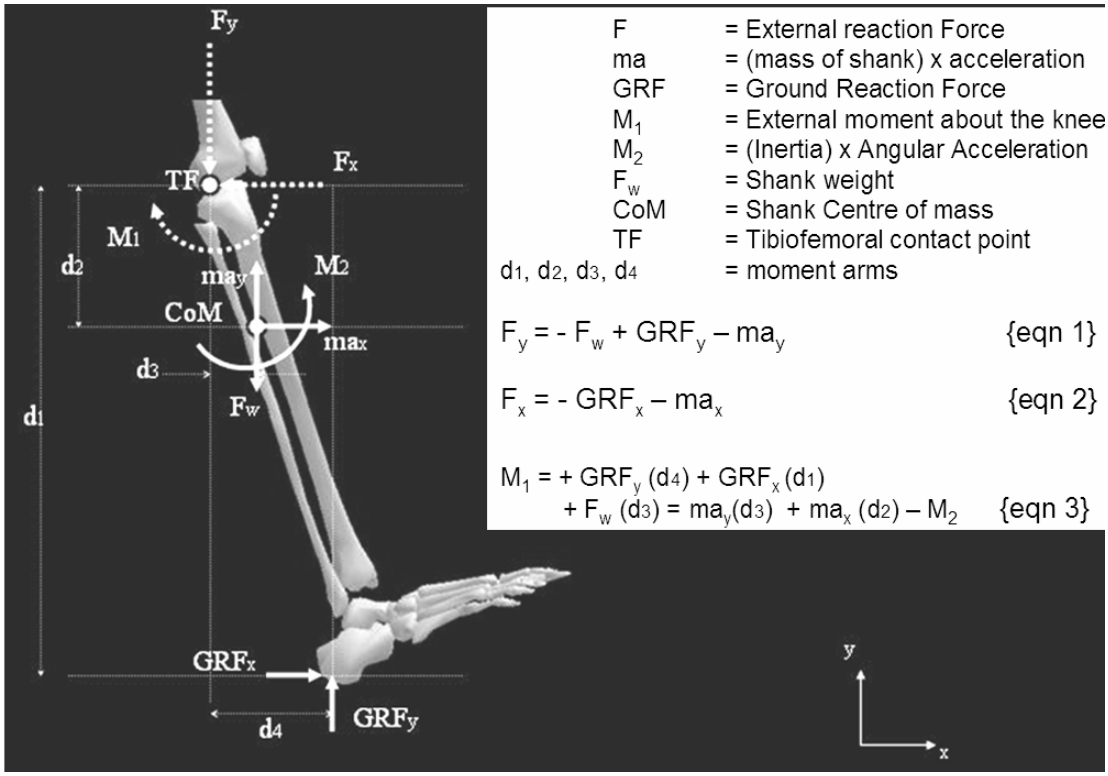
4.5.2 Description of the knee model

To validate the proposed model in the present study, a comparison of the calculations is made with that derived from earlier work on bone-on-bone contact

forces in the knee during walking [Morrison JB 1970, Schipplein OD and Andriacchi TP 1991, Andriacchi TP et al 1984].

Gait analysis data was obtained from the Clinical Gait Analysis Normative Gait Database (CGA) website (*http://www.univie.ac.at/cga/data*) with their kind permission. These were of 10 young adults compiled by the Hong Kong Polytechnic University and offered to the internet public domain. The dataset contained kinematic and kinetic data, including ground reaction force data.

Knee flexion-extension angles, moments and ground reaction forces were used for the calculation to derive joint contact (reaction) forces [Morrison JB 1970, Schipplein OD and Andriacchi TP 1991, Andriacchi TP et al 1984]. The free body diagram is shown (Figure 4.4).



F = External reaction Force
ma = (mass of shank) x acceleration
GRF = Ground Reaction Force
M_1 = External moment about the knee
M_2 = (Inertia) x Angular Acceleration
F_w = Shank weight
CoM = Shank Centre of mass
TF = Tibiofemoral contact point
d_1, d_2, d_3, d_4 = moment arms

$$F_y = - F_w + GRF_y - ma_y \quad \{eqn\ 1\}$$

$$F_x = - GRF_x - ma_x \quad \{eqn\ 2\}$$

$$M_1 = + GRF_y (d_4) + GRF_x (d_1) + F_w (d_3) = ma_y(d_3) + ma_x (d_2) - M_2 \quad \{eqn\ 3\}$$

FIGURE 4.4 Moments and forces from gait analysis derived from rigid body analysis is used as input for the boundary conditions of the knee joint where these moments and forces are balanced by internal structures to maintain equilibrium.

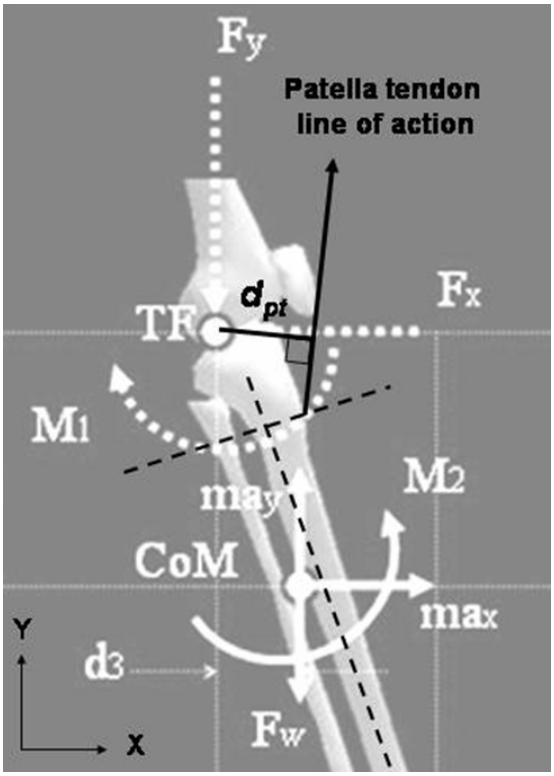


FIGURE 4.5 Schematic showing the moment arm (*dpt*) of the patella ligament assumed to be the perpendicular distance of the line of action to the tibiofemoral contact point. The orientation of the line of action of the patella ligament is an angle relative to the local anatomical axis of the tibia as shown by the dotted lines. (Refer to Fig. 4.4 for notations used)

To calculate the tibiofemoral bone-on-bone contact forces the anatomical orientation of the force bearing structures in the knee were required. These structures were simplified to the sagittal plane and consist of two opposite lines of action via the patella ligament and hamstrings tendon respectively. The lines of action of the patella ligament (α_{pt}) and biceps femoris (hamstrings) tendon (α_{bft}), *in degrees*, and the respective moment arms (d), *in centimetres*, were derived from the equations of Herzog and Read [1993] using the knee flexion angle (θ) from gait analysis (Figure 4.5):

Patella Ligament

α_{pt} = - 0.744E+02 - 0.575E-01 (θ) - 0.475E-02 (θ)^2 + 0.309E-04 (θ)^3

d_{pt} = + 0.471E+01 + 0.420E-01 (θ) - 0.896E-03 (θ)^2 + 0.477E-05 (θ)^3

Biceps Femoris Tendon

α_{bft} = 0.275E+03 - 0.872E-00 (θ) - 0.712E-03 (θ)^2

d_{bft} = 0.146E+01 - 0.926E-02 (θ) + 0.855E-03 (θ)^2 - 0.878E-05 (θ)^3 + 0.238E-07 (θ)^4

The moment arm for patella ligament (d_{pt}) and biceps femoris tendon (d_{bft}) are input into the force-moment equation to derive the force in the patella ligament (F_{pt}) and biceps femoris tendon (F_{bft}). M_p, is the external flexion (+) or extension (-) moment that was obtained from the gait analysis data using the previous model [Kadaba MP et al 1989]. The following equations were used to calculate the tibiofemoral bone-on-bone contact forces (FC) in the vertical ($_x$) and horizontal ($_y$) axes:

If M_p is positive, then:

$F_{pt} \times d_{pt} = M_p$

$FC_x = - F_{pt} (\cos \alpha_{pt} + \beta) + F_x$

$FC_y = F_y + F_{pt}(\sin \alpha_{pt} + \beta)$

If M_p is negative, then:

$$F_{bft} \times d_{bft} = M_p$$

$$FC_x = F_{bft} (\cos \alpha_{bft} + \beta) + F_x$$

$$FC_y = F_y + F_{bft} (\sin \alpha_{bft} + \beta)$$

F_x and F_y are the reaction forces derived from the ground reaction forces with the positive y-axis being upwards and the positive x-axis being perpendicular and pointing towards the line of forward progression (Figure 4.4). β is the angle the tibia rotates about the z-axis (right hand rule with x and y axes in the global reference frame). In this study, for simplicity, the tibia rotation relative to the global reference is taken as zero. F_{pt} is the tension in the patella ligament (assumed to arise from quadriceps contraction) that balances a positive external flexion moment, M_p, acting about the knee; while F_{bft} is the tension in the hamstrings tendon that balances a negative external extension moment, M_p. These forces are resolved from the line of action values derived for the patella ligament (α_{pt}) and biceps femoris tendon (α_{bft}).

An obvious exclusion from this model is the frontal plane calculations of forces. While it is acknowledged that the influence of adduction moments in the knee is an important consideration, especially in the varus knee etiology of OA, at this point the inclusion of morphological characterisation of the medial and lateral compartments is beyond the scope of this study. The focus therefore is on

calculating forces as a sum total of both compartments in which case the medial and lateral condylar morphometry becomes less relevant in the sagittal plane. The usefulness of the sum total force data will be in providing guidance to the loading protocol for in-vitro contact stress studies of the tibiofemoral joint.

4.6 Deriving contact stresses

4.6.1 Description of the In-Vitro Knee Model

In-vitro mechanical testing was carried out in this study on five cadaver knees. Loading conditions in various phases of walking and squatting were derived from previous studies [Morrison JB 1970, Wilk, K.E. et al 1996] and applied to quasi-static mechanical testing on the cadaver knees in which pressure transducers were inserted in the articulation to measure contact stresses in these various phases. Flexion angles of 5.5º, 15.5º, and 4.5º were selected [Lafortune MA et al 1992, Reinschmidt C et al 1997] to represent knee flexion angles involved at heel strike, single limb stance and toe-off respectively; the respective tibiofemoral loading for these angles were selected accordingly from previous work [Morrison JB 1970] .

In all five of the specimens, the following positions and loading conditions were prescribed:

a). Heel Strike (HS) - 5.5° flexion at 2.25 *multiples of body weight* (BW)

b). Single Limb Stance (SLS) - 15.5° flexion at 1.85 BW

c). Toe-off (TO) - 4.5° flexion at 3.5 BW

d). Deep Flexion 1 (DF1) - 90° flexion at 4 BW

e). Deep Flexion 2 (DF2) - 120° flexion at 5 BW

Body weight was assumed to be 700N. The knee joint orientations were achieved by the use of a specially constructed loading apparatus consisting of fixtures that allowed positioning (and locking in place) of the knee joint in translation and rotation in all three planes (Figure 4.6A to 4.6C). The entire loading apparatus was part of a standard materials testing machine. A preliminary protocol was implemented to all the specimens, in which a load of up to 700N to 1000N was applied at 10mm/min to allow the knee joint to locate its own mechanically stable (or 'equilibrium') position for each of the five prescribed flexion angles. To do this, the desired flexion angle was applied and the respective displacements and rotations of the tibia rotating and translating freely were facilitated until the load reached a stable point indicating equilibrium. Varus/valgus, and internal/external rotations; and anterior/posterior and medial/lateral displacements were unrestrained. To achieve the equilibrium position, under the preload, the knee is free to move in the unrestrained directions. The femoral condyles and tibial plateau articulate with the line of force passing through the center of the joint. This line of force is ensured via the design of the loading apparatus (Figure 4.6A to 4.6C) where also the central epicondylar axis of the femoral condyles remains in the flexion axis. The equilibrium position, where no more movement occurred in these rotations and translations, was recorded using scales and markers located on the loading apparatus.

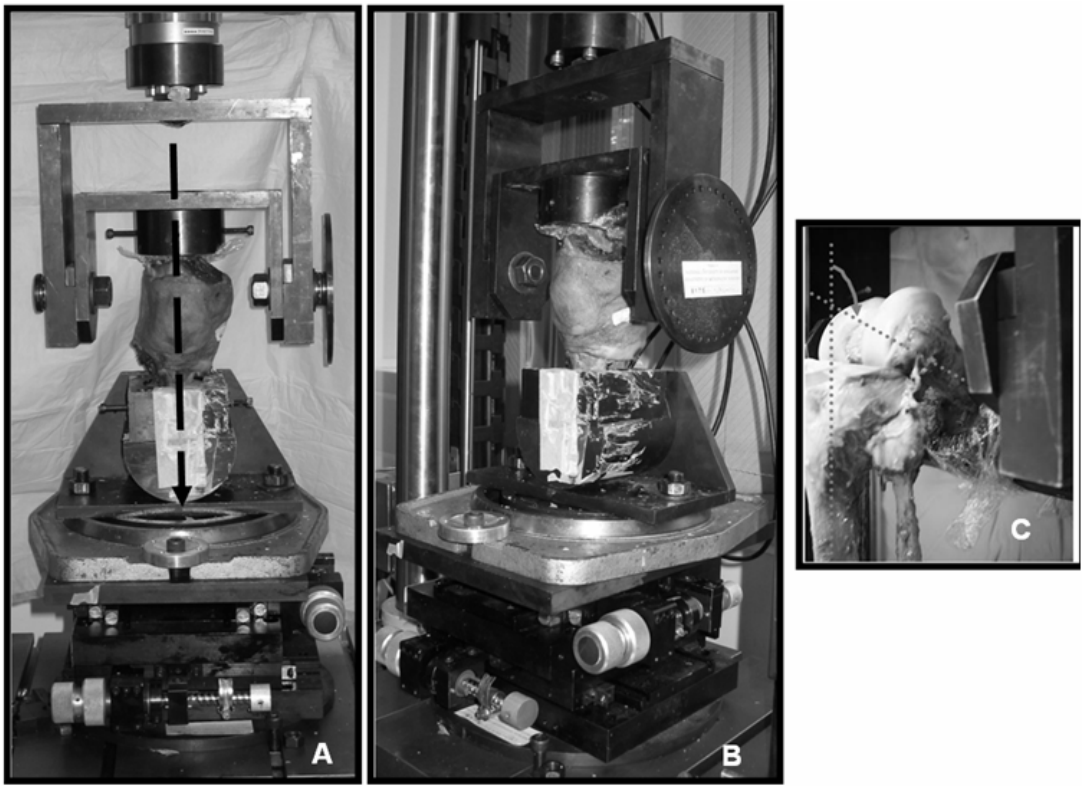


FIGURE 4.6 A to C. Except for the flexion motion which is locked at a specific desired position, the intact knee is loaded up to 1000N and allowed to move freely in the other remaining degrees of freedom to find its equilibrium position. This position is recorded. The positions are replicated after the knee has been unloaded, dissected, sensors inserted and loaded again to the maximum prescribed loading conditions estimated for these positions. A). Front view. B). Side view. C). Deep flexion position. *More detailed pictures can be found in the appendix.*

After the positions were recorded for the five prescribed flexion angles, the joint capsule was dissected and the joint disarticulated, removing all structures but preserving the integrity of the articular cartilage and menisci as well as possible. Each of the recorded positions obtained earlier were then reproduced and the relative positions of the tibia and femur were reconstructed. The joint was compressed up to loads prescribed for the five flexion conditions at a load rate of 10 mm/min . The

peak contact stress was measured in real time using sensors that were inserted into the tibiofemoral joint between the articulating surfaces.

4.6.2 Calibration of Pressure Sensor System

The pressure (contact stress) measurement system consisted of a thin (0.1mm) plastic pressure sensor (K-Scan sensor and software from Tekscan Inc, Boston, USA) (Figure 4.7) interfaced with a desktop personal computer running software that recorded and displayed in real-time the force and area values from the sensor. The system has been described previously [Harris ML et al 1999].

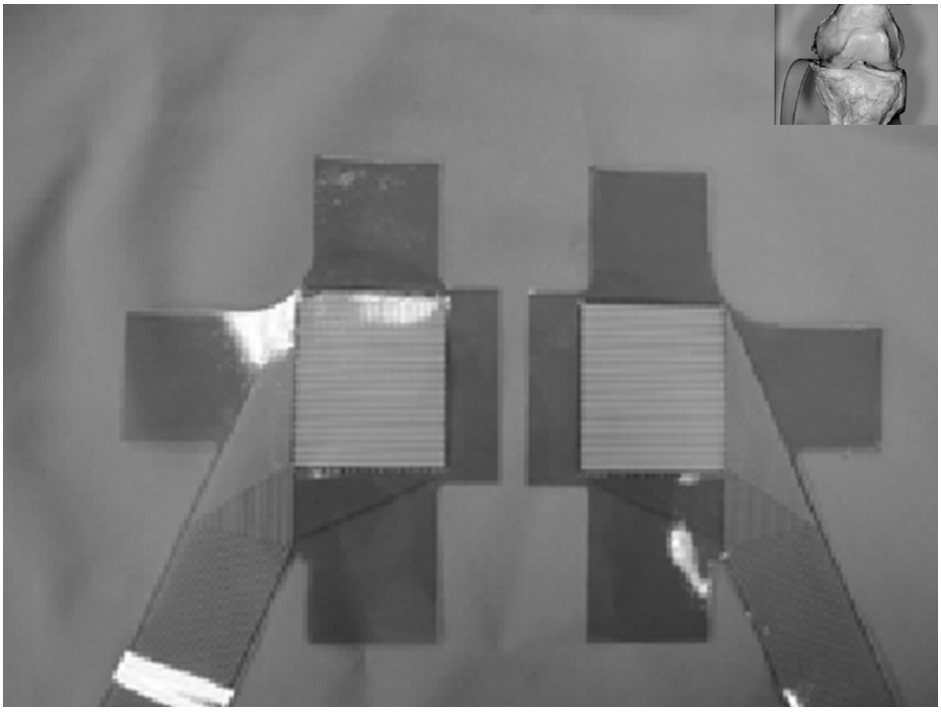


FIGURE 4.7 The sensors used to measure pressure are thin film, 9.2cm2 area sensors with 2288 sensing elements. The fine wire grid is sensitive to force and the grid layout which is known is used to indicate the way the force is distributed. Stress is thus calculated from these two parameters.

The sensors were calibrated using the load cell of the materials testing system and the flat plane end of an indenter of known area 19.6mm^2. The force output from the materials testing system is divided over the known area to establish the actual pressure when the indenter is depressed on various sites of the sensor. The pressure readings from the sensor is taken as the calculated pressure and compared with the actual pressure to define the linear relationship and multiplication factor. This factor is multiplied to the pressure measurement from the sensor. Data was streamed into an output file for statistical analysis and graphical organisation.

4.7 Characterisation of the topographical variation in articular cartilage

As mentioned in the earlier section (4.2), seven tibia specimens were obtained for this study. The specimens came from a population of male cadavers whose ages ranged from 62 to 70 years old. The specimens were obtained from bodies that had been donated to scientific and medical research, under administrative control of the Health Science Authority of Singapore. Careful gross examination was performed to exclude knees that had obvious injury or damage to the articular cartilage.

4.7.1 Grouping

Mechanical testing using an actuator with a plane-ended impermeable indenter was performed on the articular (hyaline) cartilage of the medial and lateral tibial plateaus, including the areas beneath the meniscus (Figure 4.8). Four sites of the articular cartilage on the tibial surface were thus generalised into four respective groups.

These four groups are named and described as follows:

- Group I: Lateral tibial plateau that is *not* covered by the meniscus.
- Group II: Medial tibial plateau that is *not* covered by the meniscus.
- Group III: Lateral tibial plateau that is covered by the meniscus (beneath the meniscus).
- Group IV: Medial tibial plateau that is covered by the meniscus.

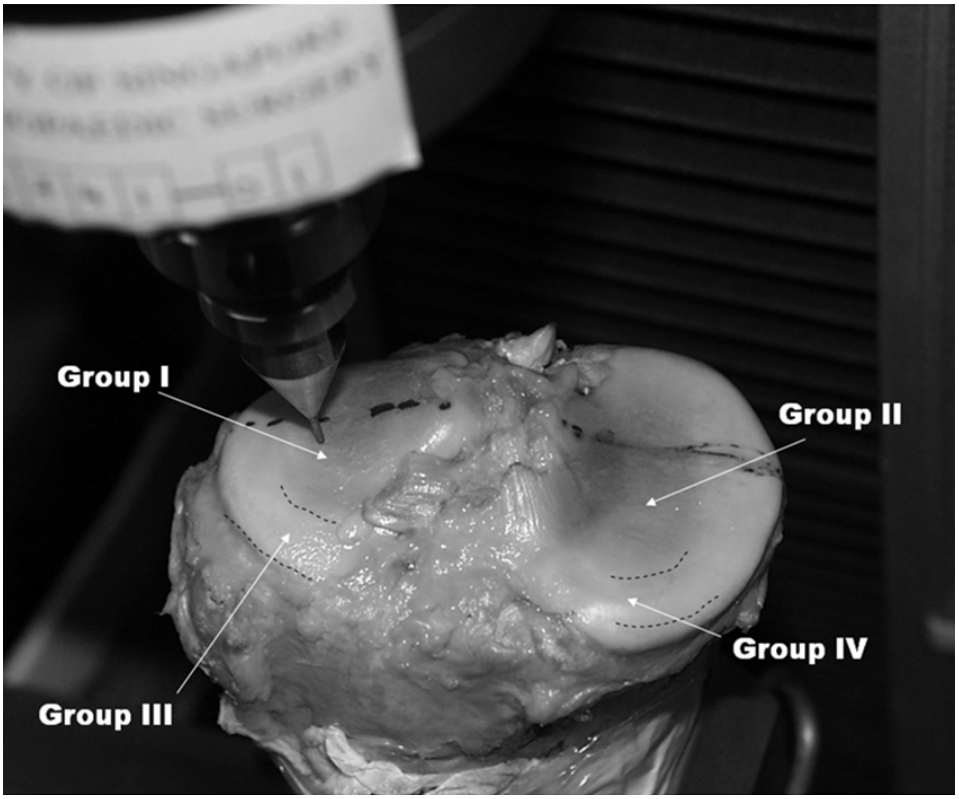


FIGURE 4.8 The dotted line represents the outline of the removed meniscus. The four sites of the articular cartilage for mechanical testing on the tibial surface were divided into four groups. Group I: Lateral tibial plateau that was *not* covered by the meniscus. Group II: Medial tibial plateau that was *not* covered by the meniscus. Group III: Lateral tibial plateau that is covered by the meniscus. Group IV: Medial tibial plateau that was covered by the meniscus.

In Groups I and II, the central section of the cartilage not covered by the meniscus was tested. This was the region of the articular cartilage subjected to direct weight-bearing. The region tested in Groups III and IV was in the posterior section of the tibial plateau beneath the meniscus. This was the region of articular cartilage most likely involved in tibiofemoral contact in the anterior cruciate ligament and meniscus deficient knee.

4.7.2 Indentation tests

Cartilage indentation mechanical tests performed in the present study followed similar testing protocols of previous methods [Hayes WC et al 1972, Lyyra T et al 1999, Mak AF et al 1987]. The properties derived in the present study to represent modulus were that obtained instantaneously and not after a process where the cartilage was subjected to long periods of creep until equilibrium was reached. The rationale for this approach is that during the instantaneous response after load application, the cartilage can be modeled as an incompressible single phase elastic material [Lyyra T et al 1999, Mak AF et al 1987]. Mak AF et al. [1987] validated their conclusions on the basis that the absolute values of instant and equilibrium shear moduli differed from each other but they revealed the same variation in topographical stiffness [Mak AF et al 1987]. In the present study, instead of measuring equilibrium modulus, the instantaneous modulus was measured. This removed the need to subject the cartilage to long periods of exposure for equilibrium to be reached. To achieve

this, a rapid loading rate was necessary to eliminate (or decrease) the effects of creep. Tibial plateau specimens were prepared with the meniscus removed (as shown in Figure 1). The cartilage was loaded in axial compression at a constant load of 0.5N, with the use of a 1-mm diameter indenter, attached to a 500N load cell of a materials testing system (INSTRON® model number 5543, Massachusetts, USA). The small size of the indenter was intended to minimize the influence of the stiff underlying bone on the registered force [Mak AF et al 1987]. The indenter start position was achieved by adjusting the specimen until the cartilage surface was just in contact and perpendicular to the long axis of the indenter. The specimen was locked in place once this position was reached by careful visual observation. The cartilage was indented with a steep ramp function (rise time < 200ms). The loading rate with this configuration was equivalent to no less than 300 kPa/s until a load of 0.5N (0.6MPa) was reached. The load was then kept constant throughout the test. The constant load was obtained by the load control system of the materials testing machine, with the gain set at 30dB for optimum feedback control. The actuator maintained a constant 0.5N load throughout the creep test that lasted for 60 seconds, following which the cartilage was unloaded. After about 5 minutes, total recovery of the indented surface was observed and the testing ended. The test was repeated until steady state was reached and repeatable response was obtained. This was done for several points in each Group (Figure 4.8). Force, extension and time parameters were recorded throughout the tests.

4.7.3 Cartilage thickness measurement

The thickness of the cartilage was determined by penetrating the cartilage with a fine needle and at a slow rate (0.1mm/sec) [Athanasiou KA et al 1991]. The thickness was calculated as the distance between surface detection and the rapid increase in force when the needle reached calcified cartilage and subchondral bone.

4.7.4 Derivation of the mechanical properties

Five parameters were derived from the available data of force and displacement (Figure 4.9) from the materials testing system. 1). Stiffness (N/mm), 2). Creep (mm), 3). Instantaneous Modulus (MPa) and 4). Creep normalised to cartilage thickness (%) (Figure 4.10).

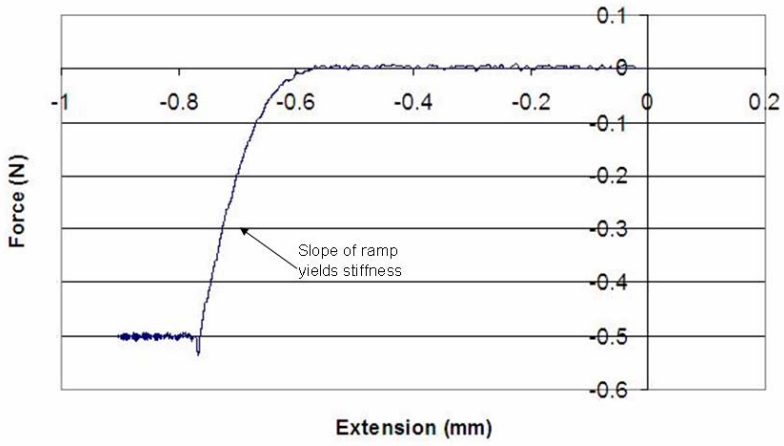


FIGURE 4.9 Typical plots derived is shown here. The force extension curve shows an initial ramp of approximately 0N up to 0.5N. This ramp is used to calculate stiffness in N/m. The steady extension or creep at constant load that follows is used to derive the creep to calculate the creep modulus at constant load 0.5N using a plane-ended indenter.

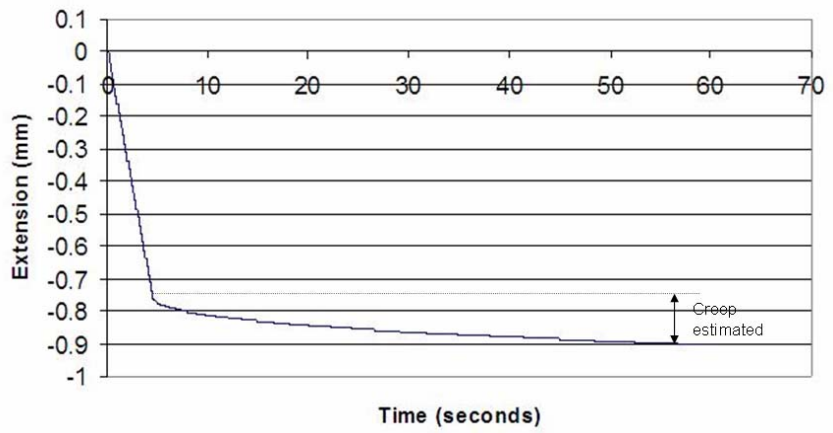


FIGURE 4.10 Here creep estimation is shown. In this study a 60-second creep value is obtained and normalised against cartilage thickness to create an index to facilitate comparison.

Creep was measured after 60 seconds with the application of the constant 0.5N load. The short creep time was used to minimise any effects that could occur from exposure of the fresh cadaver specimen to air. Saline was used to keep the specimen moist throughout the testing.

Instantaneous (Young's) modulus, E, was calculated using the methods described previously [Hayes WC et al 1972, Zhang M et al 1997] as follows:

$$E = \frac{P(1-\nu^2)}{2a\omega\kappa}$$

where:

P = Load applied (N)

ω = axial displacement of the indenter (mm)

a = radius of indenter (mm)

ν = Poisson's ratio, taken as 0.5 (assumed as incompressible) [Mak AF et al 1987, Mow VC et al 1989]

κ = f(a/h, ν) a scaling factor [from Hayes W et al 1972]

h = cartilage thickness

Several indentation tests were performed on one site (group) to ensure repeatability. The final value was used. Parameters of mean and median stiffness, creep, modulii, and creep-to-thickness ratios were calculated for the 4 sites.

4.7.4 Histological evaluation

Histological study was performed on the samples of articular cartilage procured from three tibial plateaus. Using an oscillating saw, the samples were obtained by cutting 5mm thick slices (sections) of the proximal tibia in the para-coronal plane (Figure 4.11). The sections were across the length of the tibial plateau and included regions of cartilage not covered by the meniscus as well as beneath. These sections were then halved into medial and lateral halves.

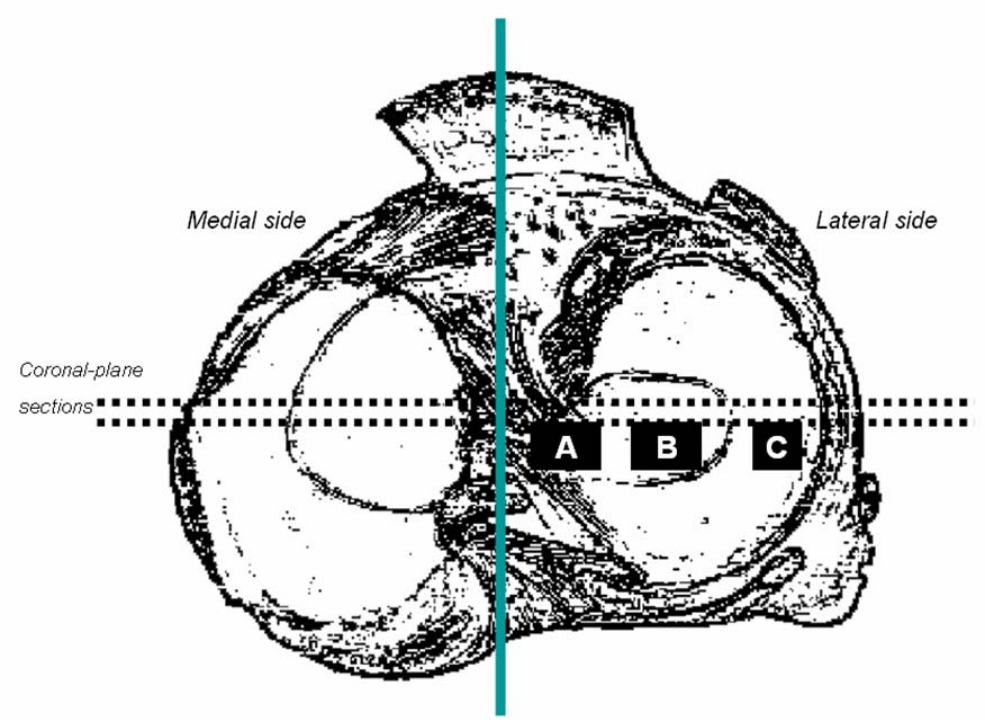


FIGURE 4.11. Coronal plane sections 5 mm thick were obtained using an oscillating saw. These sections were halved into medial and lateral. For the histological study, from each half, 10 micron-thick decalcified sections were obtained for staining with Haematoxylin and Eosin and Safranin O stains. The areas A, B and C show three distinct zones. Zone B is the cartilage that is not covered by the meniscus. Zone C is that covered by the meniscus. Zone A, close to the tibial eminence, represented cartilage not covered by the meniscus but compared to Zone B was subjected to less loading during weight bearing.

A total of twelve such halved samples were selected for histological preparation; six for the medial side and six for the lateral side. Each specimen was fixed in 10% buffered formalin for a week, decalcified in 30% formic acid for about 3 weeks, dehydrated and cleared in alcohol and toluene and finally embedded in paraffin blocks. Ten microns decalcified sections were then cut using a rotary microtome for staining with Haematoxylin and Eosin and Safranin O stains. The histological structure of the articular cartilage was studied under the microscope at a

magnification of 50 times. All the images were digitised for detailed histological analysis. The histological status of the articular cartilage was evaluated [Mainil-Varlet P et al 2003] and graded according to Mankin's scoring system [Mankin HJ et al 1971]. Digital imaging software was also used to study the thickness of articular cartilage (mm), density of subchondral bone and thickness of the calcified layer (mm). The apparent density of subchondral bone was estimated from digital image analysis that zoomed-in on the area of interest and the histogram feature of Adobe Photoshop was used [Latham et al 1999] was used to distinguish pixel intensity based on greyscale values. This area of interest was uniform for all slides investigated. It consisted of a cropped image containing only the histological representation of subchondral bone and the rest of the 'empty spaces' around it. A frequency distribution histogram facilitated the selection of the greyscale level representing the subchondral bone on the image. The number of pixels associated with the particular greyscale level was recorded as a percentage of the entire region's pixel number. This was done for all the three regions investigated.

4.8 Statistics

For the present study on the tibiofemoral bone-on-bone forces in walking, stairclimbing and deep flexion, average tibiofemoral sagittal plane forces, with standard deviations, were plotted against percent gait cycle. In walking the gait cycle is defined conventionally and consisting of a stance and swing phase. For the stairclimbing and deep flexion, stance phase is the time between the foot contact with the force plate and the time foot-off occurs. External moments about the joint were assumed to be balanced by internal moments via the action of relevant muscles. The knee flexors were considered as the hamstring muscle group and the extensors the quadriceps. Turning points in the curve were compared. Test for significant differences between the turning points and the mean force was performed using Analysis of Variance (ANOVA) followed by post-hoc Tukey with a 0.05 level of significance.

For the stairclimbing data any between-limb differences were taken as the ratio of external moments calculated for one limb divided by that of the other. For control groups between-limb differences was taken as the ratio of the right divided by the left side moments. For the patients it was the moments from the involved limb divided by the uninvolved. A *two-tailed* t-test was used to compare the between-limb difference values for the controls and patients, and the alpha level of 0.05 was used to test for significance. Four groups of limbs were statistically compared: I). Control subjects' right limbs, and II). left limbs, and

III). Patients' involved limbs and III). uninvolved limbs. An ANOVA design was implemented to test for differences between groups, followed by post-hoc Tukey. The parameters analysed were the flexion-extension angles and peak moments of the four groups of limbs studied.

The data obtained from the in-vitro contact stress studies underwent non-parametric analysis. A Wilcoxon Mann-Whitney Test of the data obtained considered *P*-values that were calculated to test for significance (<0.05) in differences between means. The means tested were those of peak contact stresses for the conditions simulating heel strike, single limb stance, toe-off and the deep flexion positions.

Data from the mechanical testing of articular cartilage, to investigate topographical variation, were from four groups (refer to Figure 4.8), while the data from the histological evaluation represented three sections (refer to Figure 4.11) of the medial and lateral sides. A comparison of the data from mechanical testing between the groups with respect to the variation was performed using non-parametric analysis with SPSS software (SPSS Inc, Chicago, USA). A Kruskal Wallis test was used to test the null hypothesis that the medians were similar for a given parameter between groups. The degrees of freedom of the Kruskal Wallis test (N=7) was three and the critical chi-square value was 7.81 (alpha at 95%) and 11.34 (alpha at 99%). Differences between groups were delineated using a

Wilcoxon signed-ranks test to investigate comparisons for: Group I vs. Group II, Group III vs. Group IV, Group I vs. Group III, and Group II vs. Group IV. The null hypothesis was that there would be no significant difference between these groups. Significant difference was taken to occur when $P < 0.05$. Correlation coefficient (r) was also calculated to study the relationship between creep and stiffness.

To examine variation in the data collected from the histological sections, a one way ANOVA design was used followed by post-hoc Tukey to define significant differences between specific sections. Significance was taken at $P < 0.05$.

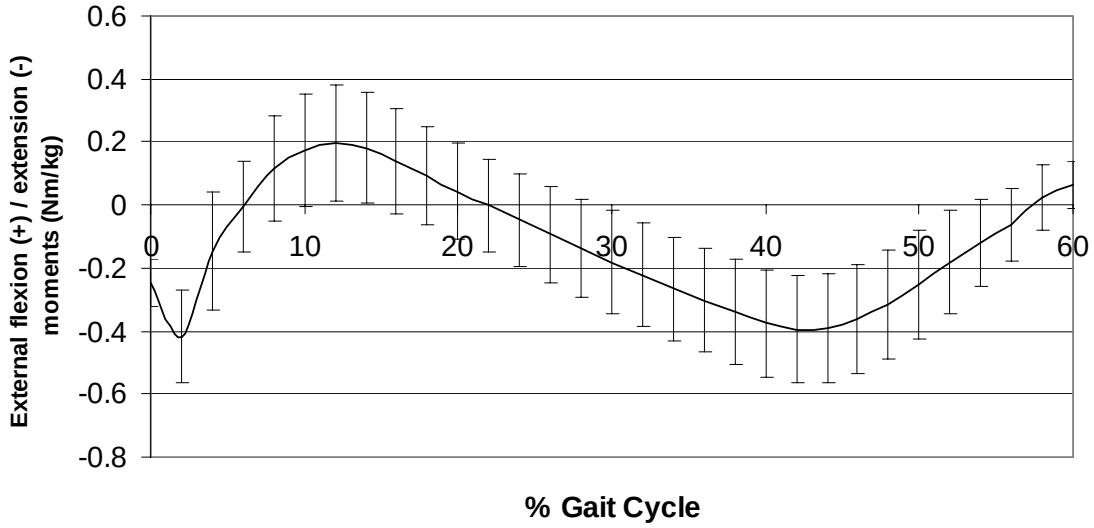
CHAPTER FIVE: Results

IN-VIVO GAIT STUDY: Walking and Deep Flexion

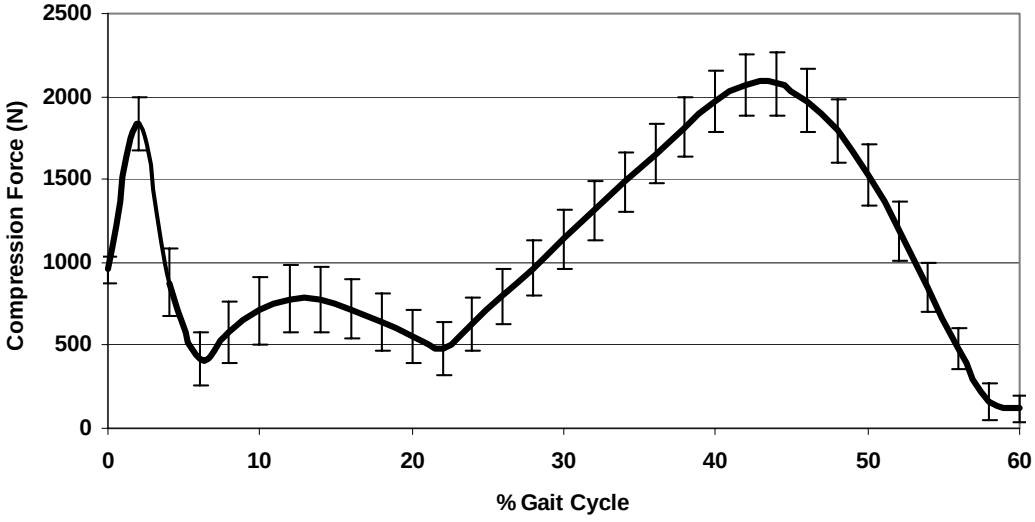
5.1 Tibiofemoral moments and bone-on-bone forces in walking and deep flexion

5.1.1 Walking

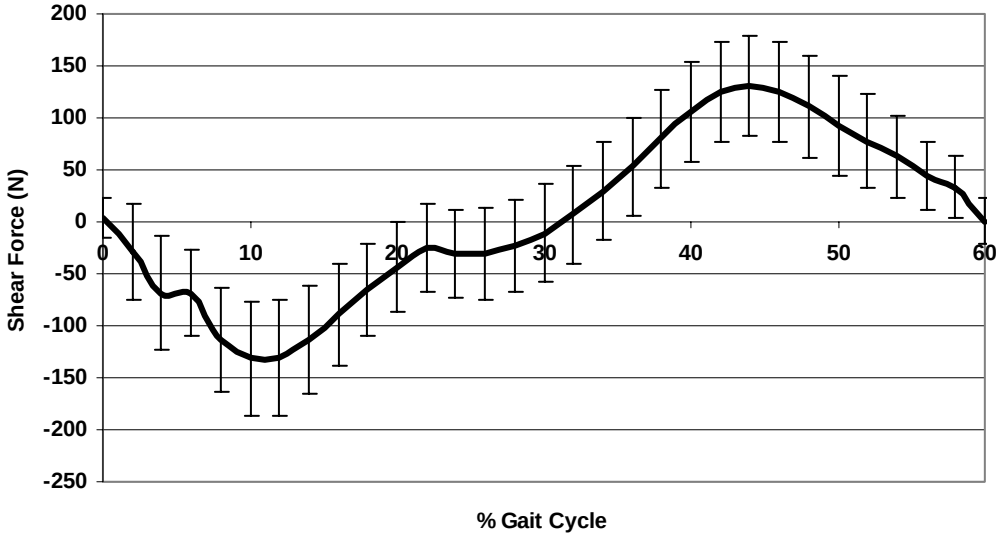
The mean external knee flexion-extension moments, bone-on-bone contact compressive and shear forces were calculated from gait data obtained from 10 adult subjects, normalised for body-weight and expressed according to one gait cycle (%) in walking (Figure 5.1) Peak external flexion moments occurred at 15% gait cycle, while peak external extension moments occurred at about 40% gait cycle (Figure 5.1 A). This peak external flexion moment in the gait cycle corresponded to the onset of single limb stance while the peak external extension moment corresponded to terminal extension and toe-off. From the ground reaction force data, it was estimated that the stance phase ended at approximately 60% gait cycle. The tibiofemoral bone-on-bone forces were reported as compressive and shear forces (Figure 5.1B and 5.1C) and calculated assuming mean bodyweight of 650N.


External flexion (+) / extension (-) moments (Nm/kg)
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
0
10
20
30
40
50
60
% Gait Cycle

A).


Compression Force (N)
2500
2000
1500
1000
500
0
0
10
20
30
40
50
60
% Gait Cycle

B).



C).

Figure 5.1. Gait analysis data of the tibiofemoral joint from normal walking, over the stance phase, averaged from data of 10 normal adult subjects. **A)** Average moments at the tibiofemoral joint; **B)** average tibiofemoral bone-on-bone contact forces (*compressive*) and **C)** average (anterior-posterior) shear force at the bone-on-one contact point. One standard deviation is shown for each of the average curves.

For the compressive forces, three points in the gait cycle were observed to correspond with three significant ($P < 0.05$) turning points in the force curves. These three turning points in the force curve corresponded with three turning points in the moment curve relative to the gait cycle. The first turning point in the compressive force curve corresponded with a peak extension moment, the second turning point with a flexion moment, and the third turning point with an extension moment again. The first turning point was at about 3% gait cycle at heel strike and the force was 1832N (SD, 161N). The second turning point occurred at 15% gait cycle. This phase corresponded approximately to the onset of single limb stance and the average peak force was 779N (SD, 203N). The third

turning point in compressive forces occurred at about terminal extension and toe-off at the end of stance phase. The force was 2075N (SD, 186N). This final rise in compressive forces occurred at about 44% gait cycle. Turning points in the shear force curves were significant ($P < 0.05$) and occurred at similar points in the gait cycle as that of the compressive forces and moments (Figure 5C). These were at the onset of single limb stance and terminal extension before toe-off. The first turning point was at -132N (SD, 34N) and at 10% gait cycle. The negative value indicated that the force was one that was oriented pointing against the direction of forward progression in the sagittal plane, that is, from anterior to posterior relative to the tibiofemoral joint. The next turning point in the shear force curve followed at about 44% gait cycle. The average force was 131N (SD, 48N).

5.1.2 Stairclimbing

(The individual plots of moments and forces for the six healthy subjects in stair ascent are shown in the Appendix.)

The flexion-extension angles in stairclimbing ranged from an average minimum of 1.5º (SD, 5º) in end-stance phase to a maximum average of 67º (SD, 16º) in swing phase (Figure 5.2). Swing here refers to the time when the foot leaves the step and proceeds onto the next step above.

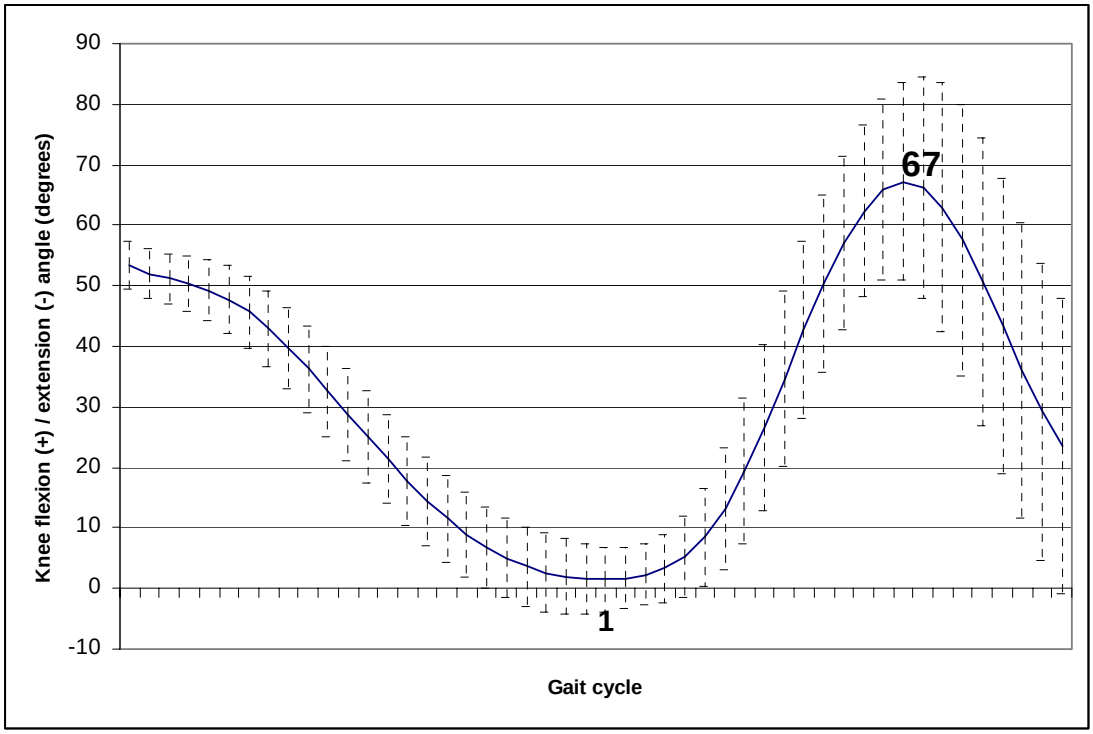


Figure 5.2. The average (n=6) knee flexion and extension angle for stairclimbing is shown here. Typical turning points in the curve are at a minimum (1º) in stance phase just before foot-off and a maximum (67º) when the limb is in transition in swing between steps.

Knee external flexion and extension moments indicated two turning points (Figure 5.3). The first was after foot contact with the force plate and at the onset of single limb stance where it was a maximum external flexion moment of 0.6 Nm/kg (SD, 0.3 Nm/kg). The second turning point was at a minimum of -0.6 Nm/kg (SD, 0.1 Nm/kg) occurring at about the moment before foot –off. These two turning points were significantly ($P < 0.05$) different.

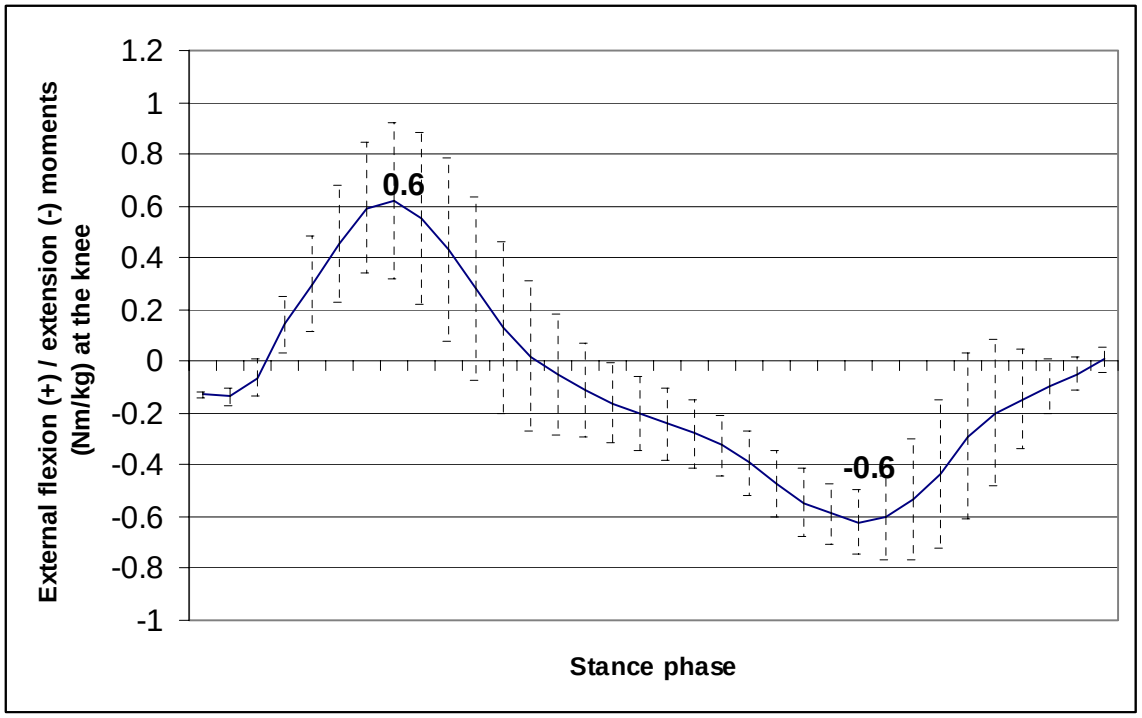


Figure 5.3. Two distinct turning points, highlighted here, were observed in the external flexion-extension moments of all subjects in stairclimbing.

Tibiofemoral bone-on-bone forces were calculated using the knee moments, angles, ground reaction forces and the methods described earlier. The peak compressive forces calculated for stairclimbing were on average 2 xBW in the first peak corresponding to the peak external flexion moment and the second typical peak was much larger at about 5 xBW occurring in correspondence with an external peak extension moment. The compressive forces calculated showed this consistent pattern of two peaks (Figure 5.4). The first peak was a smaller peak of 2 times bodyweight (xBW) (SD, 0.6 xBW). The second peak before toe-off was significantly (P<0.05) larger at 5 xBW (SD, 0.7 xBW).

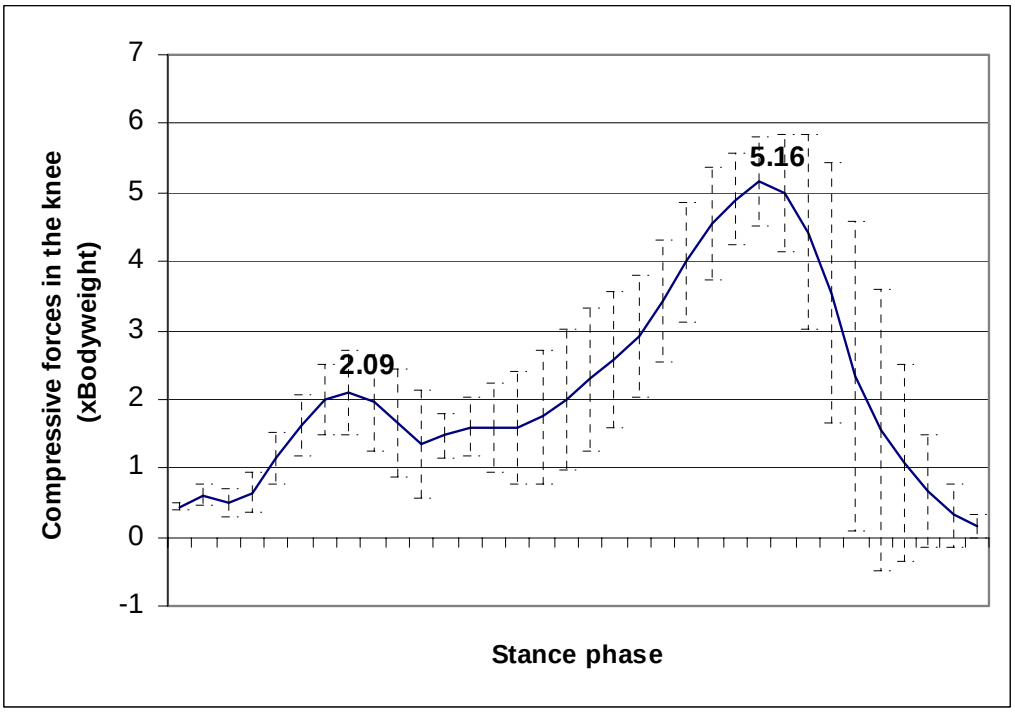


Figure 5.4 Compressive forces calculated for stairclimbing show two distinct peaks. The first occurs just after foot contact and the second just prior to foot off.

Shear forces were found to generally correspond to the shape of the compressive force profile in that two turning points were observed (Figure 5.5). The first was a minimum of -0.2 xBW (SD, 0.05 xBW) indicating a posterior-directed tibiofemoral peak shear reaction. The next turning point was at 0.4 xBW (SD, 0.4 xBW) indicating an anterior-directed peak shear reaction. The posterior-directed shear forces corresponded to the external flexion moment while anterior-directed shear corresponded to the external extension moments.

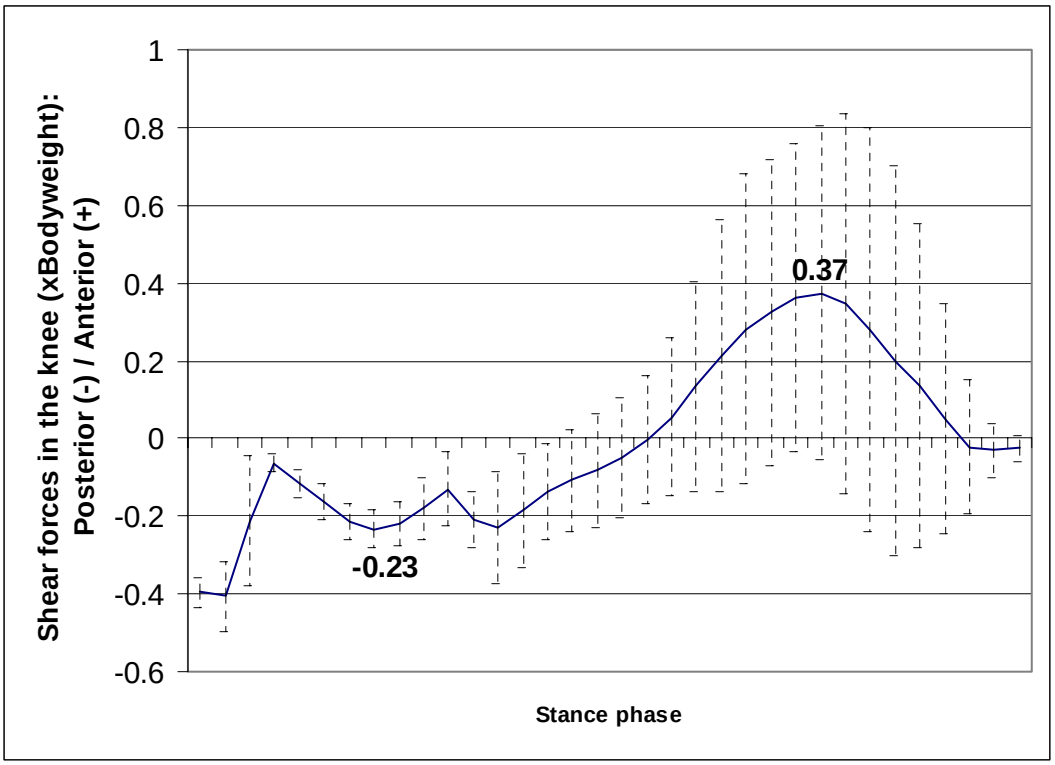


Figure 5.5 Shear forces calculated for stairclimbing indicate an initial posterior-directed shear reaction component, followed by an anterior one in end stance.

5.1.3 Deep flexion

The range of motion of the tibiofemoral joint in the sagittal plane, during the deep knee and hip flexion (or squatting) exercise was averaged over 4 normal adult subjects (Fig. 5.6). This range of motion was used as one cycle, to plot the external flexion-extension moments in the sagittal plane (Fig 5.7).

The mean flexion angle had an initial peak (20°-24°) as the knees unlocked from it full extension position (Fig 5.6). The flexion angle gradually increased, reaching a constant rate of change of flexion angle, up to about 160°, where the rate of change reduced, with the flexion angle reaching a maximum at about 170°. This was the full squat position. Immediately after which the subject rose up back to full extension. Along the external moments-exercise cycle curve (Fig 5.7), two significant peak external moments were noted. These ranged between 1.1 and 1.75 Nm/kg, and were when the deep knee flexion angle was greater that 160°. These peaks corresponded with two reverse events, the first when the knee was about to reach the full squat position, and the next after unlocking to rise up to the full standing position. In between these two peaks 1.30 (SD,0.36) and 1.45 (SD 0.37)-Nm/kg, respectively), there is a dip in the external moments as the subjects reaches maximum flexion angles (or the full squat position), and were noted to rest the posterior thigh on the posterior side of their lower leg, proximal to the ankle.

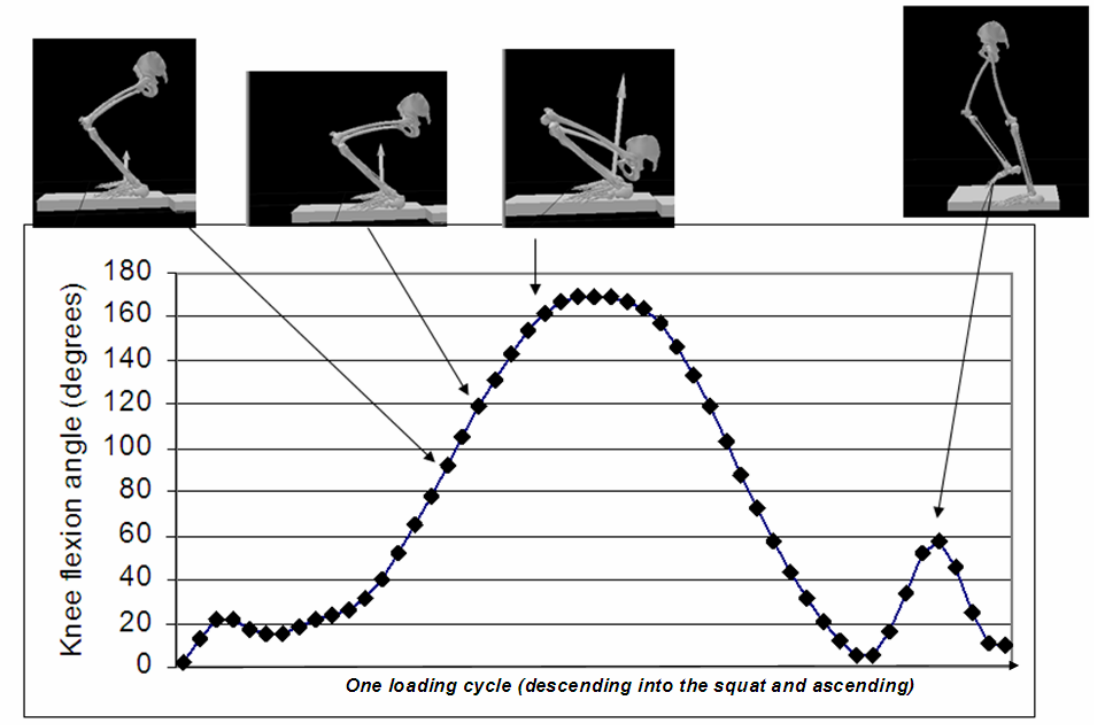


Figure 5.6. A typical curve showing flexion angles at the (right) knee when performing a squat. The maximum flexion reaches well into 160 degrees.

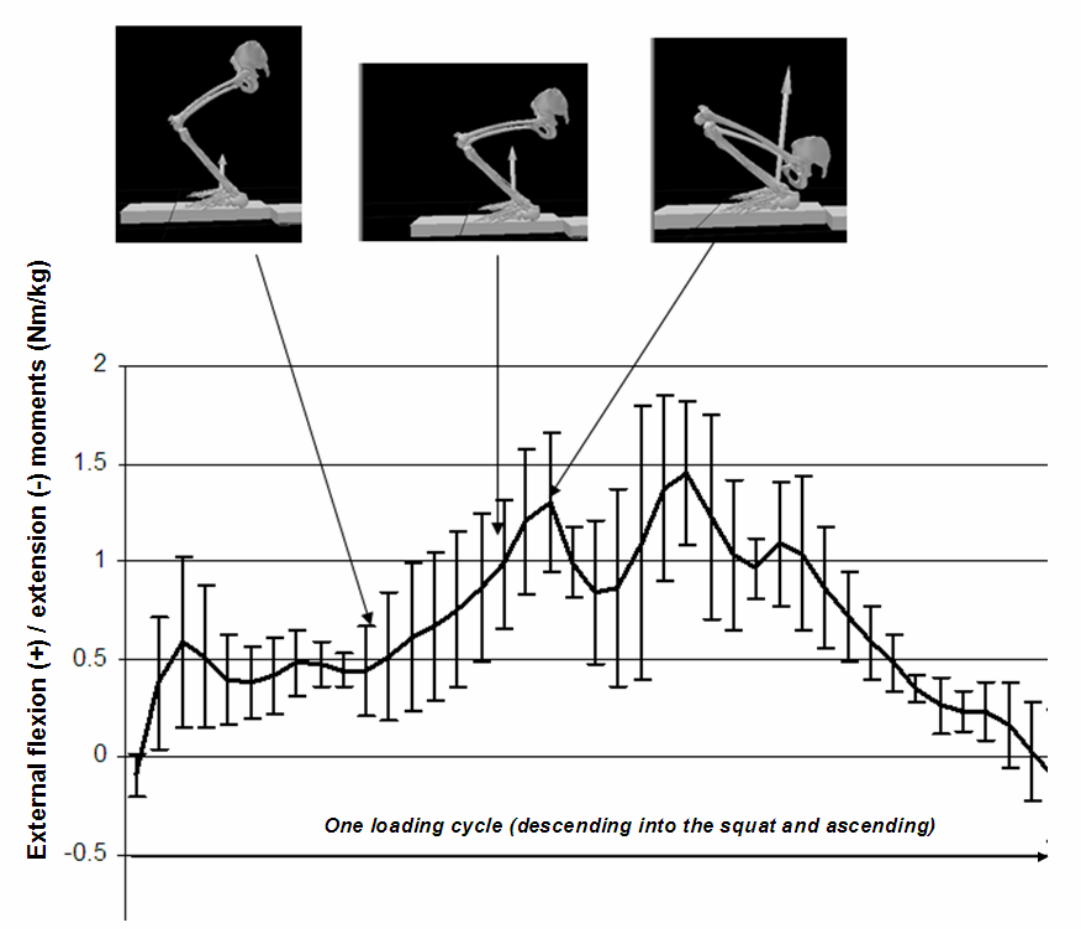


Figure 5.7. External flexion-extension moments show double-peak corresponding to the time when the subject is *going into* full squat, before coming to rest, and the second peak when the subject is *raising himself* from the full squat.

The tibiofemoral vertical contact forces had similar profiles to the moment curves. The forces were largest on the way down just before full squat, and right after full squat on the way up. Two peaks result. On the way down to the squat, the peak force is 2 times body weight. On the way up, the contact force reaches has high as 4 times body weight. The dip between these two peaks show the time when the subject rests in full squat. The shear forces indicate a similar pattern with a first peak occurring at 0.5 times body weight and a second larger peak of one times body weight. Peak moments were larger significantly ($P < 0.05$) in squatting compared to walking, and the loading in the joint to balance these larger moments are manifested more as shear forces than compressive. The data (Tables 5.1 to 5.3) indicate that peak moments were 2.5 times larger in deep flexion compared to walking (The individual force profiles are shown in Appendix A). Peak vertical contact forces in squatting was similar to peak forces in walking, whereas peak (anterior) shear forces in squatting were two to three times larger than in walking. There were no posterior shear reaction forces in deep flexion during descent and ascent in deep flexion.

TABLE 5.1. Peak values (of moments and forces in the sagittal plane) in walking.

WALKING	Subject	MOMENT (Nm/kg)	vertical force (times bodyweight)	horizontal force (x BW)	posterior shear force (x BW)
	1	0.65	3.38	0.18	-0.33
	2	0.33	5.25	0.02	-0.34
	3	0.17	2.38	0.06	-0.15
	4	0.67	3.22	0.06	-0.15
Average		0.46	3.56	0.08	-0.24
SD		*0.25*	*1.21*	*0.07*	*0.11*

TABLE 5.2. Peak values (of moments and forces in the sagittal plane) in stairclimbing.

Stairclimbing	Subject	MOMENT (Nm/kg)	vertical force (times bodyweight)	horizontal force (x BW)	posterior shear force (x BW)
	1	0.66	5.33	0.35	-0.45
	2	0.38	5.15	0.12	-0.61
	3	0.38	5.13	0.30	-0.44
	4	1.18	4.32	0.21	-0.47
	5	0.71	7.27	1.34	-0.40
	6	0.52	5.55	0.18	-0.76
Average		0.6	5.5	0.4	-0.5
SD		*0.3*	*1.0*	*0.5*	*0.1*

TABLE 5.3. Peak values (of moments and forces in the sagittal plane) in deep flexion (squatting)

SQUATTING	Subject	MOMENT (Nm/kg)	vertical force (xBW)	horizontal force (x BW)
	1	1.9	3.94	0.15
	2	0.77	2.24	0.34
	3	0.93	1.52	0.07
	4	0.98	2.86	0.17
Average		1.15	2.64	0.18
SD		*0.51*	*1.03*	*0.11*

IN-VITRO STUDY: Walking and Deep Flexion

5.2 Tibiofemoral joint contact stresses in walking and deep flexion

To achieve the 'equilibrium' position of the knee joint undergoing the 700N to 1000N load, there was some significant adjustment in the joint orientation in the different degrees of flexion. In heel strike (HS) and toe-off (TO) simulations, the knee specimens adjusted such that there was a slight varus angulation of 2º. For the single limb stance (SLS) at 15.5º flexion, besides the varus angulations, some internal rotation had to be allowed as well. This internal rotation was about 5º. At deep flexion, some anterior translation of the tibia had to be allowed, together with more internal rotation. This internal rotation in deep flexion varied from as little as 10° to as much as 20°. The amount of anterior tibial translation in deep flexion was between 10mm to 12mm. Medial and lateral translation was negligible in all flexion positions.

During the loading conditions that simulated the selected points of interest in the stance phase of gait (HS, TO, SLS) average peak contact stresses in the cadaver knee joints were 14 MPa ($\pm$ 2.5) with little variation (Figure 5.8). However, the peak stresses were significantly ($p<0.05$) larger in the deep flexion loading conditions (DF1, DF2) where it increased by over 80% to 27 MPa ($\pm$ 7.1). The contact area when peak pressure was registered (FIGURE 5.9) for the DF

position was 1.05cm^2 and 1.5cm^2 and in the position simulating single-limb stance, or SLS, the area of contact was largest at 1.75cm^2.

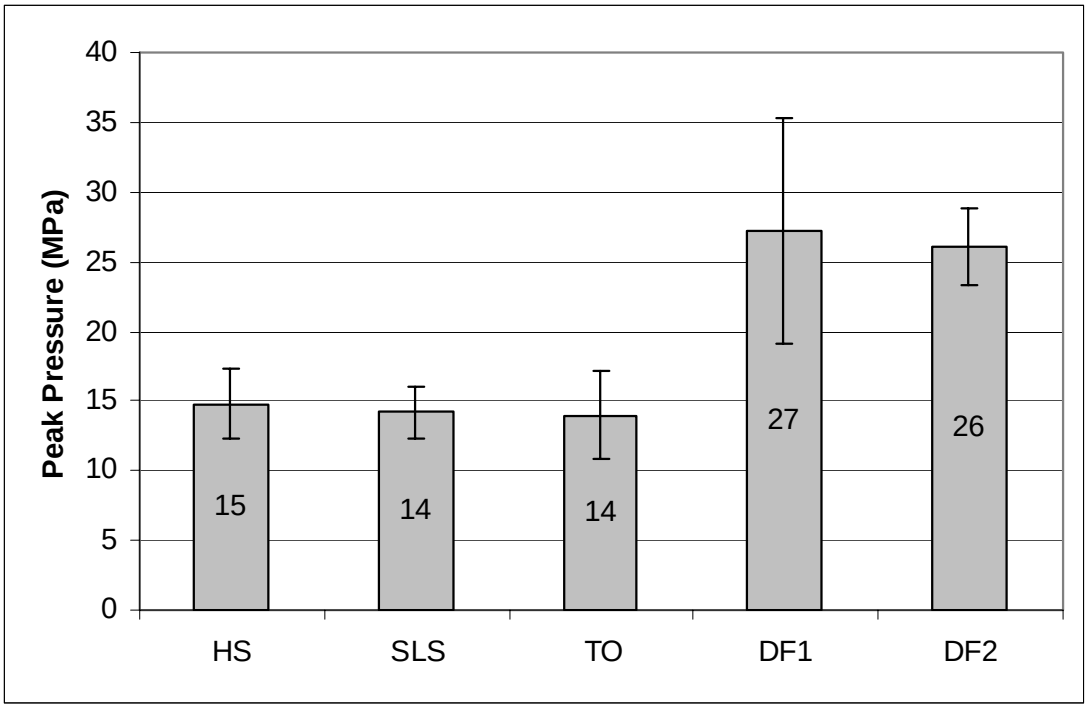


Figure 5.8 The peak pressure as derived from the five different positions of testing the tibiofemoral joint is shown here, HS (heel strike), SLS (single limb stance), TO (toe-off), DF1 (deep flexion at 90°), DF2 (deep flexion greater than 120°).

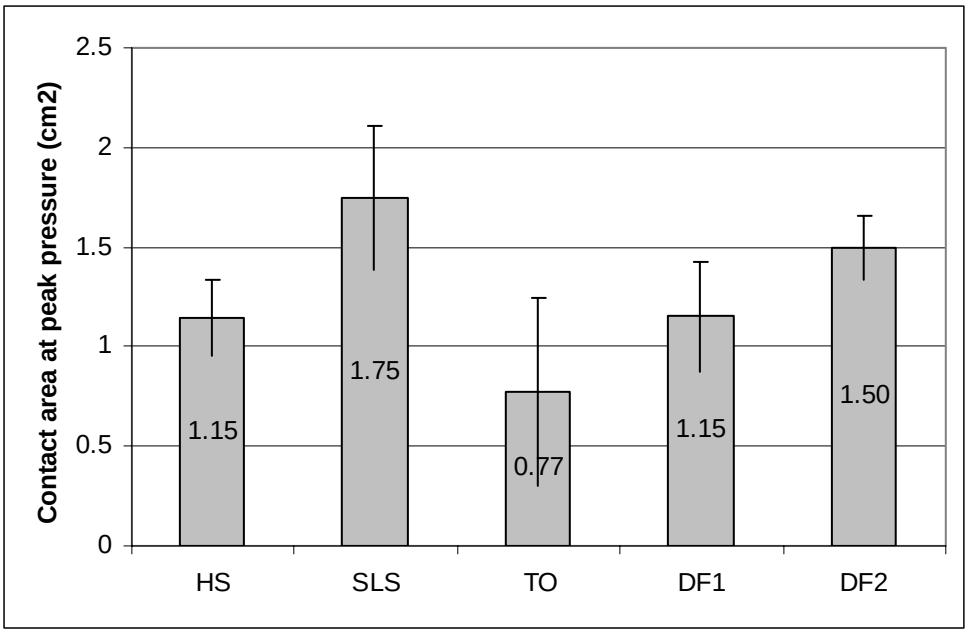


Figure 5.9 Contact area at peak pressure for the various positions tested is shown here.

The distribution of the medial and lateral contact stresses was shown to be influenced by joint position. At heel strike simulation, where the knee orientation was slightly varused at 2° and with no internal rotation of the tibia, there was minimal pressure in the lateral compartment as the compression force increased to the prescribed load. Most of this load passed through the medial compartment. The single limb stance simulation indicated a more even distribution over both compartments throughout the loading profile. In deep flexion with the knee in varus and tibia internally rotated, a fairly equal distribution was shown in both compartments in the lower load range. However in reaching the maximum load of about 4 to 5 times bodyweight, there was up to 70% larger peak pressure in the medial compartment compared to the lateral (Figure 5.10 and 5.11).

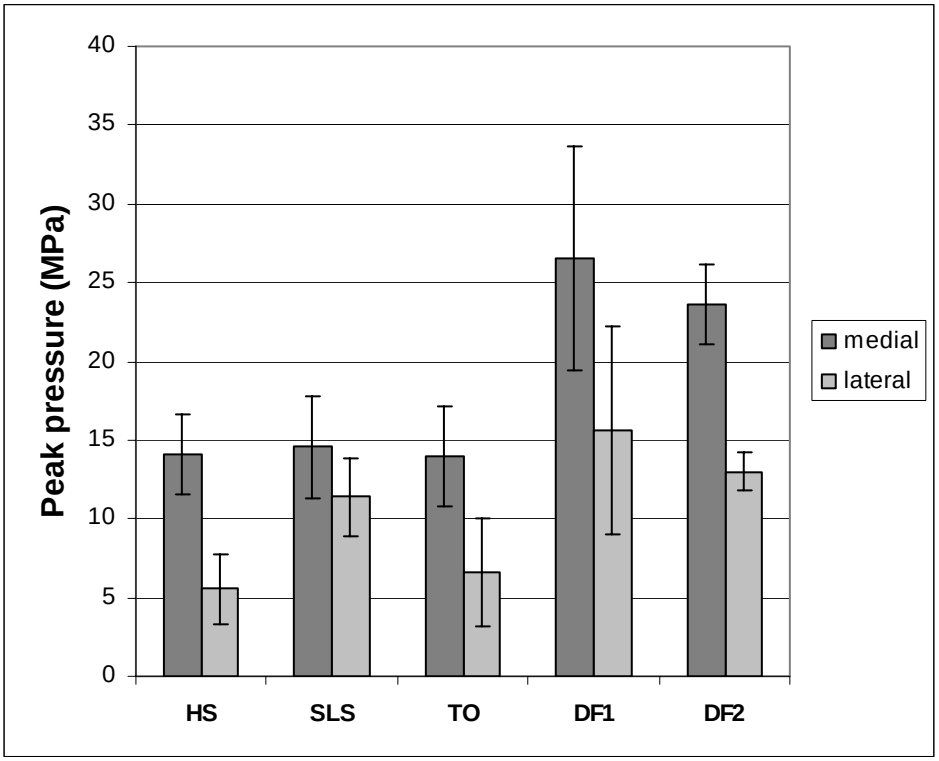


Figure 5.10 The distribution of peak stresses is shown here for the loading simulating HS (heel strike), SLS (single limb stance), and TO (toe-off). At HS the peak contact stresses are much less in the lateral compartment ($P < 0.05$). In SLS the medial and lateral compartments both experience similar peak stresses. Finally in TO the tendency is reduced peak stress in the lateral compartment. In DF1 and DF2 the difference in medial-lateral distributions are significant ($P < 0.05$).

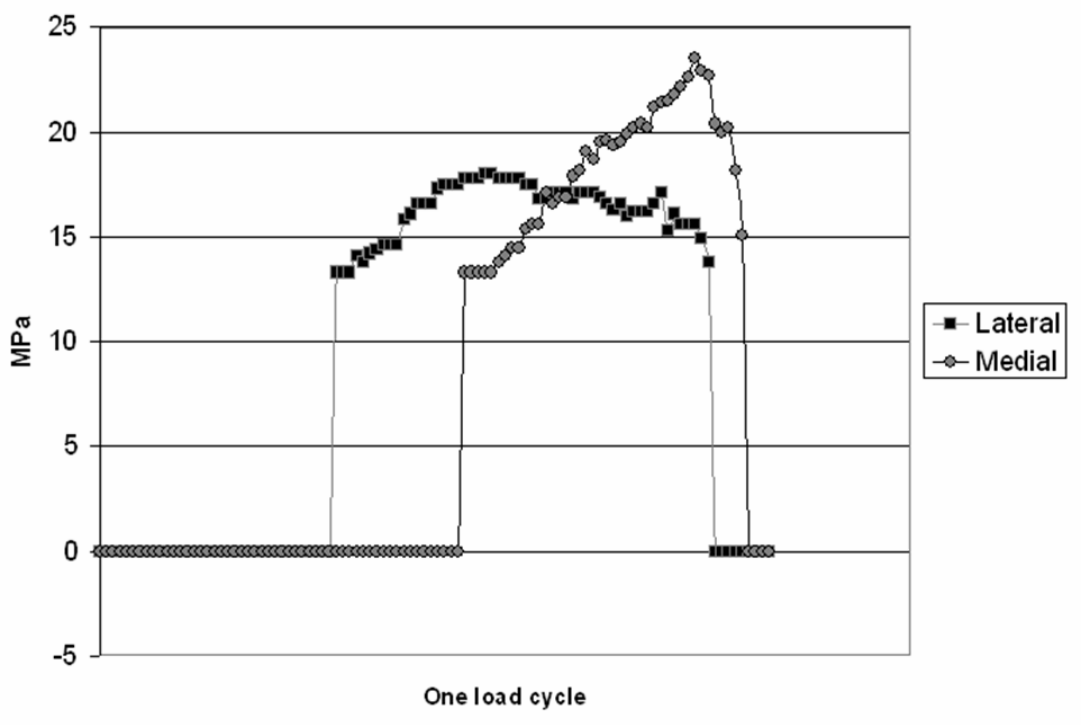


Figure 5.11 A typical plot is shown of the medial and lateral compartment peak stresses in the deep flexion loading position of greater than 120 degrees. Peak pressures tend to be larger in the medial compartment. Also the engagement of the lateral compartment before the medial compartment is consistent.

IN-VIVO STUDY: Stairclimbing and the effect of anterior cruciate ligament deficiency

5.3 Tibiofemoral joint mechanics in stairclimbing and the effect of anterior cruciate ligament deficiency

Control subjects and patients performed the task of stair climbing without pain, defined as at no time did any of the subjects complain of any discomfort. All walked up the stairs with reciprocating steps, that is, at no time between start and final rest were the feet sharing the same step. Neither control subjects nor patients used the handrail to walk up the steps. The stride characteristics (speed, percent stance, single and double limb support time, and stride length) showed that there were no significant differences between the control group and patients (Table 5.4).

TABLE 5.4. Stride characteristics of the control subjects and patients with anterior cruciate ligament deficiency.

Stride Characteristics:	**Mean (Standard Deviation)**	
	Control subjects (n=6)	Patients (n=9)
Speed (metres/second)	0.58 (0.23)	0.57 (0.28)
Single support (seconds)	0.39 (0.17)	0.32 (0.15)
Double support (seconds)	0.35 (0.18)	0.39 (0.18)
Stride length (metres)	0.78 (0.32)	0.75 (0.46)
Stance (%)	53.32 (24.42)	46.97 (29.54)

There are no significant differences (i.e. $p > 0.05$) between these two groups of data.

5.3.1. Flexion-extension angles

There were no significant differences in the mean flexion and extension angles between the left and right limbs of control subjects, or between the involved and uninvolved limbs of patients. The average minimum knee angle (Figure 5.12) of controls was about 2° (SD, 5°), whereas for the patients' involved limb it was 6° (SD, 5°). This difference was not statistically significant.

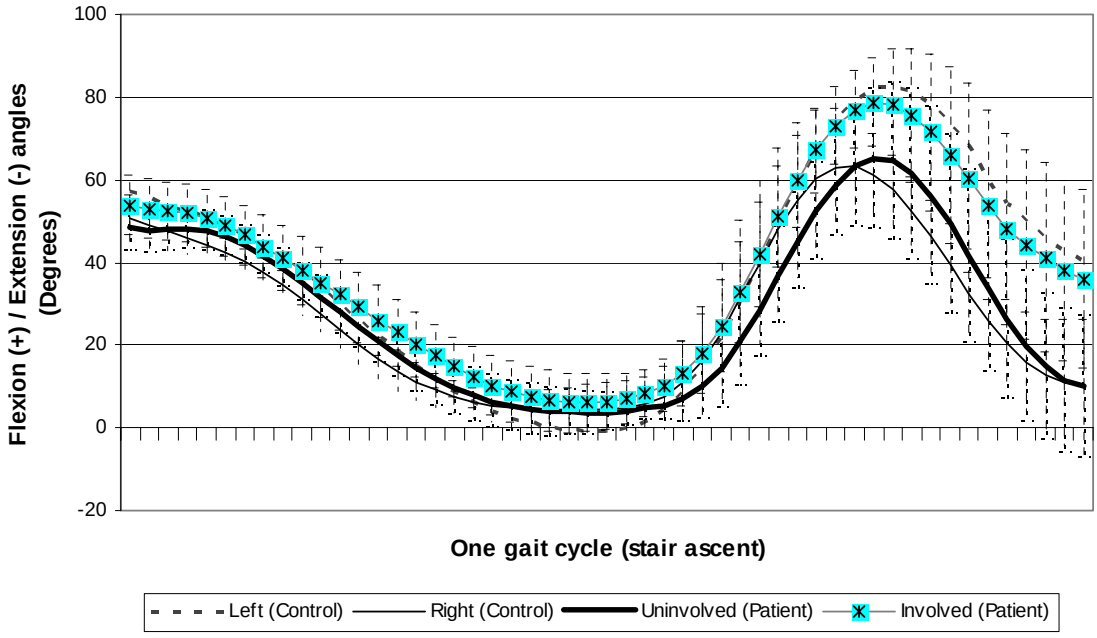


Figure 5.12 Comparison of the mean knee angles of the limbs of control subjects and patients' involved and uninvolved limbs.

5.3.2. External flexion-extension moments

At approximately 16% gait cycle, external knee flexion moments for all subjects reached a peak. This period in the gait cycle corresponded with opposite side foot off. Peak knee extension moments occurred near the end of stance at approximately 50% gait cycle. The peak moment values obtained for the control subjects' limbs are comparable with those previously published (Andriacchi TP, 1990). The knee angle when peak flexion moments occurred was not significantly different between all the groups and was about 40º (SD, 4°). Peak moments were not significantly different between the left and right limbs of the control subjects. Patients' uninvolved limbs and control subjects' limbs also did not show significant differences. However, the peak flexion moment of the patients' involved limbs was significantly smaller ($P < 0.05$) than that of the uninvolved limbs and control limbs, by up to 50% (Figure 5.13). The mean between-limb difference, the ratio of one limb to the other, in the control group was calculated as 1.08 (SD, 0.36) and for the patient group it was 0.34 (SD, 0.46) (Figure 5.14). The difference is significant ($P < 0.05$).

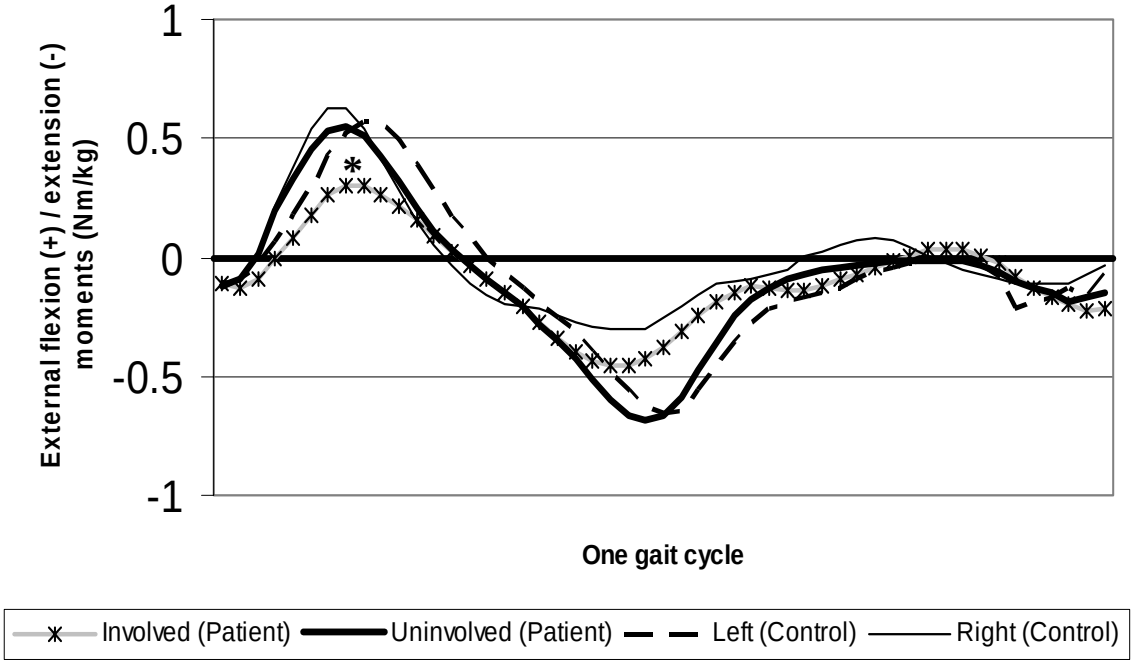


Figure 5.13 Comparison of mean knee flexion and extension moments of the limbs of control subjects, and patients' involved and uninvolved limbs. Comparison of mean peak flexion moments at the knee, normalized to percent body mass multiplied by height, indicates a significant (* $p < 0.03$) reduction in patients with anterior cruciate ligament deficiency.

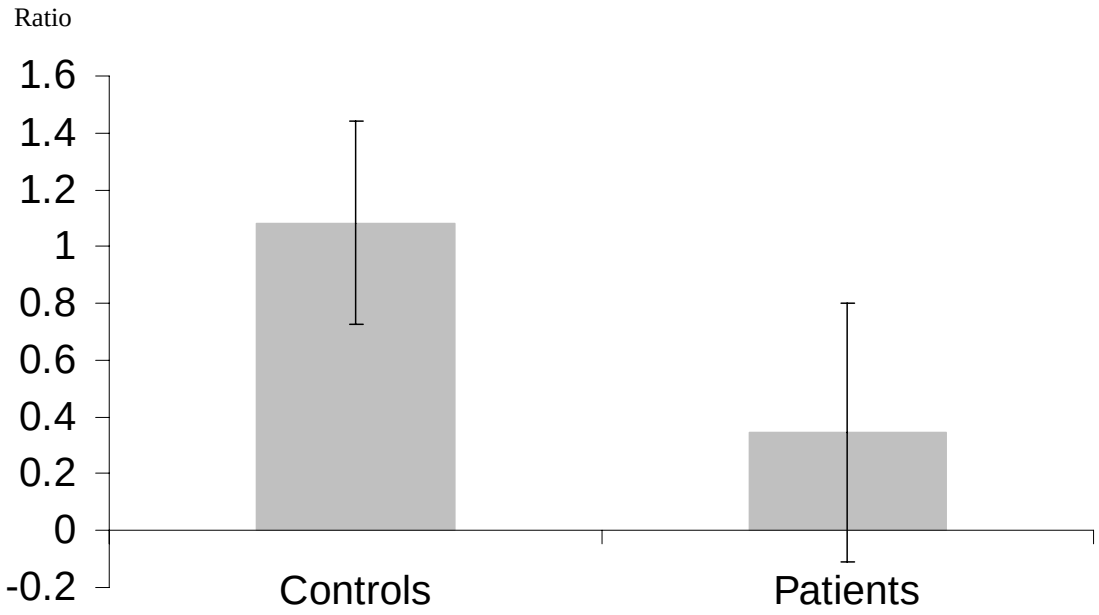


Figure 5.14 The mean *ratio* (unit less) of peak external flexion moments of one limb to the other is shown here to compare between-limb differences of controls and patients. For the controls the ratio here is the peak moments of the right limb divided by the left. For the patients it is the peak moments of the involved limb divided by the uninvolved.

5.3.3. Ground reaction forces

The vertical ground reaction force curves for control subjects and patients were typically double peaked. The peak vertical ground reaction forces were on average 1.1 *times body weight* (x BW) for the patients' involved limbs and 1.2 x BW for the uninvolved limbs; this was a small but statistically significant reduction ($P < 0.05$) in the involved limbs. The power of the test was calculated to be 0.83. The mean anterior-posterior ground reaction shear forces during

stance for the involved limbs was also significantly less than that of the uninvolved limbs (P <0.05). The mean horizontal force was in the opposite direction to forward progression in the anterior-posterior direction. For the involved limbs the force was 0.1 x BW and about 25% less than the uninvolved limb.

IN-VITRO STUDY: Topographical variations

5.4 Articular cartilage mechanical properties and morphology

Summaries of the average values and standard deviations of mechanical properties obtained for the groups studied are shown in Figure 5.16 to 5.19.

To re-cap the four groups were as follows (Figure 5.15):

- Group I: Lateral tibial plateau that is *not* covered by the meniscus.
- Group II: Medial tibial plateau that is *not* covered by the meniscus.
- Group III: Lateral tibial plateau that is covered by the meniscus (beneath the meniscus).
- Group IV: Medial tibial plateau that is covered by the meniscus.

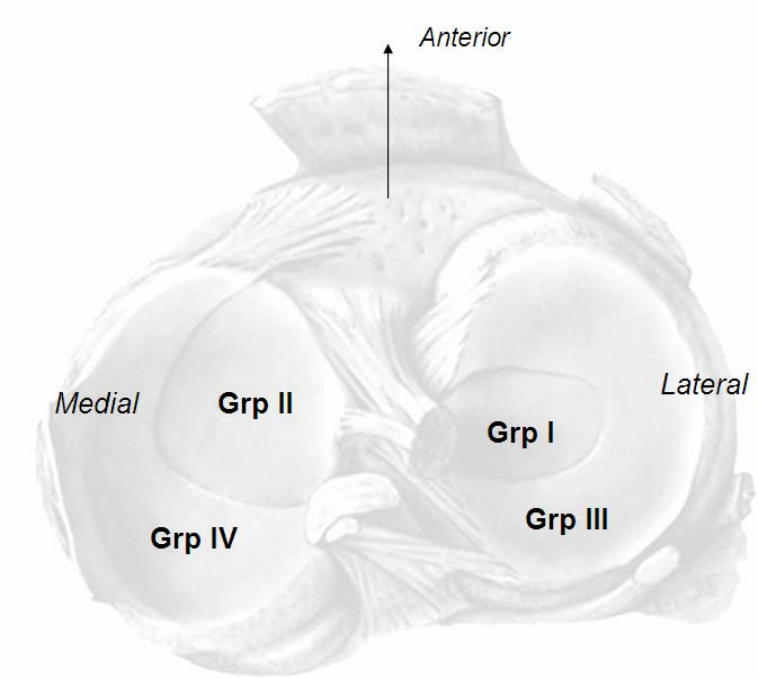


Figure 5.15 shows the four groups and the respective regions tested.

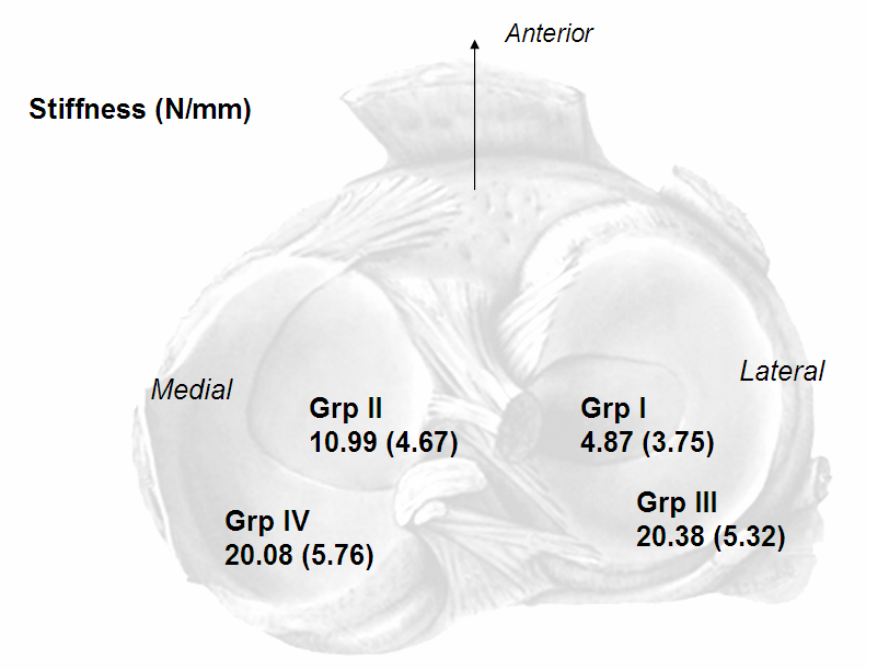


Figure 5.16 Schematic showing the topographical variation in stiffness properties in the different regions studied. *Means and Standard Deviations (in parentheses).*

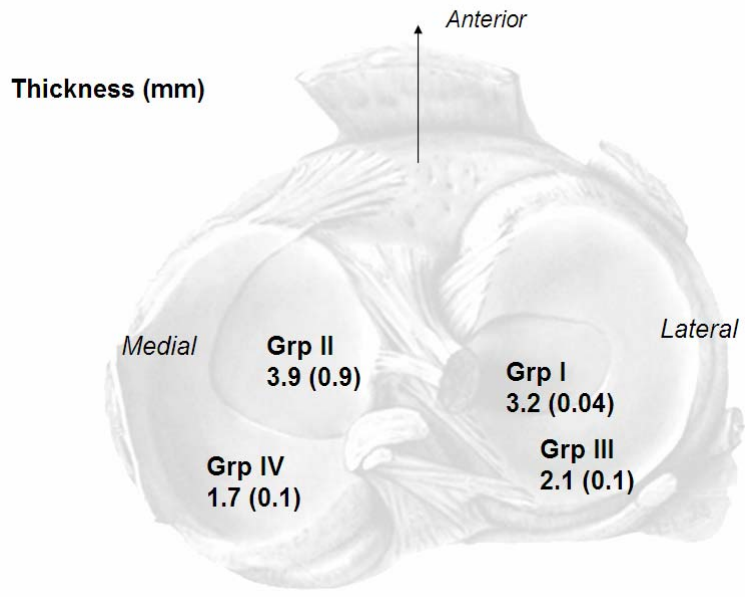


Figure 5.17 Showing a schematic representation of the topographical variation in thickness of articular cartilage measured in the present study. *Means and Standard Deviations (in parentheses).*

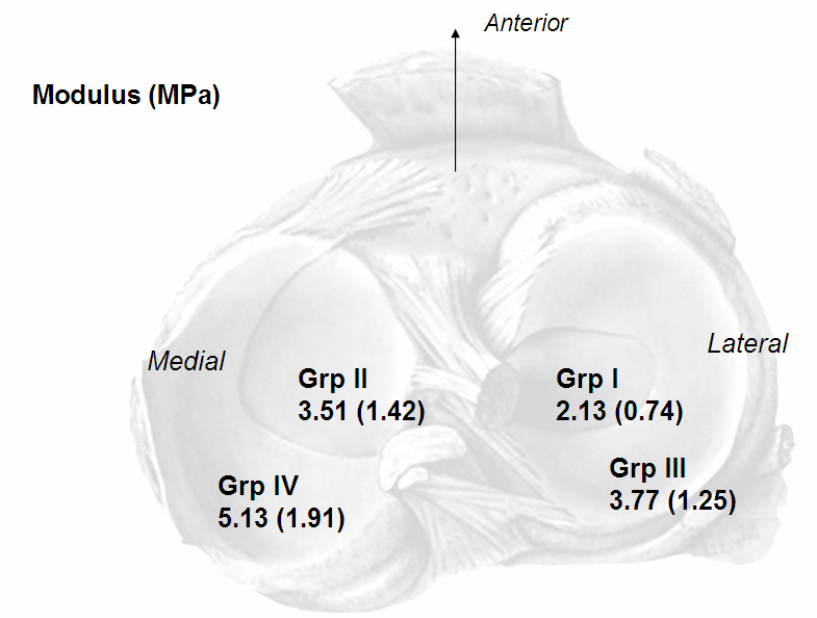


Figure 5.18 Schematic of the topographical variation in modulus as derived in the present study. *Means and Standard Deviations (in parentheses).*

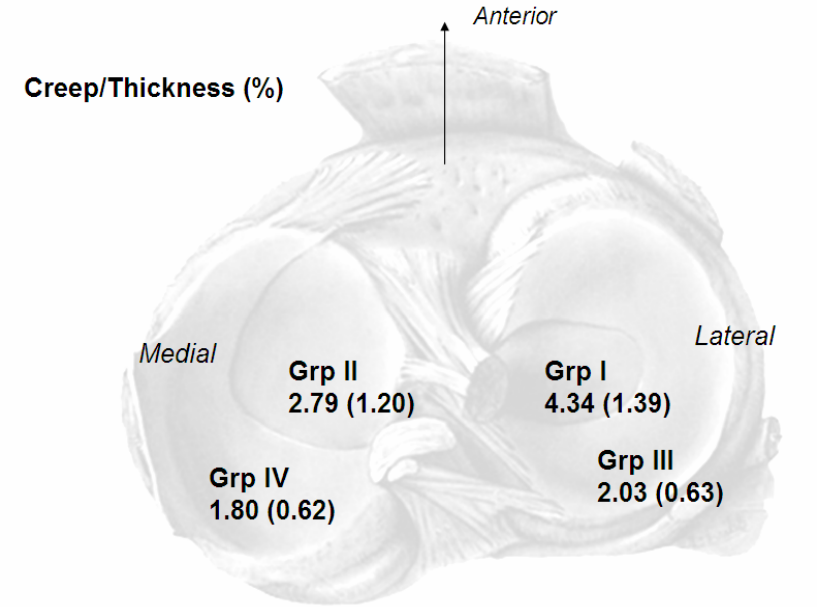


Figure 5.19 Schematic showing the creep to thickness ratio in the different regions studied. *Means and Standard Deviations (in parentheses).*

Non-parametric statistical analysis of the data using Kruskal Wallis test on the medians indicated that the mechanical properties of stiffness, creep, and modulus were all significantly different among the four groups or sites tested with chi-square values of $X^2 > 12$, ($P < 0.01$). Wilcoxon signed-ranks tests revealed that, contrary to the null hypothesis, there was a significant difference between the groups in several of the comparisons (see Table 5.5).

Table 5.5 Comparison of Articular Cartilage Mechanical Properties between Groups. P-values are shown here with significance (P<0.05) marked with asterix.

Comparison of Groups / *Parameters studied*	**I vs II**	**I vs III**	**II vs IV**	**III vs IV**
Stiffness	0.028*	0.018*	0.018*	0.735
Creep	0.018*	0.018*	0.089	0.058
Creep Modulus	0.018*	0.018*	0.063	0.028*
Creep/Thickness	0.018*	0.018*	0.091	0.176

5.4.1 Stiffness

There was a significantly ($P < 0.05$) larger stiffness recorded in Group II versus Group I (Figure 5.16). This increase, in comparing the means, was in the order of about 120%. Group IV was significantly larger by about 50% relative to Group II. Group III had significantly larger stiffness than Group I, by about 300%.

5.4.2 Creep and creep-thickness ratio

Axial creep measured after 60 seconds of constant axial load was different between the sites tested. The most creep was observed in Group I, and the least creep occurring in Group IV. Creep in Group II was significantly less than Group I by about 35%. Group III creep was also significantly less than Group I, and by about 53%. Articular cartilage thickness was found to be significantly thinner in Groups III and IV. The cartilage in Groups I and II was about 30% to 40% thicker than the articular cartilage in Group III and up to 80% thicker in Group IV respectively. A summary of the thickness measured is as follows: Group I was 3.9 mm (Standard Deviation, 0.9 mm); Group II 3.2 mm (SD, 0.04 mm); Group III 1.7 mm (SD, 0.1 mm); Group IV 2.1 mm (SD, 0.1 mm).

5.4.3 Instantaneous (young's) modulus

The modulus was significantly larger in Group II compared to Group I by about 64% (Figure 5.18). Group III modulus was also significantly larger than Group I

and by about 77%. Finally Group IV modulus was significantly larger than Group III by 36%. The difference between Group II and Group IV was *marginally* significant ($P < 0.07$).

5.4.4 Correlation between modulus and creep ratio & stiffness and creep

When correlating Stiffness (N/mm) with Creep (mm), R was negative, -0.91 and -0.77, for Groups I and II respectively, while for Groups III and IV it was -0.41 and -0.70 respectively. These correlations were stronger when the data were normalized and compared as modulus and creep-thickness ratios. The negative correlation between *Instantaneous Modulus (MPa)* versus *Ratio of creep to cartilage thickness* was significant for all Groups. The correlation coefficient (R) was less than - 0.9 for all Groups.

5.4.5 Histology

Histological analysis of the articular cartilage for all specimens stained with Haematoxylin and Eosin as well as Safranin O staining according to Mankin's scoring system gave total scores ranging from zero to 2. Our findings showed that in all specimens zones A and B gave scores of 1 (surface irregularities only) compared to a score of zero (normal) for zone C (Figure 5.20). With regard to cells all sections gave a score of zero (normal) (Figure 5.20). Safranin O staining revealed scores of 1 (slight reduction) for zones A and B, and zero (normal) for

zone C (Figure 5.21).Tidemark integrity was rated as zero (intact) for all sections in zones A, B, and C (Figure 5.22).

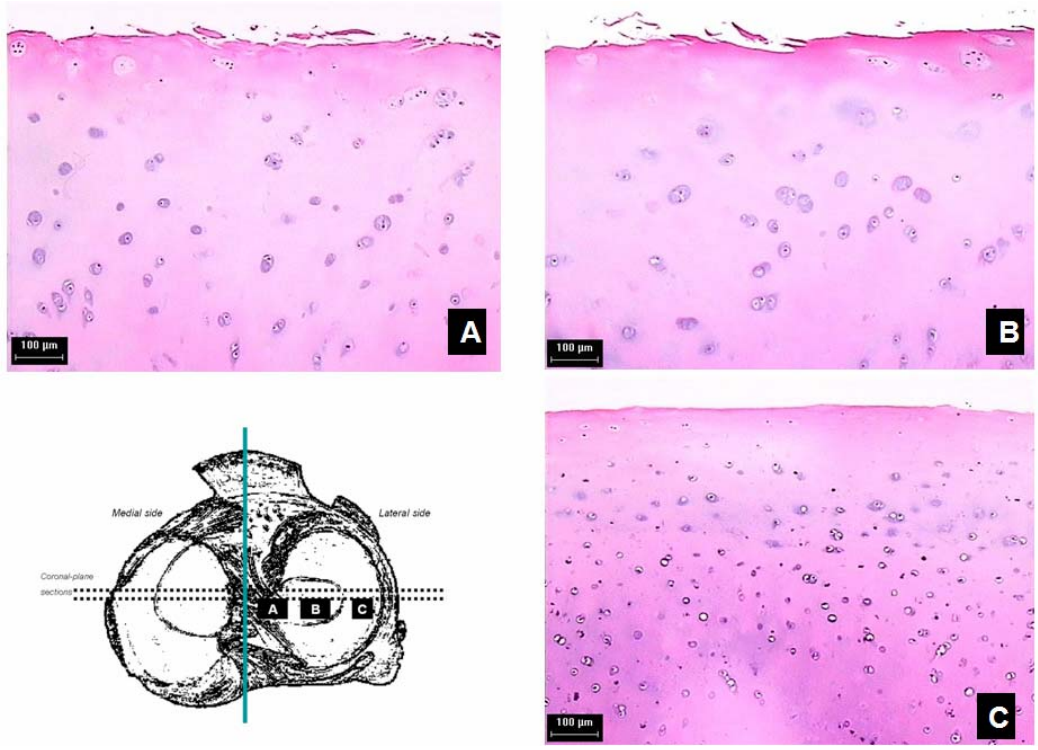


Figure 5.20 Showing at a magnification of x50 the histological sections of the zones of articular cartilage of the lateral tibial plateau of the same cadaver stained with Haematoxylin and Eosin.
A). showing cartilage in zone A, **B).** in zone B and **C)**. in zone C. Mankin score for structure was rated as 1 for A, 1 for B and 0 for C. All the cells were rated zero (normal) in zones A, B and C.

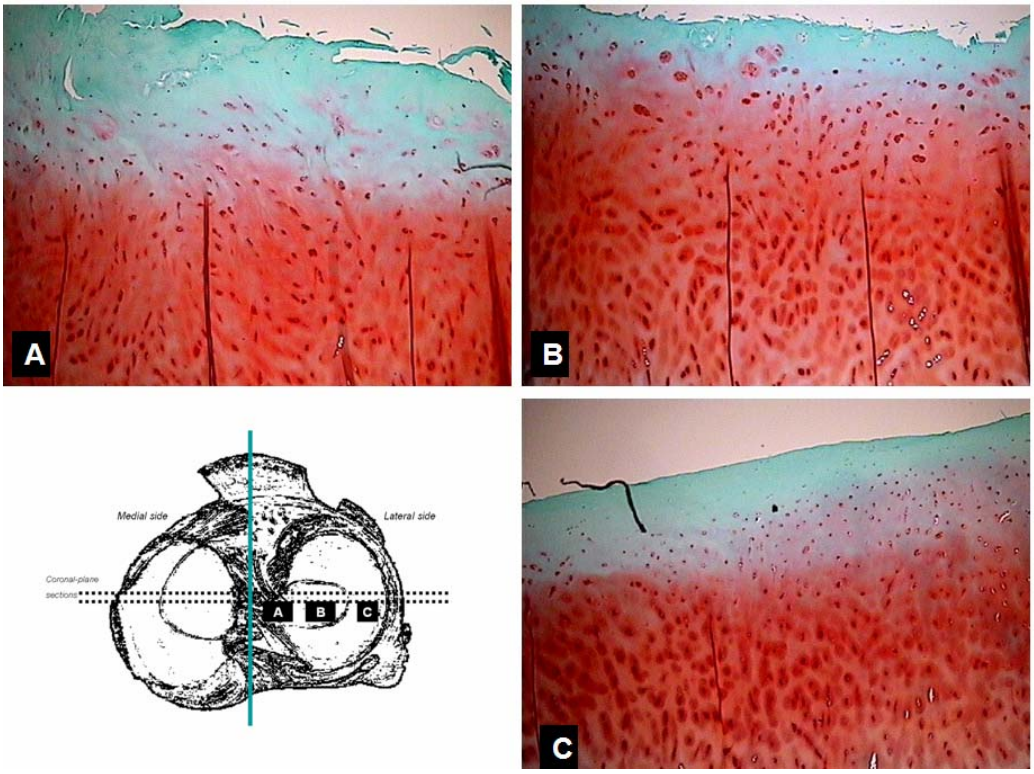


Figure 5.21 Showing at a magnification of x50 the histological sections of the zones of articular cartilage of the lateral tibial plateau of the same cadaver stained with Safranin O.
A). showing cartilage in zone A, **B).** in zone B and **C)**. in zone C. The intensity of staining was graded as 1 (slight reduction) in regions A and B, and zero (normal) in region C.

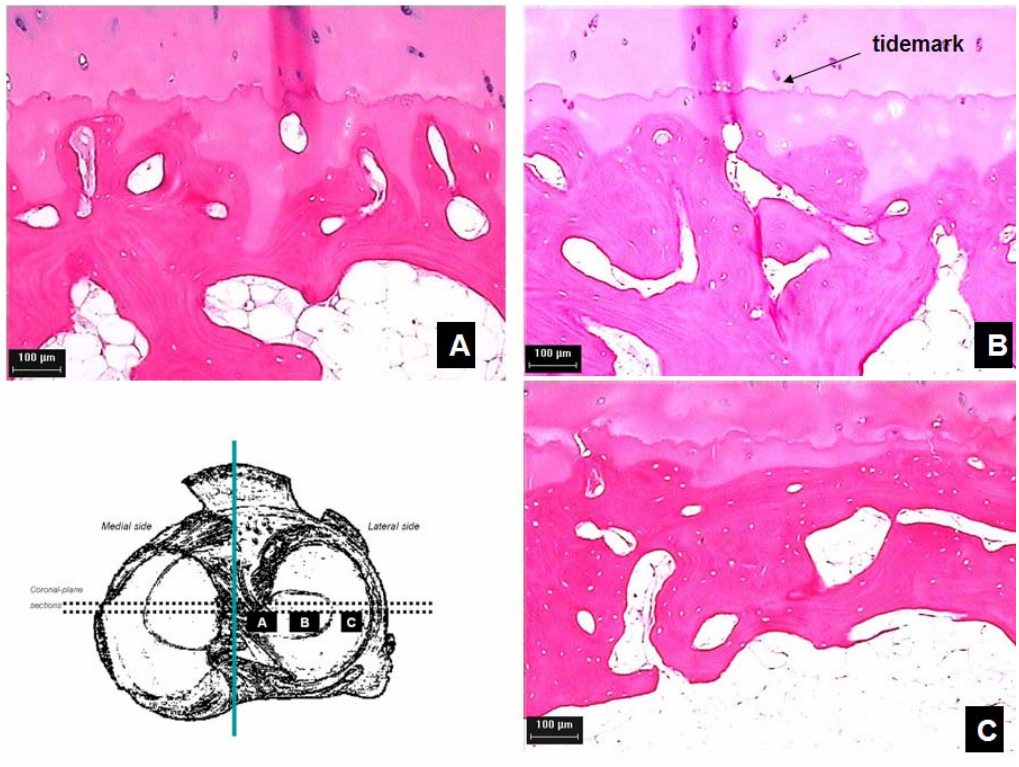


Figure 5.22 Showing at a magnification of x50 the histological sections of the zones of subchondral bone region of the lateral tibial plateau of the same cadaver stained with Haematoxylin and Eosin.
A). showing cartilage in zone A, **B).** in zone B and **C)**. in zone C. Intact tidemark with a Mankin score for tidemark integrity of zero was found in all regions.

From the digital image processing analysis the data of thickness of the articular cartilage, density of subchondral bone and thickness of the calcified region is presented (Figure 5.23 to 5.25). The morphological differences between the articular cartilage of the regions not covered by the meniscus (region B) and that covered (C) were shown to be significant. Region B, which was the area not covered by the meniscus, was most dense in subchondral bone compared to regions A and C (Figure 5.24). Region A was the section close to the tibial eminence and region C represented the area covered by the meniscus. Articular cartilage thickness (Figure 5.23) was largest in region B having thicker cartilage than region C. Less difference observed between regions A and B. The data (Figures 5.23 to 5.25) showed that the regions B versus C were consistently different in that the measurements in B were larger than C, for all the morphological parameters. A comparison of the three regions is illustrated via a composite photograph (Figure 5.26).

In summary compared to the articular cartilage not covered by the meniscus, the articular cartilage of the region beneath the meniscus was stiffer, yet thinner and had less dense subchondral bone.

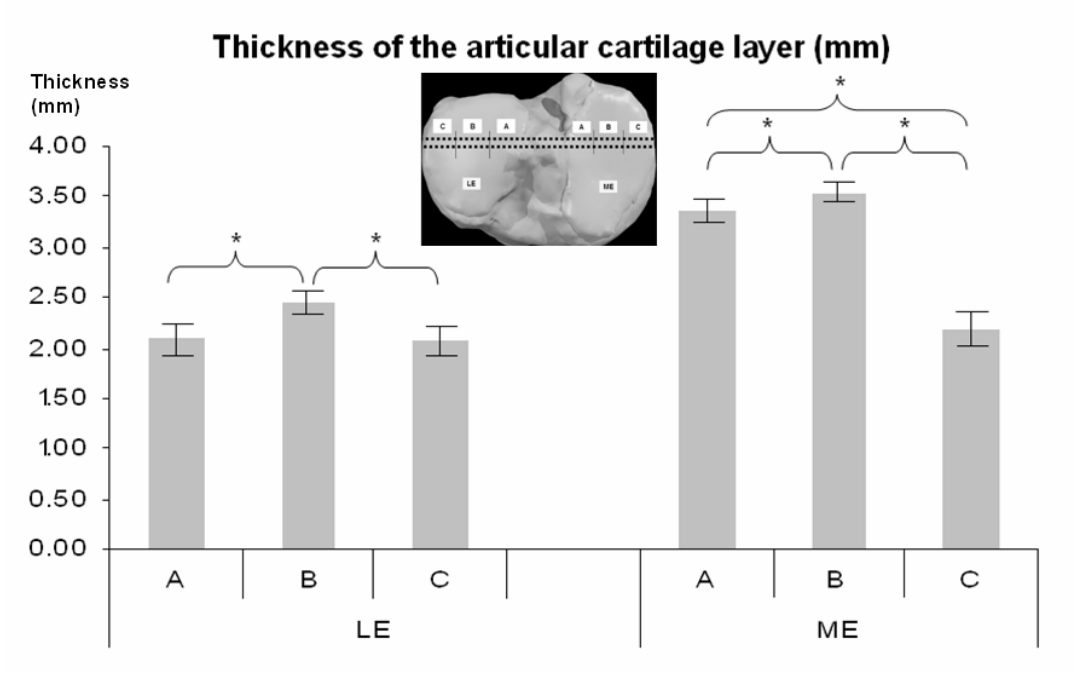


Figure 5.23 Thickness of the articular cartilage layer (mm) determined from histological sections. Lateral side (LE) and medial side (ME) differences were obvious. Also compared to the region of articular cartilage not covered by the meniscus (regions A and B) the region beneath the meniscus (C) was significantly thinner

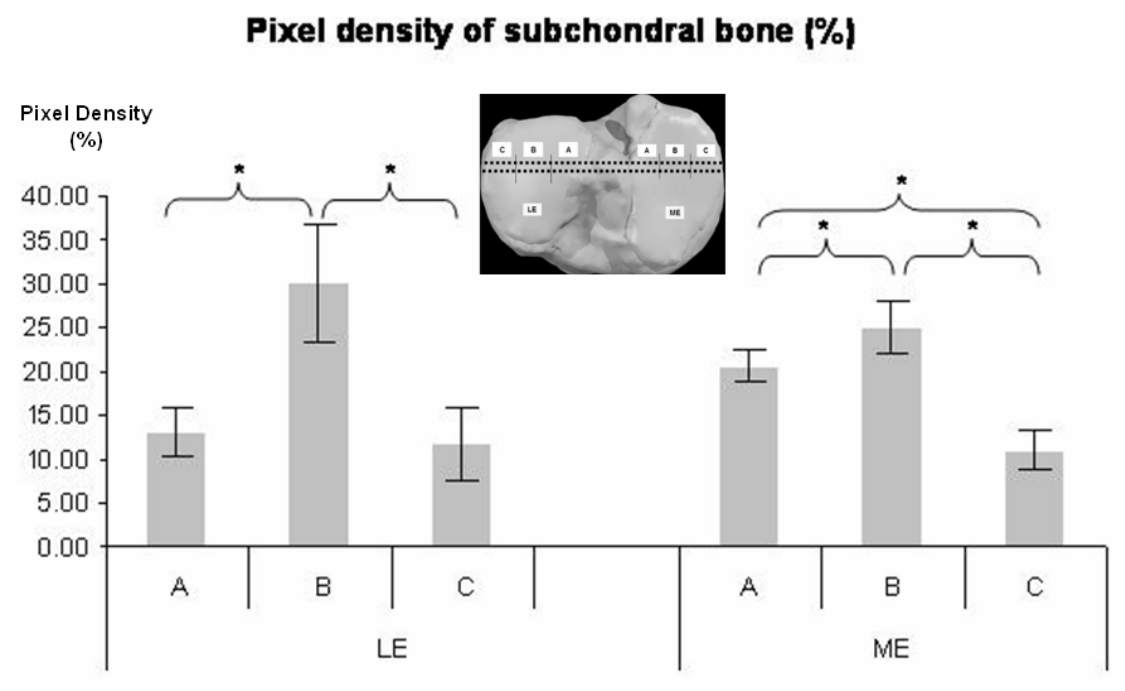


Figure 5.24 Showing the density of subchondral bone, represented as pixel number (representing stain intensity) relative to the rest of the image (%), of the lateral side (LE) and medial side (ME). For both sides, the density was shown to be largest in the region that was not covered by the meniscus and subjected to the largest loading history, which was region B.

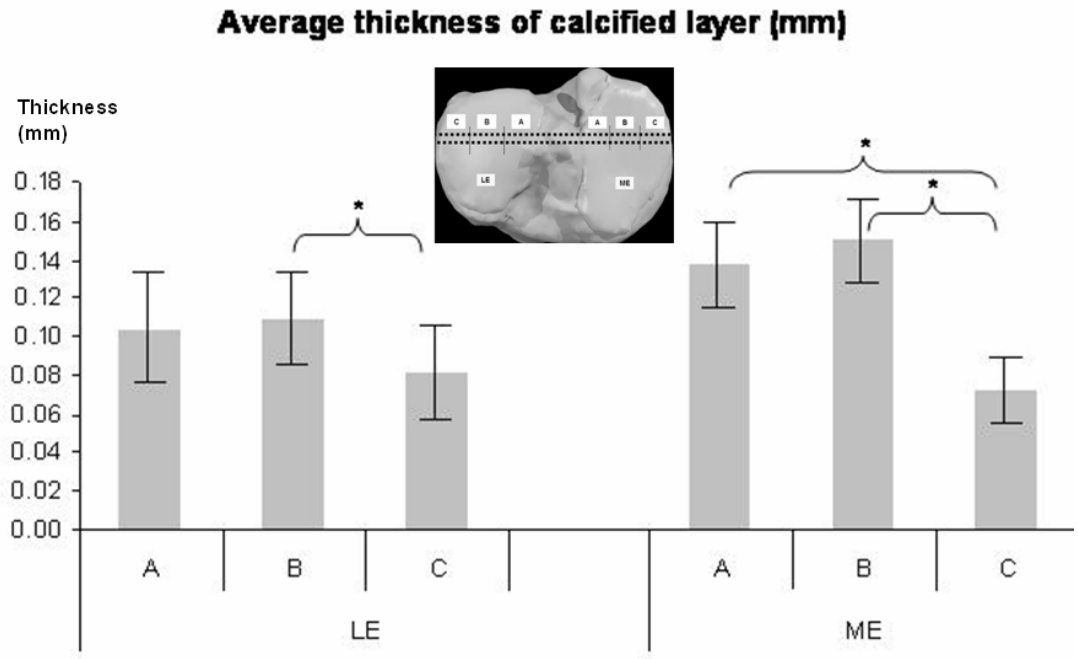


Figure 5.25 Showing the average thickness of the calcified layer (mm) of the lateral side (LE) and medial side (ME). The medial side cartilage displayed a larger thickness with significantly larger thickness in the regions not covered by the meniscus (A and B) compared to the regions beneath (C).

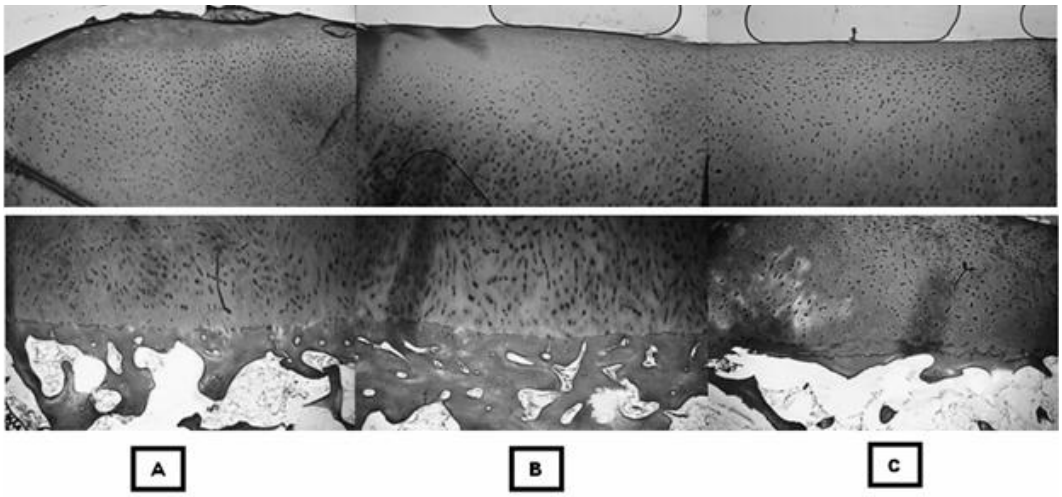


Figure 5.26 showing a composite photo of the three regions (A,B, and C) studied. The top half shows the articular cartilage including the surface, while the bottom half reveals the subchondral bone. Region B (that not covered by the meniscus) is clearly different than region C (that covered by the meniscus).

CHAPTER SIX: Discussion

6.1 Tibiofemoral joint forces in walking, stairclimbing and squatting:

6.1.1 Forces in walking

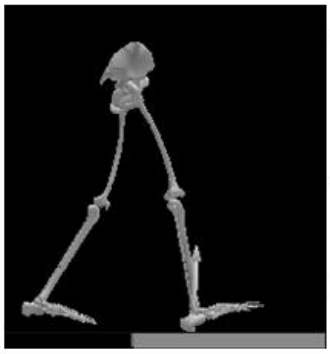
The tibiofemoral bone-on-bone contact forces for walking calculated in the present study mainly agree with previously calculated forces, showing similarities albeit some differences. (Table 6.1) Differences may be due to the variation in subjects. For example the present study used data of Asian subjects, where cultural or racial attributes may be influencing factors (Chen WL et al 2003).

Table 6.1 Three peaks in forces have generally been observed in studies on bone-on-bone tibiofemoral contact forces. The estimates from previous studies are shown here in comparison with the present study.

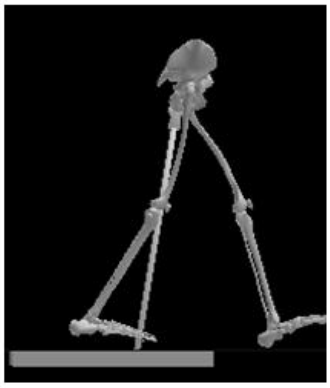
Forces (x Bodyweight)	1st Peak	2nd Peak	3rd Peak
Paul (1967)	3.2	2.2	2.8
Morrison (1970)	2.8	2.2	2.8
Schipplein and Andriacchi (1991)	3.2	2.0	2.5
***Present study* (2004)**	2.8	1.2	3.2

Both the previous and present studies report three distinct turning points or *peaks* in the force curves. The first peak in the present study reached approximately 3 times

body weight while in the previous study [Morrison JB 1970] it was reported as just above 3 times body weight. Both the previous and present studies however show the first peak to occur at about the same time in the gait cycle, that is, soon after foot contact. The second peak in the present study matches closely the second peak calculated in the previous study [Morrison JB 1970] in timing occurring at about the onset of single limb stance phase and reaching about two times body weight, again assuming 600N bodyweight for the present study's population. The third peak in the present study reached 3 times body weight at the end of stance phase, while in the previous study the third peak occurred at about the same time in stance phase and also reached about 3 times body weight. Using the current method the accuracy and consistency of the calculations are limited to that of the moment and ground reaction force data. As the horizontal force calculations use the data from the shear ground reaction force measurement, it becomes apparent that the calculation will be limited by any inconsistency in this measurement. However there is little doubt on the direction of the horizontal force in the tibiofemoral joint.



First Peak	Compressive Force(xBW)	% Gait Cycle
Present study	2.8	3
Morrison, 1970	3.0	5



Final Peak	Compressive Force(xBW)	% Gait Cycle
Present study	3.2	44
Morrison, 1970	2.8	50

Figure 6.1 Comparison of the peak forces calculated in the present study with that of a previous study (Morrison JB 1970).

Of particular interest is the posterior-directed horizontal force on the tibia at the onset of single limb stance. At this point the external moment is one that tends to flex the knee and much of the rest of the body and weight is behind the vertical axis of the knee. The knee is also partially flexed (about 15º) positioning the femur to be susceptible to rolling and sliding over the tibia. The stability here is largely controlled by muscle and ligamentous activity and restraint. The posterior-pointing horizontal force calculated in the present study therefore makes sense, and this would also be an indication of the reaction necessary to prevent rolling.

6.1.2 Forces in stairclimbing

The peak external flexion moments in stairclimbing were found to be about 0.6 Nm/kg which were about three times larger than in level walking. Peak external extension moments were also found to be larger in stairclimbing (-0.6Nm/kg) than those found in level walking (-0.4 Nm/kg). Peak compressive forces at 5 xBW were largest in stairclimbing, compared to deep flexion and level walking. The estimates of forces in stairclimbing obtained in the present study may be compared to those from a recent report of walking and stairclimbing (Taylor WR et al 2004). In the previous study (Taylor WR et al 2004), peak forces in walking reached 3.1 xBW, while in stairclimbing the forces were larger at 5.4 xBW. The previous study also reported shear forces of about 1.3 x BW, which were 2 times larger than those in level

walking (Taylor WR et al 2004). In the present study peak horizontal reaction forces were calculated to be about five times larger than in level walking (Tables 5.1 and 5.2), while peak posterior horizontal forces were about two times larger than in level walking.

6.1.3 Forces in deep flexion

The peak external flexion moments in deep flexion were found to be as much as six times larger than in walking (comparing averages of 0.2Nm/kg in walking with 1.2Nm/kg in deep flexion). The two peaks in the moment curves corresponded largely to the two points before and after the subject rests in full squat. In a previous study on deep flexion activity examining kneeling [Nagura T et al 2002] similar peaks in moments were observed just prior to and after the rest point in the maximum kneeling position. These large moments arise from the generation of significant quadriceps muscle activity to counter-balance the body by providing sufficient internal extension moment about the knee and maintain stability in the deep flexion position. With larger moments about the knee joint, the reaction forces are expected to be correspondingly large. The bone-on-bone peak forces calculated for the deep flexion activity were larger than that in walking only in the horizontal direction. Relatively more of the increases in magnitude of the forces were in this direction. If translating the vertical and horizontal forces to a local reference in terms of the tibial

orientation, then it is noted that the horizontal force is likely to be manifested as an anterior shear reaction force. This is expected given the position the knee was in, and the forces acting about it (Figure 6.2). The forces calculated for deep flexion in the present study are surprisingly small compared to previous work showing 5 to 6 times bodyweight force in squatting (Dahlkvist 1982). Probably the different techniques in the previous and present study may be the reason for the differences. (The previous study (Dahlkvist 1982) used an EMG driven model.) In the present study the forces are calculated based on input of moment arms, lines of action, external joint moments, knee angles and ground reaction forces. The ground reaction forces in performing the squat were not as large as in heel strike. This is understandable as the subject is balance on the forceplate and very little reactions are expected on the ground such as in the case of heel strike where there is a relatively strong deceleration. The fact that ground reaction forces were not significantly larger in deep flexion (squat) could be the main reason why the forces are not as large as previous estimates using other methods (Dahlkvist 1982). Another previous study (Zheng N et al 1998), using similar methods to the present found tibiofemoral (compressive) contact forces to reach peaks of only 3000N, which is not much above those measured in walking.

The combination of compression and shear forces highlights a type of loading similar to 'ploughing' [Mow VC et al 1993, Mow VC et al 1992]. In this, cartilage

is loaded, such that together with a direct compression into the cartilage, there is force acting somewhat tangential to the cartilage surface. The effects of shear forces have been discussed previously. Several studies have implicated shear forces as a critical component in the destructive profile of cartilage [review by Lane Smith R et al 2000]. Also mechanical shear stress applied to cartilage explants showed a considerable increase in the production of oxidants, and played a key role in the formation of senescent chondrocytes [Martin JA et al 2004]. Interestingly in the present study, the deep flexion activity resulted in mainly horizontal or shear-type forces in largely the opposite direction from that in walking. The direction of the shear reaction force on cartilage may be an important consideration for future work on the effects of loading direction and failure mechanisms.

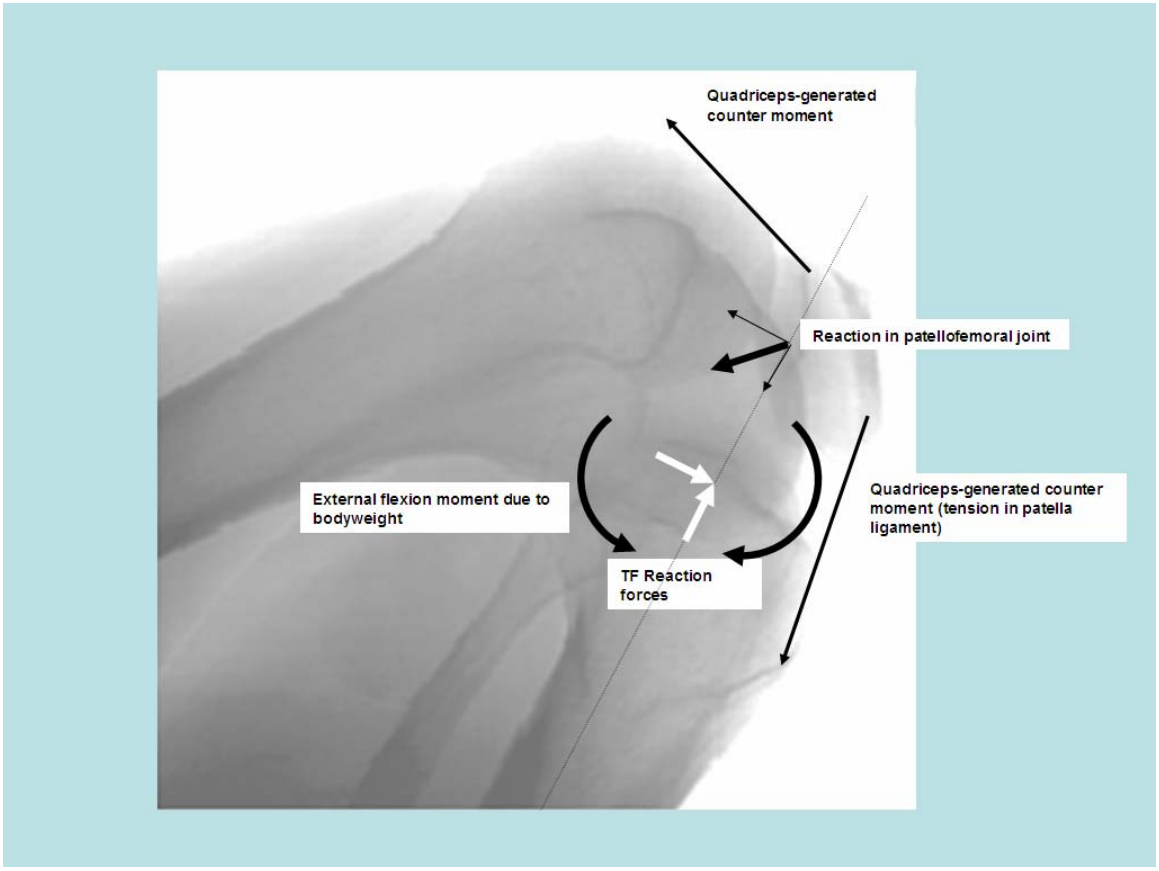


Figure 6.2 Schematic to illustrate how external flexion moments from reaction to bodyweight are balanced by internally generated moments from quadriceps activity. A backdrop of an x-ray image of a full squat is used as a reference. The reaction at the knee for equilibrium (illustrated as white arrows) shows a compression and anterior-directed shear. This simplified diagram does not include other important factors such as friction characteristics and the effects of other magnitudes and orientations of the major force bearing structures in the knee.

6.1.4 Assumptions and limitations of the model

In the present study, several assumptions for the model have been made to facilitate the calculation, including the reduction of the problem to a statically determinate one. These assumptions are as follows:

- although surface motion occurs in three planes simultaneously, the sagittal plane motion is greatest by far [Nordin M and Franklin VH 2001]. In this model, all motions in the other planes are negligible.
- The axis of flexion-extension rotation, perpendicularly intersecting the sagittal plane, is assumed to coincide with the instant center of zero velocity of the femur relative to the tibia; a point where the cruciates would intersect [Lu TW and O'Connor JJ 1996].
- The articulation of the tibia and femur is akin to that between two rigid bodies.
- The articulation vis-à-vis congruency, involves a mean surface of the tibia plateau versus a mean surface of the femoral condyles [Nisell R et al 1986].
- The tibiofemoral contact point coincides with the point where there is the shortest distance between the mean femoral condyles and tibial plateau.
- The tibiofemoral contact point also coincides with the perpendicular line drawn from the flexion-extension axis down to the tangent of the tibial plateau surface. [O'Connor JJ et al 1989]

- Knee ligaments and tendons are modeled as uniaxial tension vectors whose insertion points are fixed, and whose directions relative to the neutral position are determined by the relationships provided by Herzog and Read. [1993]
- An individual fibre in a ligament or tendon whose fibre length and insertion point may vary is not considered. The ligament or tendon is taken to be a uniform whole structure.
- The length of the ligaments and tendons can change according to the position of the knee, but the differences in tension as a result of the effects of any inherent length-tension property in the soft tissue are assumed to be negligible.
- All external forces and moments acting on the joint are assumed to be balanced by internal muscle forces and joint reactions.
- External moments tending to *flex* the knee are assumed to be balanced by internal moments generated via *quadriceps* contraction. External *extension* moments are assumed to be balanced by internal moments generated via *hamstrings* contraction. [Andriacchi TP et al 1984]
- The weight of the shank and foot is negligible as it constitutes less than one tenth body weight and changes in velocities during walking and squatting are expected to be relatively small.
- Anatomical variations play an important role in the linear measure of moment arms and lines of action [Krevolin JL et al 2004], but were not

considered in the present study. Scaling of these parameters may be achieved by using an anatomical measure, such as the femoral width. [Krevolin JL et al 2004]

- Only net external moments were considered. Hence, resolving the muscle forces during co-contractions will be considered to be beyond the scope of this model. Also beyond the scope of this model was the distributed load into the various individualized force bearing components of a particular muscle group. Hence the knee extensor (quadriceps) force was combined into one force vector via the patella ligament, and the knee flexor (hamstrings) force was combined into one force vector via the biceps femoris tendon.

The simplification to reduce the number of unknowns began with the initial step of reducing the problem to a coplanar one where three forces cancel each other out. This is similar to the assumptions made when modelling lever systems. A load, effort and fulcrum constitute the three forces that maintain equilibrium. In the knee joint, the body weight negotiated (load) is balanced by the (effort of the) muscles and ligaments over the tibiofemoral contact (fulcrum). For the sagittal plane tibiofemoral contact kinematics and kinetics, it is therefore relevant to note at this point that although knee motion occurs simultaneously in three planes, the motion in the sagittal plane is so great that it accounts for nearly all

of the motion. [Nordin M and Franklin 2001] A reasonable justification is therefore presented to consider the sagittal plane analysis sufficient to answer some of the biomechanical questions on knee joint mechanics. Hopefully this will encourage the development of more anatomical studies of lines of action and moment arms of force-bearing structures in the joint, and ultimately to also include the pathological joint as well.

6.1.5 Limitations and Assumptions in the squatting analysis

There are several limitations in the squatting force analysis and these are due to some of the assumptions made in the free body diagram used to calculate the tibiofemoral joint forces. For one the accuracy of the force measurements begin to be seriously questioned when the back of the thighs of the subject start to come in contact with the back of the calves. The additional pathway for load transmission created in this situation is not modelled and in full squat, when the subject rests, the forces in the knee could very well be reduced than what is stated in this study. The modelling of this additional pathway for load transmission is an exciting future endeavour but remains beyond the scope of the present study. This is because in the present study the peak forces were measured and these occurred when the subject was going into the squat and also when the subject was coming up form it. In these positions, muscle forces play an important role in controlling the movement and balancing the weight. The net resultant reaction forces are expected to remain within the knee joint.

A second technical criticism to note is that the polynomial equations of Herzog and Read [1991] used in the present study have not been derived from data of knee flexion beyond 120°. However the fourth-order equations tend to suggest that the range of patella tendon moment arm from 120° to 170° knee flexion is from 4cm to 8cm, while the orientation of the line of action fluctuates by about 15°. The moment arm interpretation using the data of Herzog and Read [1991] as used in the present study has also been used in a previous study on deep flexion [Zheng N et al 1998] where tibiofemoral peak compressive forces were found to be about 3100N, similar to that found in the present study. In any case, more work needs to be done in determining the true lines of action and moment arms of the major force bearing structures in the knee during deep flexion beyond 120° in order to obtain more accurate measurements.

6.2 Critique on the methodology used to derive contact stresses.

6.2.1 Limitations in the loading protocol and techniques used

One of the main concerns in the derivation of stresses to represent walking and squatting is the estimation of the knee position to accurately reflect the rotations and translations associated with the specific activities studied. Only flexion angle was duplicated and the other positions implied by allowing the knee to find its equilibrium position under a 1000N preload. This method does not include the complex loading in multiple directions for either walking or deep flexion. In order to achieve more accurate representations of tibiofemoral joint kinematics, more detailed in-vivo studies will have to be incorporated, for example obtaining data from MRI systems [Hill PF et al 200].

Previous studies have used other methods to estimate contact stresses in the natural knee joint, such as, casting techniques, the use of pressure sensitive film and stereophotogrammetry [Ateshian GA et al 1994] . A comparison of the stresses calculated in the present study is tabulated together with some of the previous reports (Table 6.2).

Table 6.2 Comparison of the stresses obtained from the present study with that obtained previously.

Tibiofemoral contact stress study	**Type of sensor used**	**Load Applied (N)**	**Medial Pressure (MPa)**	**Lateral Pressure (MPa)**	**Tibiofemoral (MPa)**
Fukubayashi and Kurosawa 1980	Pressure sensitive ink-film	1000			3 (average pressure)
Brown TD et al 1984	Piezoresistive transducers	3000			8 (peak pressure)
McKellop HA et al 1991	Pressure sensitive ink-film	2400	4.1	4.6	
Ihn et al 1993	Pressure sensitive ink-film	1200	1.9	2.5	
Riegger-Krugh et al 1998	Pressure sensitive ink-film	1960	2.52	3.86	
Present Study	Real-time thin-film electronic sensors	Up to 2400	14 (peak pressure)	0 to 11 (peak pressure)	14 (peak pressure)

The values of pressure (MPa) from the present study appear to be larger than those from the previous study especially where pressure sensitive ink film was used. One of the issues of using the ink film is that as the load is increasing beyond the threshold that causes the ink stains, it becomes difficult to relate the load applied at a given instant to the amount of ink released. It is a cumulative record of peak pressures over time that is derived from ink-staining correlated with temporal maximum local stress. If one views the film after a specific test, an

overall stain pattern may indicate a larger contact area than that obtained instantaneously and in real time. Also the contact area measured on ink film has to be carefully extrapolated to ensure that the area measured is not a summation from the entire load profile.

The present study uses the K-scan pressure measurement system to determine the contact stresses in the natural tibiofemoral joint in various knee angles in real time, such that the force and area is provided for the given time of interest. The k-scan sensor pressure measurement system has previously been used to measure contact areas in the artificial knee [Harris ML et al 1999]. Recently a study on the sensors' accuracy found that errors were on the order of 1-4% for contact force and peak pressure at 3-9% for average pressure and contact area. These errors, they reported, are comparable to those arising from inserting a sensor into the joint space or truncating pressures with pressure sensitive film [Fregly BJ and Sawyer WG 2003]. A previous study reports that the Tekscan (K-scan) System is more reliable than pressure sensitive film, and suitable for dynamic measurement of the femorotibial joint, permitting measurements to be made under more physiological conditions [Wirz D et al 2002]. While much time has lapsed since the introduction of these sensors and their acceptance for use as a reliable means of ascertaining contact stresses accurately, it is nevertheless an easy, reproducible and reliable system to derive contact areas in the tibiofemoral joint at different loads [Harris ML et al 1999].

6.3 Are the contact stresses in walking and squatting critical?

6.3.1 Inference of a factor of safety in weight bearing deep flexion

In the present study, the peak stresses observed in the cadaver knees in deep flexion were as high as 25MPa to 35MPa. This may be compared with the failure limits determined from previous studies are shown in the table (Table 6.3).

Table 6.3 The ultimate stress that can cause cartilage to fail as reported in previous studies.

Study	**Type of loading**	**Stress at which failure occurred (MPa)**
Repo RU and Finlay JB 1977	impact	25
Torzilli PA et al 1999	impact	15 to 20
Kerin AJ et al 1998	non-impact ramp loading	14 to 59 (mean 35)
Kerin AJ et al 2003	non-impact ramp loading	36

In the present study impact loading was not included. The mechanisms of failure are not expected to be the same in impact loading and repetitive non-impact type loading. Cartilage stiffness has been found to increase in high strain rate loading, via a classical elastic deformation process [Oloyede A et al 1992], and is thus likely to affect the redistribution of joint contact stresses being transmitted into the subchondral bone. Also, like engineering materials, it has been found that cartilage-bone systems display characteristics that indicate an inverse

relationship between stiffness and toughness [Broom ND et al 1996] such that the risk of crack propagation is increased with increased stiffness.

The physiological stresses derived in the present study, and the failure strength of articular cartilage as a determinable value from previous studies (Table 6.3), may be able to provide some means of understanding the implications of activities of walking and deep flexion. The factor of safety of cartilage, if this factor were to be equated as the ultimate stress of cartilage divided by the physiological peak stresses as derived in the present study, can be thus derived. Taking the ultimate stress to be about 35MPa, then the in walking the stresses derived in the present study of about 15MPa indicates that the safety factor is just above two, which may be of concern since most conservative requirements for factor of safety are not less than two[2]. This criterion becomes even more pertinent in the case of deep flexion where the safety factor may be reduced to about one. This allows for a very small margin of safety in preventing damage, especially for the unfortunate combination of poor quality cartilage (for example from aging) and or large reaction or high impact forces in the knee (for example abnormal joint loading from pathology). However, in the present study, the loads prescribed in deep flexion were four to five times body weight. The in-vivo study using motion analysis of deep flexion had revealed that compressive forces were only about three times body weight. If this is the case then the distribution of

[2] From U.S. Department of Labor Occupational Safety and Health Administration guidelines for construction regulations.

loads could be extrapolated from the in-vitro contact stress study (Table 6.4). One could combine the data of Table 5.1 and Table 6.3 with the contact area data (Figure 5.5). This would yield some values which imply that in deep flexion, about 65% of the force of 3 times body weight passes through the medial compartment engaging an area of about 1cm^2 to 1.5 cm^2 , to yield peak stresses accordingly of about 13MPa to 19MPa. Such a range is much reduced from the peak stresses measured in the present study.

Table 6.4 Extrapolated values of the distribution of stresses in Heel Strike (HS), Single Limb Stance (SLS), Toe-Off (TO), Deep Flexion (DF); 1 (90°), 2(beyond 120°)

Distribution of stresses	**HS**	**SLS**	**TO**	**DF1**	**DF2**
medial	73%	55%	68%	63%	65%
lateral	27%	45%	32%	37%	35%

The present study also showed the femoral contact on the tibial plateau to be posteriorly-located and externally rotated in deep flexion (Figure 6.3). The engagement of the more peripheral zones on the tibial plateau requires further understanding of the material properties in these areas, and of the significance of the stresses from deep flexion.

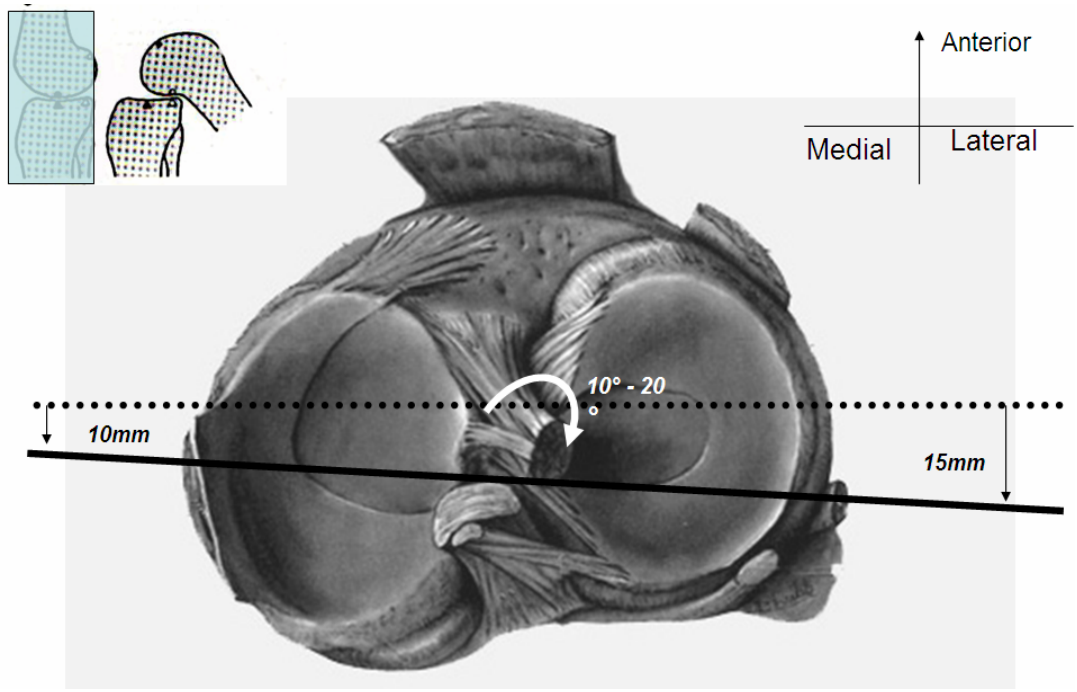


Figure 6.3 Schematic representation of the femoral contact on the tibial plateau in deep flexion showing a relative posterior translation and external rotation of the femur.

Another interesting finding from the present study is the distribution of stresses over the medial and lateral compartments in the phases simulating walking and deep flexion. In heel strike, most or all of the pressure mainly passes over the medial compartment. This is probably due to the slight 2º varus angulation that had to be implemented to the knee specimen for it to be in 'equilibrium' during loading. While it is difficult to verify these pressure readings, previous in-vivo work on knee joint kinematics using videoflurouscopy [Komistek RD et al 1999] may help to understand the present finding better. The authors of the previous study [Komistek RD et al 1999] observed condylar lift-off during heel strike of an average 1.2mm, with an inclination (towards the medial compartment) of 2.2º. In another study [Yoshimura I et al 2000] where accelerometers were used to

measure the lateral thrust during walking, it was found that 40 out of 60 normal subjects displayed this characteristic. Essentially, a lateral thrust occurs at heel strike and is observed mainly when the mechanical axis is not centred for the knee joint and is, instead, located more medially. The occurrence is notable in dynamic activities but not in a static analysis where the mechanical axis is drawn to pass through the centre of the normal knee joint [Andriacchi TP 1994]. The present study measures pressure values from a quasistatic test; however, the original orientation of the knee and the loading conditions were derived from dynamic activity. Therefore the partial loading on the medial compartment with hardly any loading in the lateral compartment during heel strike, hopefully presents a realistic interpretation.

6.3.2 Limitations in the present study on the biomechanical interpretation of deep flexion

At this time it is appropriate to address other limitations of the interpretations in the present study. The knee orientations derived were based on allowing the cadaver specimen to locate its own 'equilibrium' position and thus neglects the effects of both agonist and antagonist muscle control in joint stability. The relative tibiofemoral rotations observed in the present study correspond well with previous work on cadaver knees studying the coupling rotations that occur when passively flexing the unloaded knee joint [Wilson DR et al 2000]. Internal rotations of the tibia were found to accompany passive flexion, by as much as

25° internal rotation with 100° flexion, and the input of external loads could alter the amount of coupling motion [Wilson DR et al 2000]. This point relates well to more recent findings that show a significant variation in the tibiofemoral contact point derived from deep flexion of cadaver knees [Iwaki H et al 2000] versus loaded living knees [Hill PF et al 2000], where similar magnetic resonance imaging protocols were used. While no difference was found in the cadaver tibiofemoral contact position in deep flexion versus the unloaded living knee in deep flexion, a significant difference was found in the loaded living knee such that the medial femoral condyle translated anteriorly by up to 4mm, creating an external rotation about the tibia longitudinal axis [Iwaki H et al 2000, Hill PF et al 2000]. The difference between the present study and the previous study using passively-flexed unloaded cadaver knees [Iwaki H et al 2000] is that in the present study the tibiofemoral positions were obtained with a load of up to 1000N. The later study, which looked at live loaded knees [Hill PF et al 2000] only reported the excessive external rotation of the femur over the tibia with increasing flexion, but did not include observations on varus-valgus rotations. It is proper to assume that such an external rotation of the femur would be accompanied by varus angulation. This can be explained by the fact that the medial plateau is more concave than the lateral [Welsh RP 1980] and that the medial condyle, in the extended knee, projects lower than the lateral condyle when viewed in the frontal plane [Fowler PJ and Lubliner J 1995]. In flexion, the natural valgus of the knee is lost, as the medial condyle is no longer projecting

distally since the radius of curvature of the posterior femoral condyles of both medial and lateral sides in this position are less different. This would result in a varus angulation accompanying deep flexion, as described in the present study, which also coincides with the internal rotation of the tibia relative to the femur. In the present study, these coupling rotations were accounted for in the intact knee specimen to derive the positions of the tibiofemoral joint in various degrees of flexion. It was these positions that were used to calculate the stresses of the joint when the sensors were introduced.

From knowing the contact stresses in deep knee flexion as derived in the present study, and relating them to the published reports on epidemiological studies that have shown the relation of frequent knee bending activity to the development of osteoarthritis [Anderson JJ and Felson DT 1988], one may be able to understand a cause-effect relationship between stresses in knee bending, cartilage damage, and the development of osteoarthritis. However it is important to note that the previous epidemiological study [Anderson JJ and Felson DT 1988] had also shown that the younger age group copes well with demands on the knee in bending compared with the older age groups that tend to develop osteoarthritis. Therefore, to distinguish the role of mechanical factors on the development of osteoarthritis, more information is necessary whereby one can incorporate the effects of old age on cartilage regeneration and repair.

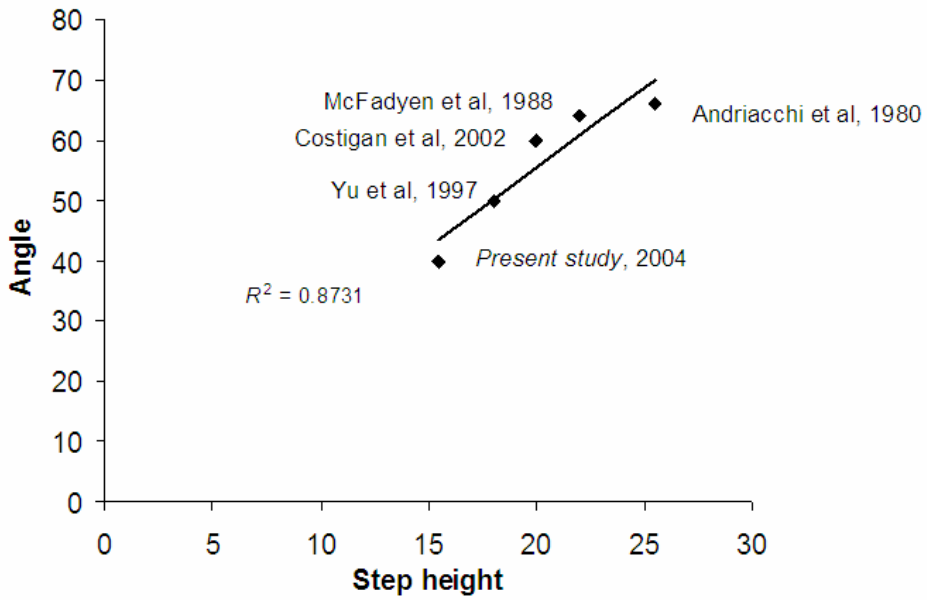
In the present study, the specimens obtained were from a population that was geriatric. Only five knees were found to be suitable for use in this study, as these contained hardly any noticeable degenerative changes. It is acknowledged that the quality of the cartilage, in truly appreciating the effects of age, has to be more than a mere visual assessment as was done in the present study. In any case, the reduced contact area that was measured when the knee was flexed at 90° and beyond 120° being the most likely cause for the increase in the pressure reading in the current study, is indicative of the general underlying principle that drastic increases in pressure from these positions are not only due to the increased external forces. Subsequently, the topographical variation in cartilage properties [Lyyra T et al 1999] becomes an issue as tibiofemoral engagement in deep flexion is different from when walking upright. For example, if the knee in deep flexion engages the more peripheral cartilage on the tibia away from the usual centre, the question of the loading response in the peripherally-located cartilage, which generally is not commonly laden as such, becomes imperative. This provides an extended scope for much of the future work investigating the mechanical causes for cartilage failure and knee OA.

6.4 The significance of adaptation in patients with anterior cruciate ligament deficiency.

In the present study the most notable difference observed between controls and patients was the between-limb difference in peak external knee flexion moments of normal controls and patients with unilateral anterior cruciate ligament deficiency. Also the moments of the involved knees of patients were found to be significantly smaller compared with those of the uninvolved knees and those of the control subjects. There are few reports [Andriacchi TP, 1993; Berchuck M *et al*, 1990] to compare the present findings with. The previous authors [Andriacchi TP, 1993; Berchuck M *et al*, 1990] showed that although gait adaptations in the form of reduced knee flexion moments occurred in level walking, patients with anterior cruciate ligament deficiencies had no significant differences in knee moments during stairclimbing. They observed that peak flexion moments occurred at approximately 66° knee flexion. These authors [Andriacchi TP, 1993; Berchuck M *et al*, 1990] hypothesized that as the knee was flexed to 66° during single limb support in stair climbing, quadriceps contraction, to provide an internal extension moment at this large knee flexion angle, instead would result in posterior translation of the tibia, and hence, reduce demand on the anterior cruciate ligament. These authors [Andriacchi TP, 1993; Berchuck M *et al*, 1990] concluded that in stairclimbing, patients with a deficient anterior cruciate ligament did not show quadriceps avoidance activity.

6.4.1 The possible effects of step height

The stair height of 25.5 cm as used in previous studies [Andriacchi TP, 1993; Andriacchi TP *et al*, 1980] is 10 cm higher than the steps used in the current study; this may be the cause of differences from the current findings, where reduced peak flexion moments were observed in patients with anterior cruciate ligament deficiencies. A larger step height implies a steeper stair slope and larger flexion at the knee. Yu (1997) reported knee flexion angles of approximately 50° during peak flexion moments when using a stair step height of 18 cm, whereas in the current study, knee angles were slightly above 40° during peak flexion moments. It has been shown that for knee angles that are closer to extension, quadriceps contraction generates an anterior drawer [Grood ES *et al*, 1984; Andriacchi TP, 1993], which probably explains the adaptation observed in the current study, where knee angles during peak moments were lower than those angles reported in previous studies. It is thus quite likely that there is a correlation between reduced peak flexion moments at the knee, the angle of flexion of the knee when these moments occur, and step height (Figure 6.4).



Study	*step height (cm)*	*flexion angle of the knee when peak external flexion moments occur (°)*
Andriacchi et al, 1980	25.5	66
McFadyen et al, 1988	22	64
Yu et al, 1997	18	50
Costigan et al, 2002	20	60
Present study, 2004	15.5	40

Figure 6.4 Using data obtained from previous published reports, this chart attempts to show the correlation (coefficient R^2) between the knee flexion angle (when peak external flexion moments occur at the knee while ascending a step) and the step height used in the respective study.

The step height used in the current study is relevant [Irvine CH *et al*, 1990] because it represents the step height that commonly would be negotiated by patients in daily living, especially in Singapore, where most buildings' stairs follow these specifications. Quadriceps avoidance gait [Berchuck M *et al*, 1990] was described as the cause for the absence of net external flexion moment in the anterior cruciate ligament deficient knee of patients during level walking. In the current study, there was a net external flexion moment in the involved knees

of the patients during stair climbing, but it was less than the flexion moments in the uninvolved knees, and in the knees of control subjects. Noyes (1992) reported reduced external flexion moments in knees of patients with anterior cruciate ligament deficiencies during level walking, indicating the presence of quadriceps activity. Measurements of the degree of lower limb muscle activity in patients with anterior cruciate deficiency have been attempted previously [Limbird TJ *et al*, 1998; Beard DJ *et al*, 1996; Bulgheroni P *et al*, 1997] with interesting results. Using electromyographic data, Bulgheroni (1997) reported a reduction in quadriceps activity during level walking gait in patients with anterior cruciate ligament deficiencies. Beard (1996) by using electromyography in conjunction with level walking gait studies, found that patients with anterior cruciate ligament deficiency did not have lowered quadriceps activity, but instead had increased hamstrings activity, giving rise to larger internal flexion moments. Other studies reported that in the stance phase of level walking, there was less quadriceps activity and more medial hamstring activity [Branch TP *et al*, 1989; Limbird TJ *et al*, 1998]. Whether it is increased hamstrings or reduced quadriceps activity, the net result for both cases is reduced external flexion moments at the knee of patients with anterior cruciate ligament deficiency. A report by Wexler (1998) indicated that as the time after anterior cruciate ligament injury increased, the reduction of external flexion moments in patients during level walking became more pronounced. This raises the question of whether the amount of reduction in external flexion moments in patients with

anterior cruciate ligament deficiency, is a reliable indicator of the development of the gait adaptation.

Another observation from the current study is the significantly reduced normalized peak ground reaction force in patients' involved limbs compared with that of the uninvolved limbs. This finding is similar to that from previous studies, where reduced peak vertical forces were found in limbs with anterior cruciate ligament deficiencies in level walking [Bulgheroni P *et al*, 1997] and running [Tibone JE *et al*, 1986]. In the present study, with no significant differences in the knee angles measured between involved and uninvolved limbs of patients and the limbs of control subjects, the reduced peak ground reaction force, especially the significantly reduced antero-posterior shear forces in involved limbs of patients, is most likely the primary contributing factor to the reduced peak knee moments. Such a reduction invariably reduces the moment arm of the resultant ground reaction force vector to the knee center, and with the vector passing behind the knee, the reduced moment arm would result in a reduced external flexion moment as observed for the patients' affected side. In the absence of a primary stabilizer, the knee therefore seems to adapt, reducing moments at the joint through some mechanism of energy absorption and less forceful foot-to-ground contact rather than an alteration in joint position.

One way the body reduces the forces from load transfer to single limb support is to reduce the inertial effects of deceleration of the mass being loaded onto the supporting limb, through muscular control. Bulgheroni (1997) observed reduced peak vertical forces in the gait of patients with anterior cruciate ligament deficiency in level walking, indicating that more care is taken with foot-to-ground interaction. The use of muscle coordination to achieve this may be the reason why patients in the present study had reduced peak ground reaction forces in their involved limbs. Gait adaptations do occur for patients with anterior cruciate ligament deficiencies, but is this adaptation good or bad for the joint? Noyes et al (1992) recorded gait adaptations of reduced external flexion moments and increased extension moments in patients with anterior cruciate ligament deficiency during level walking. They considered muscle action and calculated the soft tissue and tibiofemoral joint forces. From their model, they found that gait adaptations in patients with anterior cruciate ligament deficiency resulted in larger joint loads, which were associated with factors leading to joint degeneration. They suggested that a successful anterior cruciate ligament reconstruction that provides joint stability would tend to reduce these forces. Another study [Timoney JM *et al*, 1993] showed that after anterior cruciate ligament reconstruction, there was a tendency toward gait normalization, where a quadriceps avoidance mechanism no longer was present. At present, however, it is not appropriate to expound on the benefits of anterior cruciate ligament reconstruction surgery based on gait evaluation, given the numerous associated

variables that contribute to the complex of clinical symptoms [Noyes FR *et al*, 1985] of anterior cruciate ligament deficiency syndrome [Feagin Jr JA, 1979].

6.4.2 Limitations to the stairclimbing study

For the current study, interpretation of the results also must take into account the fact that there are variations that exist between subjects that may affect the outcome observed. These variations are knee alignment, generation of muscle force and recruitment, innate and unique gait patterns, and probably proprioceptive ability. However, it was not possible to perform gait analysis on patients before their injury, nor was it the aim of this study to quantify any additional characteristics beyond those obtained from gait analysis and the calculation of forces and moments in the knee during stair climbing. Therefore, instead of providing the definitive indication for symptomatic anterior cruciate ligament deficiency, the knee flexion and extension motion abnormalities that may be observed during stair climbing are presented in the current study to expand on the current knowledge and methods that can be developed to aid the clinician in patient evaluation. There are other limitations in the current study. For one, it was difficult to get mass-matched subjects and the importance of this criterion to a study looking at weight bearing in the knee joint is obvious. Also not documented in this study were details of patient compliance to rehabilitation and other details of the rehabilitation program. The effect of the rehabilitation program on the patients was therefore not accounted for. The gait analysis was

performed less than 12 months following injury, and is therefore unlikely to include many patients who have truly "tested" their functionality over the long term. This study also omitted examining muscle activation patterns, and it is acknowledged that the way ligament deficient patients use their muscles to stabilise their knees is important. The biarticular nature of many muscles, and the fact that the role of the other joints was not investigated in detail, is also an important limiting factor to this study.

6.5 Topographical variation in cartilage properties and the relevance to altered kinematics

The stiffness (N/mm) values obtained in this study for the articular cartilage in the regions not covered by the meniscus may be compared with previous reports [Lyyra T et al 1999]. In the previous study, the authors measured in-vivo the force required to indent 300 microns into the articular cartilage. They obtained force readings that averaged 2.4N for the medial tibial plateau and 3.1N for the lateral. These force values, when normalized to the 300 micron fixed displacement, represent stiffness values of 8N/mm and 10N/mm for the medial and lateral plateaus respectively. These stiffness values derived from the previous study [Lyyra T et al 1999] and may be compared to those from the present study where Group II (the medial side) and Group I (lateral) showed stiffness of 11N/mm and 5N/mm respectively (Figure 5.11). The differences could be due to several reasons. The most obvious reason would be that while in the previous study [Lyyra T et al 1999] the average age of the patients was 26 years, the specimens in the present study came from an older age group of donors where age-related changes may have influenced the results obtained. In the present study (according to Mankin's grading system) the articular cartilage covered by the meniscus was normal (zero), compared to a score ranging from 1 to 2 in the articular cartilage not covered by the meniscus. Also, the previous study [Lyyra T et al 1999] used a hand-held indenter in arthroscopy, and

measured in-vivo loads via displacement control; whereas in the present study the in-vitro experiment was performed via load control. However there is little evidence that this difference in load application should matter in this case.

The thickness of the articular cartilage not covered by the meniscus measured in the present study was similar to that measured in previous studies of elderly subjects [Hudelmaier M et al 2001] (Figure 5.12). Comparing with thickness measurements averaging about 1.5mm to 1.8mm from previous studies using quantitative MRI [Faber SC et al 2001], the thickness values of some 3 to 4 mm obtained in the present study on all-male cadavers were relatively larger. However, compared to earlier MRI studies [Cohen ZA et al 1999] which obtained measurements in the region of 2mm to 3mm, with maxima reaching 5mm, the present study's thickness measurements were similar. In any case, one would question the accuracy of using the needle method in the present study to determine cartilage thickness, as the method depended on the sensitivity of the measuring load cell and the point at which the needle encountered a sudden rise in resistance to its progression into the cartilage. Essentially the expectation was for the needle to encounter this sudden increase in resistance as it hit the calcified layer, a rather difficult region to define. The finding in the present study, that showed articular cartilage covered by the meniscus to be thinner than the cartilage that was not covered, supported similar findings from previous studies that reported variations in cartilage thickness in the knee [Shepherd DE and

Seedhom BB 1999, Eckstein F et al 2001]. These variations across the tibial plateau were most likely due to the load experience that indicated a tendency for thicker cartilage to be found in regions that experienced more dynamic loading activity [Adam C et al 1998].

The modulus (MPa) (Figure 5.13) of the cartilage zones note covered by the meniscus compared to previous values of 4.27 (2.89) MPa (Elliot DM et al 2003) was within the expected range. Both the modulus and creep (relative to cartilage thickness) (Figure 5.14) were parameters that had been derived through a normalization procedure where the cross sectional area of the indenter was taken into account as well as the thickness of the cartilage tested. The sites beneath the meniscus seemed to be more sensitive to the effects of this normalization, as shown by the weaker correlations when comparing simply the stiffness (N/mm) and creep values (mm). The relationship showed that the articular cartilage with the tendency to creep more had less stiffness. This relationship was only obvious when the creep measured was normalized to cartilage thickness, and when stiffness took into account radius of indenter, Poisson's ratio and strain. The creep modulus in the present study assumed a scaling factor corresponding to a Poisson ratio of 0.5, which is that of an incompressible material. Studies have reported Poisson's ratio of articular cartilage to be as low as 0.2 [Athanasiou KA et al 1991], but the scaling factors given previously [Hayes WC et al 1972] did not include those for studying

materials with Poisson's ratio less than 0.3. A more recent study [Haider MA and Holmes MH 1997] looked at the scaling factors that would be relevant to studying materials with small Poisson's ratios, and found that for the dimensionless ratio of indenter radius and tissue depth, the errors in estimating the scaling factor increased with decreasing indenter size. This made it difficult to compare measurements obtained in the various studies, including the present. In the present study, using a Poisson ratio of 0.5 and an indenter radius-to-thickness (aspect) ratio of about 0.2 (depending on the thickness of the cartilage), a reasonable estimate of the scaling factor was derived. However, more investigation has to be done with respect to the effects of Poisson's ratio, indenter size, and cartilage thickness in order to obtain a more relevant estimation of scaling factors that need to be used in these calculations. In summary, the results of the present study showed articular cartilage mechanical properties beneath the meniscus to be different from those in the region not covered by the meniscus. This corroborated the finding from a previous study [Shepherd DE and Seedhom BB 1999], where it was found that the instantaneous compressive modulus of human articular cartilage was significantly stiffer in the regions covered by the meniscus compared to the regions that were not.

The observations on morphometry from the histological sections in the present study shed some light as to what these differences in mechanical properties may

mean. From the results (Figures 5.18 to 5.20), it seems that the density of subchondral bone was largely influenced by the loading history. The results (Figure 5.19) showed that region B, which was the area not covered by the meniscus, was most dense in subchondral bone compared to regions A and C. Region A was the section close to the tibial eminence and region C represented the area covered by the meniscus. The tibiofemoral contact was likely to be confined largely to region B and hence it could be expected that the subchondral bone here would be denser due to the more intense loading history. It was interesting to note that the articular cartilage thickness (as shown in Figure 5.18) was affected by location (region B having thicker cartilage than region C) but was not as influenced by loading history, since less difference was observed between regions A and B. The effect of loading history, on the subsequent development of articular cartilage and subchondral bone morphology, therefore seemed to be different for the two types of tissue.

The mechanical testing had revealed that both the stiffness (N/mm) and modulus (MPa) increased from the region uncovered by the meniscus to the region beneath the meniscus. In summary, compared to the articular cartilage not covered by the meniscus, the articular cartilage of the region beneath the meniscus was stiffer, yet thinner, and had less dense subchondral bone. It also had relatively less capacity to creep. Creep in cartilage may be an important factor, as it has been shown that creep-loaded specimens may be up to 21%

stronger [Adams MA et al 1998]. The ability to creep also allows for increase in toughness of the material, as there is more accommodation to load over time, instead of encouraging the formation and propagation of a crack. The capacity for load bearing in the articular cartilage of the region covered by the meniscus was likely to be different from that of the region not covered by the meniscus given the differences in the morphometry and mechanical properties. A stiffer articular cartilage principally transfers loads across more directly to the next material in-line beneath it, and that would be the subchondral bone. The load transmission would thus be enhanced in the composite and the underlying subchondral bone would be the most likely to receive more loads when the cartilage beneath the meniscus is loaded. In the present study the subchondral bone content was found to be significantly reduced in the areas covered by the meniscus, areas which also showed significantly reduced thickness in the articular cartilage. The combination of these reductions provides little assurance that the regions beneath the meniscus would be adequately prepared to weight-bear in the absence of a meniscus.

Besides the obvious concern about the load-bearing differences between the articular cartilage from the two regions in relation to altered joint mechanics from an anterior cruciate ligament-and-meniscus deficient knee, there were other concerns. One worth mentioning for discussion involved bone that has suffered some form of minor fracture, such as a bone bruise. Bone bruising, an occult

trabecular microfracture of bone typically located close to a bone surface and caused by compression or impaction forces, has been found to be prevalent in anterior cruciate ligament deficient patients [Rosen MA et al 1991, Stein LN et al 1995] and those with other instabilities [Miller MD et al 1998, Mathis CE et al 1998]. This would pose an additional conundrum for the appropriate modelling of the pathomechanics of the anterior cruciate ligament deficient knee without the meniscus, when trying to include the remodelling features of the bruised subchondral bone. The knowledge of the topographical variations of articular cartilage material properties is thus an important first step for understanding the way load is transferred to the subchondral bone, because of either altered kinematics or changes in material properties, and even to bone that has suffered some microfracture. The data from the present study would be useful to colleagues for future work in this area, especially in the design rationale for biomechanical models. Such models would be useful for the analysis of the influence of knee instabilities on joint trauma, and the consequential development of the joint degenerative process as a result of such trauma. However the limitations to this study should be discussed. The specimens used were from geriatric donors which could indicate that some osteoarthritic changes, not visible, could be present. The rather low Mankin scores recorded in the present study therefore provides some assurance that the deficiencies in cartilage quality related to age is likely to be minimal. Another limitation is the generalisation of the topographical regions. The regions for each of the four

groups are quite broad. It is therefore possible that in these regions of load bearing there may be rapid changes in the properties of cartilage and thus to have consistent measurements across specimens, a better method of locating the position of each measurement would be needed. For similar reasons limitations of the histological study is that the sections were taken along the same mid-coronal plane, not considering that typical loading and OA wear patterns suggest that the anterior medial compartment and posterior lateral compartment is more frequently engaged [Weidow J et al 2002, Hill PF et al 2000]. It is possible that other morphological differences, in the anterior-posterior direction for example, were not considered in this study.

6.6 Clinical Implications: *A criterion for the risk of damage and injury from weight-bearing knee flexion.*

I). The activities of walking, stairclimbing and deep flexion were studied, as well as topographical variations in cartilage properties. In essence, the weight-bearing knee in flexion was studied. The underlying purpose for these investigations is to ultimately have some clinical relevance in the study of mechanical factors related to osteoarthritis. The basic premise is that cartilage and bone damage in the joint region is a reliable precursor to osteoarthritis. Consequently the findings from this study are put into perspective and a criterion for the risk of damage and injury is discussed. The aim is to contribute to the current knowledge on the etiology of knee osteoarthritis.

In the present study, it was found that stairclimbing and deep flexion activities result in larger loads at the knee. A simple relationship (Figure 6.5) shows the effect of larger loads and the possibility of increased risks for damage. Damage to the joint will depend on how the loads are managed and the levels of stress that develop. In the present study the stresses derived for walking and deep flexion activities are such that in deep flexion the risk for damage is increased but not critical, as the safety factor is still greater than one. Hence the indicator (as shown in Figure 6.5) is expected to be raised but not to the critical levels. The other consideration is illustrated in Figure (6.6). Here the external loading factors are assumed to be unchanged, but internal conditions have been altered.

These conditions refer to changes in the mechanical properties of the weight bearing structures and may be due to age-related degradation or injury, or even topographical variation in which regions of cartilage previously not used to loading are now engaged. This second consideration basically refers to a 'shift' in the mechanical advantage of the ability of the cartilage and bone in the joint to weight-bear.

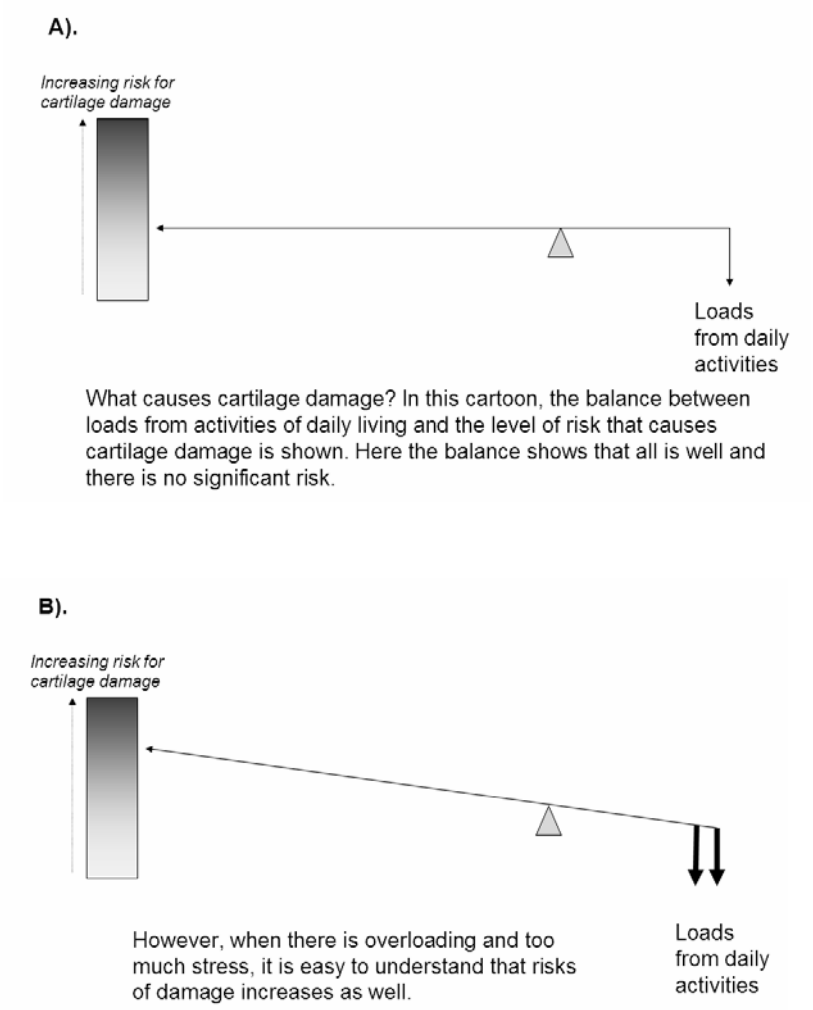
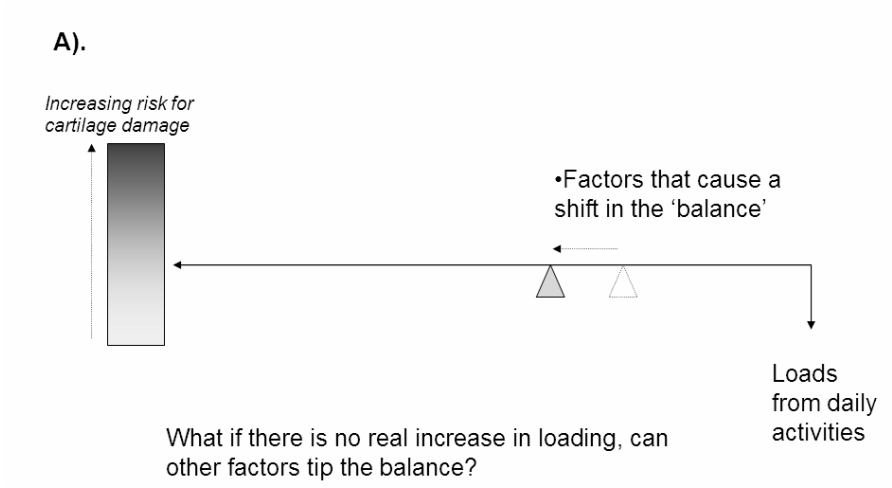


Figure 6.5. The schematic shows a proposed way in which the risk for cartilage damage may be increased. This is by an increased loading from extrinsic factors (such as deep flexion activities, or other more physically demanding activities and even obesity) leading to increased stresses.



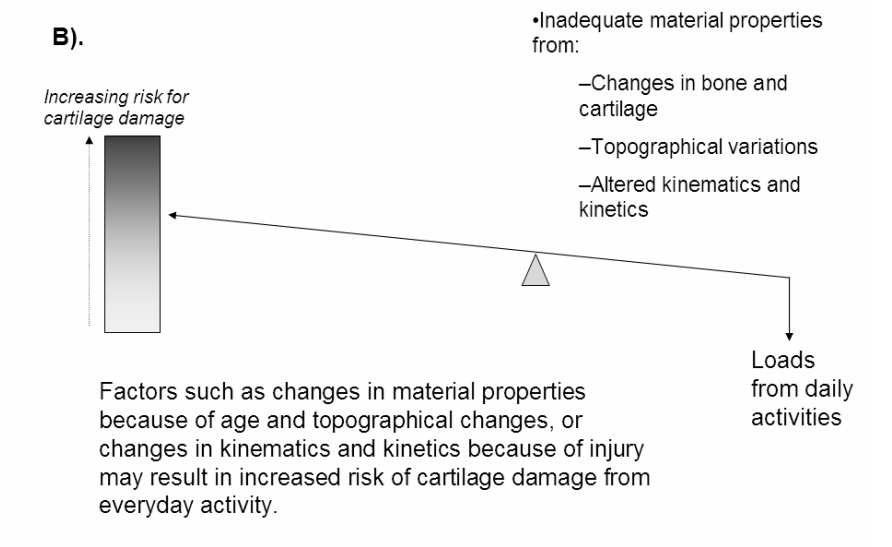


Figure 6.6 the schematic shows another proposed way in which the risk for cartilage damage may be increased. This is from more intrinsic causes of age-related changes, altered kinematics and kinetics, with no real change in the external loading conditions.

II). The fact that many activities of daily living exist that involve squatting, especially among Asians, where the incidence of knee osteoarthritis has been found to be generally higher, permits the data from the present study to have more relevance in studying the etiology of knee osteoarthritis. The moment curves obtained in the present study not only indicate increased joint moments in squatting by about three times larger than in level walking, but also a typical curve with two peaks indicating the two points before coming to rest when squatting and rising up after (Figure 6.7). The period or duration of rest between these peaks may be a significant period of concern. It may be hypothesized that long durations in the squat position may cause reduction in blood supply such that muscle activity involved in the rise-up from the squat may be altered. Another consideration is possible viscoelastic effects on the cartilage and bone material properties under continuous, almost static, loading over a period of time, as a result of resting in the squat position. A subsequent change in material response to load as a result of these effects should not be discounted.

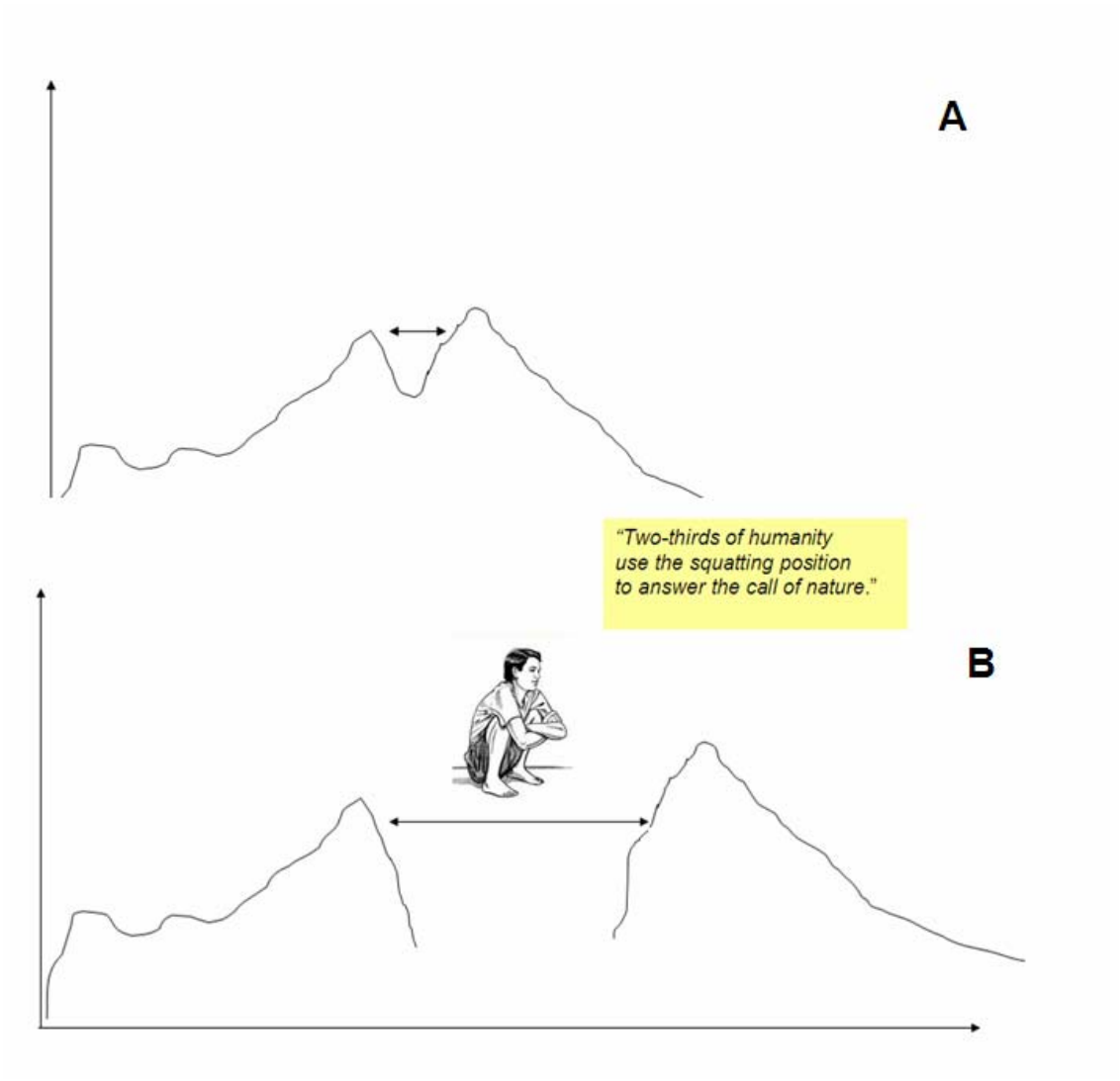


Figure 6.7 (A).The generalized moment curve for deep flexion (squat) is shown with a region indicated by the double arrow representing the time or duration the rest position is maintained. (B). The significance of this 'rest' region may be that in longer durations of rest in this position, some changes in the internal conditions may arise. This could be in altered blood supply, viscoelastic effects etc. But essentially it is hypothesized that the longer this period, the higher the risk that the loads experienced in getting up could be detrimental. (Drawing of squat position and quote from *yogaeverywhere.com*)

6.7 Future Directions

From the present study, several interesting questions arise that provide motivation for future work. These questions include the following: What are the effects of deep flexion on the blood supply to the musculoskeletal tissue relevant to the knee? What are the effects on mechanical properties of the weight-bearing structures in the knee when blood supply is affected? How do the variations in topographical properties (in the tibia) affect the load distribution in the opposing bone (femur)? Can shear stresses be accurately estimated from compressive stresses, and which of the two has more significance to causing cartilage and bone failure in the joint? Can the moments and forces derived from motion analysis be used as a means of predicting the risk of cartilage damage in relation to the etiology of osteoarthritis? Future work by the present author will hopefully try to answer some of these questions. Also to be included will be more comprehensive investigations involving several types of loading such as dynamic and impact loading, and the way cells respond to various stresses. More in-vivo cartilage studies such as that using MRI are also planned.

One of the important objectives for future work is also to expound on ways to study the biomechanical influences on the rate at which osteoarthritis (OA) is likely to develop, once damage or injury has occurred in the joint. From the information from the literature review in Chapter 2, and especially in view of the

combination of factors, both biomechanical and biological, involved in OA pathogenesis, it is important to distinguish the mechanical factors. To do this, the theory described in the earlier chapter (Chapter 2 and Figure 2.5) is complimented with a few more hypotheses, to form a larger picture on the objectives for a biomechanical approach to studying OA (Figure 6.8).

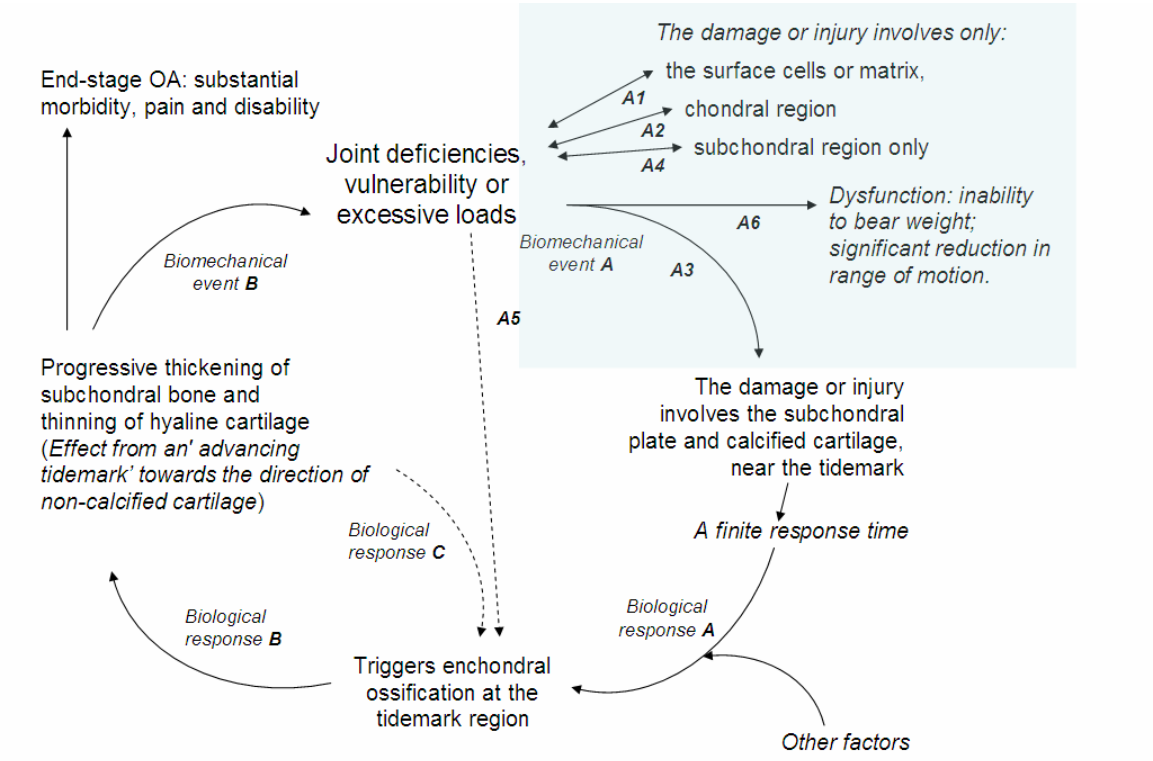


Figure 6.8. Showing the additional hypotheses (highlighted) in relation to the earlier figure 2.5. Biomechanical event A is hypothesised to consist of 6 variants. A1, A2 and A4 are processes that are not directly involved in the OA cycle as much as they are in contributing to further joint deficiency or vulnerability.

As discussed earlier, joint vulnerability or excessive loading is believed to create vulnerability to potential trauma that may trigger a series of events leading to OA [Felson DT 2004]. As such, a mechanical event is involved, which leads to some damage or triggers a response; this mechanical event is referred to in the figure (Figure 6.8) as Biomechanical event (A). Biomechanical event (A) is stipulated as having a possibility of six outcomes. One is the direct damage to the calcified cartilage near the tidemark that leads into the cycle for OA to develop and progress (A3). Another three outcomes (A1, A2 and A4) involve damage to regions other than the calcified cartilage near the tidemark. These three outcomes involve the cells or matrix, chondral or subchondral regions. Damage involved in one of these three outcomes results in all likelihood to a new level of joint deficiency or vulnerability. This new predisposition could lead to A3 type outcome and into the OA progression cycle or result in more A1, A2 or A4 type outcomes. Of course this biomechanical event could be to the extent where the joint becomes totally dysfunctional, as in a catastrophic fracture, in which the outcome is accordingly 'channelled-out' (A6) of the schematic (Figure 6.8). However this schematic does not imply that traumatic, immobilizing fractures in the long term do not lead to OA. On the contrary, it simply means that upon regaining some function (or even full function in a healed joint), the joint comes back to being defined as one with potential deficiencies or vulnerabilities. Thus, the joint is returned to the OA cycle with the probability of progressing in the cycle. An additional outcome (A5) shows the possibility of some mechanical

stimuli having a direct influence to trigger enchondral ossification, by-passing the need for damage to the calcified region near the tidemark. [Hulth A. 1993] Whether or not this type of event is likely or even possible requires more investigation, and in the present analysis the possibility of this event is not ruled out for the purpose of including a complete picture of the overall hypothesis. Biomechanical event (B) refers to the osteoarthritic-related changes in the mechanical properties of the cartilage and bone in the joint [Day JS et al 2004, Silver FH et al 2001] which could contribute to the rate of progression within the cycle of OA by increasing joint vulnerability.

In relation to both 'Biomechanical Events A and B' discussed earlier, there is a need for a biomechanical approach to study the OA problem, and in particular to address the issue of the ability of articular cartilage to safely support loads, especially in view of cartilage properties in relation to aging, injury, topographical variation, frequent repetitive loading, high impact loading, abnormal joint kinematics and lubrication properties.

CHAPTER 7: Conclusion

Referring back to the specific aims of this study (Chapter 3), the conclusions of this study are:

a. The peak moments in the tibiofemoral joint in stairclimbing were about three times larger than in level walking; and in deep flexion it was about two and a half times larger. The peak forces in the tibiofemoral joint during level walking reached about 3 times body weight, similar to those reported in previous studies. In stairclimbing peak compressive forces reached five times bodyweight, while significant peak horizontal reaction forces were about five times larger than in level walking. In deep knee flexion peak horizontal reaction forces on average were about two to three times larger.

b. In stairclimbing, and with anterior cruciate ligament deficiency, a gait adaptation to try to reduce the amount of quadriceps activity was observed in patients. This observation is believed to be a result of the knee flexion angle when peak external flexion moments occurred which was an angle about 40º.

c. The contact area in peak stresses in loaded cadaver knees was found to be as low as 1 cm^2, and in deep flexion, with the application of larger loads, the stresses are correspondingly larger.

The peak contact stresses in deep flexion were about 80% larger than that in level walking. Based on the current knowledge of the failure limits of cartilage, for deep knee flexion the factor of safety was close to one.

d. Both in deep knee flexion activity and stairclimbing with ACL deficiency, the tibiofemoral contact point is expected to be located towards the posterior periphery of the tibial plateau.
e. Compared to the articular cartilage not covered by the meniscus, the articular cartilage of the region beneath the meniscus in the posterior tibial plateau was significantly stiffer, thinner and had less dense subchondral bone.
f. The findings from the present study contribute to the explanations for two criteria on the mechanisms that can raise the risk for cartilage failure. One is the risk from significantly increased loads with reduced contact area. The other is a pathomechanical shift in the mechanical advantage of the joint as an adequate weight-bearing structure. This shift could be due to altered joint mechanics or changes in the material properties of the supporting structures.

The weight-bearing capabilities of the joint structures are generally expected to be adequate to withstand the loads from activities of daily living without damage. This is based on the force analyses, which indicate that in walking and deep

flexion, contact forces are not necessarily very large. However with abnormal loading patterns from joint instability, excessive stresses from significantly reduced contact area and the engagement of cartilage with significantly different material properties, the ability of the joint to weight-bear safely is expected to be compromised.

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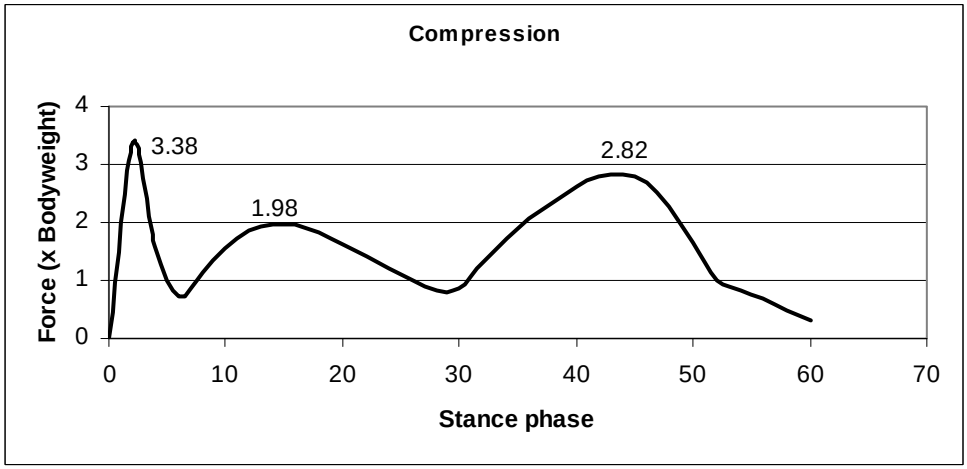
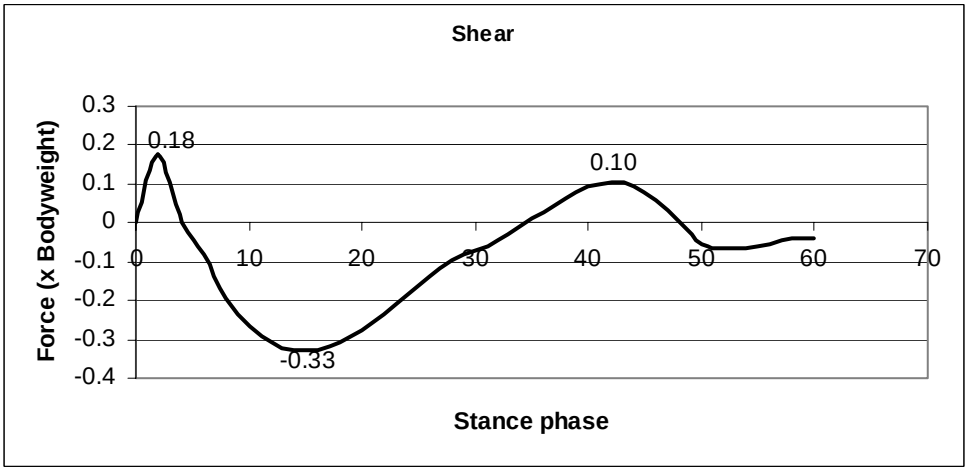
A. Relevant gait data of four subjects

9.1.1 Walking gait and forces data

SUBJECT 1: Weight(65kg); Height (165cm)

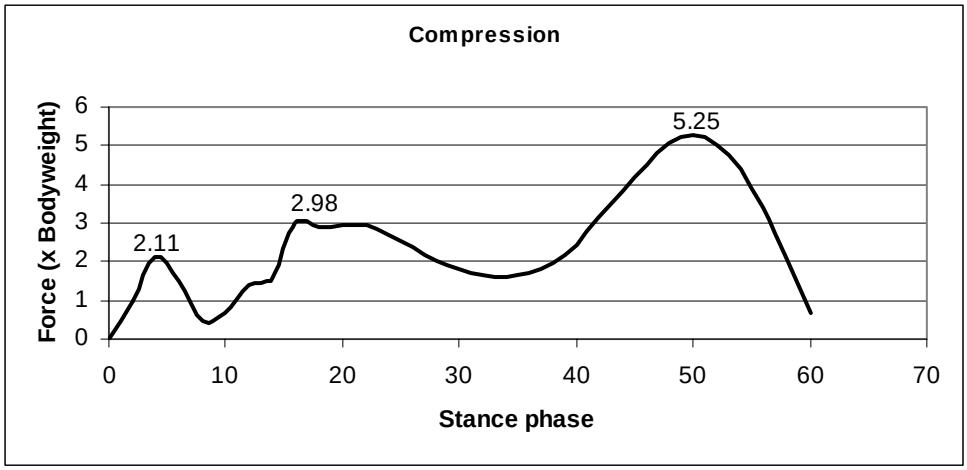
Figure A1. Calculated forces for Subject 1 in walking.

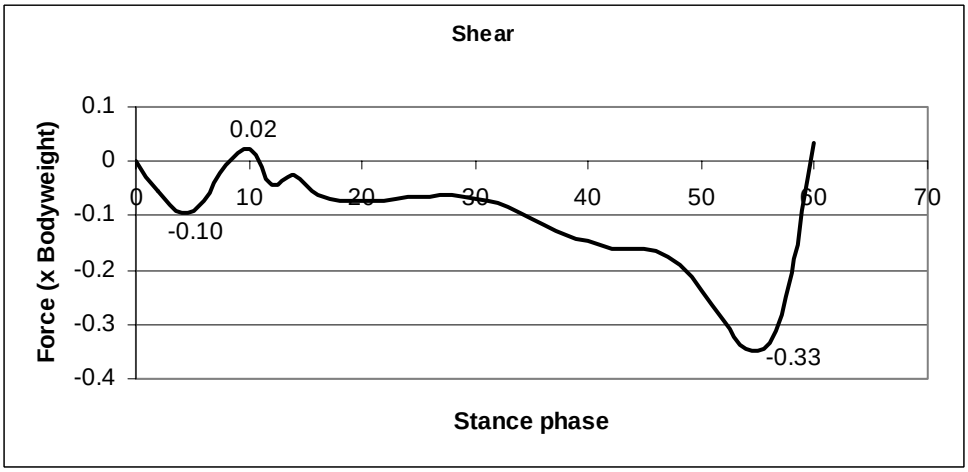




SUBJECT 2: Weight(75kg); Height (169cm)

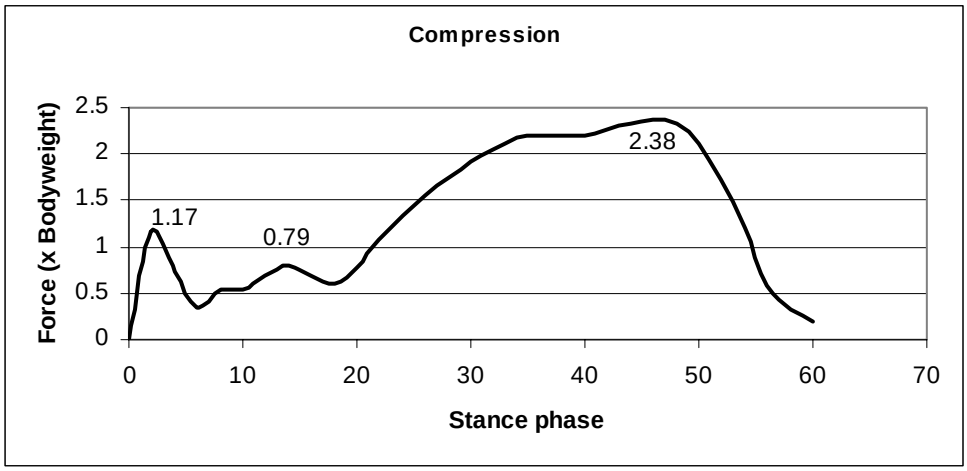
Figure A2. Calculated forces for Subject 2 in walking.

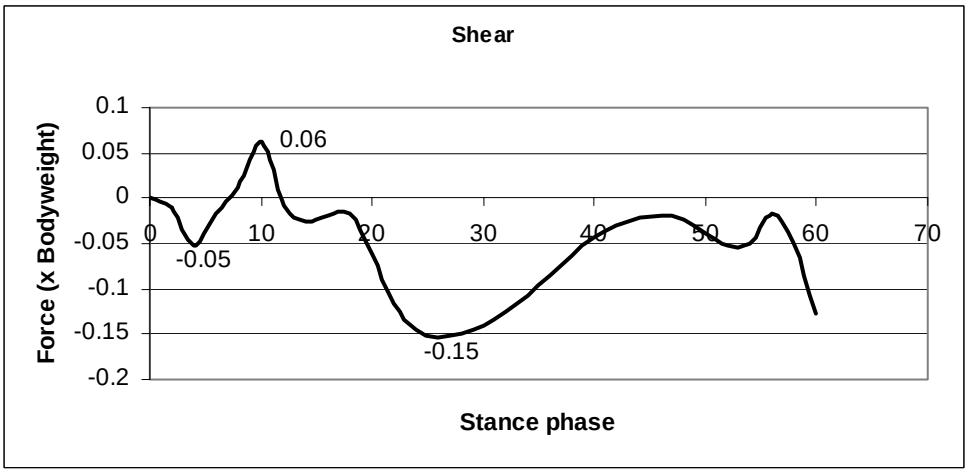




SUBJECT 3: Weight(44.5kg); Height (162cm)

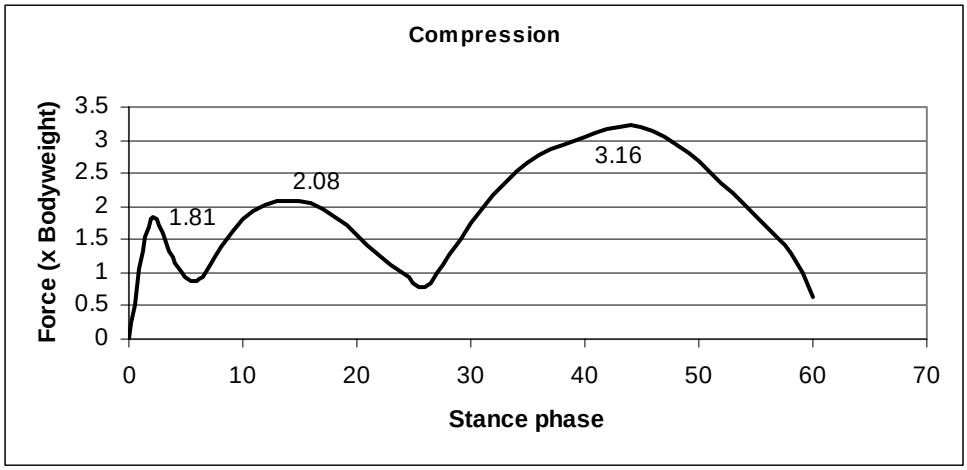
Figure A3. Calculated forces for Subject 3 in walking.

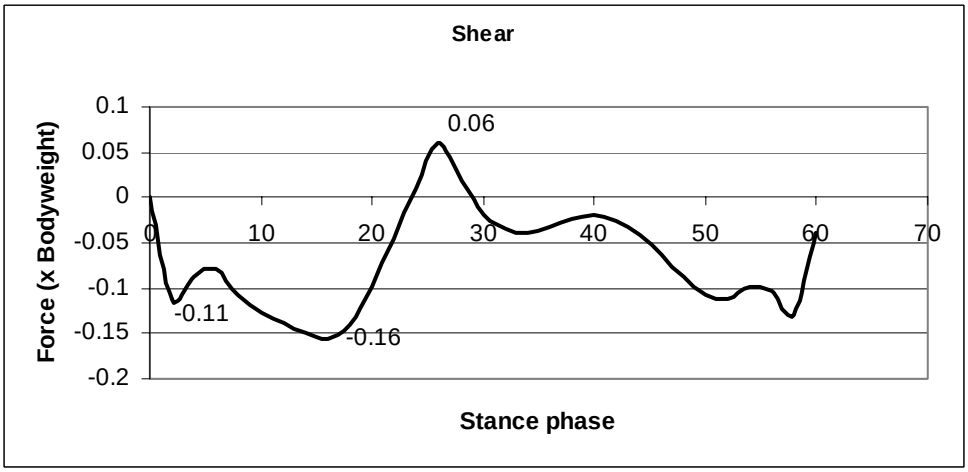




SUBJECT 4: Weight(61.6kg); Height (171cm)

Figure A4. Calculated forces for Subject 4 in walking.





9.1.2 Stairclimbing gait and forces data

Figure A5. External flexion/extension moments in stairclimbing for the six normal subjects studied.

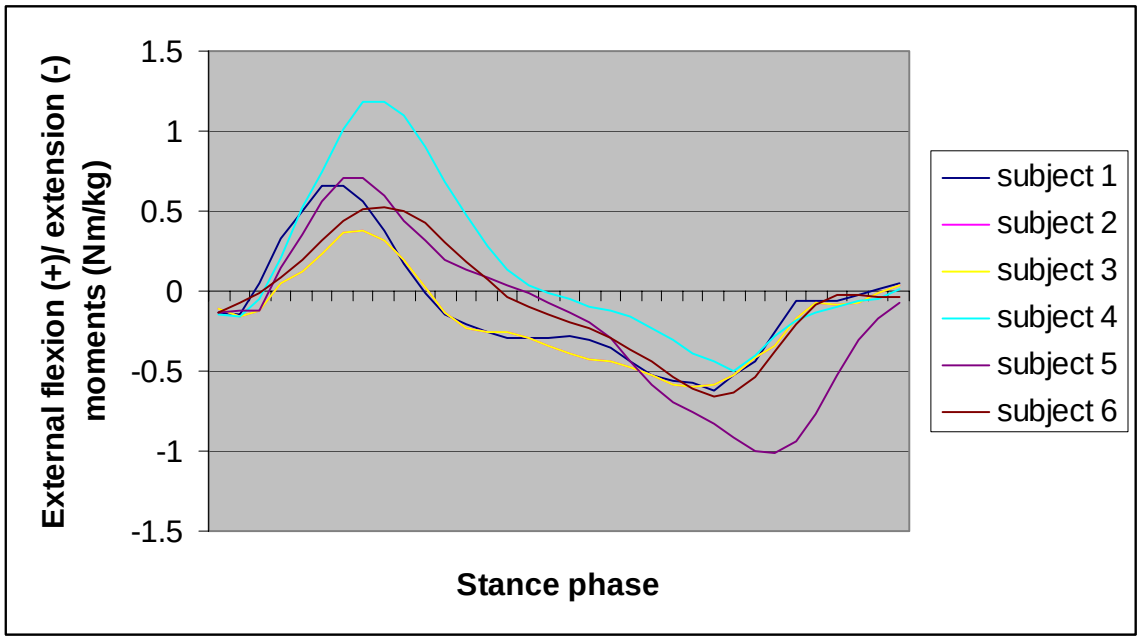


Figure A6. Tibiofemoral compressive forces for the six healthy subjects studied in stair climbing.

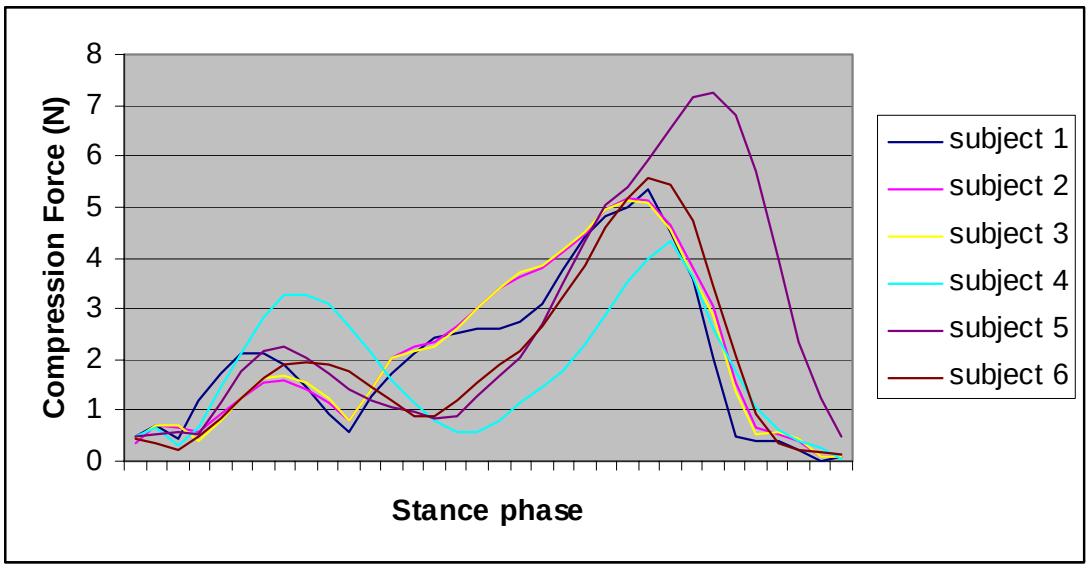
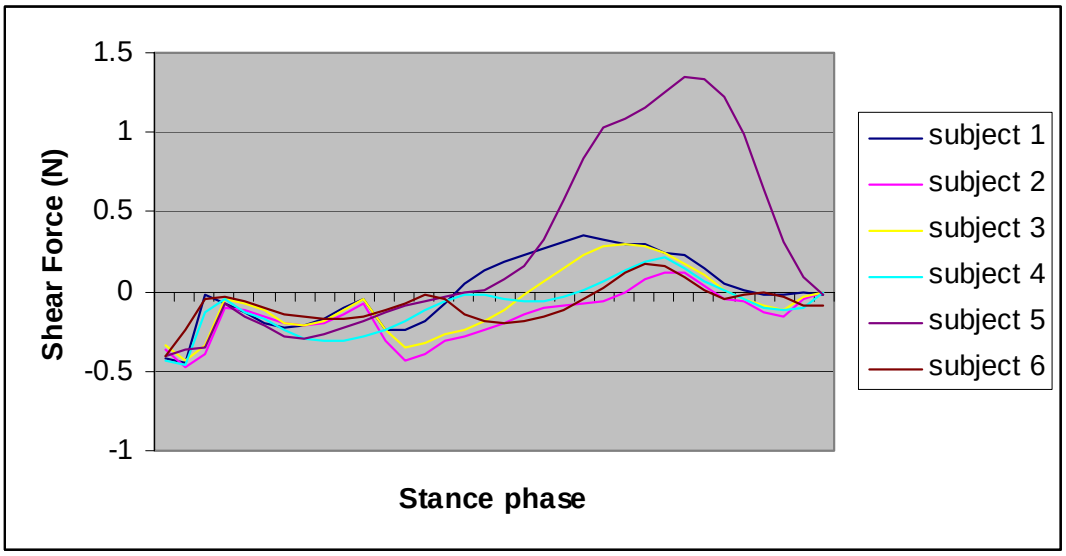


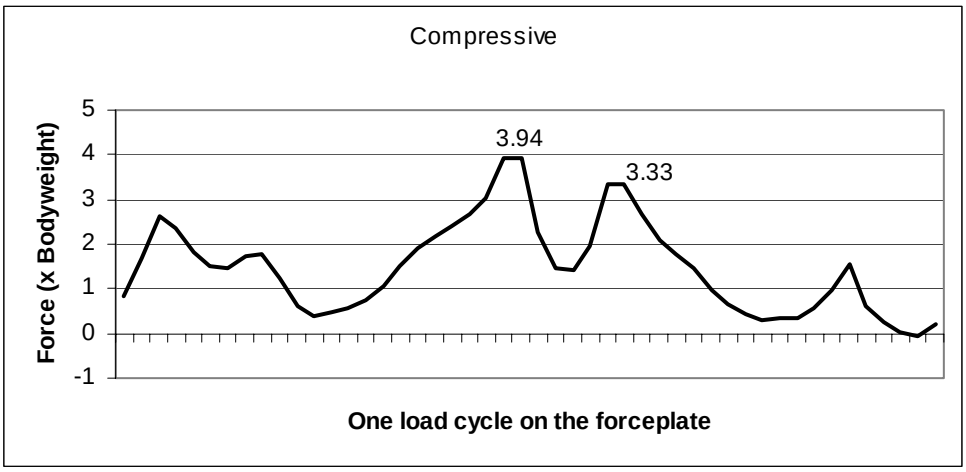
Figure A7. Tibiofemoral shear forces for the six healthy subjects studied in stair climbing.

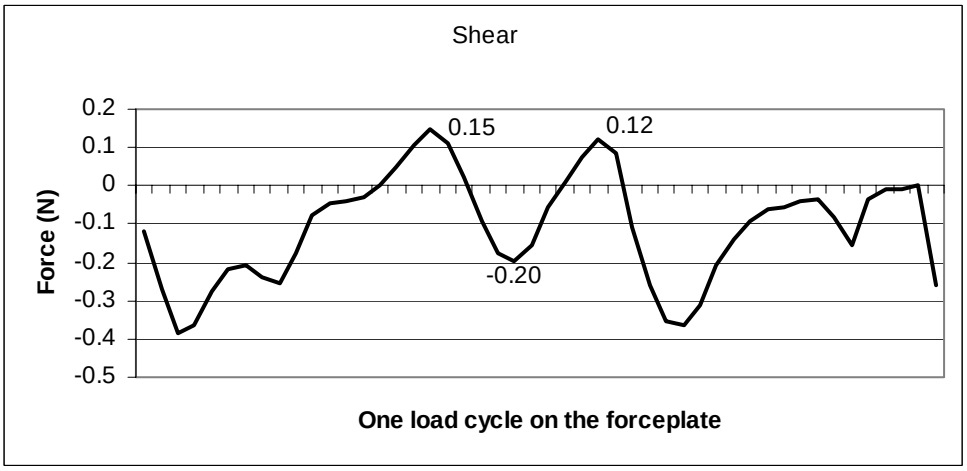


9.1.3 Squatting gait and forces data

SUBJECT 1: Weight(65kg); Height (165cm)

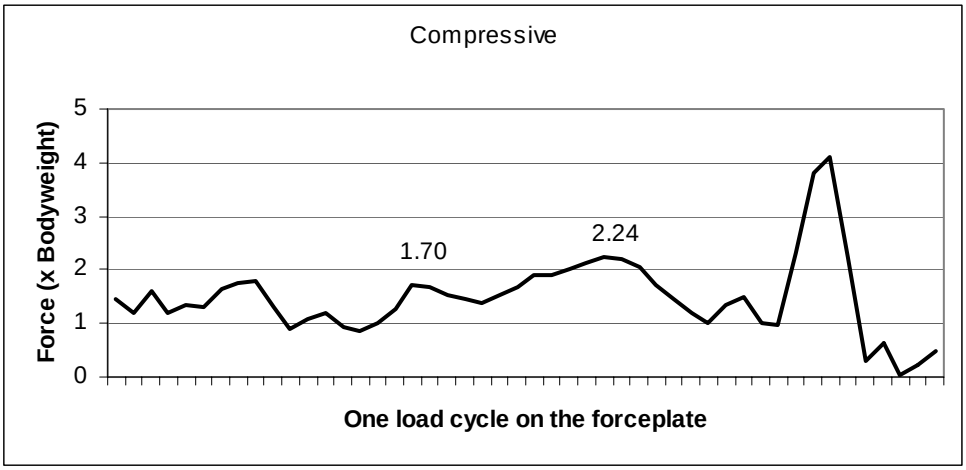
Figure A8. Calculated forces for subject 1 performing the deep flexion (squat) exercise.

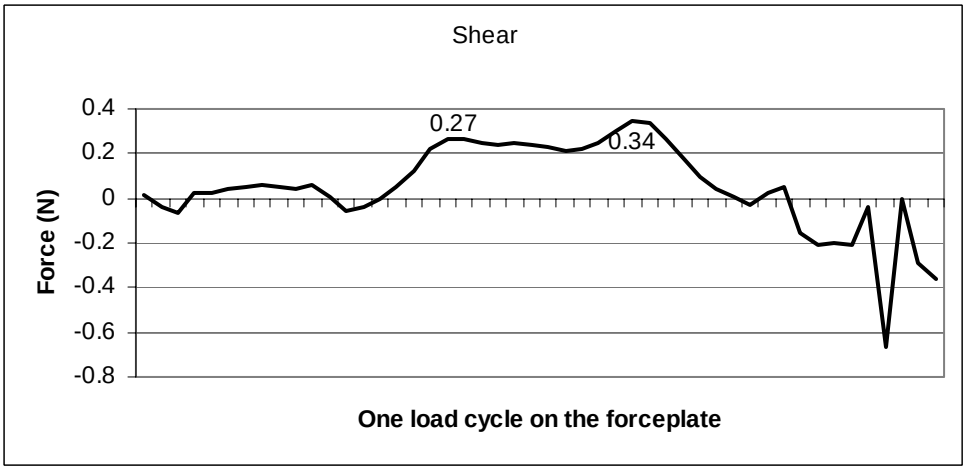




SUBJECT 2: Weight(75kg); Height (169cm)

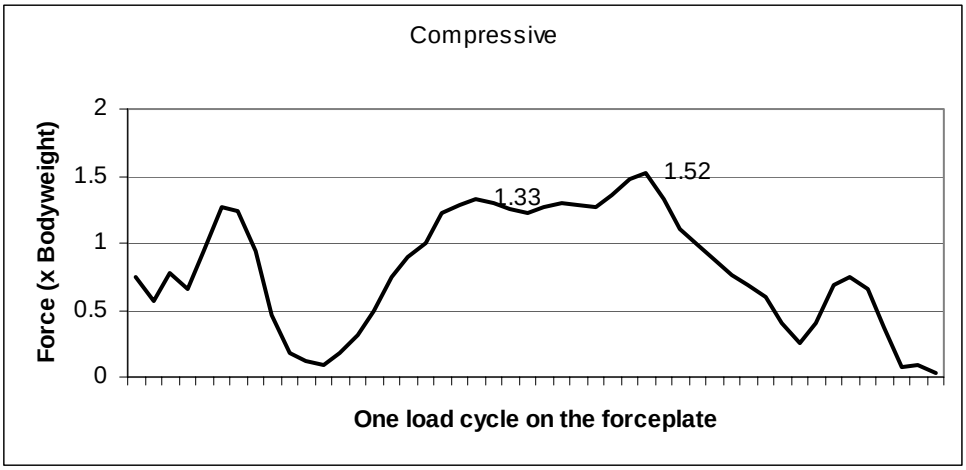
Figure A9. Calculated forces for Subject 2 performing the deep flexion (squat) exercise.

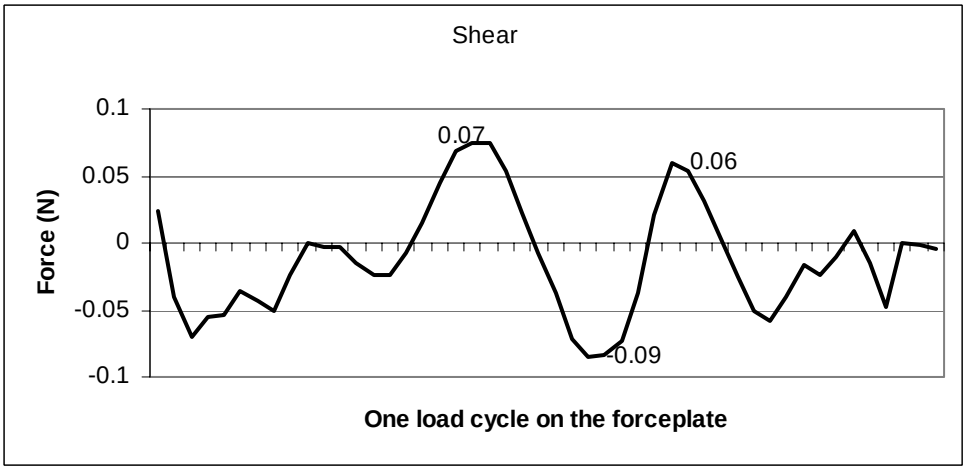




SUBJECT 3: Weight(44.5kg); Height (162cm)

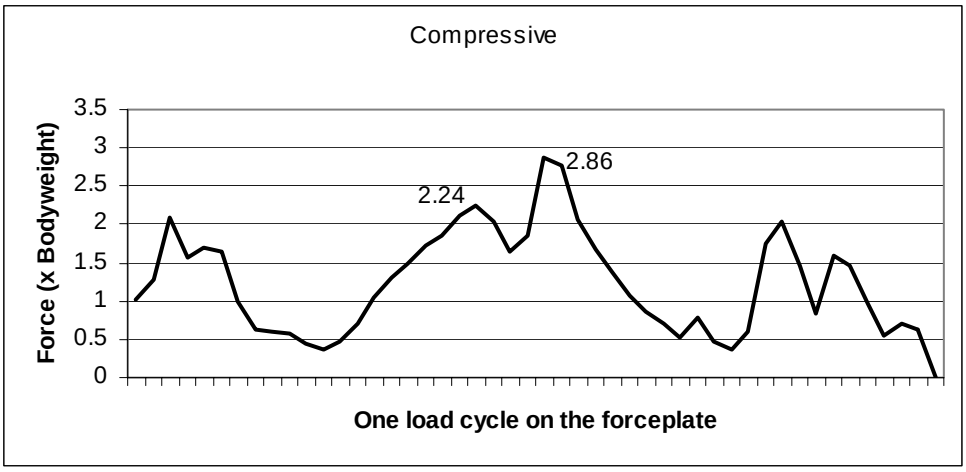
Figure A10. Calculated forces for subject 3 performing the deep flexion (squat) exercise.

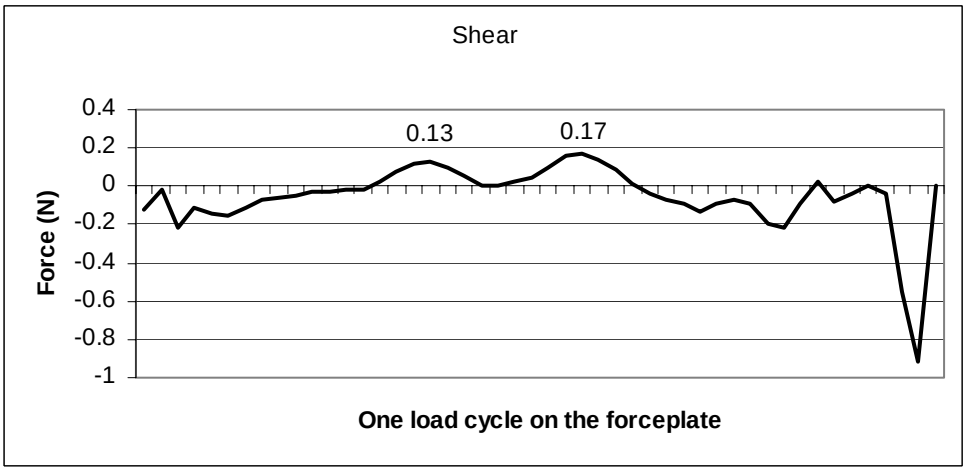




SUBJECT 4: Weight(61.6kg); Height (171cm)

Figure A11. Calculated forces for subject 4 performing the deep flexion (squat) exercise.





9.1.4 Speed and other gait data

Table B1. Relevant gait measurements for the 4 subjects

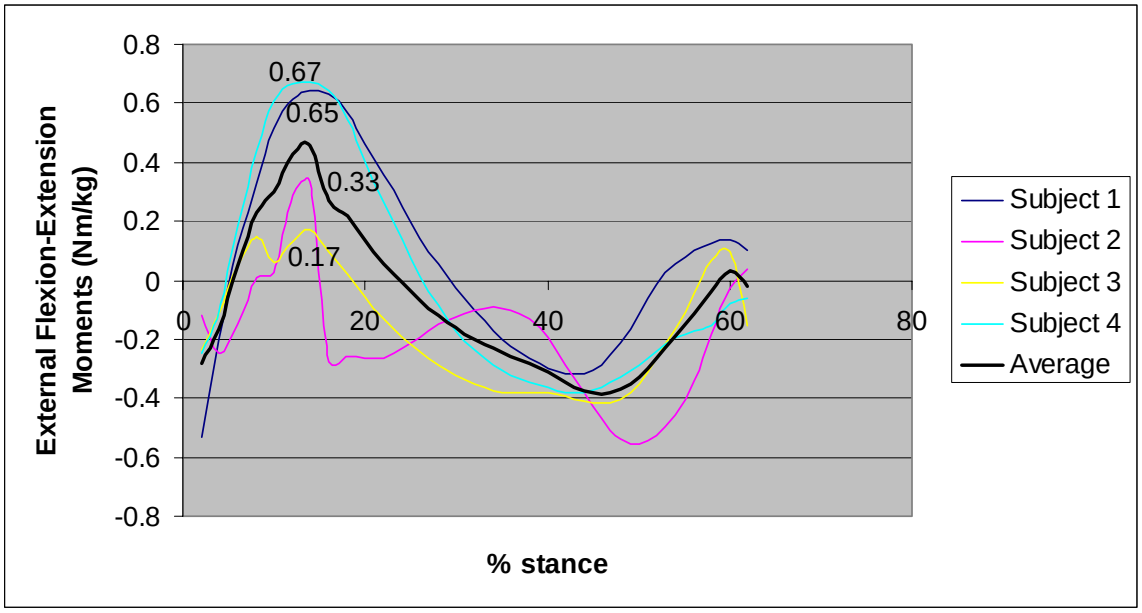
Parameters	Units	Subject 1	Subject 2	Subject 3	Subject 4
Cadence	steps/min	104.35	103.45	108.11	111.11
Stride Time	seconds	1.15	1.16	1.11	1.08
Step Time	seconds	0.58	0.57	0.58	0.55
Stride Length	metres	1.44	1.24	1.33	1.31
Step Length	metres	0.72	0.66	0.68	0.67
Walking Speed	metres per second	1.26	1.06	1.20	1.21

9.1.5 External flexion-extension moment data (Nm/kg)

Walking

Subject 1	Subject 2	Subject 3	Subject 4	Average
-0.53046	-0.12085	-0.23611	-0.24815	-0.28389
-0.19944	-0.24845	-0.11512	-0.10765	-0.16767
0.118056	-0.15099	0.047358	0.181241	0.048916
0.327724	0.011484	0.146667	0.436929	0.230701
0.517089	0.024651	0.062988	0.605212	0.302485
0.616401	0.285242	0.133492	0.664473	0.424902
0.64543	0.332527	0.172292	0.669995	0.455061
0.630989	-0.27736	0.093935	0.643928	0.272873
0.56481	-0.26151	0.018404	0.544888	0.216647
0.465128	-0.26235	-0.05454	0.404122	0.138089
0.356033	-0.26411	-0.13303	0.266123	0.056254
0.244973	-0.22834	-0.19366	0.134959	-0.01052
0.141913	-0.19379	-0.24351	0.016125	-0.06982
0.055506	-0.1483	-0.28779	-0.08702	-0.1169
-0.02448	-0.12489	-0.32366	-0.17025	-0.16082
-0.10202	-0.10302	-0.35281	-0.23567	-0.19838
-0.17179	-0.09207	-0.37576	-0.28968	-0.23232
-0.22372	-0.10402	-0.38172	-0.32519	-0.25866
-0.26447	-0.13362	-0.37889	-0.34723	-0.28105
-0.29954	-0.19392	-0.38169	-0.36228	-0.30936
-0.31967	-0.29047	-0.39505	-0.37828	-0.34587
-0.31839	-0.38298	-0.40849	-0.38144	-0.37283
-0.28691	-0.46998	-0.4178	-0.36226	-0.38424
-0.21296	-0.5382	-0.40526	-0.32747	-0.37097
-0.11347	-0.5576	-0.35077	-0.28597	-0.32695
-0.01641	-0.52371	-0.26669	-0.24064	-0.26186
0.056069	-0.45394	-0.165	-0.19536	-0.18956
0.102445	-0.33906	-0.04334	-0.17095	-0.11273
0.125256	-0.18454	0.065998	-0.1518	-0.03627
0.139586	-0.02608	0.097949	-0.07647	0.033745
0.102979	0.039827	-0.15665	-0.06391	-0.01944

Figure A12. showing the plots of external flexion moments at the knee during walking for the four subjects (subsequently studied in deep flexion squatting). The labels indicate peak external flexion moments.

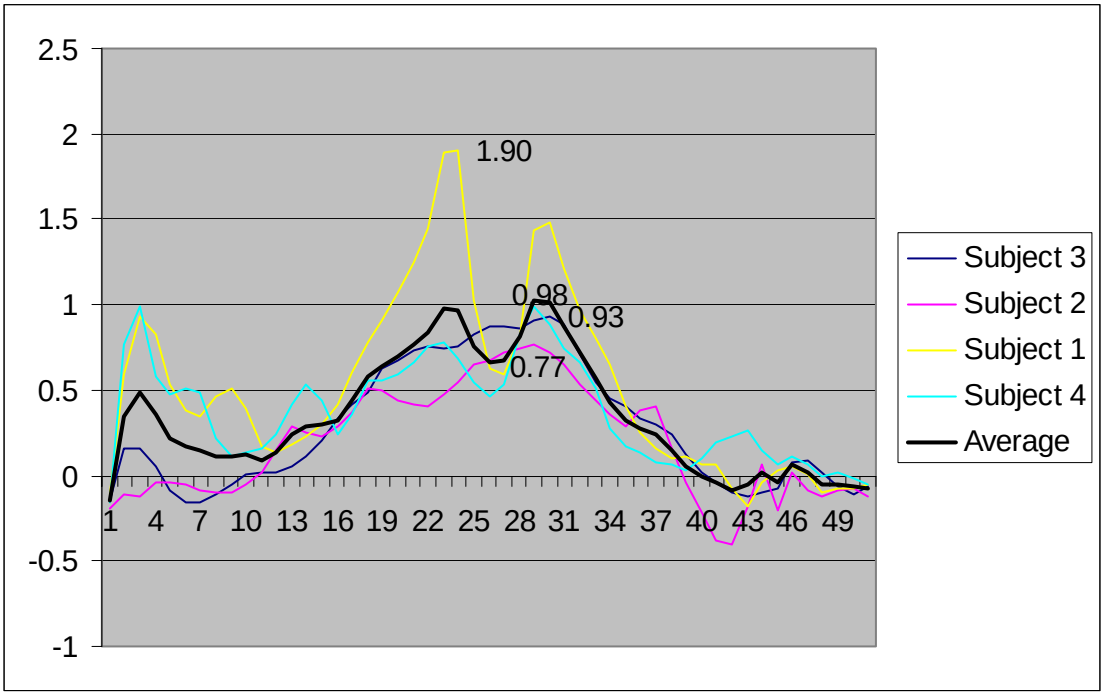


Deep flexion (Squatting)

Subject 1	Subject 2	Subject 3	Subject 4	Average
-0.10994	-0.18647	-0.14497	-0.15702	-0.1496
0.597545	-0.10863	0.155762	0.762232	0.351728
0.93646	-0.1245	0.156819	0.985555	0.488585
0.823068	-0.03544	0.048672	0.575812	0.353027
0.536064	-0.04005	-0.08168	0.469674	0.221002
0.378895	-0.04608	-0.15167	0.511437	0.173148
0.345276	-0.0879	-0.15257	0.491698	0.149126
0.463601	-0.10109	-0.11473	0.219813	0.116898
0.505185	-0.104	-0.04915	0.11653	0.117141
0.387773	-0.04829	0.009377	0.13736	0.121556
0.176152	0.014598	0.022291	0.157204	0.092561
0.136908	0.144235	0.019083	0.246316	0.136636
0.17843	0.292729	0.055718	0.419604	0.23662
0.232499	0.251785	0.11673	0.534832	0.283962
0.300089	0.231968	0.21047	0.437322	0.294962
0.421612	0.285862	0.338283	0.240119	0.321469
0.603372	0.364124	0.413532	0.358443	0.434868
0.778112	0.50521	0.483339	0.560813	0.581868
0.904888	0.492659	0.624826	0.554828	0.6443
1.069312	0.435258	0.674505	0.597381	0.694114
1.241857	0.413843	0.734465	0.659354	0.76238
1.445898	0.406662	0.751822	0.751928	0.839078
1.895456	0.474666	0.745955	0.782803	0.97472
1.900083	0.547316	0.755661	0.684776	0.971959
1.028179	0.652886	0.820295	0.544683	0.761511
0.629922	0.672438	0.8757	0.467631	0.661423
0.587486	0.717023	0.877264	0.537019	0.679698
0.813992	0.748393	0.863473	0.826292	0.813038
1.438465	0.769771	0.912991	0.984845	1.026518
1.487333	0.721057	0.934608	0.890205	1.008301
1.210124	0.651745	0.886774	0.744692	0.873334
0.965927	0.533113	0.709386	0.660633	0.717265
0.798255	0.438734	0.541012	0.515627	0.573407
0.644714	0.35455	0.456967	0.272059	0.432073
0.406553	0.291829	0.409264	0.168052	0.318925
0.249181	0.385361	0.34006	0.1346	0.2773
0.162453	0.407136	0.300769	0.082688	0.238261
0.106087	0.161882	0.244376	0.069323	0.145417

0.114473	-0.03533	0.118979	0.030082	0.057051
0.069105	-0.21141	0.023833	0.099445	-0.00476
0.059525	-0.38528	-0.04299	0.192162	-0.04415
-0.07273	-0.40814	-0.10338	0.231243	-0.08825
-0.18589	-0.18302	-0.1165	0.263153	-0.05556
-0.03465	0.063278	-0.10258	0.144258	0.017576
0.034406	-0.20897	-0.06947	0.066577	-0.04437
0.054096	0.019126	0.071424	0.115569	0.065054
0.002534	-0.08517	0.088466	0.070443	0.019067
-0.0949	-0.11964	0.019048	-0.00669	-0.05054
-0.07602	-0.08578	-0.06159	0.015423	-0.05199
-0.08073	-0.07599	-0.10516	-0.01553	-0.06935
-0.05039	-0.12521	-0.05783	-0.05456	-0.072

Figure A13. showing the plots of external flexion moments at the knee during deep flexion squatting. The plots also include an 'uncorrected' average plot. The corrected average plot is shown in the main text of the results section where the timing of the double peak is matched. One loading cycle refers to the time the subject steps on the forceplate, performs the deep flexion squat and then moves away.



9.1.6 Typical moment arms obtained: comparison between walking, stairclimbing and squatting

Figure A14.Typical PATELLA TENDON MOMENT ARM in relation to knee flexion angle (cm) for walking, stairclimbing and squatting

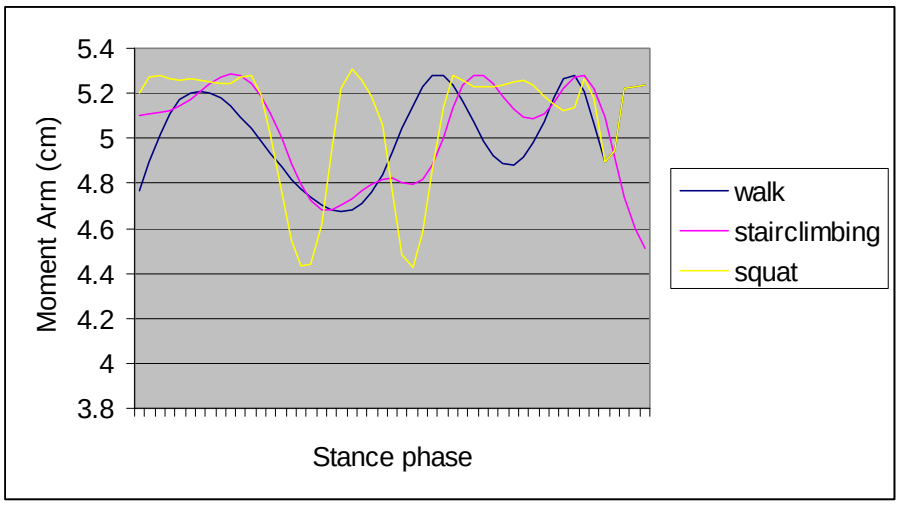
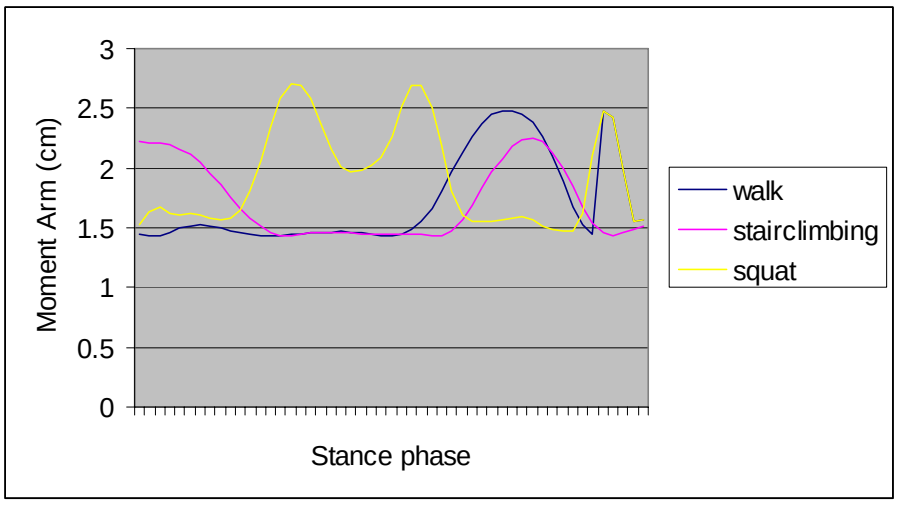


Figure A15. Typical HAMSTRINGS MOMENT ARM in relation to knee flexion angle (cm) for walking stairclimbing and squatting



B. Details on the loading apparatus and related instrumentation for the contact stress study

9.2.1 Knee loading jig

The apparatus to hold the cadaver knee while loaded was designed to facilitate positioning in all axes.

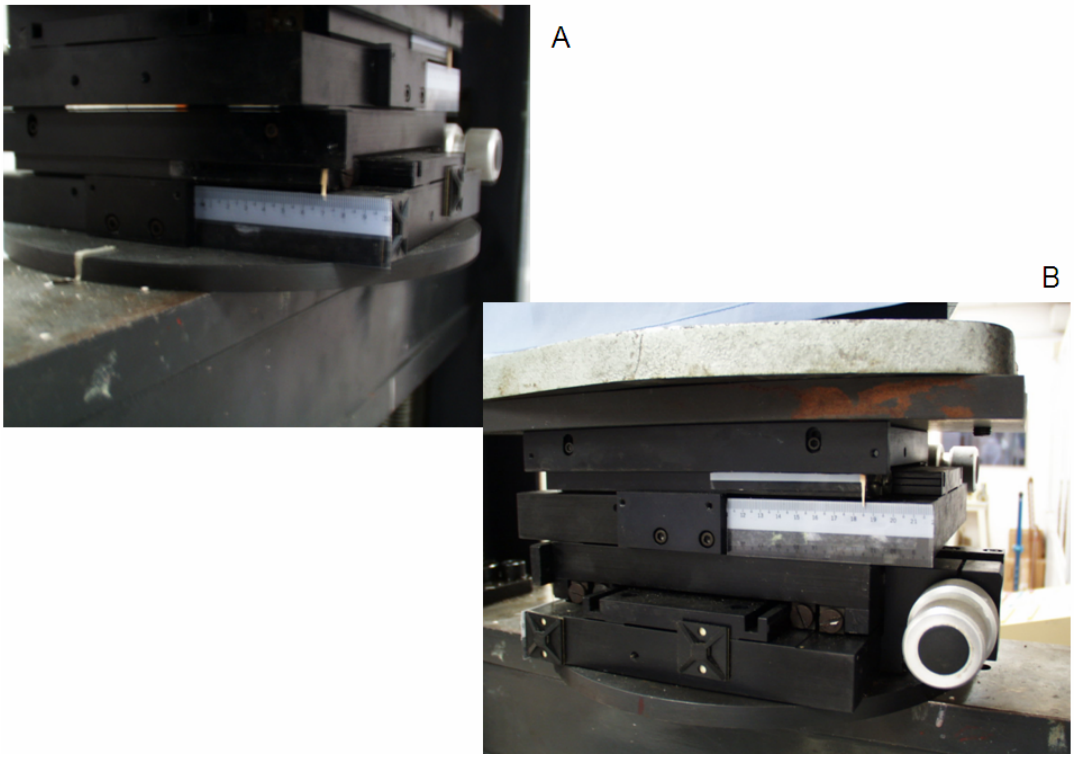


Figure B1. Sturdy X-Y tables were used to facilitate anterior-posterior (A) and medial lateral (B) positioning.

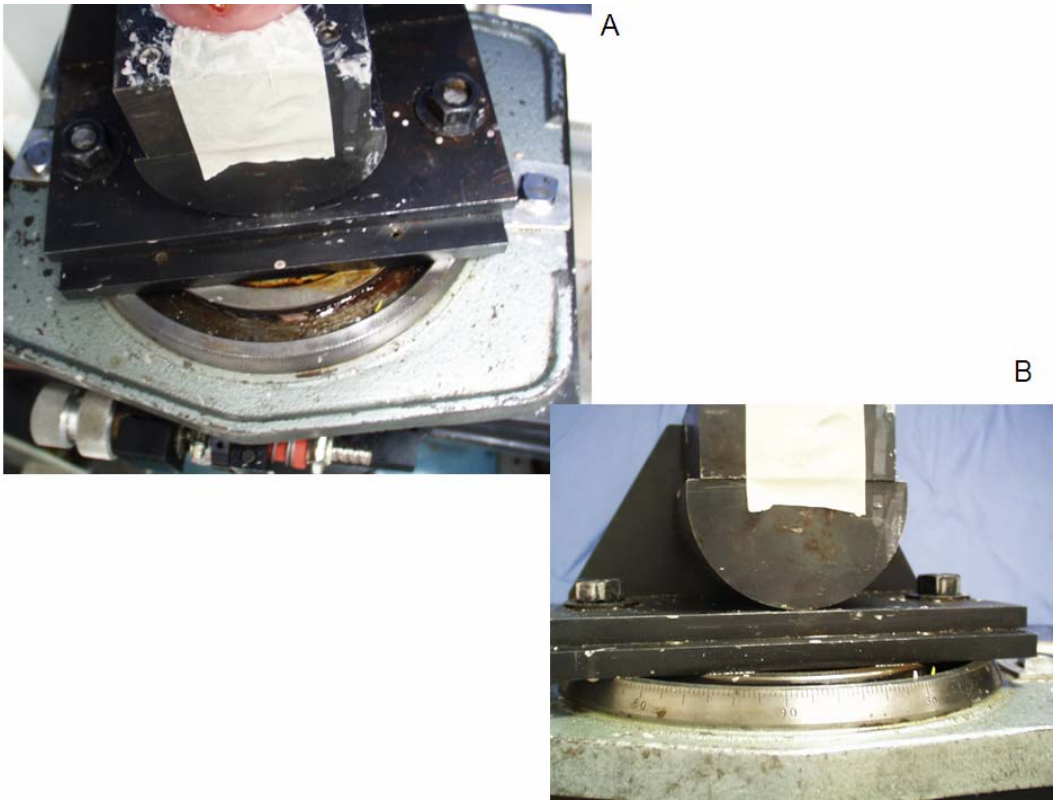
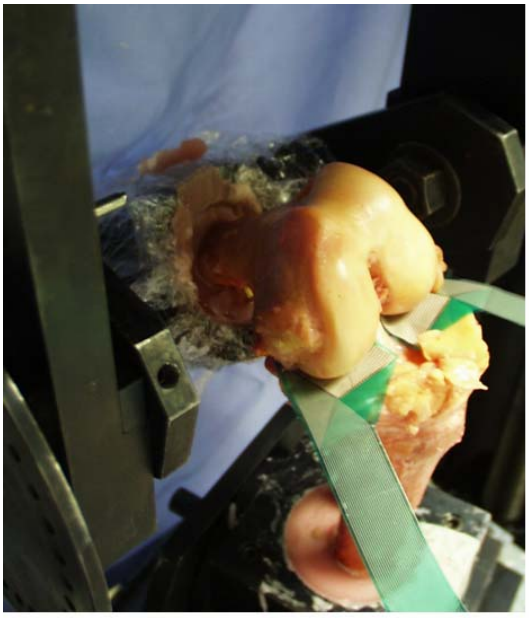
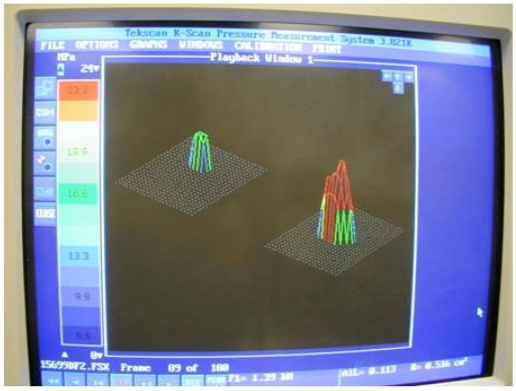


Figure B2. Rotating platforms and semi-circular bases with locking mechanisms to maintain position were used to achieve the desired internal-external rotation (A) and valgus-varus rotation (B).



A



B

Figure B3. The joint could be compressively loaded in deep flexion and with the k-scan pressure sensors inserted in the joint space, stresses are presented via the K-scan visual display.

9.2.3 Summary of pressure data collected.

Table B1. Contact area (mm2)

Specimen	**HS**	**SLS**	**TO**	**DF1**	**DF2**
1	125.00	202.48	117.73	150.54	130.60
2	87.99	131.02	77.54	131.46	162.04
3	101.61	140.00	77.54	78.65	150.86
4	127.02	197.58	113.60	101.45	136.19
5	131.25	202.48		114.75	168.27

Table B2. Peak Pressure (MPa)

Specimen	**HS**	**SLS**	**TO**	**DF1**	**DF2**
1	12.4	12.9	11.4	18.6	27.6
2	15.5	16.1	16.7	21.3	25.7
3	17.9	16	11	35.6	29.5
4	16.1	12.1	16.7	36	22.1
5	12	13.8		24.4	25.7

C. Moment graphs of anterior cruciate ligament deficient patients in stairclimbing

Figure C1 to C9 showing plots of external flexion-extension moments at the knee during stairclimbing for unilateral anterior cruciate ligament deficient patients. The plots are labeled as, C, the contralateral or uninvolved knee, and X, the involved deficient knee. Except for subject 4 and subject 6 (Figure D4 and Figure D6 respectively), all the plots indicate a relatively reduced peak external flexion moment in the involved knee.

Figure C1.

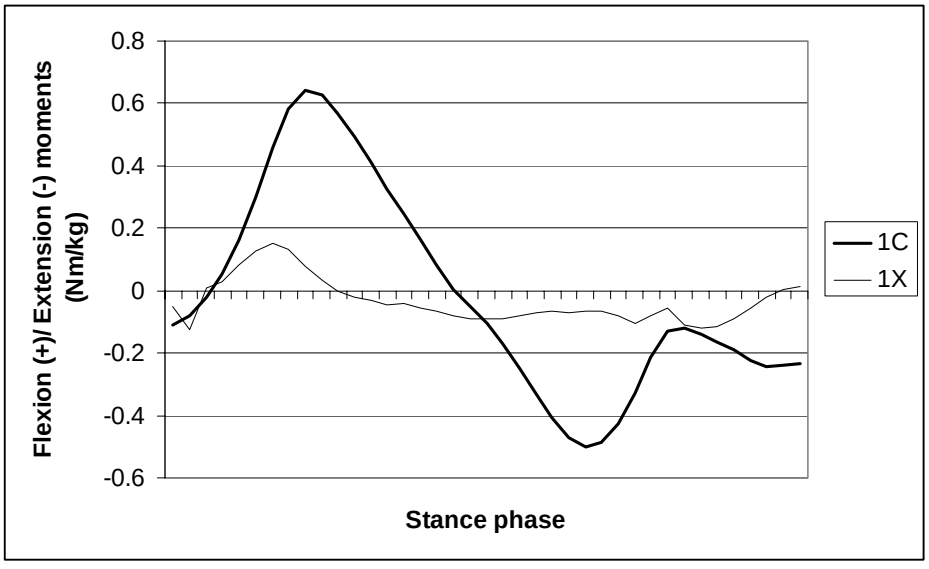


Figure C2.

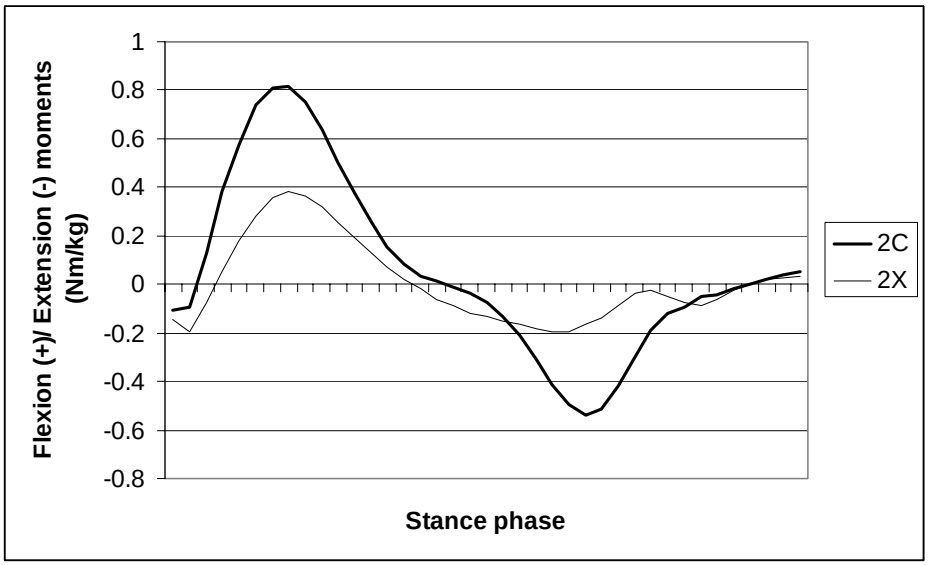


Figure C3.

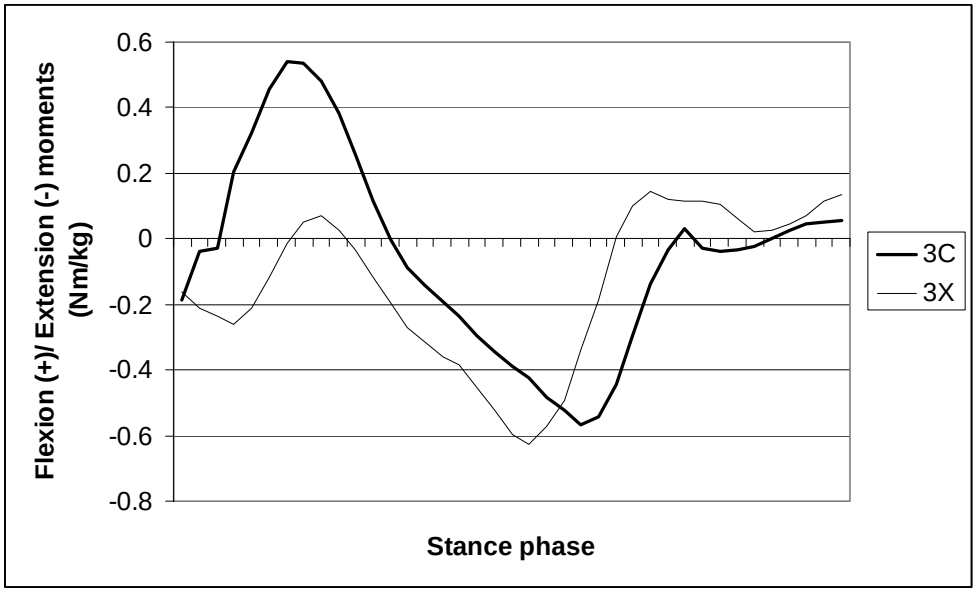


Figure C4.

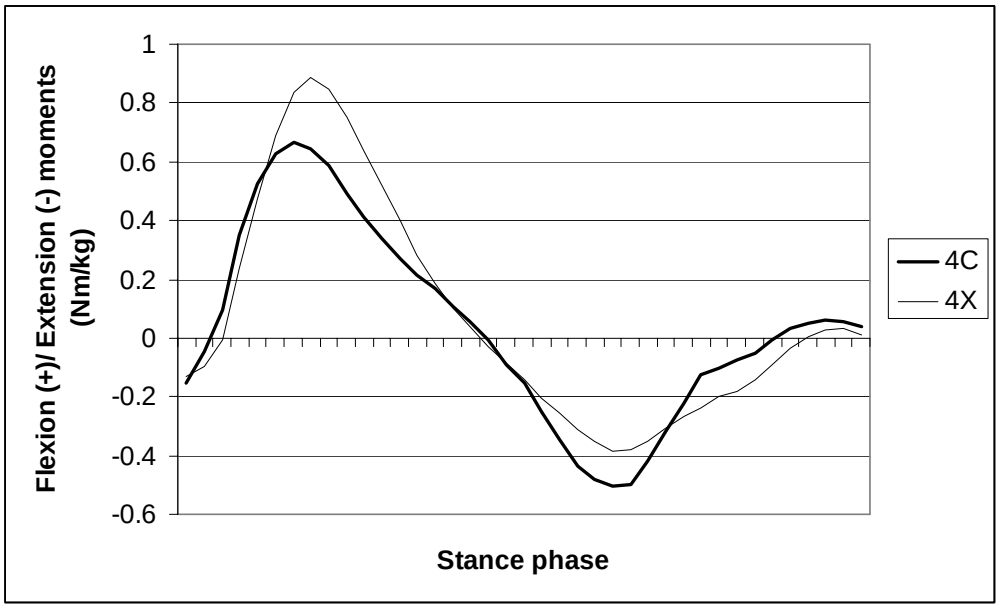


Figure C5.

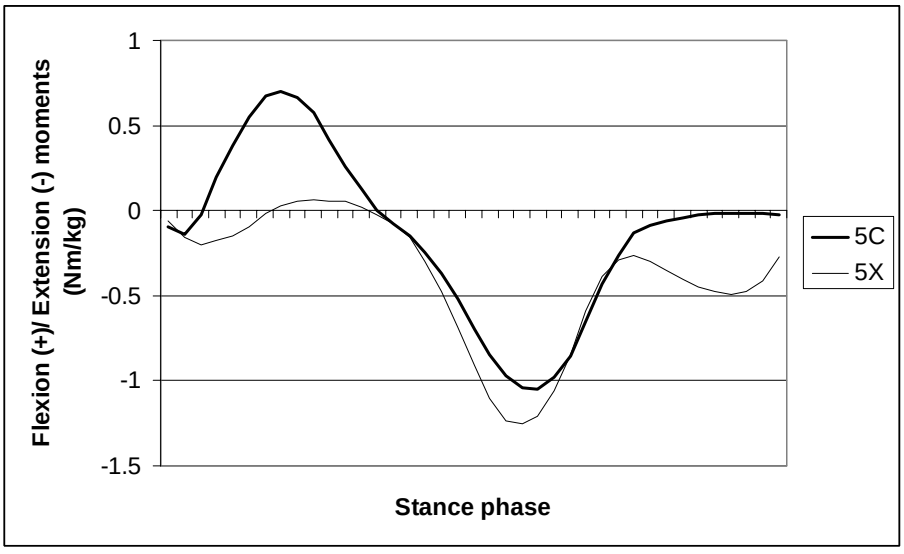


Figure C6.

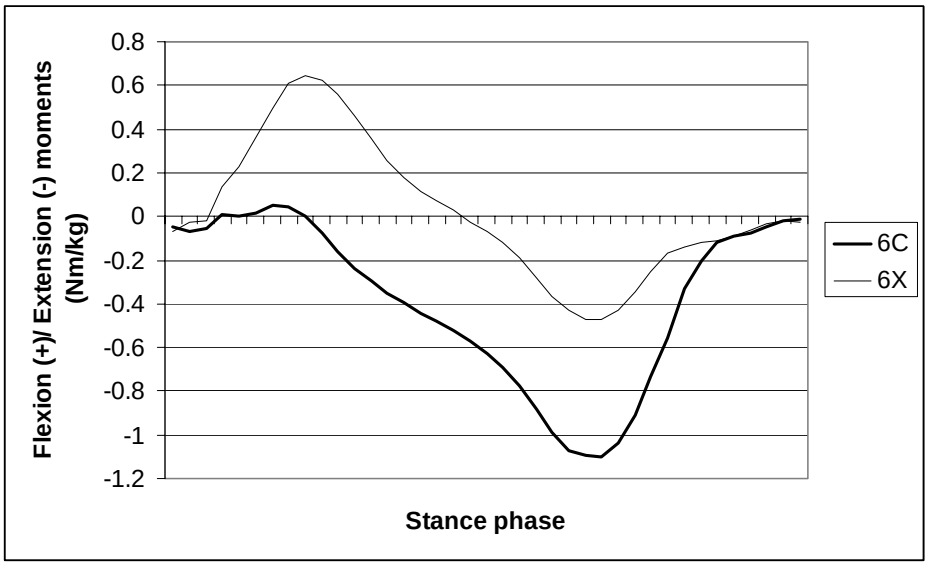


Figure C7.

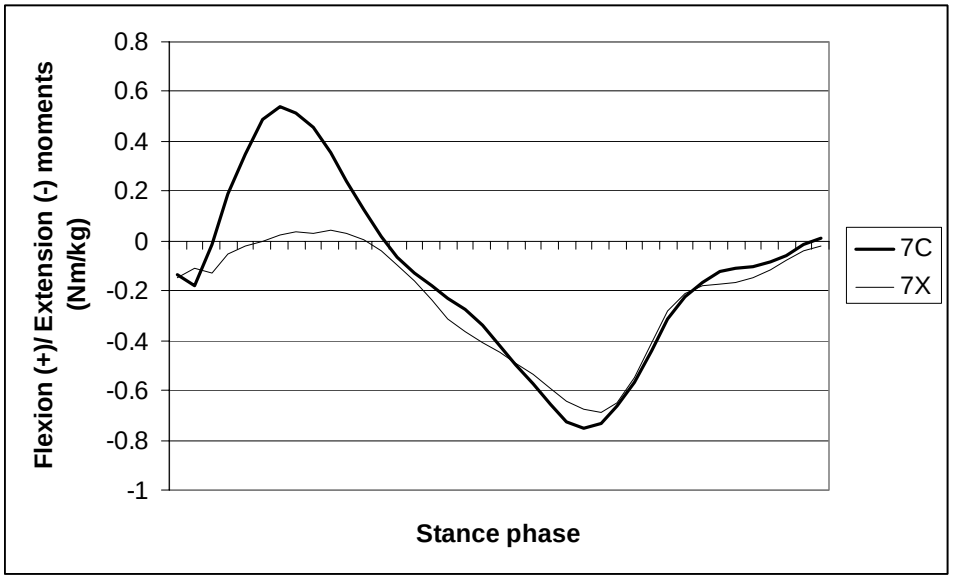


Figure C8.

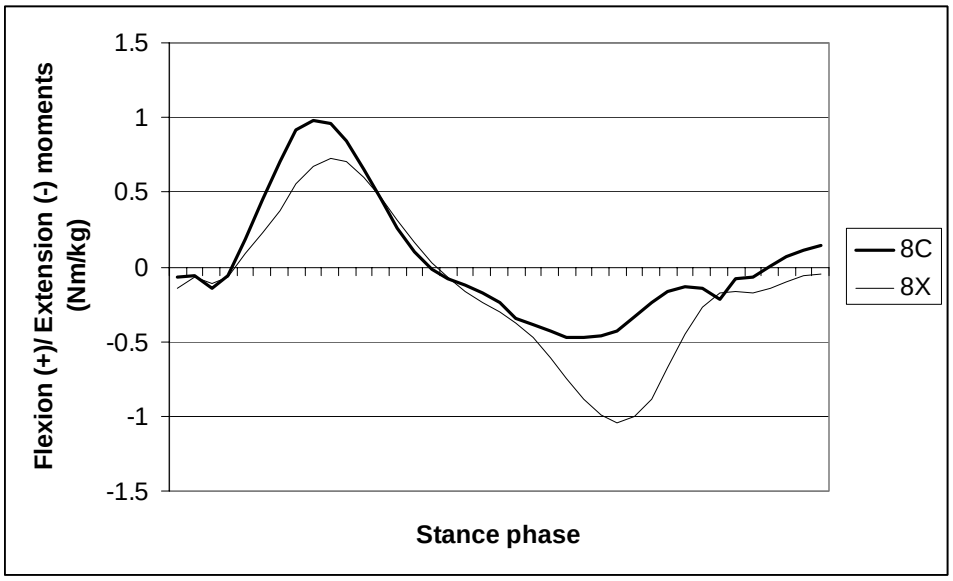
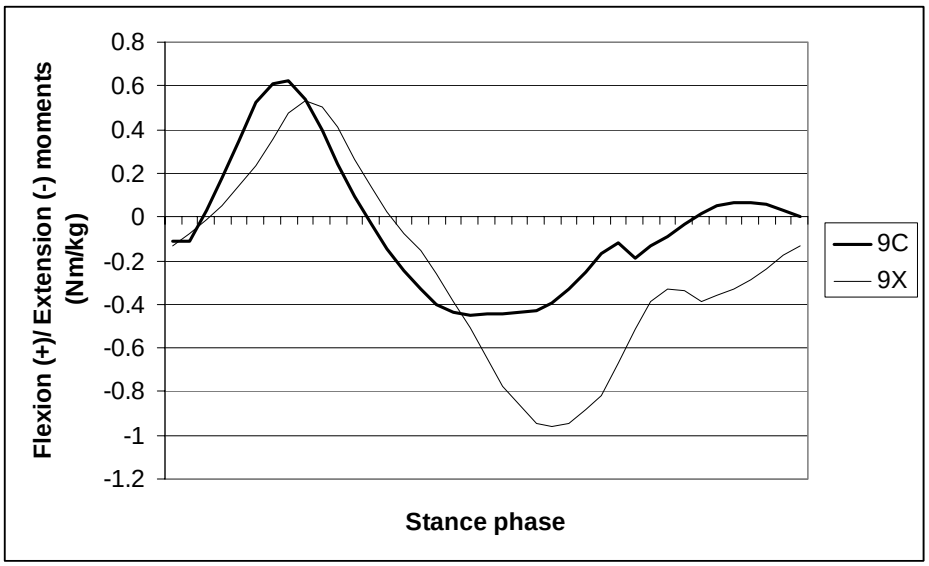


Figure C9.



D. Summary of data from the articular cartilage topographical variation study

9.4.1 Design of the indentation device

The following diagrams provide a schematic of the indentation apparatus used.

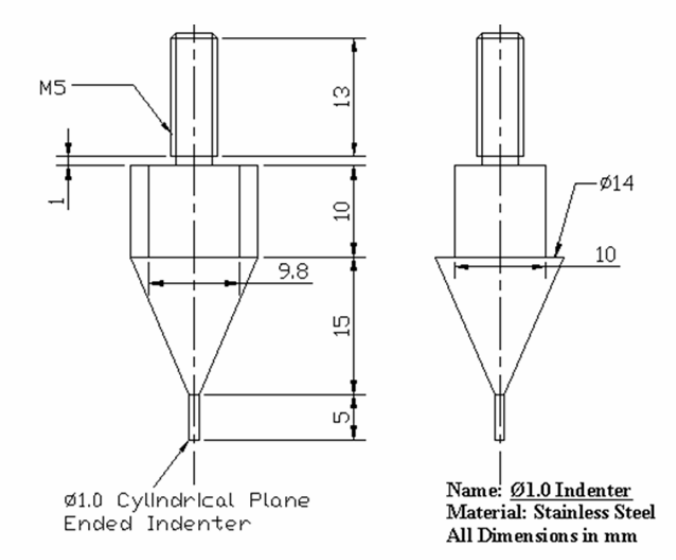


FIGURE D1. The design of the indenter used is shown here. With the application of 0.5N constant load the effective pressure on the cartilage is 0.6MPa which is adequate for assessment of the material properties yet non-destructive to the cartilage.

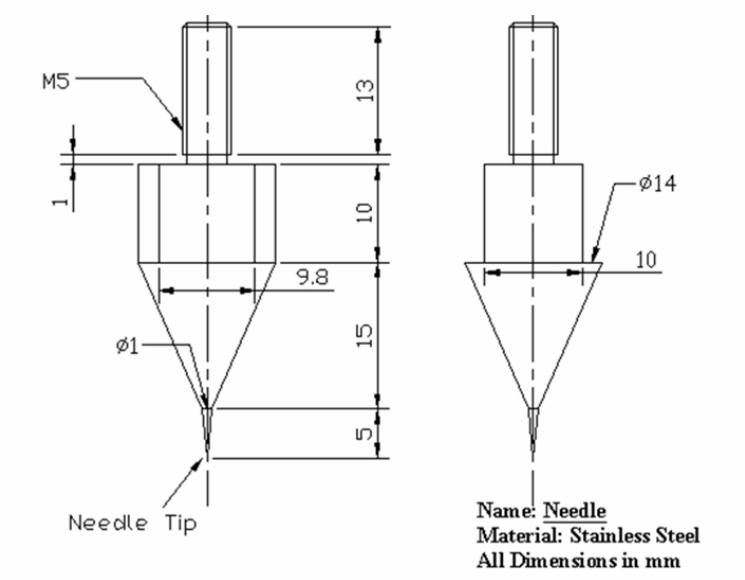


FIGURE D2. A needle indenter was used to measure the thickness of the cartilage. The needle pierces the cartilage and when it spikes against bone, the end point of its travel is represented as a sharp rise in force reading and the thickness noted.

9.4.2 Table of stiffness, modulus and creep measurements

TABLE D1. The averages and standard deviations of the values obtained from mechanical testing. Groups I and II represent articular cartilage that is not protected by the meniscus while Groups III and IV are articular cartilage that lies beneath the meniscus. Groups I and III are the lateral aspect of the tibial plateau while Groups II and IV are the medial.

(N = 7)		**Stiffness (N/mm)**	**Creep (mm)**	**Modulus (MPa)**	**Creep/Thickness (%)**
GROUP I (unprotected cartilage; lateral side)	Mean	4.87	0.17	2.13	4.34
	SD	3.75	0.05	0.74	1.39
GROUP II (unprotected cartilage; medial side)	Mean	10.99	0.11	3.51	2.79
	SD	4.67	0.05	1.42	1.20
GROUP III (protected cartilage; lateral side)	Mean	20.38	0.08	3.77	2.07
	SD	5.32	0.02	1.25	0.63
GROUP IV (protected cartilage; medial side)	Mean	20.08	0.07	5.13	1.82
	SD	5.76	0.02	1.91	0.60

9.4.3 P-values from comparison between groups

TABLE D2. The statistical comparison of measurements taken between sites (groups) is shown here in terms of P-values obtained from Wilcoxon Signed-Ranks tests. Significant difference* ($p<0.05$) is shown in the means of parameters across many group comparisons. There is significant difference in stiffness between all groups except groups III and IV which represent the lateral and medial sites beneath the meniscus.

Comparison of Groups / *Parameters studied*	**I vs II**	**I vs III**	**II vs IV**	**III vs IV**
Stiffness	0.028*	0.018*	0.018*	0.735
Creep	0.018*	0.018*	0.089	0.058
Modulus	0.018*	0.018*	0.063	0.028*
Creep/Thickness	0.018*	0.018*	0.091	0.176