

*IN-VITRO CHARACTERISATION OF
ARTICULAR CARTILAGE WITH
APPLICATION TO
HEMIARTHROPLASTY*

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This dissertation is submitted for the degree of Doctor of Philosophy

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ABSTRACT

Faculty of Engineering

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In-Vitro Characterisation of Articular Cartilage with Application to Hemiarthroplasty

by Maryam Imani Masouleh

Osteoarthritis (OA) is a common form of arthritis that causes joint degradation and affects one in five adults over 45 years of age in the UK. It is characterized by chronic and irreversible degeneration of articular cartilage (AC). Hemiarthroplasty (HA) is a surgical procedure, where the diseased cartilage on one side of the joint is replaced with an implant, while the other side remains intact. The main aim of this study is to analyse the mechanical and frictional response of different shoulder humeral component materials against the natural glenoid. This has been developed as a two-stage process. In a simple geometry HA model, the cartilage coefficient of friction, mechanics and wear have been examined in a pin-on-plate cartilage testing device. In the first stage of this study, friction and wear properties of four different grades of human osteoarthritic AC were measured using pin-on-disc technique against three major types of implant materials used in hemiarthroplasty including Cobalt-Chromium (Co-Cr), Ceramic (Al_2O_3) and Polycarbonate-urethane (PCU) polymer. Mechanical and frictional properties of the samples were characterised by compression, shear tests and surface roughness measurements using white light interferometry (WLI). Results indicated that at the same stage of OA, the cartilage tribological and mechanical properties deteriorated when using Co-Cr. The second stage of this study focuses on creating a more anatomically realistic model of the hemi-replaced shoulder joint and assesses the cartilage frictional behaviour for both healthy and enzymatically digested AC. A custom-made joint simulator has been built and has been used to investigate the response of shoulder joints under representative loads. The glenoid has been tested against different humeral component materials to understand the friction/wear response of the cartilage. The correlation between

enzymatically damaged and healthy cartilage has been investigated. Histological analysis will be performed on the tissue to observe any structural changes due to wear. The results from this study can aid the surgeons to choose the best possible material for hemiarthroplasty according to the disease state of the patient. In the joint simulation of HA, the cartilage coefficient of friction, surface roughness has been studied for both metal and ceramic humeral heads articulating against glenoid cartilage in a pendulum friction simulator. It was demonstrated that: 1) The coefficient of friction increased when metal implants were used compared to ceramic. 2) The COF was higher for enzymatically digested AC compared to healthy samples. 3) Ceramic heads produced lower surface roughness parameters compared to metal implant.

The methodologies and findings obtained in this thesis have opened a new line of research and can be adopted for related future studies; additionally, the anatomic pendulum friction natural joint simulation could be used for pre-clinical studies in less invasive procedures.

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LIST OF ABBREVIATIONS

AC	Articular Cartilage
ADL	Activities of daily living
ASTM	American Society for testing g and materials
AVN	Avascular necrosis
BS	British standard
BW	Body weight
HA	Hemiarthroplasty
COF	Coefficient of Friction
CoCr	Cobalt Chromium
COR	Center of rotation
ECM	Extra cellular matrix
FBS	Fetal bovine serum
FCD	Fixed charge density
FEA	Finite element analysis
GAG	Glycosaminoglycans
HA	Hyaluronic acid
HEPFIE _x	Hemi-endoprosthesis flexion extension
HFRR	High frequency reciprocating rig
ICRS	International cartilage repair society
ISO	International organization for standardization
MMP	Matrix Metalloproteinase
NBF	Natural buffer formalin
NSAIDS	Non-Steroidal anti-inflammatory drugs
OA	Osteoarthritis
PBS	Phosphate buffer solution
PCU	Polycarbonate-urethane
PG	Proteoglycans

PMMA	Poly methyl methacrylate
RC	Rotator cuff arthroplasty
RA	Rheumatoid arthritis
ROM	Range of motion
SAL	Surface amorphous layer
SZP	Superficial zone protein
SF	Synovial fluid
TB	Toluidine blue
TSA	Total shoulder arthroplasty
RSA	Reversed shoulder arthroplasty
UHMWPE	Ultra-high molecular weight polyethylene
WLI	White light interferometry

LIST OF NOMENCLATURE

μ	Coefficient of friction
F	Vertical force
N	Normal force
E	Young's modulus
I	Second moment of area
y	Surface of neutral axis
M	Bending moment
M_{friction}	Frictional bending moment
M_{direct}	Direct bending moment
L_s	Distance from the contact point
P	Frictional force
θ	Angle of the main arm
$\epsilon_{\text{friction}}$	Frictional strain
$\epsilon_{\text{measured}}$	Measured strain
ϵ_{direct}	Direct strain
σ	stress
σ_{direct}	Direct stress
α	Range of motion angle
r	Radius from COR to contact point
v	Voltage
R	Resistance
R_a	Average roughness
R_q	Root mean square (RMS) roughness
R_z	Average maximum height
R_t	Maximum surface height
S_{sk}	Surface Skewness
S_{ku}	Surface Kurtosis

1 INTRODUCTION

1.1 Project background

The diarthrodial synovial joint is the most common type of joint in the human body and it is particularly essential for the study of human movement. Synovial joints are characterised by a small space between the bones called the joint cavity, and the ends of the bones of this joint are covered with a soft tissue called the articular cartilage (AC) (Karen, 2015). The AC has remarkable lubricating and biomechanical properties, and this provides a surface with a low coefficient of friction (COF), allowing smooth motion and protecting the joints from abrasive wear (Pearle et al., 2005). Moreover, the AC has the ability to absorb stress, spread the load, and reduce stress at any contact points (Mow et al., 1992; Rieppo et al., 2003a).

Although cartilage survives for the lifetime of a person, factors such as obesity, joint injury, genetics, excessive stress and anatomical abnormalities can promote cartilage degeneration and cause joint diseases such as osteoarthritis (OA) (Gersing et al., 2016). OA affects up to 15% of the adult population, the majority of which are over 65 years old (Felson and Zhang, 1998; Guccione et al., 1994). OA causes the tissue to change structure and composition, leading to changes in tribological and mechanical performance, which eventually leads to AC wear and joint degeneration.

At present, there is no simple test for the early diagnosis of OA and, usually, by the time a definite diagnosis is made using imaging techniques, the disease is in its advanced stages. Hence, one of the biggest challenges until now has been the early diagnosis of OA. Knowledge of OA progression requires a comprehensive understanding of the mechanics and structure of cartilage. The mechanism and initiation of cartilage breakdown remain unknown; however, it is thought that the mechanical environment plays an important role, causing structural and biochemical changes in tissue.

Currently, there are three ways of managing OA: non-pharmacological, pharmacological and surgical. Joint replacement surgery is usually recommended if the patient has severe pain or mobility issues. Hemiarthroplasty (HA) is a surgical technique where only one side of the joint is replaced by an implant. This procedure results in less surgical time and allows for early weight bearing and recovery when compared to total arthroplasty. HA has gained importance in the last few decades due to the development of new biomaterials. In the clinical routine, the material used for HA surfaces includes the long-

standing cobalt-chromium (CoCr) alloy, various ceramics such as zirconium (ZrO₂) and aluminium oxide (Al₂O₃), and polymers such as polycarbonate urethane (PCU). Cartilage wear after HA remains a problem in orthopaedic surgery. The main cause of cartilage wear, is generally considered to be the tribology of the material surface (Jung et al., 2008). Hence, there is an urgent need to reduce the complications associated with the tribological behaviour of biomaterials in contact with cartilage in an attempt to increase implant longevity. HA is the most common treatment for hip fractures and is used in 20–45% of all shoulder joint replacements. However, the use of HA in the shoulder is very controversial, as reflected in the significant variation in usage. There are strong regional preferences for the alternative procedures despite the significant problems of these options. Due to a lack of understanding of the factors affecting cartilage wear, the clinical outcome of the HA procedure is unreliable, and the procedure is in decline (Boese et al., 2015; Morsi et al., 2016).

HA needs to be able to function in the presence of tissue affected by OA and a key factor in determining the longevity of this type of reconstruction is the tribological properties of the material in the OA environment. The tribology of HA biomaterials in the various OA environments has never been investigated before and there is a lack of knowledge regarding the tribology of these materials in the HA joints. Moreover, since there are different stages of OA, it is necessary to consider the performance of these biomaterials against various grades of OA and indicate when a revision to total arthroplasty is required.

Most in vitro studies have been carried out to investigate the friction and wear response of cartilage against biomaterials in a pin-on-plate experimental set-up. However, to date, studies that have investigated the tribological response of cartilage against biomaterials with the use of natural joint simulation are limited. Therefore, with these considerations in mind, in the first stage, (which consists of tests performed in collaboration with a previous PhD student) this thesis investigates the tribological behaviour of biomaterial-cartilage contact in HA in order to improve the reliability and long-term performance of this procedure. As part of this project, a joint simulator will be developed, which will enable the investigation of the behaviour of both OA-like and healthy joints at a larger scale, with the joint subjected to physiological loading in a lubricated environment. This can ultimately allow the exploration of the biomaterials' performance in terms of their size and shape. In the second stage, a joint simulator will be developed, which will enable

the investigation of the behaviour of both OA-like and healthy joints at a larger scale, with the joint subjected to physiological shoulder loading in a lubricated environment. This can ultimately allow the exploration of the biomaterials' performance in terms of their size and shape.

1.1 Research objectives

Over the past decade, the study of the mechanical properties of the AC using various techniques, such as experimental, numerical or analytical, has started drawing much attention in the scientific literature. However, it is evident that the mechanical, tribological and wear properties of the AC are not completely understood. Moreover, intensive research studies are required to understand the tissue degeneration mechanism. In this thesis, the reader will appreciate the overall practical scope of this study, aimed at providing insight for future clinical contribution to early surgical intervention in the treatment of OA HA.

Thus, the main objectives of this study are as follow:

- To assess the performance of three commonly used biomaterials against the AC affected by various grades of OA in order to understand the behaviour of biomaterial-AC contact in an OA environment.
- To characterise the mechanical and frictional response and the structure of AC affected by various degrees of OA and also study the effect of mechanical degradation.
- To finalise the development of an in-vitro tribological joint simulator to replicate physiological loads and motion in the shoulder joint and to be compatible for the minimum testing of two hours with CoCr and alumina implants.
- To design and implement a system to measure frictional forces at the joint interface.
- To test the system and carry out experiments towards understanding the tribological response as a biomechanical system of the HA joint with various implant materials.

1.2 Thesis outline

The structure of this thesis is outlined below:

Chapter 2 provides a literature review, which highlights the most important work undertaken in this area of research to date and is a crucial step to ensure existing knowledge is built upon and the significant gaps in past research are adequately bridged. This chapter provides the reader with the necessary information to fully understand the studies carried out throughout this research. It provides a description of the shoulder joint regarding anatomy and biomechanics. It also provides an overview of the complex structure and composition of the AC and its constituents. The various mechanical measurement techniques utilised to determine the properties of cartilage tissue are discussed. Problems associated with OA and enzymatic degradation of cartilage and the effect on the mechanical properties of tissue are also described. Following this, a comparable overview of shoulder OA treatment options, particularly shoulder HA and its complications, is provided.

Chapter 3 introduces the details of the experimental techniques, methodology and the testing protocols used throughout this project. The experimental techniques have been chosen and designed in order to assess various properties of the tissue: mechanical, tribological, and biochemical properties, as well as surface topography. This will allow us to obtain a complete characterisation of the tissue, which is essential for a complete understanding of the healthy and damaged tissues' responses under various loads.

Chapter 4 explains the mechanical and structural properties of non-OA and OA human cartilage. Moreover, OA-like AC was, for the first time, compared to human osteoarthritic tissue to investigate the role of mechanical degradation, as well as the role of proteolytic enzymes in the pathology. Finally, the performances of three common biomaterials, CoCr, Al₂O₃ and PCU, articulating against the various grades of OA, were compared. The work in this chapter was carried out in collaboration with a previous PhD student (Ajdari, 2016) and is in the process for paper submission.

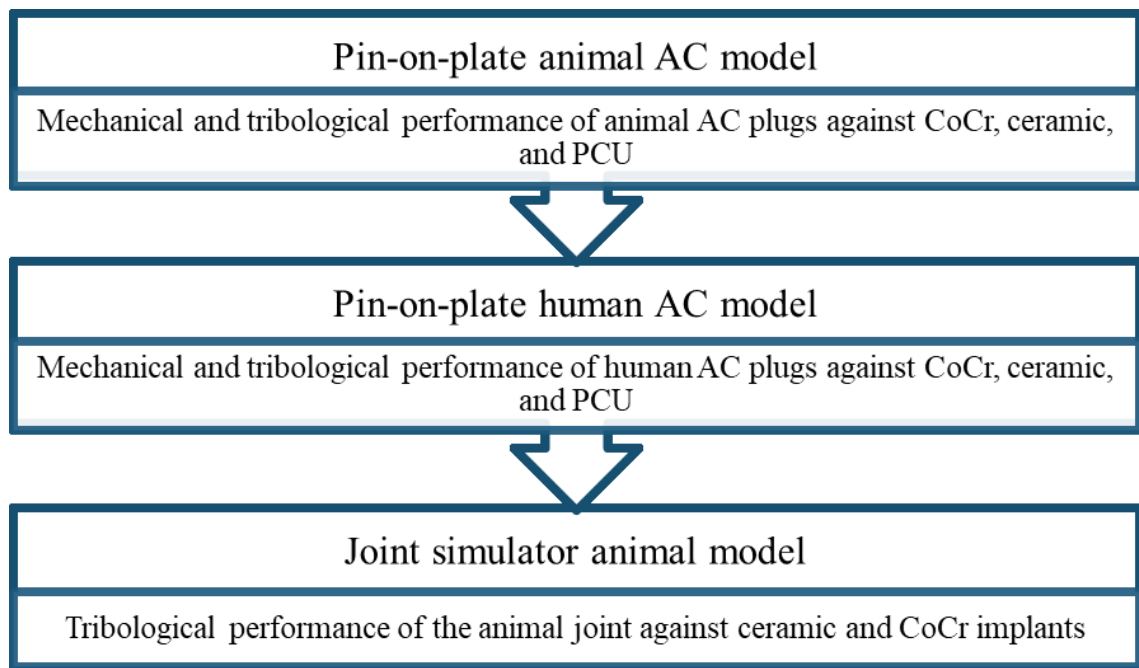
Chapter 5 focuses on the joint simulator update and modifications. A friction measurement system consisting of strain gauges attached to the sides of the motion arm and connected to a National Instrument card has been designed, implemented and calibrated for use. All the mechanical and electrical components of the joint simulator are

explained thoroughly. A preliminary full system test was developed and carried out in dry contact against the ceramic implant head to ensure the strain gauges function properly.

Chapter 6 includes a comprehensive study of the frictional behaviour of native and OA-like enzymatically digested porcine glenoid against the humeral head implants of two different biomaterials: CoCr and ceramic. Following this, surface topography and histology measurements were performed to assess the AC structure after the friction test.

Chapter 7 discusses the conclusion, recommendations and future research to improve this multi-disciplinary study.

A graphical summary of the progression of the studies reported in this thesis is schematically reported below.



2 LITERATURE REVIEW

2.1 Literature review- Part 1: Articular Cartilage structure and function

The literature review in this PhD has been divided into two parts. Part 1 of this literature provides the reader with the necessary background to fully understand the studies carried out throughout this research (mainly chapter 4 of this thesis). First and foremost, an overview of the complex structure and composition of the articular cartilage and its constituents are described. Furthermore, the various mechanical measurement techniques utilised to determine the properties of cartilage tissue, as well as the problems associated with osteoarthritis (OA) disease and the enzymatic degradation of cartilage and the effect on the mechanical properties of tissue, are also described. The findings from this chapter help the reader to gain a deeper understanding of chapter 4. Part 2 of this literature focuses on the shoulder joint's detailed anatomy and biomechanics; this is followed by a comparable overview of shoulder OA treatment options, particularly shoulder hemiarthroplasty (HA) and its complications. This section aids the reader to obtain an overview of the state-of-the-art in relation to chapters 5 and 6 of this thesis.

2.2 Articular cartilage

Articular Cartilage (AC) is a highly specialised avascular, viscoelastic and anural tissue that provides a resilient and almost frictionless surface for the pain-free distribution of load across diarthrodial joints (Akkiraju and Nohe, 2015). The mixture of fluid and the extracellular matrix (ECM) provides the biomechanical and low friction properties of the AC. The AC is composed of 68–85% water, 10–20% collagen, 2–5% chondrocytes (which are involved in synthesising the matrix), and 5–10% of proteoglycans' (PGs') wet weight (Mow et al., 1992). The action of all these constituents together provides the cartilage with mechanical support within the synovial joint (Hani et al., 2011; Pearle et al., 2005).

2.2.1 Articular cartilage composition

Based on previous in vitro studies, AC composition and thickness differ between joints depending on the magnitude of mechanical loading applied and age (Athanasίου et al., 1991; Eckstein et al., 2006; LeBaron and Athanasίου, 2000; Wong and Carter, 2003). The ECM comprises two segments: the fluid segment, consisting of water and electrolytes, and the solid segment, containing chondrocytes, collagen fibrils, PGs and glycoproteins

(Mow et al., 1992). Fox et al. (2009a) stated that the combination of these components allows the preservation of water inside the ECM, which is vital to sustain its mechanical properties. The number of cells present has little effect on the volume of tissue, approximately 1% in human AC. However, in species such as small animals, the concentration of cells is considered much more (Buckwalter and Mankin, 1998a).

2.2.2 Interstitial fluid

Considering the composition of cartilage, 65–80% of wet weight is water and interstitial fluid, where 80% exists in the superficial zone and 65% in the deep zone ((Buckwalter and Mankin, 1998b). The lubrication of the joint and the delivery and distribution of essential nutrients to chondrocytes is obtained by the flow of interstitial fluid within the cartilage. The main function of the AC is to serve as a bearing material for diarthrodial joint, supporting relatively large loads while providing low friction wear. In healthy cartilage, the permeability of the tissue is very low, and fluid is moved through the ECM by applying pressure to the solid matrix of tissue. Interstitial fluid supports most of the joint contact load and helps to transfer it away from the solid matrix, therefore reducing a low friction (Caligaris and Ateshian, 2008). The combination of frictional resistance and fluid pressurisation across the matrix provides the basic mechanism for the cartilage to withstand successive significant loading (Fox et al., 2009). However, during OA, the amount of water rises to more than 90%, initiated by an increase in permeability and interference to the matrix. Consequently, the modulus of elasticity decreases, which also causes the load-bearing capability of the AC to decrease (Lieber and Burkholder, 2008; Wu et al., 2008).

2.2.3 Collagen network

Collagen is an abundant protein consisting of three triple helix polypeptide chains. It contains 10–20% of the wet weight and 50% of the dry weight of the AC; type II collagen composes of 90–95% of the macrofibrillar framework, which offers tensile strength to the cartilage (Fox et al., 2009; LeBaron and Athanasiou, 2000; Mow et al., 1992; Wu et al., 2008). At least 28 different types of collagen have been found so far. The most common type of collagens are the fibrillary collagens, mainly type I (Hulmes, 2008). The predominant solid component of cartilage is collagen type II, which represents 90–95% of the collagen in the ECM and contributes to the shear and tensile properties of the tissue

(Pearle et al., 2005). Collagen types I, IV,V, VI, IX, and XI are present in slight proportions. Within the collagen structure, three polypeptide chains are held together in a helical conformation by hydrogen bonds (Pawelec et al., 2016; Shoulders and Raines, 2009). Each peptide chain consists of repeating amino acids, such as glycine, hydroxyproline and proline (Shoulders and Raines, 2009). Each polypeptide chain contains a region characterised by a repeating amino acid, Gly-X-Y, where Gly is glycine and X or Y can be any amino acid. Glycine forms the core of the protein, while the X and Y amino acids are exposed at the surface (Sherman et al., 2015). Many three-stranded type I collagen molecules pack together side by side, forming fibrils with a diameter of 50–200 nm. In fibrils, adjacent collagen molecules are displaced from one another by 67 nm. This staggered array produces a striated effect (Lodish et al., 2000) (Figure 2-1). The fibrous structure of collagen plays an important role in the structural and mechanical properties of the AC. Type I collagen fibrils are about 50 nm in diameter and have very high ultimate tensile strength, as they are quite large fibrils that are packed side by side in parallel bundles called collagen fibres. The collagenous network is stabilised by cross-linking the collagen fibrils, and the stiffness of the collagen network is influenced by the number of cross-links that have been formed (Akizuki et al., 1986a; Mow and Huiskes, 2005; Ottani et al., 2001). The orientation of the collagen fibrils varies throughout the cartilage depth, which results in various properties within the tissue. At the articular level, the collagen fibres are arranged parallel to the surface in the tangential layer. The transitional layer is found under the tangential layer. Here, fibres are crossing over each other to the mid cartilage region, where the fibres are arranged perpendicular to the surface layer and retain their alignment through the calcified zone. This model is known as the Benninghoff arcade model and it was first proposed as a theoretical model by Benninghoff in 1925 (Figure 2-2) (Benninghoff, 1925; Moger et al., 2007; Zheng and Xia, 2009).

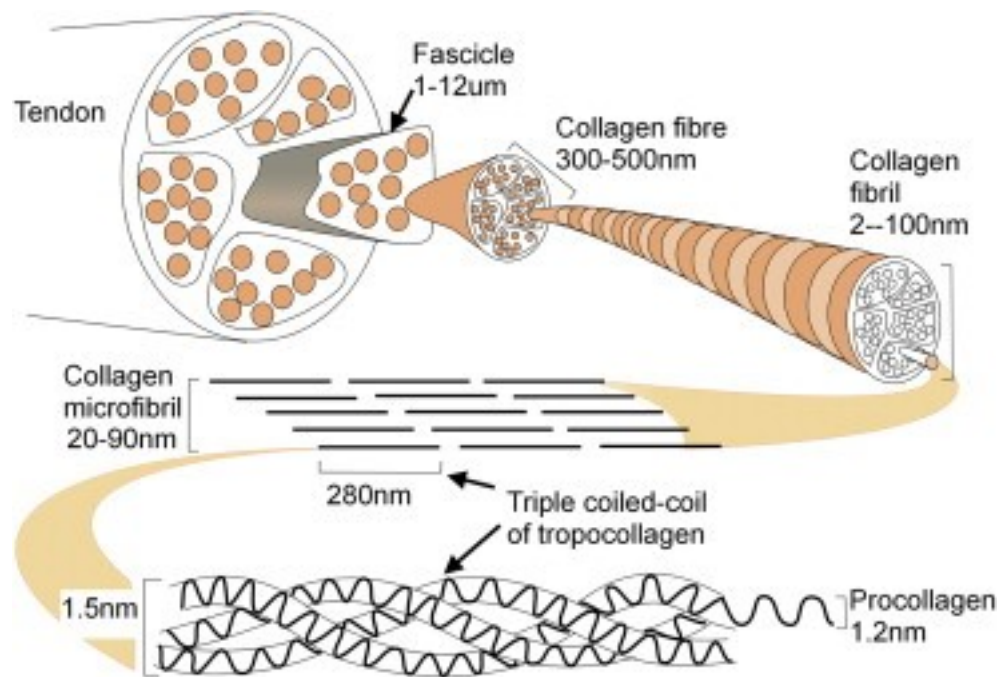


Figure 2-1 The hierarchical structure of collagen fibres. Initially, three polypeptide chains form a left-handed triple helix. Thereafter, several triple helices assemble to produce collagen fibrils that, in turn, align to form a mature collagen fibre. Image adapted from (Scarr, 2011)

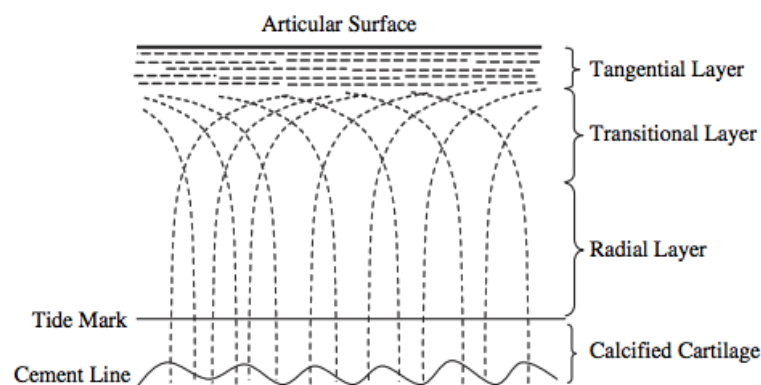


Figure 2-2 A schematic diagram demonstrating the collagen arrangement in cartilage, showing the tangential, transitional and radial layers in the AC and the calcified zone. Image adapted from (Moger et al., 2007)

2.2.4 Chondrocytes

Chondrocytes (mesenchymal stem cell origin) are the only cell type within the AC that assists in joint articulation. These cells are metabolically active cells that synthesise a large volume of the ECM components, such as collagen, glycoproteins and PGs (Akkiraju and Nohe, 2015; Fox et al., 2009; Horký, 1993). They vary in shape, size and number. The metabolic activity of chondrocytes is affected by many factors that are present within their chemical and mechanical environment. These include mechanical loading,

hydrostatic and osmotic pressure changes, injury and degenerative diseases (Williams, 2007). Cytokines, such as interleukin-1, are known to have an important catabolic and anabolic effect that play a role in controlling the balance between matrix macromolecular degradation and synthesis (Buckwalter and Mankin, 1998b). Since cartilage is avascular tissue, chondrocytes rely on a diffusion of nutrients from the articular surface (Poole, 1997). The cartilage healing response to injury is limited because chondrocytes have limited ability to replicate, as their survival is dependent on an optimal mechanical and chemical environment (Fox et al., 2009).

2.2.5 Proteoglycan aggrecan

PGs, the main macromolecule in cartilage, contain protein polysaccharide particles that create 10–20% of the wet weight, as well as offer compressive strength to the AC (Bhosale and Richardson, 2008; Buschmann et al., 1998). PG consists of a protein core structure to which a large number of chondroitin sulphate and keratin sulphate chains are covalently attached. This chain is referred to as a glycosaminoglycan (GAG), which has a toothbrush-like structure. This structure can bind or aggregate to a backbone of hyaluronic acid (HA) (Figure 2-3) (Hascall, 1977; Mansour, 2013). GAGs attract water and repel each other due to their electronegativity, producing a swelling pressure that is controlled by the collagenous meshwork. The compressive stiffness of the cartilage is positively related to both GAG concentration and to the hydration of the tissue. In general, the collagen network resists the tensile and shear stresses, while the PGs resist fluid flow and compressive stresses (Buschmann and Grodzinsky, 1995; Laasanen et al., 2003; Woo and Buckwalter, 1988).

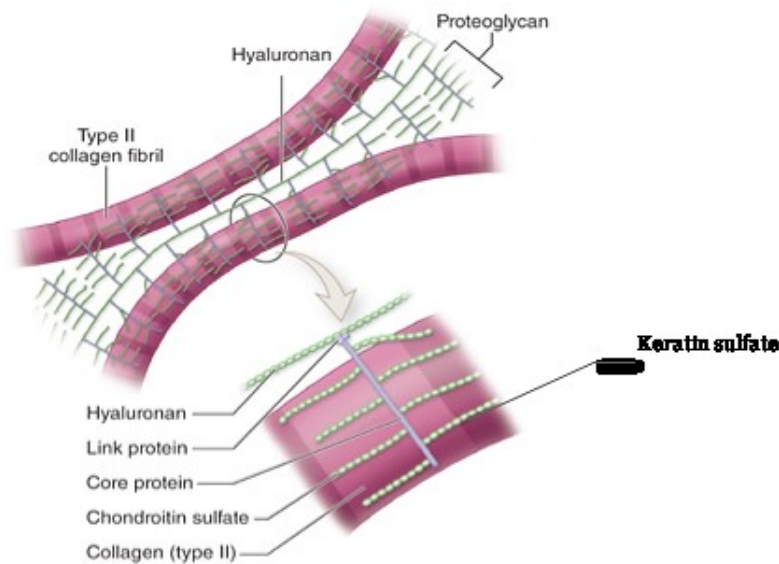


Figure 2-3 The schematic structure of Proteoglycans (a) demonstrating details of PG monomer structure showing chondroitin sulphate and keratin sulphate chains and the interaction of the monomer with the hyaluronate chain and link proteins; (b) molecular conformation of a typical PG aggregate showing the size of the molecule; (c) an electron micrograph of a PG aggregate. Image adapted from Merscher (2016)

2.3 Articular cartilage structure

The AC has an organised layered structure that reflects its functional role and is composed of four various zones: the superficial (tangential) zone, the middle (radial) zone, the deep zone and the calcified zone (Pearle et al., 2005; Sharma et al., 2013) (Figure 2-4). The appearance of these zones and their sizes differ among the same species, and zonal organisation has a functional significance. Each zone varies in water content, aggregate sizes, PGs, collagen concentration, and chondrocytes orientation relative to the articular surface (Buckwalter et al., 2005). The tissue material strength depends on the extensive cross-linking of the collagen and the apparent zonal changes in fibrillar architecture with tissue depth (Eyre et al., 2006). It has been demonstrated clinically that the loss of collagen fibres from the AC surface in load-bearing areas results in fibrillation, arthritis and wear (Akeson and Bugbee, 2007; Eyre et al., 2006; He et al., 2013).

2.3.1 Superficial zone

The thinnest zone of the AC is the superficial zone, which makes up approximately 10–20% of cartilage thickness (Fox et al., 2009). Superficial cartilage consists of a highly structured network of ECM proteins, PGs, collagen, and non-collagenous proteins, which maintain high water content. Its role is to protect and maintain the deeper layers of the

cartilage (Frantz et al., 2010). In this zone, chondrocytes are flattened and aligned parallel to the surface. These cells are surrounded by polarised collagen fibrils (mainly type II and IX collagen) that are packed tightly in parallel to the cartilage surface. This zone is in contact with the synovial fluid and provides the highest tensile properties, enabling the cartilage to resist tensile, compressive and shear forces during joint movement (Poole et al., 2001). The chondrocytes form a matrix that contains a high concentration of collagen and a low concentration of PG in relation to the other zones. Cells from the superficial zone degrade PGs at a faster rate and create less collagen and PGs compared to cells from the deeper zones (Zhang et al., 2009).

2.3.2 Middle (radial) zone

The middle zone is below the superficial zone, with lower cell density and represents 40%-60% of AC volume (Fox et al., 2009). The ECM in this layer has high PG aggrecan content with more rounded chondrocytes. The collagen fibrils are arranged randomly and have a larger diameter (Poole et al., 2001). This middle layer contains randomly orientated collagen fibres with large chondrocytes. Compared to the superficial zone, the transitional zone is much larger in volume, containing cells with a high concentration of synthetic organelles, endoplasmic reticulum and Golgi membranes. These spheroid-shaped cells form a matrix with randomly arranged large-diameter collagen fibrils, a high concentration of PG, and a low concentration of water and collagen in contrast to that of the superficial zone. This zone consists of spheroid-shaped chondrocytes arranged in columns at right angles to the joint surface. Furthermore, the collagen fibrils in this zone are thicker compared to superficial zone (Bhosale and Richardson, 2008; Buckwalter and Mankin, 1998b).

2.3.3 Deep zone

The deep zone is situated between the calcified cartilage and the middle zone and represents 30% of the AC volume (Fox et al., 2009). This zone contains the largest diameter collagen fibrils, the highest proteoglycan content and lowest chondrocytes cell density (Poole et al., 2001). The collagen fibres in the deep zone are arranged in vertical columns separated by collagenous fibrils. Chondrocytes in the deep zone are terminally differentiated and actively synthesise collagen type X (Akkiraju and Nohe, 2015).

2.3.4 Calcified zone

This thin zone of calcified cartilage consists of a small volume of cells implanted in a matrix with a low metabolic rate. Hypertrophic chondrocytes in this zone form type X collagen, which offers structural stability and acts as a shock absorber. Cells in this zone are smaller in volume and consist of small quantities of endoplasmic reticulum and Golgi membranes compared to the radial zone. The borderline between the deep zone and the calcified cartilage is labelled as the tidemark. The calcified layer supports the attachment of the cartilage to the bone by fixing deep-zone collagen fibrils to the subchondral bone (Fox et al., 2009). Differences in the calcified cartilage zone provide the matrix with three different regions: these include the pericellular region, the territorial region and the interterritorial region (Bhosale and Richardson, 2008; Buckwalter and Mankin, 1998a).

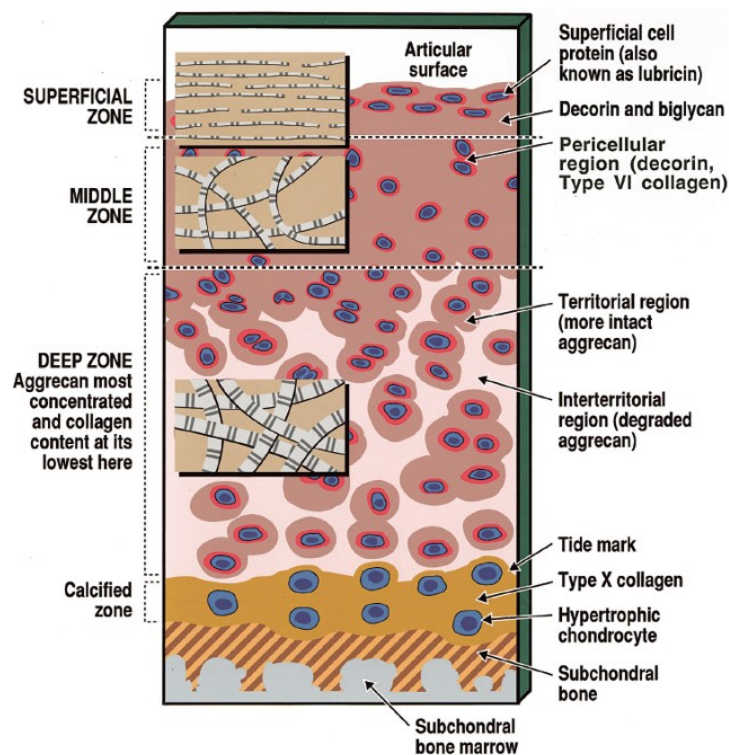


Figure 2-4 Diagrammatic representation of the general structure of an adult human AC, showing various zones, regions, and relationships with the subchondral bone adapted from (Poole et al., 2001)

2.4 The mechanical behaviour of articular cartilage

The biomechanical behaviour of a diarthrodial joint is dependent on the composition and structure of the cartilage. The collagen network of the cartilage protects the chondrocytes and resists tensile forces produced by compression. Furthermore, the collagen network

fight against interstitial swelling, provides attachment for PGs, and anchors the cartilage to the subchondral bone. Cartilage that is subjected to high loads frequently demonstrates a thicker superficial zone and a high degree of collagen orientation (Panula et al., 1998). Below describes various biomechanical behaviour of AC.

2.4.1 Compressive behaviour

The time-dependant and stress-dependant mechanical properties of the AC during compression is regulated by the exudation of interstitial fluid in and out of the tissue through the porous and permeable ECM (Fung, 1981; Mow et al., 1980a). The mechanical properties of the AC when loaded are believed to depend on specific interactions between the collagen and PGs of the ECM (Khalsa and Eisenberg, 1997). The negatively charged PGs contribute to compressive resistance and provide a high osmotic pressure within the tissue, which supports the load applied (Han et al., 2011). In contrast, the collagen network contributes to the tensile and shear properties of the AC (Korhonen and Jurvelin, 2010).

When the cartilage is loaded axially, collagen fibres become more compact and water is forced out from the tissue, resulting in a decrease in tissue volume and lateral tissue deformation and an increase in the osmotic pressure of the PG (Kaplan et al., 2017). This causes swelling of the tissue, and the tissue is straightened as water molecules are forced out from the ECM (Wells et al., 2015). The overall negative charge of aggrecan is called the fixed charge density (FCD), which attracts cations from the synovial fluid. The Donnan ion distribution law states there are always more charged ions in the tissue than the surrounding fluid (Donnan, 1924; Urban et al., 1979). This difference in ion concentration generates a positive osmotic pressure, which results in the swelling of the tissue (An and Martin, 2003a). The combination of osmotic pressure and fibril direction contribute to the anisotropy nature of the cartilage and results in a Poisson's ratio that is greater than 0.5 from the axial to lateral direction (Edelsten et al., 2010). Furthermore, it has been noted that an increase in the density of PGs creates a reduction in water content and hence an increase in the compressive modulus (Sah et al., 1997; Setton et al., 1997, 1994). Cartilage has a depth-dependant matrix composition, which includes low PG content in the superficial zone and high PG content in the middle zone. Respectively, the compressive modulus is lowest at the surface and increases with depth (Chen et al., 2001).

2.4.2 Swelling behaviour

Swelling is the electrochemical behaviour of the AC. Swelling of tissue arises from a high density of negatively charged PGs (FCD) in the matrix that generate a high interstitial swelling pressure (Narmoneva et al., 2002). The Donnan osmotic pressure effect, based on physicochemical motive force, and the chemical expansion effect, based on mechano-electrochemical motive force, contribute to the total swelling behaviour of cartilage (Nordin and Frankel, 2001). The swelling behaviour is regulated by a balance between the swelling pressure and the restraining force generated within the collagen solid network. In damaged and fibrillated tissue, there is an imbalance between the swelling pressure and the restraining force; therefore, swelling is elevated. The chemical expansion is caused by the compacted arrangement of PGs in the ECM and depends on the concentration of ions in solution floating around the PGs, as these ions protect the charged groups from interacting with each other (Cohen et al., 1998). The repulsion force between these molecules results in the swelling of cartilage, pressure difference and the flow of the fluid from surrounding areas into the cartilage (Comper, 1996; Mow et al., 2012).

2.4.3 Tensile loading

The collagen fibres in the ECM are responsible for the tensile properties of the AC; consequently, the orientation of these fibres influences tensile behaviour (Cohen et al., 1998). When a cartilage is under tensile loading, the collagen fibres resist extension by reorienting towards the direction of the load and thus narrowing the sample. The PGs provide secondary resistance by restricting the degree of reorientation and narrowing the sample (Bell, 2010). The tensile modulus of the cartilage depends on the collagen fibril density, fibril orientation and the degree of collagen cross-linking (Akizuki et al., 1986b). Research has shown that the tensile behaviour of cartilage depends on the rate of loading (Verteramo and Seedhom, 2004), and tensile stiffness increases with higher applied strain rates. Moreover, the tensile strength of cartilage decreases with increasing depth from the articular surface (Sokoloff, 2014).

2.4.4 Viscoelastic behaviour

The AC is a highly viscoelastic tissue, meaning that it possesses three distinct characteristics of viscoelastic material: stress relaxation, creep, and hysteresis (Pal, 2014). Due to the non-homogeneous distribution of collagen and PG molecules, the AC exhibits

mechanical inhomogeneity and anisotropy. Primarily, it is a viscoelastic tissue; therefore, it responds to constant load changes with time. The drag force of the intrinsic fluid flow and the time-dependant deformation of the solid component are two important mechanisms establishing viscoelastic behaviour (Mak, 1986a, 1986b). Kempson et al. (1971) pioneered a study of cartilage as a viscoelastic material. The group observed viscoelastic behaviour in cartilage during indentation and uniaxial tension tests. There are two distinct viscoelastic behaviours. The first is: 1) flow dependant, which is the main mechanism driving creep and stress relaxation in the tissue (Figure 2-5). This is caused by frictional force due to the drag flow of interstitial fluid in the solid matrix, also known as strain-dependant permeability. The second is: 2) the flow independent mechanism, which is caused by the intrinsic viscoelastic properties of the ECM that is mainly related to collagen fibrils (Boschetti et al., 2004; Huang et al., 2001; Mow et al., 1980a; W. Wilson et al., 2005a). The combination of these two mechanisms has been shown to cause a mechanical response in the tissue, which is a function of the loading rate and time (Kempson et al., 1971; Woo et al., 1980).

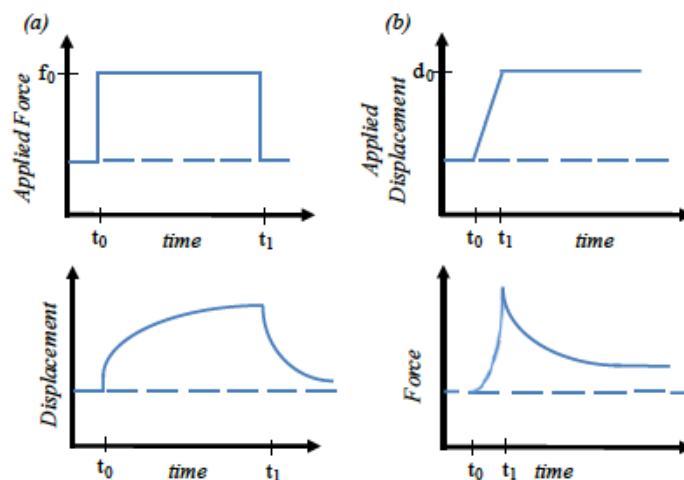


Figure 2-5 Schematics of load-deformation viscoelastic behaviour of the AC. (a) Creep: A viscoelastic material behaviour where a constant load is applied over time. (b) Stress relaxation: A viscoelastic material under constant strain. The displacement results in an increase of load followed by stress relaxation until equilibrium is reached. (Lu and Mow, 2008)

2.5 Experimental mechanical testing of the articular cartilage

This section explains the three main types of loading experiments (Figure 2-6). Each experiment defines the different mechanical properties of cartilage. From a biomechanical point of view, the AC can be viewed as a multiphasic, fibre-reinforced

permeable material consisting of both a solid and fluid phase with nonlinear viscoelastic properties (Moutos, 2009; Mow et al., 1980a; Zhang et al., 2009). The low volume of the AC means that the amount of force and energy that can be absorbed by this cartilage during typical daily activities is much less than the muscles, tendon, and subchondral bone around the cartilage (Hu, 2005; Zhang et al., 2009). Cartilage composition also plays a vital role in the mechanical properties of tissue. As discussed previously, the principle components of the AC are the tight and organised collagen fibres with the charged PGs that contribute to the tensile properties of cartilage (Wilson et al., 2005b). It has been noted that there is a strict relationship between the mechanical properties of AC and its zonal composition and structure. Since various zones have a different collagen diameter and organisation, the tensile properties subsequently change within each zone (Li and Herzog, 2004; McAdams et al., 2010; Peretti and Pizzini, 2010).

Akizuki et al. measured the tensile modulus of the human knee joint in terms of healthy and osteoarthritic cartilage. The regions that were studied were taken from four different tissue zones, which included both areas that can withstand high and low loads. The superficial zone had the highest modulus (10.1 Mpa) compared to the middle and deep zones (5.5 Mpa and 3.5 Mpa respectively). They also found that the high load-bearing areas have lower tensile modulus than the low load-bearing areas (Akizuki et al., 1986b). The tensile modulus of the AC depends on the collagen fibril density, fibril orientation and the amount of collagen cross-linking. When a tensile load is applied on the cartilage, the collagen fibrils and PG molecules align and strain along the axis of loading (Roth and Mow, 1980; Mow et al., 1980a; Wilson et al., 2005). For healthy human cartilage, the tensile modulus is between 2–25 Mpa (Akizuki et al., 1986b; Guilak et al., 1994; Mow et al., 1980a).

2.5.1 Confined compression

Confined compression is mainly used to determine the material properties of cartilage. In a confined compression test (Figure 2-6(a)), cartilage plugs are harvested with some underlying subchondral bone from a cadaver joint. This is placed in a confined and impermeable chamber that prevents radial formation and fluid discharge from the sides (Mow et al., 1992). A permeable plate loads the cartilage samples axially; therefore, fluid exudation only occurs through the top surface of the cartilage sample via a permeable plate. This configuration is used to estimate material properties, such as hydraulic

permeability and aggregate modulus (Armstrong and Mow, 1982; Buschmann et al., 1992). The confined compression is used in creep and stress relaxation mode, where a constant load is applied and the displacement of the tissue is measured as a function of time. During stress relaxation mode, a constant displacement is applied to the tissue and the force is measured as a function of displacement (Mansour, 2013). In 1997, Schinagl et al. investigated the modulus of bovine AC under confined compression; they found that the compressive modulus increased with depth from the surface of the cartilage. It was the lowest in the superficial zone (0.079 ± 0.039 Mpa) and highest in deeper zones (2.10 ± 2.69 Mpa) (Schinagl et al., 1997).

2.5.2 Unconfined compression

An unconfined compression test (Figure 2-6(b)), is similar to a confined compression test; the only difference is that the cylindrical cartilage plugs are between two rigid impermeable plates, allowing outward radial deformation. As a result of this configuration, the porous solid matrix doesn't undergo a volumetric strain and Young's modulus of the solid phase determines deformation at equilibrium. During the unconfined compression test, the material properties are independent of the sample size (Boschetti et al., 2004; Hasler et al., 1999; Korhonen et al., 2002). This test is usually performed on full thickness cartilage with no bone attached; this allows the axisymmetric problem to be modelled as a one-dimensional problem along the radial direction (Li et al., 1999). The unconfined compression test is more widely used in testing cartilage mechanics, as it is a closer model to the physiological environment than confined compression. The impermeable plate limits the flow in a similar way to the subchondral bone (Park et al., 2003). Unconfined compression, together with appropriate theoretical models, is extensively used to find the elastic material parameters of the solid phase, such as Young's modulus of tissue (Korhonen et al., 2002).

2.5.3 Indentation testing

The indentation test (Figure 2-6(c)), is a less invasive method of determining the mechanical behaviour of cartilage, as it does not require the excision or preparation of the cartilage since the discs of the cartilage are not removed from the underlying bone. It is also suitable for testing cartilage in small joints (Accardi, 2012; Bell, 2010; Mansour, 2013). An indentation test is performed under constant load and it involves applying axial

compression using a solid or porous cylinder indenter with either a flat or hemispherical end against an intact specimen, while recording the deflection and resistive force. This configuration requires optical determinations of the Poisson's ratio in order to extract the Young's modulus of the sample (Hasler et al., 1999; Lai et al., 2004).

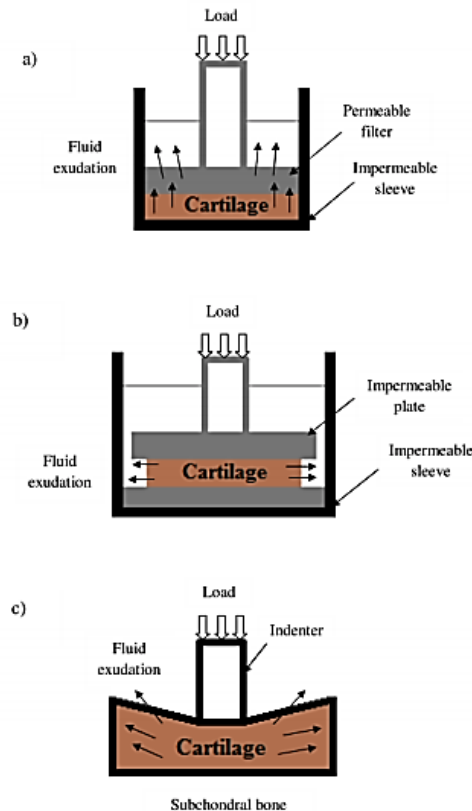


Figure 2-6 Schematic representation of experimental configurations on AC samples: (a) confined compression; (b) unconfined compression; (c) indentation test.

2.5.4 Biotribology of the articular cartilage

The main load-bearing parts in the human body are the knee, hip and ankle, which all go through multidirectional movements. Due to the slow repair mechanism in the AC, the biphasic nature of this tissue has an important role to play in protection. Ultimately, understanding the lubrication mechanism of the AC is essential for a better understanding of the damages caused in the AC, such as OA and how it is initiated. The low friction and wear of the AC layer is related to mixed modes of lubrication, which consist of fluid film lubrication by the synovial fluid, boundary lubrication by a variety of candidate molecules in the synovial fluid cartilage, and lubrication by pressurisation of the interstitial fluid in the cartilage (Ateshian, 2009).

2.5.5 Friction

Friction is a force that resists the relative motion of two surfaces and is classified as static or kinetic friction (Malik, 2015). This friction is quantified through a COF, and it is defined as the ratio of friction over the normal force (Brockett et al., 2007). Human diarthrodial joint surfaces have a very low COF (approximately 0.02) due to the presence of the synovial fluid, which lubricates the tissue during joint movement and acts as a cushion. In the absence of the synovial fluid, the tissue will degrade and the friction and wear increase, which will eventually reduce mobility and cause pain as a result of the tissue softening and fibrillation (Whiting and Zernicke, 2008). Synovial fluid consists of hyaluronan molecules, PGs, phospholipids, superficial zone protein (lubricin) and water (Accardi et al., 2011; Jayanth Katta et al., 2008; Schmidt et al., 2007). Lubrication decreases the frictional resistance between two bearing contact surfaces; there are several lubrication mechanisms in the joint that have been proposed by various authors.

The higher load leads to a higher COF value, and this result is also affected by the lubricant type. The higher concentration of proteins in the lubricant increases the COF for all implant types, with the exception of metal on metal implants, which benefit from a protein later deposited over the bearing surfaces. Reliable friction measurements require the use of lubricants with a rheological response as close to the synovial fluid. In *in vitro* simulator studies, 25% bovine calf serum is commonly used as a lubricant (Puccio and Mattei, 2015). A study carried out by Brockett et al. (2007) demonstrated that increased serum concentration will result in a significant reduction of the friction factor.

Few studies have demonstrated that contact stress levels have an effect on the wear and friction of the AC (Ateshian, 2013; Katta et al., 2007; Malcom, 1976; Pickard et al., 1998). The general trend is that an increase in contact stress results in a decrease in COF. The COF shows the time-dependant performance of cartilage against robust materials. At a certain stress level, the COF stops decreasing and begins to increase, causing wear of the cartilage due to the constant loading of the tissue and the reduction of fluid support. However, the rehydration of previously loaded cartilage in cartilage-against-cartilage contact provides a stagnant low COF value. The COF of cartilage gliding on cartilage has been measured as low as 0.002, which means that a contact force of 1 KN across the joint produces a frictional force of 2 N at the cartilage surface (Guilak, 2005).

2.5.6 Wear

Wear is the deterioration of material as a result of both contact surfaces mechanically interacting with each other and causing friction. In the AC, wear can occur both mechanically and biologically. Mechanical wear of the AC includes adhesive, abrasive and fatigue wear. In the case of biological wear, cartilage tissue is affected by a reduction in PGs or modifications in the collagen network (Mow et al., 1992). The location of the joint also affects the wear of the AC, since the medial section of the knee is the most common area to be affected by OA. All factors mentioned increase cartilage wear above that of natural repair (Jayanth Katta et al., 2008).

2.5.7 Lubrication

Lubrication is the action of fluid to reduce friction and wear between solid surfaces (Hori, 2006). It is defined as a complicated process that depends on the tribological, chemical and mechanical condition of a system (Puccio and Mattei, 2015). The cartilage tissue is attributed to a combination of both interstitial fluid and solid constituents resulting in biphasic behaviour. Lubrication of articular cartilage can be divided into two categories: boundary lubrication, and fluid film lubrication (Dawson and Wright, 1973).

2.5.7.1 *Boundary lubrication*

The Boundary lubrication (Figure 2-7 (a)) exists when the fluid film thickness is smaller than the average surface roughness; therefore, surface contact occurs (Taylor, 2012). In the boundary condition, the separation of the bearing surfaces is of molecular dimensions. It is more likely to occur during low-speed activities, such as walking after standing still for a finite period of time (Unsworth, 1991). In such cases, the interaction of the lubricant molecules within the film or surface layer determines the load-bearing properties of the AC. This interaction of molecules is important for the maintenance and protection of cartilage; each load-bearing surface is covered with a thin layer of molecules that form a gel to protect the opposite surfaces from touching each other. In human joints, these layers contain the lubricin that remains on the cartilage surface and are effective at low loads. In the absence of lubricin, the AC surface is vulnerable to frictional damage, as evidenced by the accelerated progression of joint degeneration in individuals with OA (Levangie and Norkin, 2011a).

2.5.7.2 Fluid film lubrication

Fluid film lubrication (Figure 2-7(b)) is a form of lubrication in which the interfaces are separated by a viscous fluid with a thickness greater than the surface roughness to prevent contact (Cowin and Doty, 2006). The fluid forces that support the applied loads from the interacting surfaces are generated through hydrostatic and hydrodynamic mechanisms (McNary et al., 2012). The classical representation is two rigid surfaces set at an angle to each other and producing a wedge-shaped gap. When one surface is caused to move tangentially relative to the other in the direction shown, the fluid that is present is drawn into the diminishing gap by viscous forces. This lubrication mechanism is associated with very low friction since the load is entirely supported by the hydrostatic pressure of fluid film (Bhushan, 2000).

Another mechanism encountered by fluid film lubrication is squeeze film lubrication (Figure 2-7(c)), which is characterised by the existence of a film of fluid that completely separates the interacting surfaces. Therefore, the pressure in the fluid film supports the load on the surfaces. This pressure can be maintained by the continuous motion of the surfaces or by pumping the fluid externally. If two articular surfaces are loaded perpendicular to each other, the hydrostatic pressure of the fluid film will increase. This fluid film is responsible for load support; however, eventually, the lubrication will squeeze out of the gap and is thus only effective for a short period of time unless the film is replaced. This is believed to occur in a cyclical manner through hydrodynamic lubrication (Accardi, 2012; Dowson and Wright, 1973).

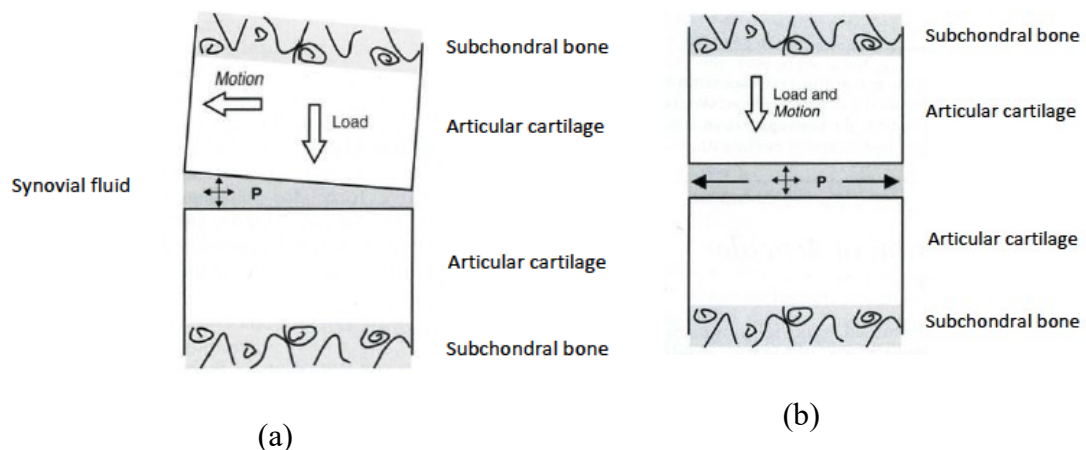


Figure 2-7 The schematic of different lubrication regimes: (a) Fluid-film lubrication; The wedge effect of hydrodynamic lubrication, (b) squeeze film lubrication

2.5.7.3 Biphasic lubrication

Cartilage is a biphasic material that is composed of a porous solid phase and an incompressible fluid phase. The mechanism of successive loading onto two phases is known as biphasic lubrication (Figure 2-8(a)). Biphasic lubrication is a mode of lubrication produced between bearing surfaces, where at least one of the two contacting materials consists of a relatively soft, deformable and porous medium. This biphasic medium consists of a porous-permeable solid and a fluid phase. The solid phase is characterized by the ECM, which is porous and permeable. The relationship between proteoglycans and interstitial fluid provides compressive resilience to cartilage via negative repulsion forces. Biphasic lubrication is effective when the interstitial fluid pressurises to support a significant fraction of the contact load. The friction force acting on the bearing surfaces is proportional only to the fraction of the load transmitted through solid-on-solid contact (Ateshian, 2013). When the load is applied to the cartilage, the interstitial fluid flows from high pressure regions of the joint, through the ECM into the lower pressure regions. The flow of interstitial fluid through the ECM results in a high frictional drag force, which is due to low permeability of the ECM to the interstitial fluid. These high frictional drag forces cause pressurisation, which leads to fluid phase loading—as a result the fluid phase withstands 90% of the load, protecting the solid phase from high loads. When all the interstitial fluid is released from the tissues, other lubrication regimes, such as boundary lubrication, become effective to prevent friction in the joint due to the articulating surfaces coming close to each other (Nordin and Frankel, 2001). Two mechanisms, weeping and boosted lubrication, are proposed to take place when AC is loaded.

2.5.7.4 Weeping lubrication

Weeping lubrication is generated by the release of interstitial fluid from inside the tissue when the AC is loaded out towards the contact zone, creating a film between the contacting surfaces and therefore reducing solid-to-solid interaction. Stresses transmitted through solid-to-solid contact compress the cartilage matrix, pressurising the ECM and inducing interstitial fluid exudation. In weeping lubrication, the cartilage acts as a “self-pressurised” hydrostatic bearing and this method of lubrication is most effective when the surface is fully loaded, as it will cause the tissue to be fully pressurised where the fluid will form a film in the contact zone (Lewis and Mccutchen, 1959; McCutchen, 1959).

2.5.7.5 Boosted lubrication

Boosted lubrication (Figure 2-8(b)), occurs under joint loading conditions that force the fluid back into the ECM, effectively increasing the concentration of the lubricant confined at the articular surface (McNary et al., 2012; Walker et al., 1968). The permeability of the AC plays an important role in this mechanism. The AC is only permeable to water and other small solutes and, when it is loaded, the water in the synovial fluid is filtered through the AC. Consequently, as a result of this filtration process, there will be a higher concentration of hyaluronate molecules in the joint space, which act as a boundary lubricant on the tissue surface, as well as improving the load-carrying capacity of the synovial fluid due to an increase in viscosity (Accardi, 2012; Neu et al., 2008; Walker et al., 1968). Weeping and boosted lubrication are the key mechanisms in the AC (Accardi et al., 2011). McCutchen (1959) first proposed that the interstitial fluid of the cartilage may be responsible for its load-bearing properties. This phenomenon was explained through ‘weeping bearing’ properties in animal joints (Jayanth Katta et al., 2008; Lewis and Mccutchen, 1959; McCutchen, 1959). In 1968, Walker and co-workers first proposed the boosted lubrication mechanism. In contrast to weeping lubrication, due to the porous and permeable structure of the AC, when it is loaded, the synovial fluid (without hyaluronate) flows back into the tissue. A hyaluronic gel remains between the two articulating surfaces, which acts as a boundary lubricant and protects the joints (Callaghan, 2003; Walker et al., 1968).

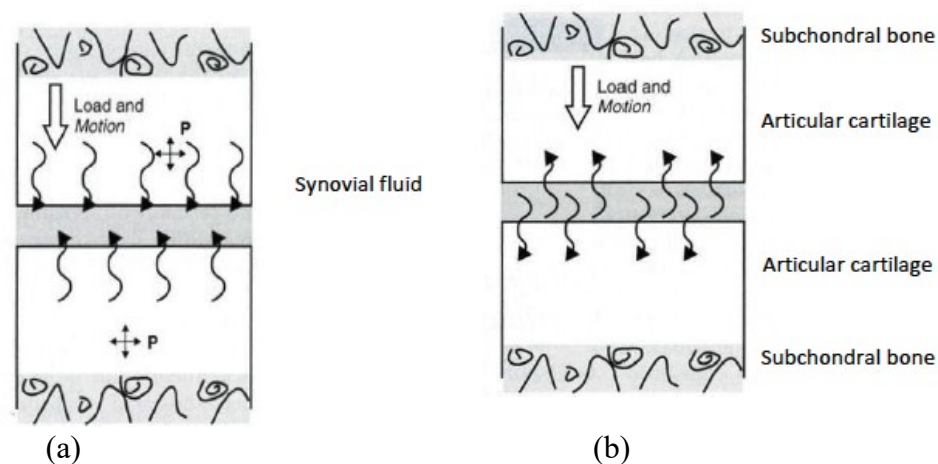


Figure 2-8 The mechanism of (a) weeping lubrication (the black arrows represent the influx of interstitial fluid from the cartilage matrix to the joint cavity); (b) boosted lubrication (the black arrows indicate the flow of the smaller molecules, such as wastes and electrolytes).

2.6 Osteoarthritis

Osteoarthritis (OA) is a progressive degeneration of the AC and is the most common type of joint disorder. OA affects 15% of the population, the majority of which are over 65 years old. The elderly experience symptoms of inflammation, which include impaired mobility, stiffness and pain. The hands, knees, hips and spine are the most affected areas and the disease may require total hip and knee replacement (Felson, 2000; Felson and Zhang, 1998; Guccione et al., 1994, 1994; Pelletier and Pelletier, 2010; Tchetina, 2011). OA affects the whole joint structure, which includes the subchondral bone, ligaments, the synovial membrane and periarticular muscles, as well as the cartilage itself. The treatment of OA focuses on the management of the disease symptoms, as there is no cure currently available for this disease and the pain and inflammation of the joint is reduced by using non-steroidal anti-inflammatory drugs (NSAIDs).

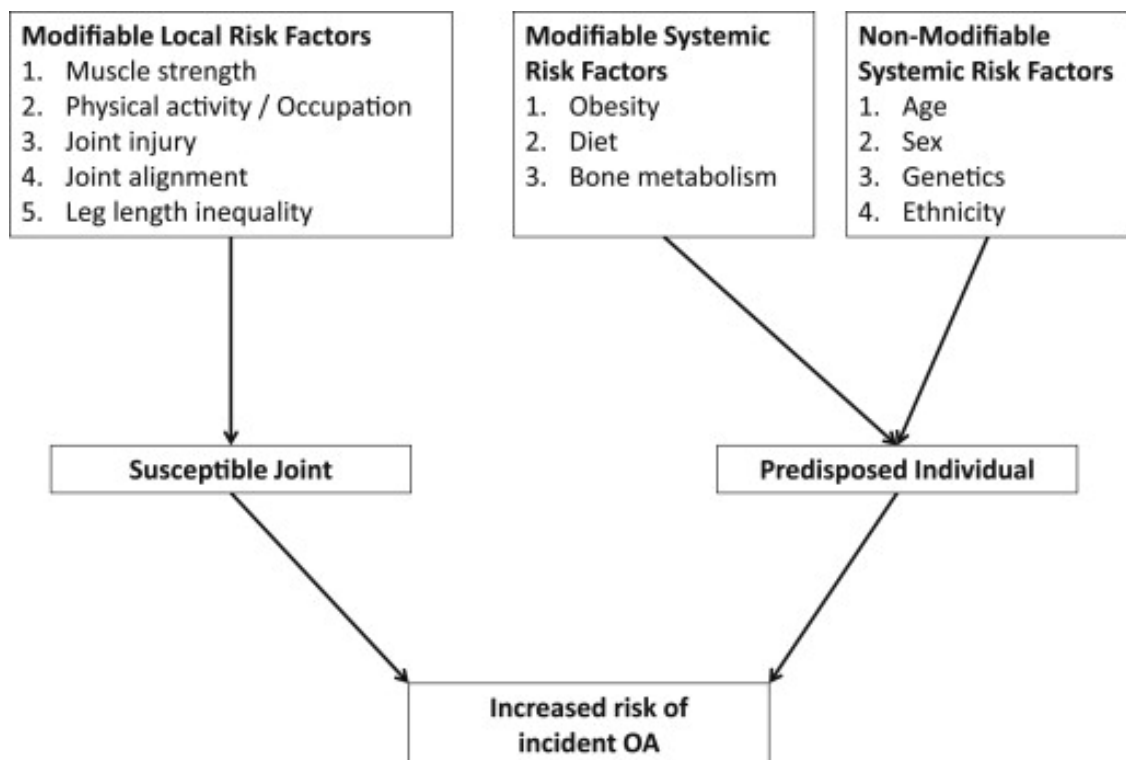


Figure 2-9 Potential risk factors for susceptibility to OA incidence, each with different degrees to support their association (Johnson & Hunter, 2014).

2.6.1 Effect of osteoarthritis on the articular cartilage

Cartilage has a limited healing capacity and damage to the surface will eventually lead to deterioration and premature arthritis (OA) (Ahern et al., 2009; O'Driscoll, 1998). Early OA is characterised by the disruption of the superficial collagen network, loss of PGs, increased interstitial fluid content, tissue swelling, decreased extracellular osmolality, and increased chondrocyte volume (Arokoski et al., 2000; Korhonen et al., 2010; Venn and Maroudas, 1977). Figure 2-10 shows schematic representation of articular cartilage composition and morphology in healthy and damaged osteoarthritic cartilage. In the healthy cartilage (A), the orientation and density and concentration of the collagen fibres and PGs varies according to location within the cartilage layer and regionally within the joint. In early osteoarthritis (B), PGs and GAGs leak from the cartilage and the collagen fibers changes in size and orientation. These initial disease process occur without macroscopic alterations in cartilage morphology. During the later OA stages (C), morphologic changes of the cartilage appear (Oei et al., 2014).

During the ageing process, the load-bearing components of the ECM – PGs and collagen type II, which offer tensile and compressive stiffness – experience structural changes. The ability for the chondrocytes to remodel the cartilage ECM deteriorates with ageing, which consequently decreases its anabolic capacity (Felson and Zhang, 1998; Fitzgerald et al., 2004; Loeser and Shakoor, 2003; Pelletier et al., 2001; Wells et al., 2003). According to Saamamen and co-workers, the mechanical exercise of the knee joint in vivo contributes to an increase in the density of aggrecan in the cartilage. On the other hand, if the knee joint is inactive, the density decreases (Behrens et al., 1989; Slowman and Brandt, 1986). Dynamic loading and fluid exchange with the synovial fluid are important in maintaining cartilage homeostasis. Overloading and under-loading the cartilage can affect matrix synthesis and cell viability (Vanwanseele et al., 2002). Normal cartilage can withstand peak loads as high as 15–20 Mpa in vivo; any load higher than this may cause tissue injury and initiate cartilage degeneration and reduce PG synthesis, which causes cell death and will ultimately lead to OA (Lee et al., 2011; Loening et al., 2000; Wilson et al., 2003).

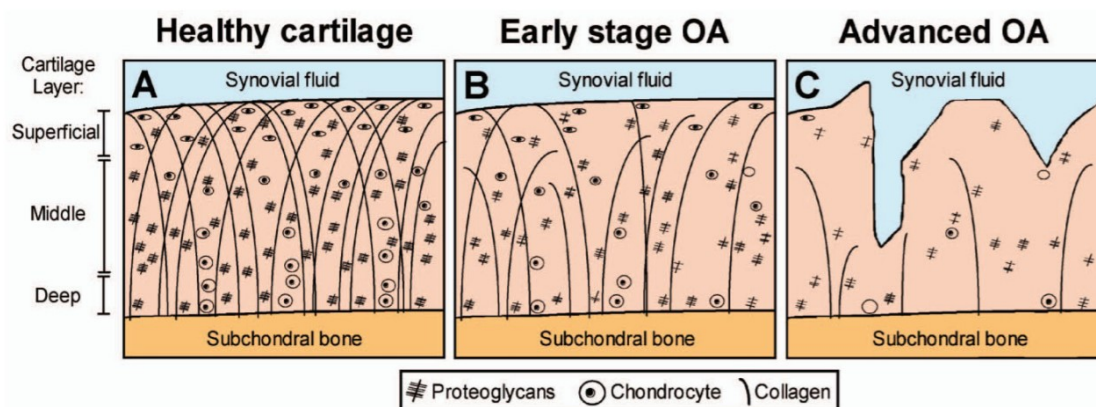


Figure 2-10 Schematic representation of articular cartilage composition and morphology in healthy (A), early-stage osteoarthritic (B), and advanced-stage osteoarthritic cartilage (C) (Image adapted from (Oei et al., 2014))

2.6.2 The effect of osteoarthritis on the mechanical properties of the articular cartilage

As mentioned previously, mechanical loading is the most important factor that regulates the maintenance of the cartilage. Both overloading and under-loading this tissue will result in damage eventually. The pathways leading to OA are not well understood; hence it is vital to quantify factors that create tissue damage. Studies have demonstrated that excessive mechanical loading can directly damage the cartilage ECM and change the equilibrium in chondrocytes to favour catabolic activity over anabolism. Factors such as strain rate and peak stress contribute to cartilage damage (Sun, 2010). The critical load threshold for cell death and collagen damage as a result of single impact load in bovine cartilage is 15–20 Mpa (Torzilli et al., 1999). In another study carried out on bovine explants by Leoning et al., the degradation of the collagen matrix occurred in the 7–12 Mpa range and chondrocyte apoptosis occurred at the 4–5 Mpa range (Loening et al., 2000). Kurz et al. studied the effect of injurious loading on cartilage repair and degradation. A strain rate of 0.01 s^{-1} resulted in the peak stress of 12 Mpa and no effect on the cells, whereas a strain rate of 0.1 s^{-1} and 1 s^{-1} resulted in the peak stress of 18 and 23 Mpa correspondingly, which decreased the protein and PG biosynthesis. Increase in strain rate also increases peak stress, which results in decreased cell viability and injury. Moderate cyclic compression loading of the cartilage over a range of frequencies can increase chondrocytes' biosynthesis of matrix macromolecules. Despite significant work in the area of cartilage injury, the molecular mechanisms underlying these biochemical changes remain poorly understood (Kurz et al., 2001; Ryan et al., 2009).

2.6.3 In vitro enzymatic degradation of the articular cartilage

It is generally believed that the degeneration of cartilage in OA occurs in two phases: a biosynthetic phase and a degradation phase. In the biosynthetic phase, chondrocytes in the cartilage attempt to repair the damaged ECM. In the degradation phase, the ECM is digested by the activity of enzymes produced by chondrocytes and the event of cartilage erosion is accelerated (Howell, 1986; Lu et al., 2013). The link between the mechanical and the structural properties of the cartilage is key to better understanding the pathogenesis of OA. As described in the section above, the earliest sign of OA seems to involve changes in the composition and structure of the superficial cartilage (Buckwalter and Mankin, 1998a). In vivo animal models have been used extensively in OA research; however, ethical issues, high costs and the extended time span of experiments burden the use of animal models. Moreover, under in-vivo conditions, it is challenging to trace early pathophysiological changes and to experimentally study the structure-function relationships of injured cartilage, as multiple structural and functional changes occur simultaneously, and the first alterations do not cause pain. Hence, the enzymatic digestion of cartilage provides an experimental model that reveals the structure-function relations of cartilage tissue and the changes associated with early stage OA (Rieppo et al., 2003b). This procedure allows us to understand how the degradation of individual constituents affects the mechanical behaviour of the tissue.

2.6.3.1 Enzymatic degradation of collagen

Matrix metalloproteinases (MMPs) – such as stromelysin (MMP-3) and collagenase 3 (MMP-13) (Durigova et al., 2008), and ADAMTS (the disintegrin and metalloprotease with thrombospondin motifs), namely ADAMTS-4, -5, -8, -9, -1 and -15 (Verma and Dalal, 2011) – are responsible for early aggrecan cleavage and are believed to have a key role in the destruction of the joint during OA. The enzymatic activities of MMPs are controlled by tissue inhibitors of the metalloproteinase (TIMP-1, TIMP-2, TIMP-3, and TIMP-4). Hence the equilibrium between MMPs and TIMPs in the synovial fluid and local tissue may be a determinant of whether the MMPs attack the cartilage ECM (Verma and Dalal, 2011; Yoshihara et al., 2000). The MMPs have been considered the main enzymes responsible for the degradation of aggrecan and collagens in cartilage (Nagase and Kashiwagi, 2003). Many enzymes have demonstrated the ability to cleave the protein backbone of the aggrecan (Mahmoud et al., 2005). ADAMTS-4 and ADAMTS-5 have

been identified as the known enzymes that are the most capable of cleaving aggrecan (Glasson et al., 2004). A number of reports have mentioned the increased contribution of ADAMST-4 in joint disease with inflammatory cytokines (Yamanishi et al., 2002). To study the contribution of such enzymes in the development and progression of OA, knock-out mice can be used, to characterise aggrecan degradation (Glasson et al., 2004).

2.6.3.2 Enzymatic degradation of proteoglycans

Artificial degradation through enzymes is a typical method to experimentally induce the depletion or decomposition of one or two components, stimulating the pathological changes of the AC. The major ECM protein in cartilage is collagen, and it is important for cartilage integrity. Collagen is damaged in degenerative diseases that affect the cartilage, such as OA (Deng et al., 2007). This produces a model that resembles early stage OA, including loss of superficial collagen fibrils and PGs. The degree of artificial degradation can be controlled through the choice of enzyme, concentration, and the duration of treatment (Moody et al., 2006b). In OA, tissue breakdown initiates from the superficial zone and the surface of the AC; it is characterised by the degeneration of the two principle macromolecular components of cartilage ECM: the type II collagen fibrillar network and the PG aggregates (Brocklehurst et al., 1984; Hollander et al., 1995).

To reproduce the OA disease process in vitro, researchers use a number of enzymes with similar properties to those found in vivo to cleavage the PG molecule (Moody et al., 2006a). These include trypsin (Hardy et al., 2005; Jakob et al., 2003; Qin et al., 2002; Wang et al., 2008a), cathepsin K and D to denature collagen type II fibres (Dejica et al., 2008; Kempson et al., 1976; Sapolsky et al., 1973), chondroitinase ABC (Bautista et al., 2016; Koob, 1989) and elastase (Rieppo et al., 2003b). The study of enzymatic digestion of cartilage begins with some variations in samples before the process of degradation starts. Factors such as sample size, thickness, PG distribution in the tissue affects the results. PGs are the major component of the cartilage ECM and, due to their size, they are able to apply high pressures within the collagen network, providing cartilage with the ability to resist compressive forces (Bartholomew et al., 1985).

2.6.3.3 Effect of enzymatic damage on the mechanical properties of cartilage

When degrading a single constituent of the ECM during its enzymatic digestion, more than one mechanical property is affected due to the tissue's complicated interrelation

between its constituents and mechanical properties (Accardi, 2012). In the early stages of OA, the loss of cartilage constituents (GAGs) results in the softening of the tissue; thus, understanding the breakdown of the mechanical properties of cartilage in patients with OA would be useful for the early detection of OA (Hardy et al., 2005). Experimental studies have demonstrated that GAG digestion decreased the compressive modulus and increased the permeability and water content of the tissue (Fung, 1981; J. Katta et al., 2008; Korhonen et al., 2002). The depletion of PG is shown to reduce collagen degradation and have no effect on the instantaneous compressive response of the tissue. In terms of compressive response, the collagen is responsible for an instantaneous response and PGs for the compressive modulus of the tissue (Bader et al., 1992; Lyyra et al., 1999).

2.7 Literature review- Part 2: Shoulder anatomy

As explained previously, Part 2 of this literature focuses on shoulder joint's detailed anatomy and structure and biomechanics followed by an overview of shoulder OA treatment options, particularly shoulder hemiarthroplasty (HA) and its complications, is given. This section aids the reader to obtain an overview of the state-of-the-art in relation to with comprehending chapter 5 and 6 of this thesis.

The structure of the shoulder makes it the most mobile joint in the body and also the least stable. It is due to this extreme mobility that the shoulder is more susceptible to the risk of injury. The shoulder complex consists of the clavicle, scapula, and the humerus, and it includes the following joints: the glenohumeral joint, the sternoclavicular joint and the acromioclavicular joint as shown in Figure 2-11 (Davies, 2006; Hendrickson, 2002).

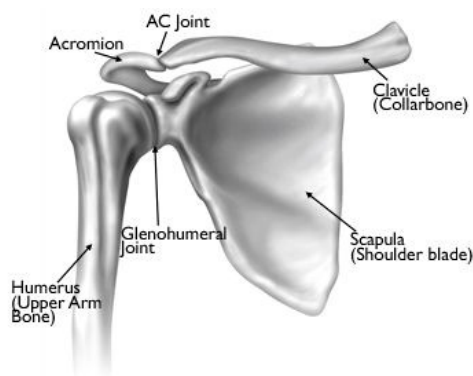


Figure 2-11 Glenohumeral anatomy showing various components of the shoulder joint

2.7.1 Glenohumeral joint anatomy

The glenohumeral joint is remarkable for its relative lack of bony constraints, relying significantly on the congruent articulating surfaces and surrounding soft tissue for static and dynamic stability (Bigliani et al., 1996). It is a ball-and-socket synovial joint that is formed by the articulation of the rounded large humeral head and smaller glenoid fossa with three rotatory and three translator degrees of freedom. This instability is due to a lack of bony congruity in its articulating surface. The shoulder joint has to rely on the ligaments for stability; therefore, they are very susceptible to injury and degeneration. The collective role of the glenohumeral ligaments is to strengthen the anterior and inferior walls of the joint capsule by providing some limitation to the lateral rotation of the shoulder, particularly between 0–90 degrees of arm elevation (Culham and Peat, 1993).

The shoulder joint has three degrees of freedom of movement, allowing the motions of flexion/extension, abduction/adduction, and medial/lateral rotation (Halder et al., 2000; Levangie and Norkin, 2011b; Reese and Bandy, 2016). The radius of the curvature of the glenoid cavity and humeral head depends on cartilage thickness. Cartilage is thicker at the centre of the humeral head and the rim of the glenoid cavity. The average glenoid to humeral head surface area ratio is 3.12 and 2.90 for males and females respectively. The average cartilage surface area of the humeral head for males and females has been measured to be 1734 ± 204 and $1336 \pm 220 \text{ mm}^2$ respectively (Iannotti et al., 1992; McPherson et al., 1997).

2.7.2 Humerus

The humerus is the longest bone in the upper extremity of the body, whose head is approximately one-third of a sphere (Peterson and Bronzino, 2014). The head of the humerus is considerably larger in area than the glenoid and its surface is more acutely curved, giving it a smaller radius of curvature. The degrees of the radius of curvature of the humeral head and the glenoid are close. This difference in size of the articular surfaces also influences the type and range of motions (ROMs) that can occur between these two surfaces (Pratt, 1994). The articular surface of the humeral head is almost a sphere shape of 120 degrees, with an average diameter of 43 mm and it is tilted 45 degrees relative to the humeral shaft (M. Halder et al., 2000; Rockwood, 2009) (Figure 2-12). The humeral head's average radius of curvature in the coronal, anteroposterior, and axillary planes are $24 \pm 2.1 \text{ mm}$, $13.1 \pm 1.3 \text{ mm}$ and $22.9 \pm 2.9 \text{ mm}$ respectively (Iannotti et al., 1992; McPherson et al., 1997). Sometimes, a substantial force on the shoulder can result in glenohumeral joint dislocation, with a possibility of fracture at the proximal humeral head. The humerus fracture incident increases with age: people over 40 years of age are at greater risk due to osteoporosis (Terry and Chopp, 2000).

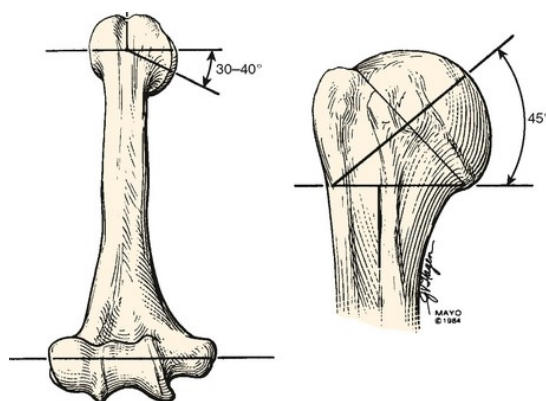


Figure 2-12 The two-dimensional orientations of the articular surface of the humerus with respect to the bicondylar axis (Hadler et al., 2000)

2.7.3 Scapula

The scapula is a large flat triangular bone that is thicker at both superior and inferior angles; its main function is to carry a large number of powerful muscle attachments. The scapula forms a connection between the humerus and the thorax, which consists of three processes: the acromion, spine and coracoid processes (Halder et al., 2000; Persad, 2016) (Figure 2-11). The scapula has a slight superior directed tilt of three degrees to five degrees and is rotated 30 degrees forward relative to the frontal plane (Oosterom, 2004). The end of the scapula, known as the glenoid, meets the head of the humerus to form the glenohumeral cavity that acts as a flexible ball-and-socket joint (Abulkhair, 2012).

2.7.4 Glenoid cavity

The glenoid is part of the lateral scapula; it is a shallow, pear-shaped socket, tilted upward at about five degrees (Löhr et al., 1998) (Figure 2-13). The spinoglenoid notch separates the base of acromotion from the glenoid. It has a slightly concave surface with a radius curvature that is larger than the humerus. Its total surface area is three to four times smaller than that of the humerus. The central area of the glenoid has thinner cartilage compared to the edges of the glenoid (Halder et al., 2000). The surface of the glenoid is 25–35% of the humeral head, which results in only part of the humeral being in contact with the glenoid at any position of the shoulder joint (Culham and Peat, 1993).

The glenoid of the scapula serves as the proximal articular surface for the glenohumeral joint, and the humeral head is the distal articular surface of the glenohumeral joint. The glenoid fossa is commonly described as pear-shaped or having an inverted shallow

comma shape. The shallowness of the glenoid fossa and the disproportionate size and lack of congruency of the articular surfaces make the joint inherently unstable. Also, the glenoid provides only a small articular surface for the humeral head; therefore, the glenohumeral joint possess some instability (Kaar et al., 2010).

2.7.5 Glenoid labrum

The glenoid labrum is a triangular, dense fibrous rim overlying the peripheral circumference of the glenoid that contributes to the stability of the glenohumeral joint. Its base is attached to the margin of the glenoid by fibrocartilage and fibrous bone. It is attached to the glenohumeral ligaments, and its function is to increase congruity, generating a suction effect and thereby enhancing the stability of the glenohumeral joint (Halder et al., 2000; Wilk et al., 1997). The glenoid labrum supplies nutrition to the glenoid cavity and maintains joint lubrication (Hill et al., 2008). The labrum does receive a blood supply, where the vascularity is limited to its periphery. A study by Cooper et al. (1992) showed that the superior and anterosuperior parts of the labrum have less vascularity in comparison to its posterosuperior and inferior parts. Vessels supplying the labrum originate from either the capsular or periosteal vessels and not from the underlying bone. Working as a valve, the glenoid labrum covers the joint from atmosphere pressure, therefore sustaining negative intra-articular pressure. Any labral damage would break this seal and could increase joint instability and cartilage strains in the joint (Cooper et al., 1992; Ferguson et al., 2001; Habermeyer et al., 1992; Hill et al., 2008).

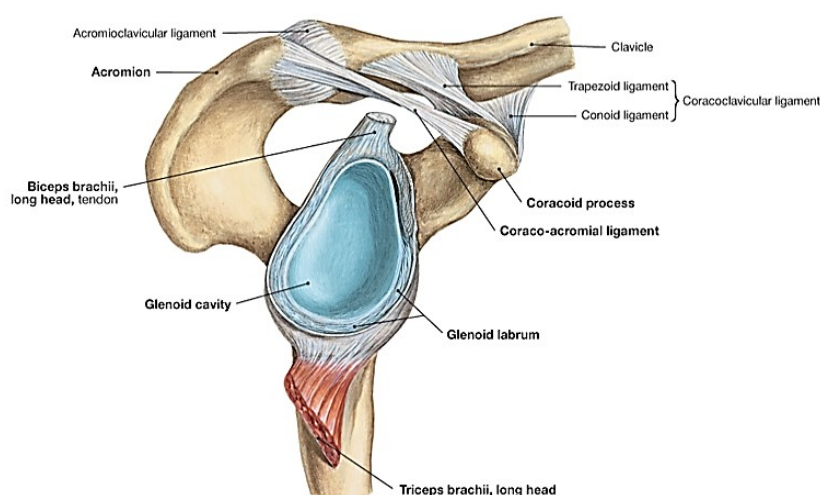


Figure 2-13 Anatomy of the glenoid labrum Adapted from Sabotta

2.8 Shoulder joint mechanics

Shoulder kinematics is concerned with shoulder joint movement and its degree of freedom (Haering et al., 2014). In contrast to the more singular load-bearing ball-in-socket behaviour of the hip, the shoulder joint is a complex ensemble of multiple elements and muscles requiring extraordinary mobility to perform complex motion. However, the type of articulation between the hip and the glenohumeral joint is rather similar, although the latter receives active assistance from the scapula (Oosterom, 2004).

Table 2-1. Normal range of motion (ROM) (degree) for the hip and the glenohumeral joint values are adapted from (Reese and Bandy, 2010))

Motion of joint	Glenohumeral joint (degree)	Hip joint (degree)
Flexion	0–180	0–120
Extension	0–60	0–30
Abduction	0–180	0–45
Adduction	0–140	0–30
Medial rotation	0–70	0–45
Lateral rotation	0–90	0–45

The centre of rotation (COR) of the glenohumeral joint has hardly been measured and is still a subject of discussion, due to the unknown location of the COR relative to the thorax (Shklar and Dvir, 1995; Veeger, 2000). In 1976 and 1977, Poppen and Walker and Jackson et al. stated the position of the COR relative to the humeral head during abduction based on a two-dimensional estimation (Jackson et al., 1977; Poppen and Walker, 1976). Recently, Amabile et al. (2016) used a camera optical motion tracking system to obtain shoulder kinematic data in order to calculate the glenohumeral joint's COR. Furthermore, studies carried out by Soslowky et al. (2001) and Kelkar et al. (1992) concluded that the COR is fixed, at least as long as the humeral head and the glenoid shape remain spherical (Kelkar et al., 2001; Soslowky et al., 1992). In the glenohumeral joint, three different types of motion may occur: spinning, sliding, and rolling. Spinning occurs when the

contact point on the glenoid remains the same, while the humeral head contact point changes. Sliding is the pure translation of the humeral head on the articular surface of the glenoid that occurs at the extreme motion, when the contact point on the glenoid is moving while the contact point for the humerus remains the same. Rolling may also occur at the glenohumeral joint; this is a combination of the humeral head sliding and spinning relative to the glenoid, such that the contact point changes on both the glenoid and the humeral head (Krishnan et al., 2004). Table below shows the average radius of curvature of the glenoid cavity and humeral head for both male and female.

Table 2-2 The radius of the curvature (mean $\pm$ SD) (mm) of the glenoid cavity and the humeral head for male and female subjects, measured with and without the cartilage layer (Soslowsky et al., 1992)

<i>Radius of curvature (mm)</i>	<i>Including cartilage</i>		<i>Excluding cartilage</i>	
	<i>Male</i>	<i>female</i>	<i>Male</i>	<i>Female</i>
<i>Humeral head</i>	26.85 $\pm$ 1.40	23.27 $\pm$ 1.69	26.10 $\pm$ 1.41	23.15 $\pm$ 2.09
<i>Glenoid cavity</i>	26.37 $\pm$ 2.42	23.62 $\pm$ 1.56	34.56 $\pm$ 1.74	30.28 $\pm$ 3.16

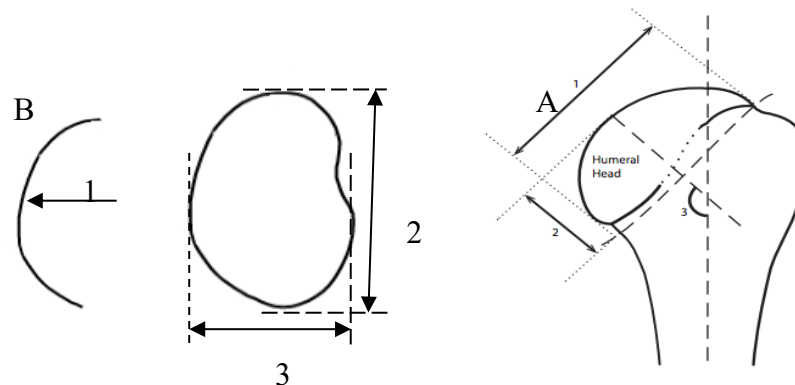


Figure 2-14 A) Humeral head's anatomical dimensions in the coronal plane: 1) humeral head diameter; 2) humeral head height; 3) humeral head angle. B) Glenoid cavity: 1) glenoid curvature; 2) maximum height; 3) maximum width

2.8.1 Range of motion and joint forces

The functional ROM is defined as the ROM needed to comfortably and efficiently perform 'Activities of Daily Living' (ADL) (Brumfield and Champoux, 1984). During ADL, the shoulder complex must be able to pick up forces that can be as high as several times one's body weight (BW) and still be stable enough to prevent joint dislocation. The

shoulder joint allows for a large ROM, approximately 180 degrees abduction, 50 degrees adduction, 75 degrees internal and external rotation, 120 degrees flexion and 13 degrees extension (Figure 2-15) (Morrey and An, 1990). Although the wrist and elbow functions have been well investigated, less is known about the ADL ROM requirements of the shoulder. Using the clinical studies of the wrist and elbow as a model, Namdari et al. (2012) carried out a study to characterise the functional ROM of the shoulder. Table 2-3 shows some of the shoulder motions needed to complete the ADL task (Namdari et al., 2012). While the shoulder joint is not weight-bearing, contact forces can reach several times one's BW (Oosterom, 2004). It has been found that an arm abduction to 90 degrees results in joint contact forces between 370–650 N (0.5 times BW and 0.89 times BW respectively) (Poppen and Walker, 1978; van der Helm, 1994). If weights are added to the joint, forces increase to 2,070 N (three times BW) (Buechel et al., 1978). During articulation, the contact area between the glenoid and the humeral head depends on the elevation angle and ranges between 87 and 507 mm² (from 0 degrees to 120 degrees abduction) (Soslowsky et al., 1992).

Table 2-3. Average ROM (degree) in dominant and non-dominant arms while performing ADL. Values adapted from Namdari et al. (2012)

Tasks of daily living	Measured humeral motion	Dominant arm	Non-dominant
Comb hair	Forward flexion	107.8±3.0	109.0±2.6
	Adduction	86.1±2.9	91.3±2.4
Tuck in shirt behind back	Extension	45.5±2.4	45.9±3.2
	Internal rotation	88.3±9.1	86.9±8.7
Reach overhead shelf without bending the elbow	Forward flexion	118.6±1.4	123.1±1.6
	External rotation	29.5±2.0	26.2±1.8
Wash the back of the opposite shoulder	Forward flexion	94.9±2.4	92.6±2.5
	Adduction	115.8±2.2	115.9±1.9

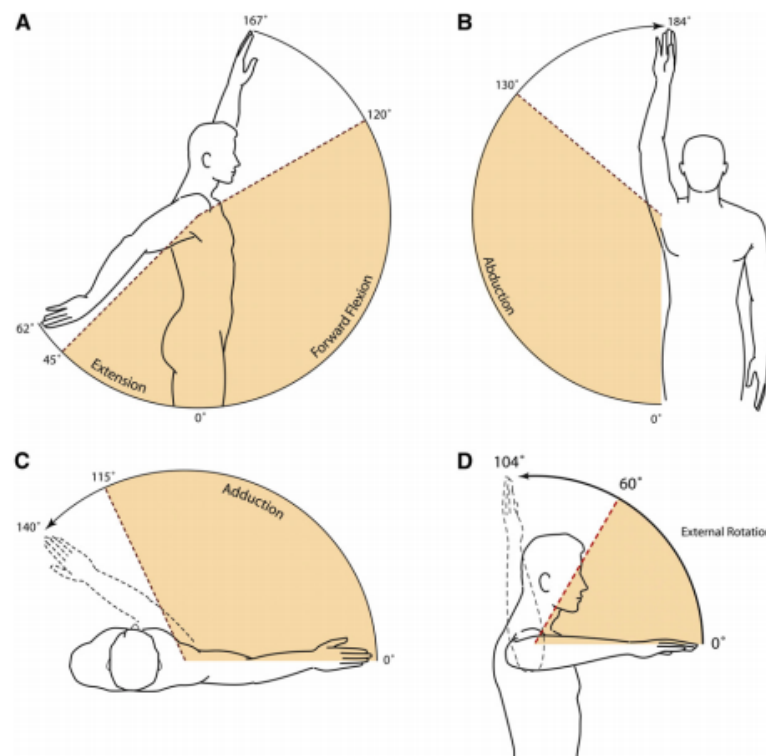


Figure 2-15 The diagram demonstrates the functional arcs of the shoulder motion (shaded) compared with the normal anatomic ROM in (a) forward flexion and extension; (b) abduction; (c) adduction; and (d) external rotation. Images adapted from Namdari et al. (2012)

2.9 Shoulder joint pathology and shoulder replacement

Common shoulder joint pathology can be classified into four different areas: Rotator Cuff (RC) Arthroplasty, Avascular Necrosis (AVN), Glenohumeral OA, and Rheumatoid Arthritis (RA). RC arthroplasty is characterised by RC insufficiency, reduced acromiohumeral distance and arthritic changes in the glenohumeral joint (Funk et al., 2007). Neer et al. (1983) hypothesised that a massive RC tear leads to the initial event in the degeneration of the shoulder joint. A deficient cuff may allow excessive upward migration of the humeral head and result in abrasion and the erosion of the glenoid (Neer et al., 1983). The articular surface receives nutrition from the synovial fluid and a RC tear violates the closed joint space, allowing the synovial fluid, with its nutrients and other biochemical constituents, to leak into the surrounding soft tissue (Zeman et al., 1998). The prevalence of RC disease increases with age, obesity, diabetics and chronic diseases that affect the strength of the shoulder (Greenberg, 2014). This is also demonstrated by increased glenohumeral instability, as the joint compression force has disappeared.

AN is an uncommon cause of glenohumeral arthritis described first by Cruess in 1976, where a region of the humerus bone is permanently lost as the result of poor blood supply and the subsequent death of osseous tissue (Orfaly et al., 2007). This can occur when blood vessels in the bone are injured due to traumatic impact or when the disease produces areas of abnormal circulation (Hollis and Yamaguchi, 2008). The early stage of this disease is difficult to recognise, as there is no pain or a decrease in joint functionality. In the later stages, it can be seen as a decrease in bone density. As the collapse of the humeral head occurs, hemiarthroplasty (HA) and total shoulder arthroplasty (TSA) become the most appropriate surgical treatments. For younger patients, HA is carried out to preserve glenoid cartilage; for older patients with or without glenoid wear, TSA is performed, this would be explained in further details in the next section (Hollis and Yamaguchi, 2008).

Glenohumeral OA, also known as the degenerative joint disease of the shoulder, is a common cause of shoulder pain that involves a gradual, progressive, mechanical and biochemical breakdown of the cartilage (Millett et al., 2008). As the AC surface wears, friction in the joint increases, causing progressive loss of the normal load-bearing surfaces along with pain and disability (Hytinen et al., 2001). Although little is known about the initiation events in cartilage degeneration, some studies suggest that changes of the superficial layer are among the earlier events. The tensile stiffness and strength of the cartilage's superficial layer is decreased by 40–60% in the human experimental OA model and the tissue water content is increased (Akizuki et al., 1986b). Radiographic findings of glenohumeral OA include joint space narrowing, circumferential osteophyte formation, subchondral cyst formation, posterior wear or bone loss of the glenoid. Shoulder OA may be primary or secondary. Primary OA is believed to be rare in the shoulder, yet it is becoming an increasingly recognised source of pain and disability (Gupta et al., 2004).

RA is an autoimmune inflammatory joint disease, affecting both the bone and the surrounding tissue of the shoulder region. This is a progressive disorder that results in pain, as well as loss of ROM and functional stability (Chen et al., 2003). In RA, the body releases enzymes that attack its own healthy tissues and destroy the linings of joints. The radiological progress of joint destruction was measured by Larsen et al. A normal joint is stage 0 and the complete destruction of the joint is stage 5 (Larsen et al., 1977; Luukkainen et al., 1983).

2.9.1 Current shoulder joint replacement systems

Shoulder replacement surgery is employed in the treatment of the joint pathologies explained above. The main aim of shoulder arthroplasty is to improve function, pain, and quality of life. Three different replacements are available: HA, total shoulder replacement (TSR) and reverse shoulder replacement (RSR). HA and TSR are indicated in patients with intact RCs, and RSR is used for cuff-deficient older patients. Outcomes are favourable, with the majority of patients seeing improvement in terms of shoulder pain and function. In patients with OA, the debate over TSA and HA remains. HA has a shorter operative time, is low cost and requires less demanding technical expertise. TSA, on the other hand, is suitable for more young and active patients, has implant longevity and less glenoid loosening (Garcia et al., 2016). Humeral head replacement was introduced by Neer for the treatment of select proximal humeral fractures (Neer, 1955) and approximately 90% of patients treated with shoulder HA showed minimal pain, despite a wide range of function, motion, and strength (Armstrong and Murthi, 2016). A study by McCarty et al. (2008) evaluated 21 HA procedures and reported an 81% rate of return to physical activities (McCarty et al., 2008).

Modern shoulder arthroplasty was first introduced by Neer in 1950s for the treatment of the proximal humeral head fracture (Van Den Bekerom et al., 2013). The common surgical options for OA are HA with or without the stem, removal of the humeral head, and TSA. TSA is applied for patients with an indication of glenohumeral OA, RA and complex humeral fractures. Managing complex proximal humeral fractures is a challenge for clinical physicians, particularly in the case of severe dislocation. HA has proven to generate satisfactory results for the treatment of complex proximal humeral fractures (Yang et al., 2009).

The potential advantages of HA are that the operation time is reduced, blood loss is decreased (therefore, it is easier to perform), and the procedure is less technically difficult and avoids issues associated with glenoid loosening. However, there is still concern regarding the progression of the disease and glenoid erosion with this procedure; hence, the need for future revision surgery. TSA is associated with an increase in blood loss and operation time. This is technically more challenging to perform and incurs the risks of potential glenoid loosening and polyethylene wear. Whether to use HA or TSA is still controversial. Some surgeons choose TSA for fractures without glenoid impairment,

while others consider that TSA has a high incidence of implant loosening created by glenoid component loosening (Yang et al., 2009). When deciding to perform HA or TSA, two factors are very important: the possibility of glenoid loosening in TSA versus the possibility of glenoid erosion when performing HA (Carroll et al., 2004; Sandow et al., 2013; Yang et al., 2009). Studies by Gartsman et al. (2000a) and Edwards et al. (2003) have recommended that TSR would provide more short-term pain relief but there are concerns of long-term glenoid failure and problems regarding revisions of failed TSR. Sandow et al. (2013) investigated the short-term efficiency of HA and TSR in patients with OA and intact RC. They demonstrated that patients who underwent TSR had better function and less pain compared to HA within two years; results also showed no deterioration of TSR function at 10 years. Reverse shoulder arthroplasty has emerged as a very attractive alternative for patients with cuff tear arthroplasty. Complications after shoulder arthroplasty may include infection, instability, neurovascular injury, stiffness, cuff tears, glenoid erosion and component loosening (Sanchez-Sotelo, 2011).

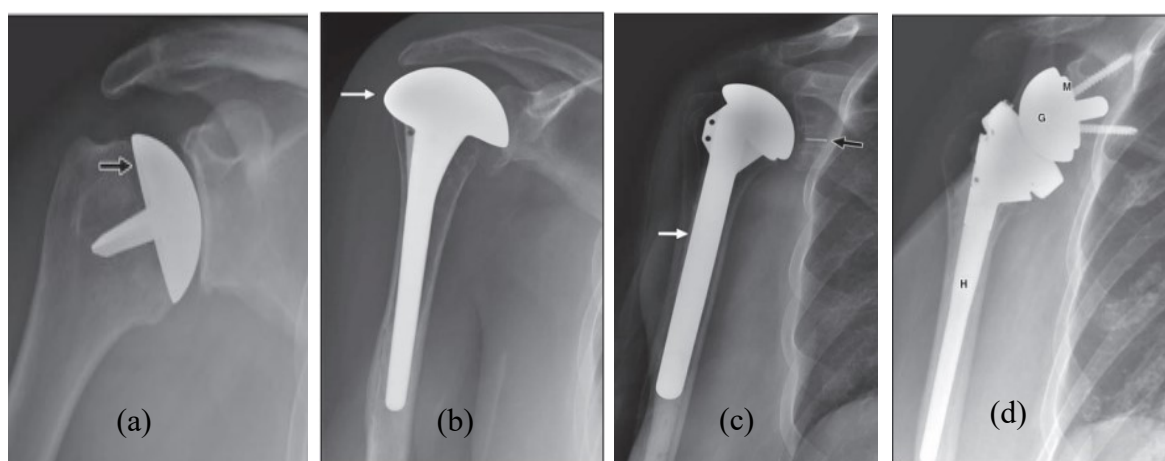


Figure 2-16 Different shoulder replacement systems: (a) shoulder HA without the stem with humeral head resurfacing of a humeral head with AN; (b) shoulder HA with stem with osteonecrosis humerus; (c) TSA placed for primary OA; (d) reverse total shoulder arthroplasty (RTSA). Images adapted from Ha et al. (2012) and Petscavage et al. (2012)

2.9.2 Results and complications after shoulder replacements

The success of shoulder arthroplasty depends on multiple factors – proper height, retroversion and tuberosity healing (Bigliani et al., 1996; Boileau et al., 2006a) – but its main advantage is that it is a simple procedure that avoids the risk of glenoid component loosening (Levine et al., 2012). Bad results are correlated to the degree of glenoid wear (Levine et al., 1997). Patient outcomes are sometimes shown to be less successful than

with total arthroplasties (Dean et al., 2016; Ferrel et al., 2015; Sebasti  -Forcada et al., 2014). Painful glenoid arthrosis is the most indication for the revision of HA (Ferrel et al., 2015; Gartsman et al., 2000; Sperling and Cofield, 1998). Rispoli et al. (2006) showed that 18% of HAs used primarily in treatment of shoulder OA were revised for painful glenoid arthritis; Ferrel et al.'s (2015) study showed that 4% of HAs were revised for fractures. There is a general uncertainty about the cause of seemingly accelerated cartilage wear in HAs (Champion and McNally, 2004; Haidukewych et al., 2002; Hasan et al., 2002; Hedtmann and Werner, 2007; Parsons et al., 2004; Sperling et al., 2002). One of the main factors in determining the longevity of this type of reconstruction is the resulting damage and wear of the cartilage. Revision from HA to reverse shoulder arthroplasty does not appear to improve outcomes (Acevedo et al., 2014; Schairer et al., 2015). In the clinical routine, the material used for HA surfaces include long lasting cobalt -chromium-molybdenum alloy, various ceramics such as zirconium (ZrO_2) and aluminium-oxide (Al_2O_3), and polymers such as polycarbonate-urethane (PCU).

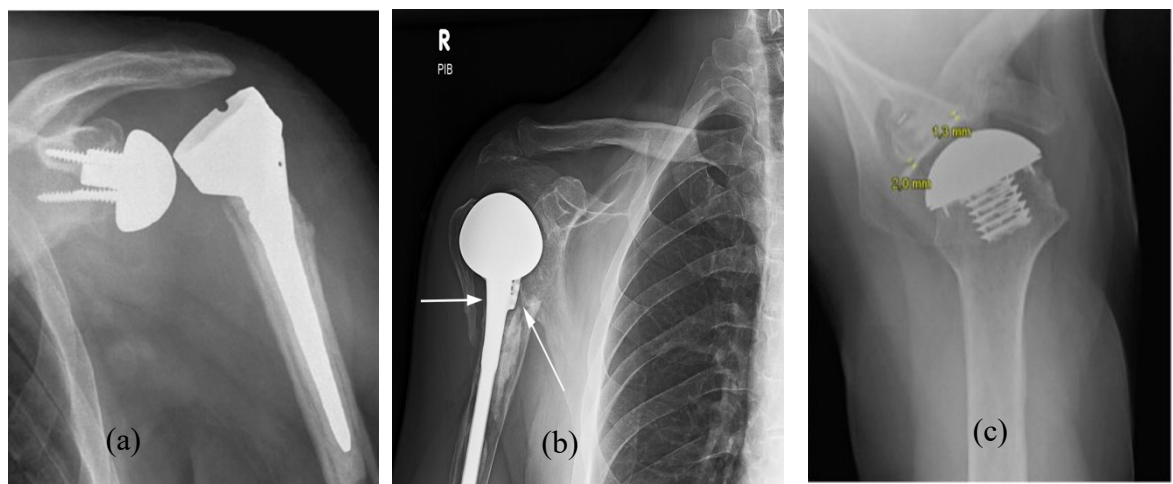


Figure 2-17 Overview of common complications after shoulder replacement: (a) anteroposterior view of a reverse TSA with dislocation (failure of fracture healing with loosening and osteolysis) (Farshad and Gerber, 2010); (b) radiograph of the right shoulder after a six-month cementless TSA indicating the loosening of the glenoid component (Venjakob et al., 2015); (c) shoulder HA failure shows cartilage wear and the narrowing of the glenohumeral joint

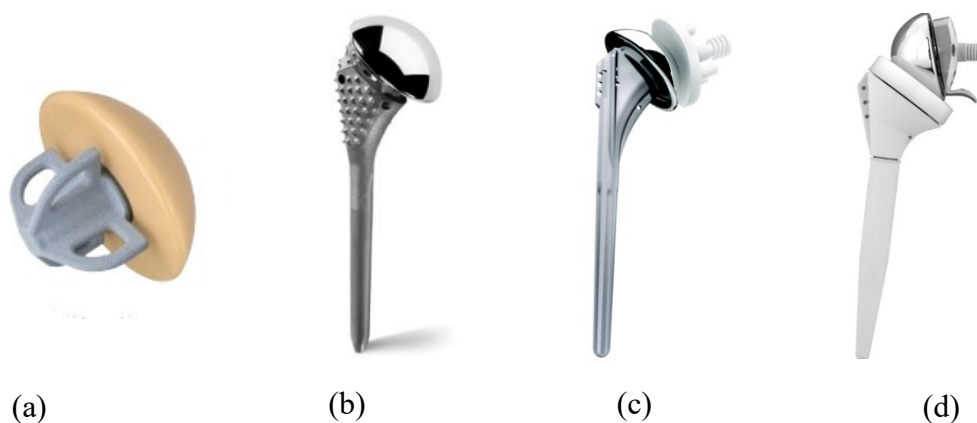


Figure 2-18 Common shoulder implants in the market. (a) Mathys humeral head; (b) Zimmer Biomet anatomical shoulder HA system for fracture; (c) DePuy GLOBAL ADVANTAGE shoulder arthroplasty system; (d) GEO RTSA

2.10 Literature review of the current shoulder joint simulators – In vitro tribological experiments on cartilage

A number of model systems have been developed to stimulate various aspects of the mechanical loading forces experienced by cartilage (Fitzgerald et al., 2004). During normal daily activities, cartilage is exposed to static and dynamic mechanical loads. Hence, to understand how these *in vivo* joint loading patterns affect the cellular regulations of anabolic and catabolic activities, the response of cartilage explants from animal models under static and dynamic loads have been studied (Griffin and Guilak, 2005). A physiological loading system for cartilage is essential for the maintenance of the AC by regulating tissue remodelling in the form of catabolic and anabolic processes. Several groups have used mechanical conditioning in the form of uniaxial compression to modulate the response of chondrocytes; the PG metabolism in humans can be studied *in vitro* (Lafeber et al., 1993). The mechanical forces influence both the ECM and chondrocyte metabolism. *In vitro* models of cartilage have been developed and they are used prior to *in vivo* models for validation (Cook et al., 2014).

Cartilage explants have been used to study the effect of mechanical forces on the cartilage metabolism; these studies are important as they provide important information on the behaviour of chondrocytes in the ECM. The explant studies have a major problem, as the mechanical forces are extremely difficult to characterise. The normal synovial joint can withstand repetitive loading during normal activities for a lifetime without developing OA. Mechanical forces that exceed the tolerance of the AC surface have an important

contribution in the development of OA. Studies suggest that repetitive loads on the joint are associated with early OA (Buckwalter et al., 2005). Experimental studies show that excessive mechanical stress can directly damage the AC and subchondral bone, and it can alter chondrocyte function, including the balance between synthetic and degenerative activity. In vitro studies are sometimes superior to in vivo studies due to a number of reasons: 1) they are cheaper, as they reduce the number of animals used; 2) the assessment of OA development is more controlled and data can be achieved at different stages of OA; and 3) it is more ethically acceptable (Polli, 2008).

Although many studies (Kienle et al., 2015; Liu et al., 2015; Morrell et al., 2005; Wimmer et al., 2004) have investigated the damage and wear of cartilage in the natural joint as related to the initiation and progression of OA, very few studies (Dombroski et al., 2009; Krawczyk et al., 2008) report on the breakdown of cartilage when articulated against a prosthetic material as related to HA. Moreover, the latter studies describe the behaviour when the prosthetic head is articulated against intact cartilage (Bülhoff et al., 2017a; Lizhang et al., 2011; Parsons et al., 2004). Furthermore, even in a case where the cartilage is initially intact for an HA of the hip, OA almost invariably develops postoperatively (Herschel et al., 2017; Kofoed and Kofod, 1983; Parsons et al., 2004; Sen et al., 2009; Yamagata et al., 1987). Thus, most HAs need to be able to function in the presence of tissue affected by OA. The wear and tear of cartilage caused by the femoral or humeral prosthesis in the various OA environments has never been investigated before, and there is a lack of knowledge regarding the tribology of these prosthetic materials in the HA joints.

Pin-on-disk configurations have been the most commonly used in vitro set-ups to study cartilage tribology: these have a higher degree of control in terms of the experimental variables but they lack biochemical and biomechanical synergies that are found in a synovial joint (Farizon et al., 1996; Saikko, 2014; Shi et al., 2011, 2012). In a pin-on-disk set-up, variables such as the stroke length and sliding velocity control the friction properties of the system and the wear of cartilage surfaces. Synovial joints typically operate in a mixed lubrication regime; thus, slow sliding (1–4 mm/s) velocities are generally adopted in these pin-on-plate set-ups to reproduce these conditions in vitro, while also avoiding non-physiological hydrodynamic lubrication between the surfaces. The output of this test is a curve of friction coefficient versus time, which (following the

appropriate interpretations) provides an understanding of the tribological behaviour of the material. Oungoulia et al. (2015) tested different materials for HA and showed that considerably more damage occurred in the cartilage samples tested against stainless steel (10 nm roughness) and the low carbon CoCr alloy (27 nm roughness) compared to glass (10 nm) and smoother low or high carbon CoCr (10 nm). PCU is a new material developed for the acetabular component in total hip arthroplasty (Cadossi et al., 2013; Moroni et al., 2012).

Cartilage has been demonstrated to be a structure rather than a material, which makes it impossible to remove small samples for testing without disrupting its structural integrity. Obeid et al. (1994) reported that a 8-mm diameter cartilage plug offered a rather reasonable flat surface, and this dimension was less disruptive of the collagen network. Therefore, the overall aim of this study was to provide information to help determine the most appropriate prosthetic material for HA, and if this material selection might be affected by the severity of OA suffered by the patient. The specific objectives were to assess the damage and wear of human cartilage when tested against three orthopaedic materials in a pin-on-disc test set-up, and to carry out this assessment on cartilage with different degrees of OA. Specifically, the CoCr alloy, alumina ceramic (Al_2O_3) and PCU were tested against five different levels of OA, varying from intact cartilage to severely OA-degraded cartilage (Obeid et al., 1994b). All the previous studies have been developed on pin-on-plate studies; as part of this project, a joint simulator will be developed that will enable the investigation of the behaviour of both OA-like and healthy joints on a larger scale, with the joint subjected to physiological loading in a lubricated environment. This can ultimately allow the exploration of the biomaterials' performance in terms of their size and shape.

2.11 Summary

In this chapter, the literature review was divided into two different sections as each part aided the reader with understanding different chapters of this thesis. In the first section, several aspects of articular cartilage ranging from the structural description of the tissue to its mechanical properties have been illustrated. In the second section, detailed anatomy description and mechanics of the shoulder joints, as well as different modes of joint arthroplasty, were discussed. It is only by thoroughly understanding the relationship between the biological and the engineering principles that a successful investigation into

osteoarthritis and choosing an optimum biomaterial for a shoulder joint replacement can be made. Having provided the reader with the necessary foundations to comprehend such a study, the basic experimental techniques which have been used during this research in terms of tissue preparation and analysis will be described in the following chapter. These techniques are found to be common through chapters 4, 5 and 6, in-depth explanation of experimental methods used specifically for the results presented in each of these can also be found in each of them.

3 MATERIALS AND SAMPLE PREPARATION

3.1 Introduction

This chapter introduces the experimental techniques and the testing protocols and procedures used throughout this research. The experimental techniques have been outlined and designed in order to assess various properties of the tissue: mechanical, tribological, and biochemical properties as well as surface topography. This will enable us to obtain a complete characterisation of the tissue which is essential in order to have a complete understanding of the healthy and damaged tissue's response under various loading. This study was separated into different phases. Initially, tests were carried out on animal articular cartilage plugs to define and validate the precise protocol necessary in order to assess mechanical and tribological response of the tissue. The findings from animal studies will help to prepare a protocol for human tissue studies. Secondly, the damage was induced on the animal tissue and was compared with the real OA human samples in order to shed light on the possible initiation routes of the pathogenesis. Furthermore, to study this in larger scale a tribological joint simulator was developed, which allowed the wear and friction testing of animal joints. The various details of the rig development will be thoroughly explained in chapter 5.

3.2 Lubricants

3.2.1 Phosphate buffer saline

Phosphate buffer solution (PBS) (Sigma Aldrich Ltd., Dorset, UK, Catalogue No: P4417) is a water-based salt solution and it is commonly used in biological research. According to the manufacturer's instruction, one tablet was dissolved in 200ml of Deionized water to yield 0.01M phosphate buffer (0.0027 M potassium chloride and 0.137 M sodium chloride) with PH 7.4 at 25°C. The prepared PBS was stored at room temperature and used within two weeks.

3.2.2 Bovine calf serum

Animal serum is commonly used to supplement basal media formulations for the optimal growth of many cell types. Iron fortified bovine calf serum (IF-BCS) is collected from formula-fed calves that are 4-6 months old. Because the calves' diet is designed for weight gain by fattening, the serum is high in lipids and lipid proteins. While serum from formula-fed calves contains approx. double the protein level of Fetal Bovine Serum

(FBS), it is deficient in iron, which is essential component to achieve optimal growth with most cells. To effectively preserve the integrity of the serum, it should be stored at -10°C to -40°C and protected from light. (Sigma Aldrich Ltd., Dorset, UK, Catalogue No: 12138C).

3.2.3 PMMA bone cement

Poly methyl methacrylate (PMMA) bone cement was used to secure the tissue samples in to the correct position and orientation in the shoulder simulator sample holder fixture. Both simplex rapid powder (cold cure) and liquid (rapid repair) were obtained from Kemdent (Swindon, UK) and mixed according to the instructions. For ideal thick custard consistency, appropriate quantity of liquid is measured and then the powder is added. For optimised handling and physical properties, after 60 seconds the liquid will absorb the correct amount of powder. The resultant mixture can be poured easily for optimum control and once cured it is very strong and can tolerate high loads and less likely to fail. This process was carried out under a fume hood at room temperature.

3.3 Sample preparation

3.3.1 Choice of animal model that was used to represent human cartilage

In this research study cartilage samples were taken from various porcine and human joints. The use of animal tissue can be extremely useful for methodology development. The porcine cartilage has been used in order to prepare OA-like samples. Porcine cartilage was used as it closely replicates human cartilage. The porcine joint size, weight bearing requirements, and cartilage thickness more closely imitate the human condition than smaller animal models (Chu et al., 2010). Shepehrds et al. reported the thickness of human femoral head cartilage to range between 1.08-2.40 mm, whereas ovine was only 0.68mm in this area, porcine 1.14 mm and bovine 1.53 mm. Cartilage from human groove ranged between 1.76-2.59 mm, ovine cartilage is much thinner, 0.86 mm, porcine was 2.04 mm and bovine 1.52 mm. Porcine cartilage has higher GAG content compared to bovine. this data demonstrated that porcine cartilage thickness was within the range of human cartilage thickness (Shepehrd et al.,1999). A study by Kaab and co-workers also demonstrated by freeze-fracture scanning electron microscopy analysis that the collagen fibre arrangement in pig cartilage is very similar to the arrangement found in human (Kaab et al., 1998). Furthermore, porcine shoulder joints are more readily available when

compared to another animal models and also are cost effective in providing proof of concept data to serve as a bridge between in-vitro experiments and more costly in-vivo large animal pre-clinical studies. Many studies have used porcine plugs as part of pre-clinical in-vitro studies. Bowland et al. (2018) assessed tribological performance of porcine joint in presence of osteochondral allografts. In another study, Men and colleagues utilised porcine cartilage discs to investigate changes in the mechanical properties of defected and injured articular cartilage via a novel non-contact method (Men et al., 2017).

The first part of this study was carried out in collaboration with previous researchers in our research group and data on porcine and human joints were already available. For the pin on plate studies the plugs were taken from the knee joints due to larger cartilage size. The porcine tissue was obtained from the local butcher (Lidgate butcher, London, UK); knee joints and shoulder joints were obtained for various parts of this study. The human tissue was obtained in collaboration with Dr Abel from Charing Cross hospital, Surgery Department. The femoral heads were from patients with hip replacement surgery caused by OA or fracture. The femoral heads were individually classified by Dr Kittle, a trauma surgeon, using the ICRS OA classification.

3.3.2 Extraction of human and porcine articular cartilage plugs

The cartilage samples used in this study were taken from healthy adult porcine knee joint (4-6 months) obtained from a local butcher and the dissection of the knee was performed within 4h of death. The human femoral head samples were obtained in collaboration with Dr Abel from the surgery department of Charing Cross Hospital. To study the tribology of HAs, human femoral head AC was used in this study. These femoral head samples were obtained from patients following hip replacement surgery as a consequence of fracture or OA. The joints were either used on the same day or they were stored in the -20°C freezer. Previous studies have shown that freeze-thaw treatments do not affect the frictional properties of articular cartilage (Froster and Fisher, 1996). Prior to preparation, two hours before, the joint was taken out the freezer and left to thaw. A surgical scalpel was used to strip off the fat and muscle around the knee joint very carefully. It was necessary to ensure that there was no contact with the cartilage surface. The anterior cruciate ligament, menisci, patella, medial and lateral ligament were taken off in order to expose the underlying cartilage. Using a surgical coring device which makes a perfectly

round hole in the bone, 10mm diameter osteochondral plugs were removed from the various load bearing regions of the joint and using a sharp surgical scalpel, full thickness AC was carefully removed from the underlying subchondral bone. Particular care was exercised while performing this procedure as it was important not to cut through the cartilage plugs. Cartilage has a complex structure rather than a homogeneous material, which makes it impossible to remove small samples for testing without disrupting its structural integrity (Obeid et al., 1994). Obeid et al. (1994) reported that a cartilage plug of 8 mm in diameter is less disruptive to the collagen network and also offered a reasonably flat surface. In the current research, specimens with a diameter of 10 mm were utilised with the aim of interpreting their local properties without causing too much disruption to their structures.

Figure 3-1 (a) and (b), illustrate an image of porcine femur with cartilage plugs extracted and the map of AC plugs location. The thickness of the samples was measured using a Venire calliper and due to nonhomogeneous structure of the cartilage this was done at 10 different points across the plugs and the average was taken and for consistent results only samples with thickness > 2mm were chosen. The samples were stored in plastic containers filled with Phosphate Buffer Solution (PBS) to prevent dehydration. If the test was not conducted on the same day of sample extraction, they were stored in the -42°C freezer. It has been noted that freezing the samples and using PBS solution will not effect on the mechanical properties of cartilage samples (Szarko et al., 2010).

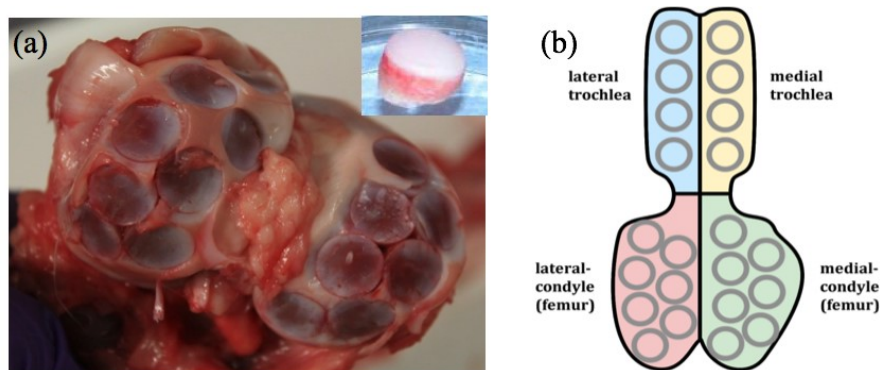


Figure 3-1(a) Porcine femur with locations of AC plug explants, (b) Map of AC sample locations.

3.3.3 Grading of human femoral head

The femoral head samples were obtained in collaboration with Dr Abel from the surgery department of Charing Cross Hospital. To study the tribology of HAs, human femoral head AC was used in this study. These femoral head samples were obtained from patients following hip replacement surgery as a consequence of fracture or OA. Using the International Cartilage Repair Society (ICRS), the cartilage lesion classification system, the femoral head samples were individually classified and determined by Dr Kittl, a trauma surgeon at Imperial College London, upon visual inspection of the typical defects associated with OA, such as fibrillation, erosion and cracking (Figure 3-2). The tissue was graded as ICRS Grade 0 to 4, where Grade 0 and Grade 4 represent non-OA and OA tissue (with severely exposed subchondral bone) respectively. In brief, according to ICRS classification, superficial fissures and cracks are considered grade 1 cartilage defects whereas lesions extending down less than 50% of the cartilage thickness are considered grade 2 defects. Grade 3 defects are defined as those extending down more than 50% but not involving the subchondral bone. Defects involving the subchondral bone are classified as grade 4 defects according to ICRS classification (Brittberg et al., 2003). The accurate determination of the defect locations depends on the surgeon's experience. Niemeyer et al.(2011) showed that inexperienced surgeons tend to overestimate defect size when compared with experienced surgeons. Human femoral head AC plugs were extracted from the femoral heads using the same procedure used for porcine AC described above.

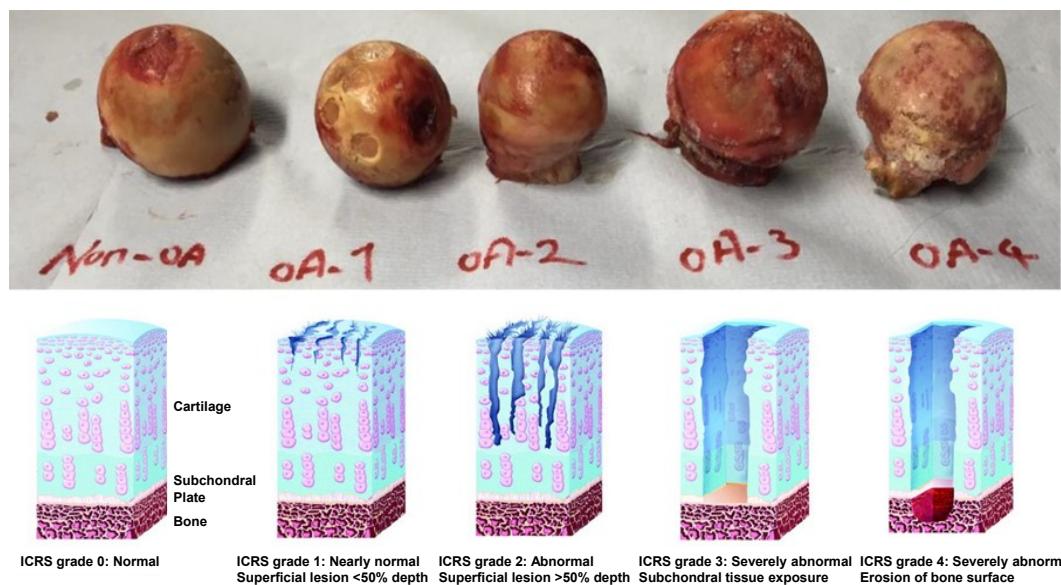


Figure 3-2 Non-OA- and OA-graded femoral head samples collected from patients following operations. Each sample is presented with the corresponding ICRS classification.

3.3.4 Harvesting porcine glenoid

For the second part of this research, porcine glenoid has been used. Porcine glenoid is a good alternative to human glenoid and is readily available compared to human samples. Healthy porcine complete shoulder joints (6-8 months old) were obtained from the local butcher (Lidgate Butcher, Nottingham gate, UK) 24 hours after slaughter. The shoulder joint was dissected as shown in the images below- as explained in chapter 1, the shoulder joint includes the Scapula, Humerus and fused radius and ulna and glenoid. The entire joint was cleaned from all soft tissue (muscles, ligaments, and tendons) and the glenohumeral joint was dislocated using a surgical scalpel (Figure 3-3). Care was taken not to damage the cartilage on the glenoid side. The tendons and ligament around the glenohumeral joint capsule were cut and the entire scapula was removed.

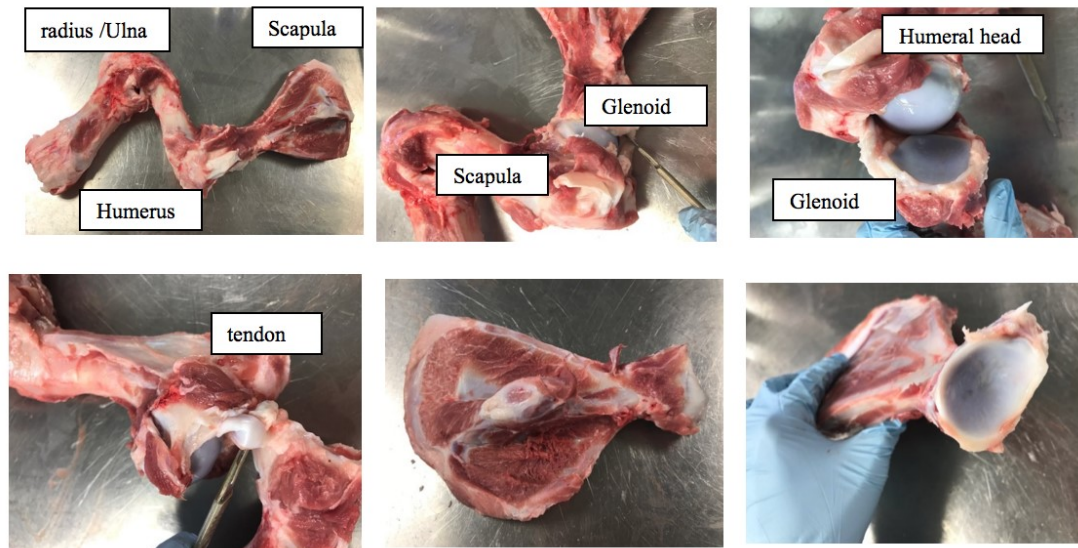


Figure 3-3 Step-by-step process of glenohumeral head and glenoid dislocation

After the scapula was clamped and the excess tissue around the glenoid bone was removed to ensure the glenoid fits within the simulator sample holder. Using a bone saw the glenoid with approximately 10-15mm of bone was sawn off. The glenoid was placed in a PBS soaked tissue and was inserted in a re-sealable bag and frozen at -20°C until ready to test (Figure 3-4).

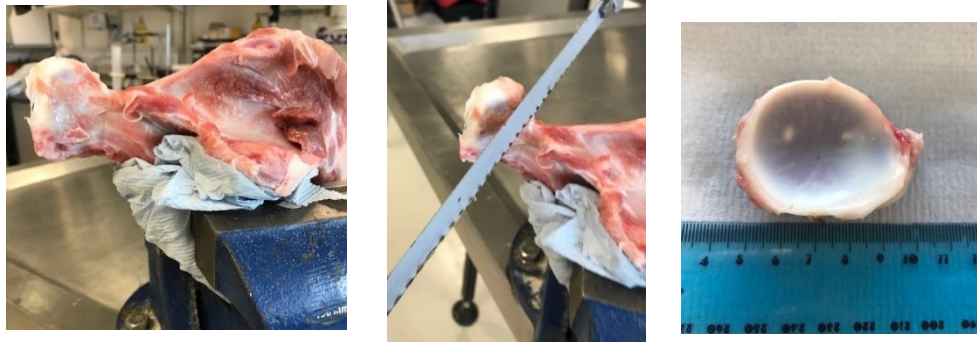


Figure 3-4 Cutting and extraction of porcine glenoid

3.3.5 Extraction of porcine glenoid articular cartilage plugs

The third part of this study focuses on creating enzymatically digested whole glenoid cartilage. As this technique has not been done previously, it was important to develop the technique on cartilage plugs before applying it on the whole joint. Therefore, as previously discussed, same porcine joints were obtained from the butchers and dissected (protocol as section 3.2.1). A surgical coring device was used to remove osteochondral plugs 10mm in diameter from the surface of glenoid. Approximately, depending on the size of the glenoid, five plugs can be extracted from each glenoid (Figure 3-5). After, they were immediately placed into plastic jars filled with PBS and they were either immediately tested or stored in -42°C freezer.

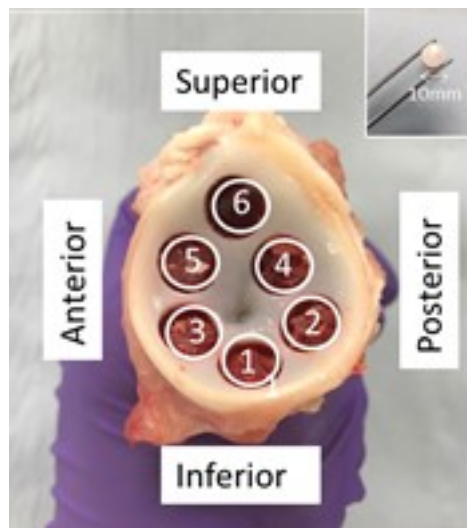


Figure 3-5 10mm diameter Articular Cartilage plug extracted from the glenoid

3.4 Microset silicon polymer compounds

Microset 101RF fluid component (Microset Products Ltd., Leicestershire, UK, Figure 3-6) was used to replicate the glenoid surface, with the aim of measuring the radius of curvature of the glenoid. The typical application of the Microset silicon replicating compounds are, assessment of surface damage and crack detection. The reason for measuring the cartilage replica rather than the cartilage itself were as follows:

- It is well known that the cartilage dehydrates fast. Its dehydration could create inaccuracy of volume measurements, which were not desirable.
- Talysurf tip and other measuring devices might damage the cartilage surface.

The replica is designed to obtain a high resolution (0.1 microns) replications. It a high strength elastomeric material; therefore, it can be removed without damage to itself and replica surface. It can be stored limitlessly for future reference with shrinkage of less than 0.1%. After curing, it is dimensionally stable for geometric measurements and It can be assessed with various technique such as Talysurf, WLI, and SEM. The replicating compound has been used in cartilage studies. In order to know the right size of shoulder implants required for the study, it was important to measure the size of radius of curvature of porcine glenoid. In order to do this, the glenoid surface was dried with lint free paper and covered with aliminum foil to ensure easy replica compound removal. Using the aluminum foil also enxured the microset does not come into contact with cartilagea nd the it does not affect its mechanical or structural properties. The joint was held tight upward and clamped on to a bench (Figure 3-7). The glenoid was filled with silicon using microset dispenser and left to dry for one hour. Once dried the mould is removed from the joint to measure their radius of curvature. Three different joint were utilised to obtain three different replicas. Initially Talysurf Stylus was used to measure the curvature, but the tip was not long enough.

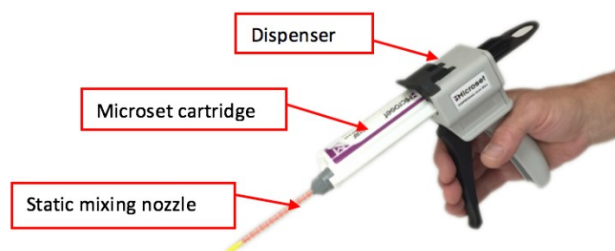


Figure 3-6 Microset compounds (Image taken from Microset.co.uk)

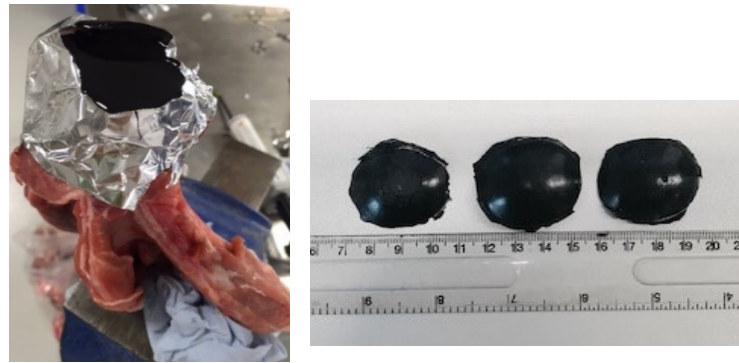


Figure 3-7 Glenoid joint filled with Microset polymer, The replica compound

3.5 Calculation of Radius of curvature

The shape and dimensions of glenoid was determined from the Microset moulds. Five measurements were taken of the width and height of mould and averaged. The equation below was used to measure the radius of curvature and choose the right glenoid implant. This was calculated based on measurements from glenoid diameter (GD) and glenoid height (GH). The following formula was used for calculating the right glenoid radius of curvature. For the calculation, it was assumed that the glenoid is fully curved and forms a perfect sphere.

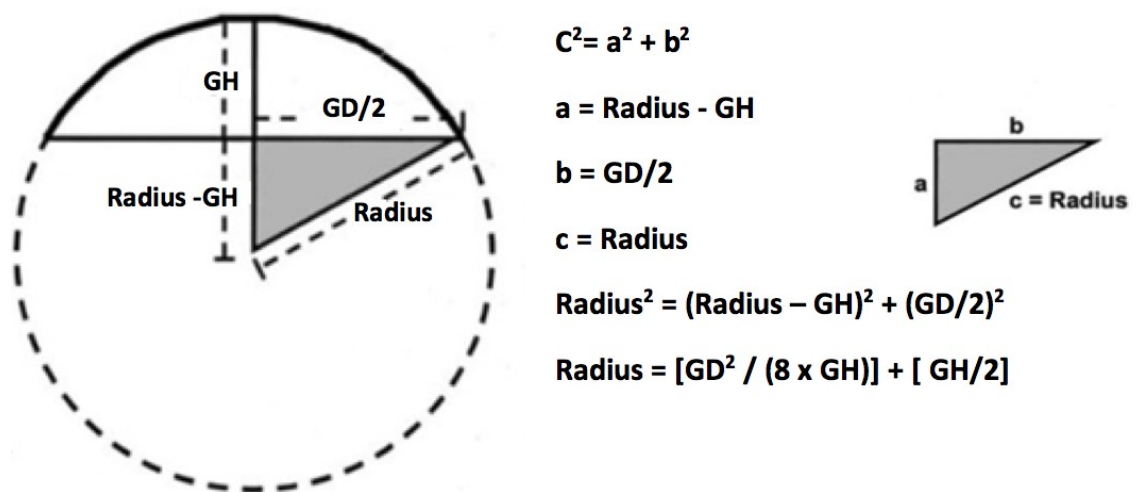


Table 3-1 shows the measurements taken from the moulds of three different glenoid joints. The implants provided by the company (Mathys orthopaedics Ltd, Switzerland).

Table 3-1 Porcine glenoid and humeral head implant radius of curvature

<i>Porcine glenoid</i>			
	<i>Diameter</i>	<i>Height</i>	<i>Radius of curvature</i>
<i>Glenoid 1</i>	34.69 ± 1.11	7.86 ± 0.23	23.06
<i>Glenoid 2</i>	36.23 ± 1.28	8.52 ± 0.46	23.61
<i>Glenoid 3</i>	34.58 ± 0.57	8.19 ± 0.42	22.34
<i>Humeral Implants</i>			
<i>Ceramic</i>	45	16.8	23.46
<i>Metal</i>	45	16.8	23.46

[7]

3.6 Multiaxial Compression and Shear Testing Rig (MCSTR)

A custom-made Multiaxial Compression and Shear Testing Rig (MCSTR), was developed previously in our research group to test the cartilage plugs against different contact surfaces of different sizes and geometries (Accardi, 2012). The shape and surface of upper specimen was fully customisable, allowing for different contact surfaces of various biomaterials (such as Co-Cr alloy, ceramic and PCU) to be mounted and tested as the upper specimen. The MCSTR rig is able to move both in compression, vertically, and in shear, horizontal, via a piezoelectric load cell and linear variable differential transformer (LVDT), allowing measurement of force and displacement respectively. The specifications of the rig are: vertical and horizontal frequency (0.1-5Hz), maximum vertical load (100N), resolution of vertical and horizontal transducers ($\pm 1\text{mV}$). The vertical and horizontal motion are driven by the action of two solenoids, where the horizontal solenoid is damped by a viscous damper (silicon oil) to avoid instability during shear test. During vertical solenoid, the solenoids return to the 'home' position upon power removal via the action of gravity and during horizontal solenoid via the action of a spring pulling the horizontal slide back. The rig design is such that the upper specimen is secured in place whilst the lower specimen is allowed to move vertically and horizontally. The cartilage sample is placed in the sample holder and it is fully immersed in either Phosphate Buffer (PBS) solution or Bovine calf serum (BS). A sample size of 10mm is standardised throughout the experiment as it allows the global response of the tissue under compression and shear to be measured. The sample holder used for shear contains 3mm deep and 10mm diameter recess. Depending on the height of each plug, an insert was used to raise the sample from the recess therefore making it visible for shear testing. The holder for unconfined compression test contains a flat homogenous surface and does not contain any recess. A schematic of the front view of the rig is shown in Figure 3-8.

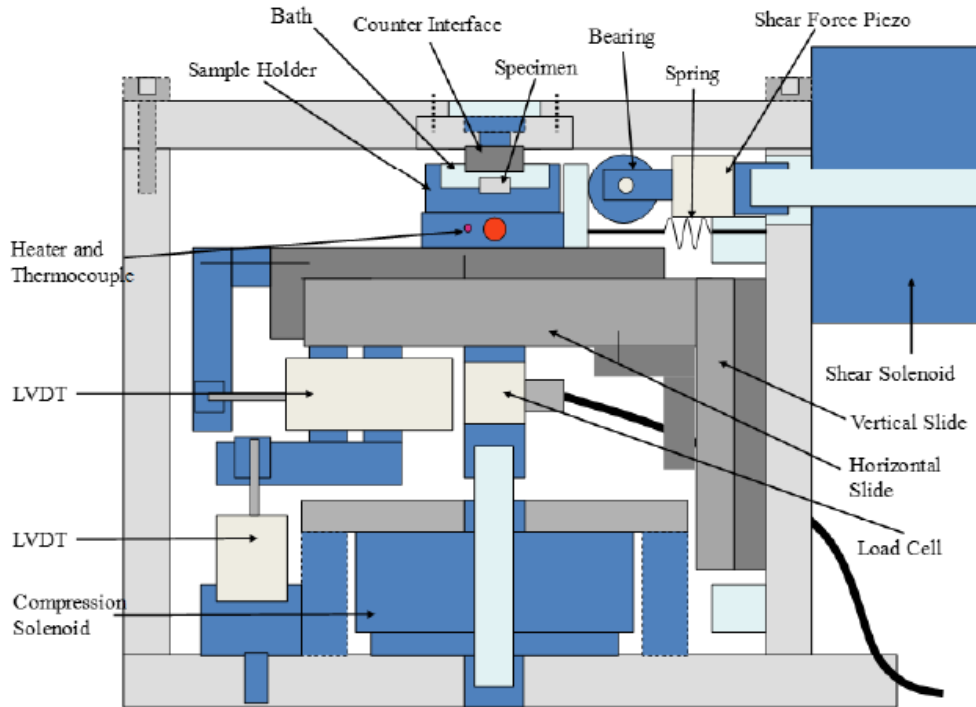


Figure 3-8 Schematic of MCSTR rig, Image adapted from (Accardi, 2012)

3.6.1 Unconfined compression test on porcine cartilage plugs

The unconfined compression test was carried out using rig shown on Figure 3-9, according to the method described in chapter 2. The stress-relaxation test was chosen due to the considerable amount of literature data available for validation of the obtained results as well as ease of performing the test. The samples were taken out of the freezer and thawed until defrosted. Two hours prior to testing, if frozen, the samples were left to thaw at room temperature. Typically, from experience, it took approximately 1-2 hours for the 10mm cartilage plugs submerged in PBS to fully defrost at room temperature. Osteochondral plugs with the thickness of 10 mm were removed from the joints using a surgical scalpel. The thickness of each plug was measured using a digital Vernier calliper at five different locations around the sample's surface and average thickness of the sample was recorded. The AC plugs were then placed in the sample holder and immersed in PBS. The holder was raised gradually until the AC sample was in contact with the fixed upper specimen. The contact was noticeable when there was a small increase in compressive reaction force measured by load cell on the LabVIEW screen, which was measured approximately 0.1N. Once the contact was found, the AC was left to equilibrate for fifteen minutes prior to test initiation. This position was considered to be "zero" displacement.

For unconfined compression test, the applied vertical strain in terms of vertical displacement, the desired ramp time for applying the selected displacement followed by the total length of the test was accurately selected and specified as inputs to the rig via the LabVIEW software. The test was started and reaction force was measured and recorded at intervals of 0.05 seconds. Once the test had been stopped, before retesting, the sample was left to equilibrate in PBS for at least one hour. As the applied strain was not high enough to cause any damage, the samples could be retested in compression. The test was performed three times on each plug to ensure repeatability.

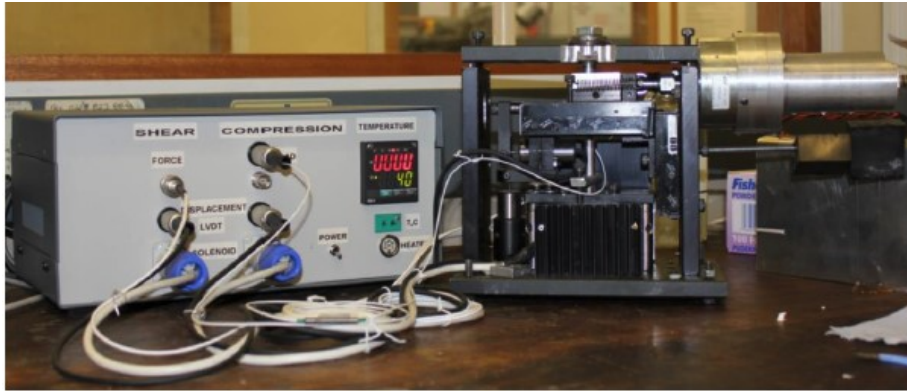


Figure 3-9 The rig and the respective control box, Image adapted from (Accardi, 2012)

3.6.2 Unconfined compression test on human cartilage plugs

The same procedure described above, was followed for testing human AC samples. The human femoral head specimens had been ICRS grade and 10 mm diameter plugs were excised. The AC plugs were kept hydrated throughout the experiment. Following the procedure explained in section 2.5.1, the sample was placed in the sample holder and submerged in bovine calf serum (Sigma-Aldrich, 12133C) with a total protein content of 4.5–6.5 mg/ml. This is higher than the protein content in synovial fluid, and it is usual to dilute bovine serum to a 25% w/w concentration for hip simulator tests. The bovine calf serum solutions were stored at less than -20°C , and just before testing were removed from the freezer and brought to room temperature. The solutions were diluted with deionised water (Sigma-Aldrich, S-37531-356) to the suitable w/w concentration. The bovine serum was selected for this set of experiments to replicate conditions closer to those in the existence of synovial joints. For the upper specimen, three types of biomaterials commonly used in HA were considered: 1) Co-Cr alloy, 2) ceramic and 3) PCU. Using a super glue, each of these materials was fixed as the upper specimen compressing against the AC.

3.6.3 Shear Testing

For shear testing, a modified sample holder was used with diameter of 10mm and depth recess of 3mm which was utilised to press fit the samples in place and provide a lateral constrain during shear. If required, depending on the thickness of the plugs, thin Ultra High Molecular Weight Polyethylene (UHMWPE) discs with different thickness was used to bring the surface to required height and avoid contact between the specimen and holder. Once appropriate frequency and stroke length was chosen, the shear test was carried out by applying a load to AC samples against the upper specimen and powering the horizontal solenoid which moved the tray in a reciprocating action. For human AC samples, different biomaterials were fixed to the specimen holder and tested against all five groups of non-OA and OA (grades 1-4) cartilage samples. This will be described in further details in chapter 4.

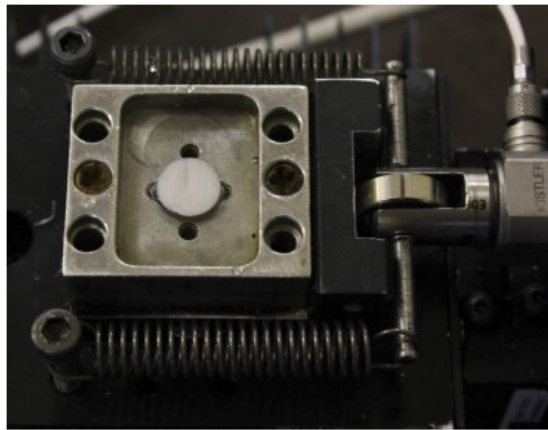
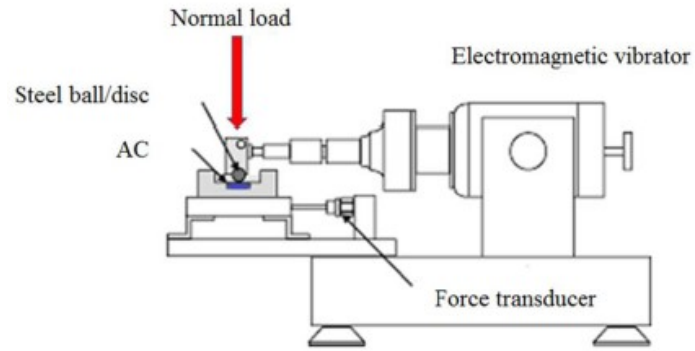


Figure 3-10 Sample placed on a UHMEPE disc support prior to shear testing

3.7 High Frequency Reciprocating Rig (HFRR)

As an alternative to MCSTR, High Frequency Reciprocating Rig (HFRR) (PCS Instruments, London, UK, Figure 3-11) was utilised to perform shear testing on porcine plugs, in order to be able to have a reliable comparison based on the same experimental protocol and conditions. HFRR is computer controlled and provides fast assessment of wear properties of soft tissue. HFRR was also chosen to induce damage to porcine specimens and it also enables testing under various configurations and higher frequencies. AC samples with radius of 10mm were placed in the sample holder and immersed in PBS. Steel ball with 6mm diameter was placed in the upper sample holder and used as a counter surface material for this HFRR test. Since the thickness of AC plugs is 1.0-3.0 mm, a

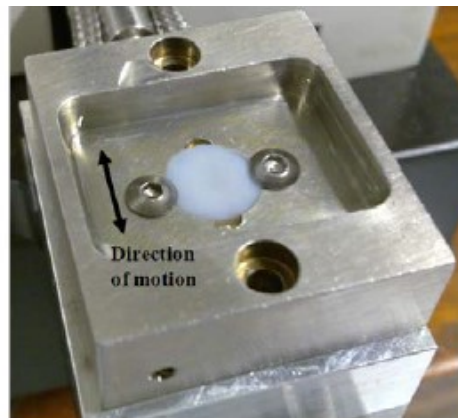
UHMEPE disc with various thickness was utilised to elevate the AC surface up to the required height. To mechanically fix the samples in the holder, cartilage plugs were held in the holder via screws (Figure 3-11(c)). A constant normal load was applied to the specimen during the test using dead weights. According to the previous study performed with the same configurations (Accardi et al., 2011), a load of 600 was required, in order to mechanically test the AC under physiological conditions. This load resembles an average contact pressure of the knee in the lower range (1.6Mpa) (Accardi, 2012). The temperature of the holder was set at 37°C during the test. The stroke length and frequency range in the HFRR are 20 µm- 2mm and 10-200 Hz respectively. Test with different duration time were performed and friction was recorded.



(a)



(b)



(c)

Figure 3-11 (a) Schematic of HFRR, (b) Sample placed in the HFRR sample holder, (c) AC place in HFRR sample holder

3.8 Surface characterisation of Articular Cartilage

The surface roughness of the human and porcine cartilage plugs, prior and post damage, was characterized using White Light Interferometry (WLI) (Wyko NT9100 by Veeco, see Figure 3-12). WLI microscope is used for noncontact surface topography measurement of articular cartilage plugs. The test area is scanned in vertically scanning interferometry (VSI) mode, which creates a 3-D topographical surface map of the object and provides a fast data acquisition. Prior to testing, if frozen, all the samples were thawed thoroughly. Lint-free paper was used in order to remove all the moisture from the samples. Care was taken to confirm no damage was caused to the samples through the application of excessive force. The sample then was positioned and levelled using the handles before the scan started. A scan length of 150 μm with a lens objective of x20 magnification was adopted. Finalisation of the scan generates a dataset with no post processing, which increases the number of scans to be taken thus eliminating surface dehydration. Surface measurement were performed on the samples before and after shear test to visualise surface topography. Five positions at each plug were chosen to achieve average roughness and minimum of three scans were taken from each point (Figure 3-12(b)). The image obtained using WLI was of 312x234 μm^2 . After the test, the results were processed and analysed to reduce noise and normalize the data using, tilt correction, Masking, filtering and data restore.

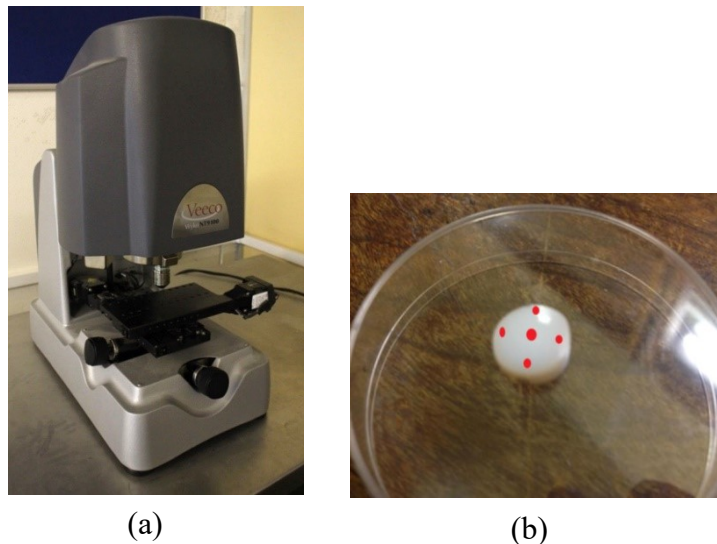


Figure 3-12 White Light interferometry (WLI) device a) Wyko NT9100 by Veeco, b) A schematic of typical White Light interferometer

3.8.1 Hirox digital optical microscope

After the friction test the glenoids were analysed on a digital microscope (RH 2000 coupled with MXB-2500 REZ objective, Hirox Co. Ltd. Figure 3-13). The microscope was utilised to capture and visualise any worn surfaces on the cartilage samples in real-time. This system allows fast macro inspection up to highest resolution, the microscope has three different resolutions; low, mid and high range (from 0.1x up to 10,000 x) with large depth of field and working distance. Furthermore, this optical microscope captures images with high resolution and a wide field of view simultaneously. The images can tilt in X and Y directions in real-time. The microscope is capable of creating 3D images. Before the friction testing the potted glenoid was taken and placed under the microscope and tilted in a way that the lens is parallel to the surface of cartilage. Images from 10 different location across the surface of glenoid were taken at low and high magnifications. Post testing, once the AC plugs were taken out, they were secured with blue tag on a V-shape sample holder. Extra care was taken not to touch the surface and images were taken as quickly as possible to avoid dehydration of the samples. Once the images were taken, the plugs were placed in 10% formalin fixative for histological analysis which will be described in the next section.

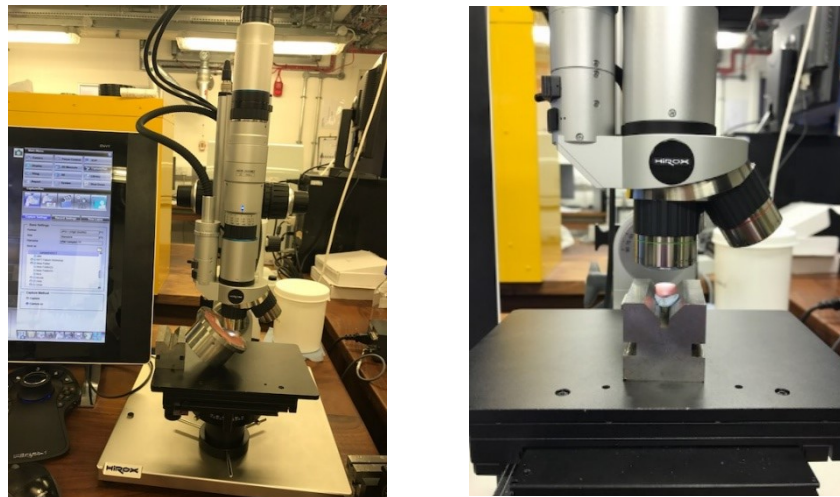


Figure 3-13 An image of digital Hirox microscope to visualise surface wear of round cartilage plug and whole glenoid

3.9 Basic histological techniques

3.9.1 Tissue preparation

Paraffin histology is a powerful tool to study the internal structure of cartilage at a cellular level. In this study, histology was used to assess the structure of cartilage before and after the mechanical testing. Fresh Intact porcine shoulder joint was obtained from the local butcher (Lidgate butchers, Nottingham gate, London, UK), 10mm plugs were taken from the porcine glenoid or human humeral head and placed in the fixative for 48 hours. The rest of the joint was kept in the freezer for future use. The following protocol was applied to all the plugs.

3.9.2 Tissue fixation

Fixation is the first step of histology process and it rapidly preserves the tissue structure; therefore, the existing form and all of its structures is maintained. Fixatives kill the tissue as well as any bacteria that are present in the tissue. Fixation involves cross linking of proteins, making them insoluble and the removal of water. A commonly used fixative is made of Formaldehyde. The amount of time the samples are left in the fixative is dependent on the size of the samples and type of fixative. Cartilage samples were dissected as described in section 3.3. Fresh cartilage plugs were placed in the large volume of universal 10% Natural Buffered Formalin for 48 hours (constant agitation), as soon as they were dissected from the acetabulum to achieve a complete fixation prior to dehydration step, constant agitation is required. It is important, to cut the cartilage sample to the smallest size as possible for better fixation. In case of osteochondral plugs, this is impossible as the bone is hard, but the cartilage plugs with no bone attached can be cut to ensure optimal fixation. Figure 3-14 shows the orientation that the cartilage plugs were cut (An and Martin, 2003b). If there is bone attached to the cartilage plugs, it is necessary to perform the decalcification process after fixation, if not there is no need for the decalcification step.

3.9.3 Decalcification

The cutting of hard tissue such as bone is impossible, hence it must be treated to remove calcium phosphate through a process called “decalcification”, thus the tissue becomes soft enough to be cut into thin sections via a microtome (Lynch and Raphael, 1976).

Decalcification is the process of removing inorganic components such as calcium from hard tissue (Skinner, 2003). Calcified tissue must be decalcified before processing otherwise the tissue cannot be sectioned. Depending on the size, density and tissue type of the tissue, varying length of time and different concentration of the decalcifying solution is required. Decalcifying is carried out by specific chemical agents, such as acid to form soluble calcium salts. After the cartilage samples were fixed, if they have any subchondral bone attached, they were placed into decalcifying agent for further processing at room temperature (Sangeetha et al., 2013). Strong acid, decalcifies tissue in less time, therefore there might be a great risk of over decalcification (Skinner, 2003). Once the removal of salts has been completed, the decalcification process reaches to its “end point”, when all the inorganic material is removed from tissue, leaving the remainder of organic matrix intact. Precise determination of this end point is critical for optimal staining. Decalcified tissue should be soft enough for paraffin and dehydration processing.

Post fixation, the NBF was changed to 10% formic acid (Sigma-Aldrich) in order for decalcification to initiate. This was carried out at room temperature, on a rotating roller for gentle agitation. The solution was changed every 24 hours for period of 7 days for optimal decalcification. After 3-4 days, the plugs were cut into half along the longitudinal axis (Figure 3-14) to ensure the decalcifying solution penetrates into entire tissue adequately. If the samples were difficult to cut, this means that they are not decalcified enough and should be placed back in the formic acid until they are soft enough to be cut. Full decalcification, was tested by lightly squeezing the sample, if they were resistant to bending they were placed back in the formic acid for another 24 hours.

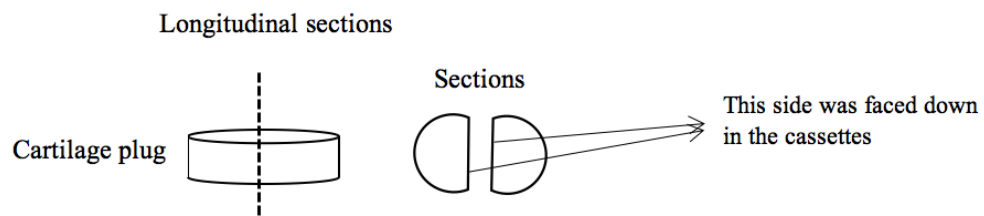


Figure 3-14 Orientation of cartilage plugs for histology, the round plugs were bisected before being placed in the histology cassettes, the cut surface was faced down in the wax, so the longitudinal sections that are cut with the microtome show the entire view of cartilage zones.

3.9.4 Dehydration

For optimum wax infiltration, the tissue has to be fully dehydrated and all the water has to be removed. Ethanol is the most commonly used dehydrating agent. Dehydration step is carried out by immersing the tissue in series of ethanol dilutions, from 50% to 100%, leaving the samples for an hour in each dilution. During this process water, soluble protein and lipids are also removed from the tissue. It is necessary to ensure the dehydration process is completed on the same day as excessive dehydration can result in over-dehydrating by removal of bound water from the sample and in some cases, may result in brittle blocks.

3.9.5 Clearing

Once the samples are dehydrated, they are placed in Histo-Clear II (National Diagnostics, Atlanta, US) to clear the samples, as ethanol and water are immiscible, overnight followed by two changes of each two hours the following day. Histo-clear will remove the ethanol in the tissue and in turn will be placed with paraffin wax later. Insufficient clearing before infiltration process, may result in poor infiltration with wax due to ethanol leftover in the tissue. When the tissue is completely infiltrated with clearing agent, it becomes translucent. Another vital role of clearing is to remove excess fat from tissue, which otherwise creates an obstacle for wax infiltration.

3.9.6 Infiltration

The step following clearing is called “Infiltration” and it consists of replacing the clearing agent with paraffin wax (Fisher Scientific, UK) in an oven at 60 degrees for total of 4 hours, with wax being changed every 2 hours. Paraffin wax is miscible with Histo-clear, but it is not miscible with alcohol. As previous steps, the optimal infiltration time for each tissue type/size must be determined for optimal results.

3.9.7 Paraffin wax embedding

After the tissues have been fully fixed, they are taken to the embedding station (KD-BM Kede tissue embedding system, Figure 3-15). The samples are placed in cassettes, and left to cool on the cold plate, after the blocks are set, they are left to set overnight in the freezer. A microtome (Leica RM2255) was utilised to cut 5 µm sections. Sectioning the block will create ribbons. The ribbons are floated on a warm water bath for a few minutes,

until the wrinkles from slicing are removed. The ribbons are picked up using microscopic glass slides and left in the 60-degree oven to remove any excess paraffin wax attached to the slides. Staining with Toluidine blue and Safranin-O were conducted using the protocol set out in Table 3-2 and Table 3-3. The stained sections were visualised under a Zeiss light microscope.



Figure 3-15 Articular cartilage samples in the mould on the cold plate

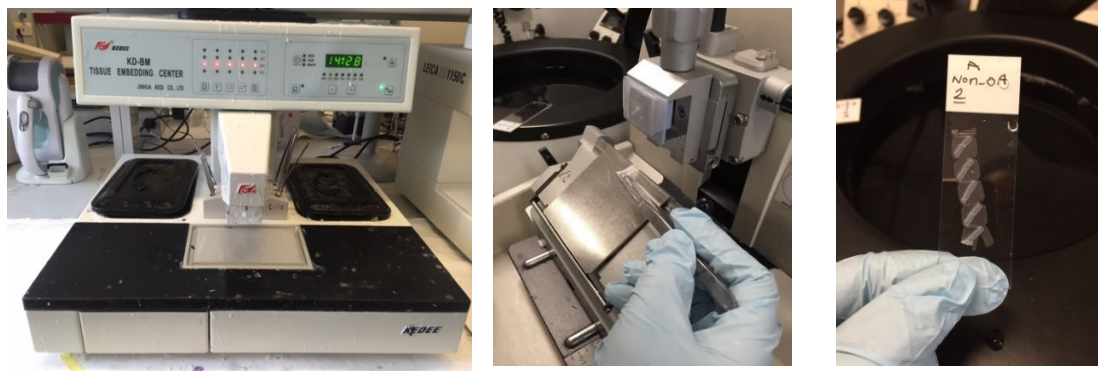


Figure 3-16 (a) embedding station, (b) Sectioned samples in ribbon form, (c) Ribbons removed from water bath and placed on a glass slide

Table 3-2 Histological protocol for processing porcine Articular Cartilage

Step	Chemical	Duration	Notes
Fixation	10% NBF	48 hrs	Change every 24 hours
Decalcification	10% Formic acid	7 days	Change every 24 hours
Dehydration	50% Ethanol	1 hr	
Dehydration	60% Ethanol	1 hr	
Dehydration	70% Ethanol	1 hr	
Dehydration	80% Ethanol	1 hr	
Dehydration	90% Ethanol	1 hr	
Dehydration	100% Ethanol	1 hr	
Clearing	Histoclear	Overnight	
Clearing	Histoclear	2 hrs	
Clearing	Histoclear	2 hrs	
Infiltration	Paraffin wax	2 hrs	
Infiltration	Paraffin Wax	2 hrs	
Embedding			
Sectioning			

Table 3-3 Toluidine Blue and Safranin O/Fast green staining protocol

Toluidine Blue		Safranin O and fast green	
Solution	Duration (minutes)	Solution	Duration (minutes)
Histo-clear II	4	Histo-clear II	5
Histo-clear II	4	Histo-clear II	5
Histo-clear II	4	100% Ethanol	1
100% Ethanol	2	100% Ethanol	1
95% Ethanol	1	100% Ethanol	1
95% Ethanol	1	Wash	1
Distilled water	1	Acid Alcohol	20s
0.04% Toluidine blue	5	Wash	1
Distilled water	1	Blueing water	1
Warm air	9	Fast Green	6
100% ethanol	1	Acetic Acid	15s
Histo-Clear II	1	Wash	1
		Safranin O	2
		Wash	1
		100% ethanol	1
		Histo-Clear II	1

3.10 Enzymatically induced damage

One of the aims of this study is to create artificially degraded cartilage through enzymatic treatment in order to produce a model that resembled early stage osteoarthritis, including loss of proteoglycans and superficial zone collagen fibrils. A major purpose of modelling degeneration is to understand the biomechanics of cartilage in health and in different stages of the disease (Chen et al., 2017). Animal tissue have different sizes and are non-homogenous, therefore, a protocol needs to be set out in order to measure the amount of time that is needed for digestion (Korhonen et al., 2003; Nieminen et al., 2002; Rieppo et al., 2003a). The degree of degradation is controlled through the choice of trypsin concentration and time. Initially the protocol was set for the porcine plugs and later was accordingly adapted and applied to whole glenoid joint. Native AC plugs were subjected to enzymatic degradation using Porcine Pancreas Trypsin powder (Sigma Aldrich, Dorset, UK, T4799). Normal and intact porcine shoulders were obtained from the local butcher 24 hrs after the slaughter and the glenoid were dissected. Five, 10mm plugs were taken out of each glenoid and placed into PBS filled bottles. If the plugs were not used on the same day, they were placed into a -20 freezer and thawed for 1 hour on the day of the experiment. For the digestion process, it is best to use the freshly dissected samples. Trypsin is most active in a solution of PH 7-9 (Moody et al., 2006b). The Trypsin solution was made up outside the cell culture fume hood, and once transferred into the hood it had to be filtered to avoid any bacterial transfer (

Figure 3-20). The effect of various trypsin concentration and time on cartilage digestion was examined by immersing each plug in 25%, 0.1mg/ml, 0.5mg/ml, and 1mg/ml trypsin and PBS saline solution for different durations. The petri dish was disinfected thoroughly and placed into the 37°C incubator for various hours (See protocol), After 1, 2, 3, 4 hours, each set of plugs were taken out of the trypsin solution and washed with PBS and placed into 10% natural buffer formalin for 48 hours and processed further for histological examination. Like all biological tissues, the physical and morphological structure of cartilage is different depending on the location of the sample. Factors such as weight and skeletal structure can affect the cell and PG density, matrix distribution of the tissue, therefore the results from this will not be consistent, and it varies for every tissue (Moody et al., 2006b). Table 3-4 shows previous studies that used trypsin on various tissue in different sizes and different concentration of trypsin and time.

Table 3-4 Literature review on various trypsin studies

Author	Sample	Trypsin concentration	size	Duration (hrs)	Temp (°C)
(Rojas et al., 2014)	Femoropatellar grooves of 1–2-week-old bovine calve	0.1 g/mL, Sigma, T4665	6mm AC plug	12	37
(Brown and Chen, 2016)	normal bovine patellae sample	0.1 g/mL, Sigma, T4665, dissolved in 0.15 M phosphate buffered saline	Whole patella	4	37
(Moody et al., 2006)	Bovine patella	0.15M saline and 0.1mg/ml	Whole patella-removed every 2h took biopsy	24	37
(Zheng et al., 2001)	Bovine patella groove	1 g/L	Bovine patella groove	1-2	37
(Hardy et al., 2005)	Femoral condyle of knee	2.5% (25g/l) porcine trypsin	1cm diameter	5-15	Room temp
(Wang et al., 2008b)	Porcine patella	0.25% Porcine trypsin	6.35mm bovine patella cartilage bone plug	0.6	Room temp

Table 3-5 Enzymatically induced articular cartilage samples with different concentration and time

Enzymatic degradation	Trypsin Concentration/time
Low	0.1mg/1h
	0.1mg/2h
	0.1mg/3h
	0.1mg/4h
Medium	0.5mg/1h
	0.5mg/2h
	0.5mg/3h
	0.5mg/4h
High	1mg/1h
	1mg/2h
	1mg/3h
	1mg/4h

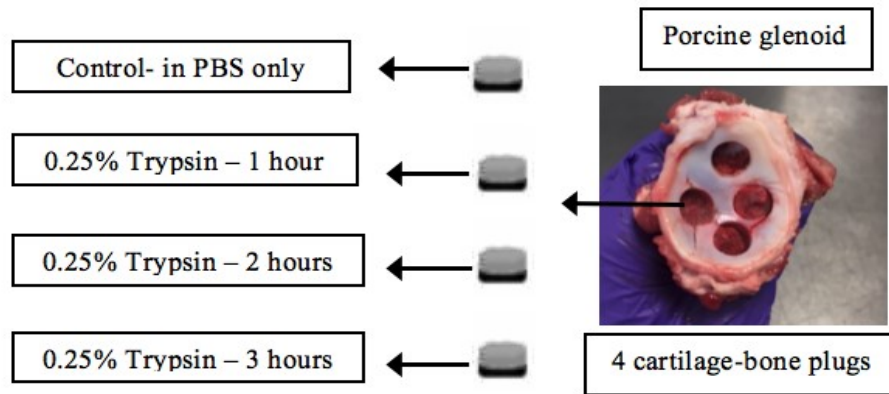


Figure 3-17 Digestion process for 0.25% Trypsin on porcine glenoid cartilage

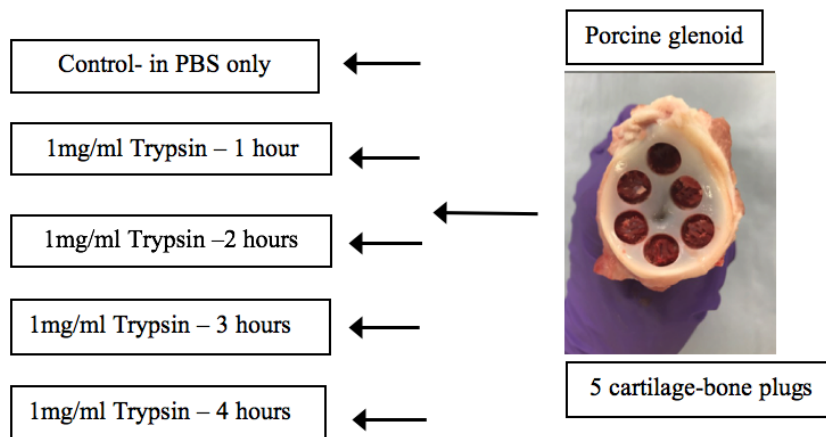


Figure 3-18 Enzymatic digestion process for 1mg/ml Trypsin on porcine glenoid cartilage

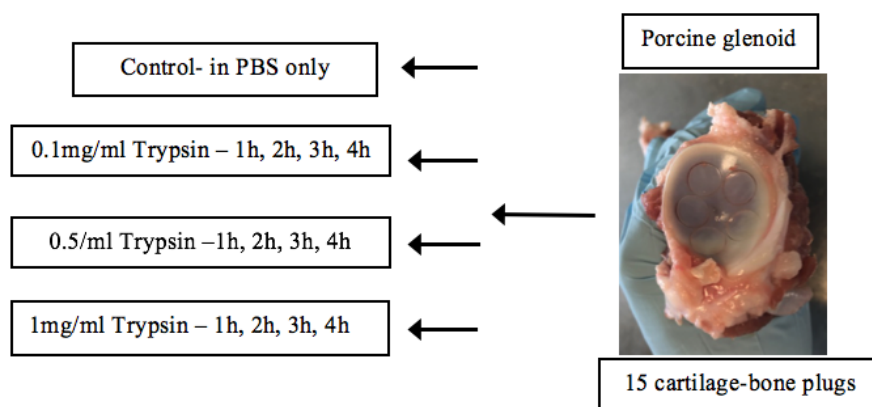


Figure 3-19 Enzymatic digestion process for 0.1, 0.5, and 1mg/ml Trypsin on porcine glenoid cartilage

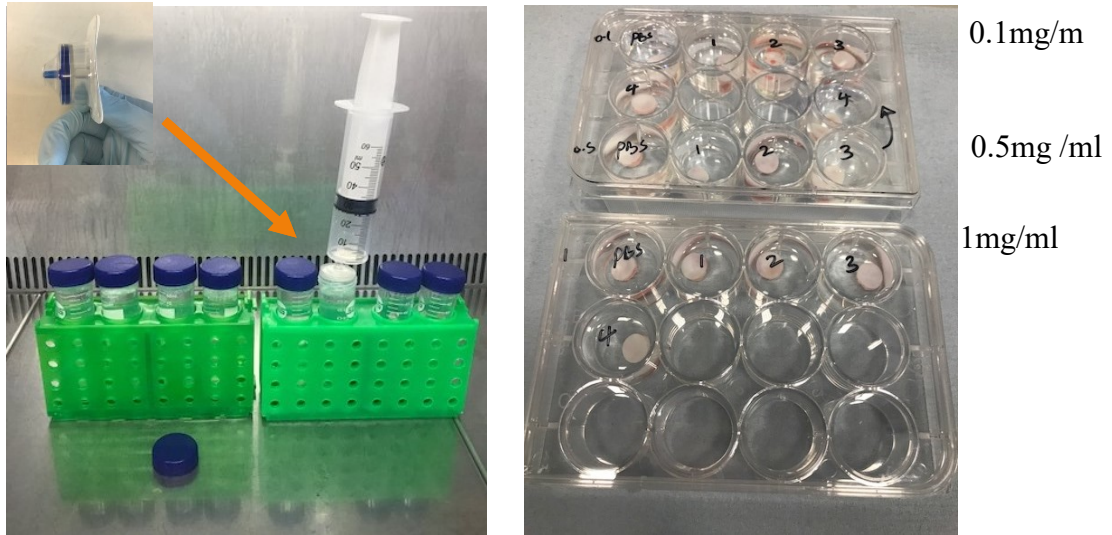


Figure 3-20 a) Filtering process of Trypsin solution under sterilised conditions, (b) cartilage plugs submerged in three different concentrations of Trypsin for various durations

Once the protocol was developed using cartilage plugs, the optimal combination of trypsin concentration and time was applied on a whole glenoid and consequently was utilised in simulator study which will be explained in further details in chapter 6. Due to Limited number of samples, only two glenoid per concentration were used. One concentration (0.5mg/ml) at two different durations were chosen as representative of low and high damage, 1hr and 3hrs respectively.

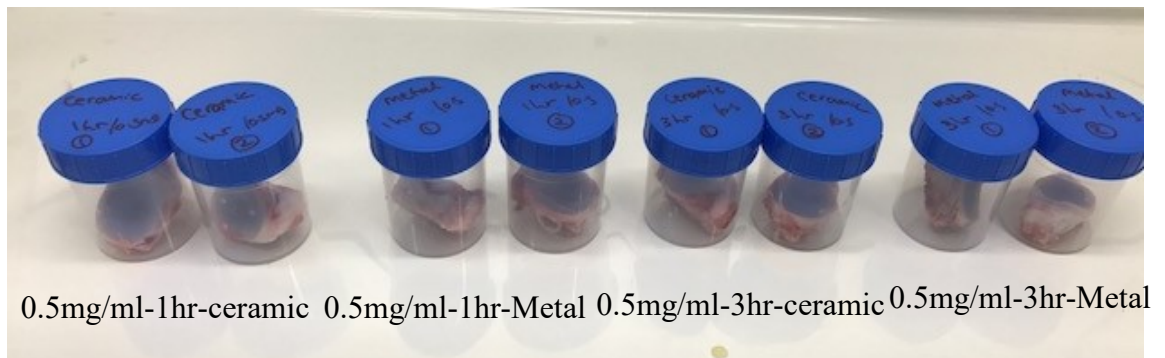


Figure 3-21 Glenoid joints in containers filled with various concentration of trypsin and duration

3.11 Chapter Summary

In summary, the first scenario of this research includes a human study on articular cartilage plugs (healthy and OA). Initially, the surface roughness of human AC sample was measured using WLI (Figure 3-22). The mechanical characterisation of the samples was carried out by performing the unconfined compression test. To investigate the behaviour of each of the three biomaterials, the shear test was performed using the MSCTR with cartilage and each of the biomaterials a counter-surfaces. The evaluation of the performance of each biomaterial was carried out by repeating the surface roughness measurements and an unconfined compression test after the shear test, and comparing the values with the initial values. Furthermore, a comparison between the two scenarios was made in order to shed light on similarities and differences between them and to estimate the damage to the human OA samples.

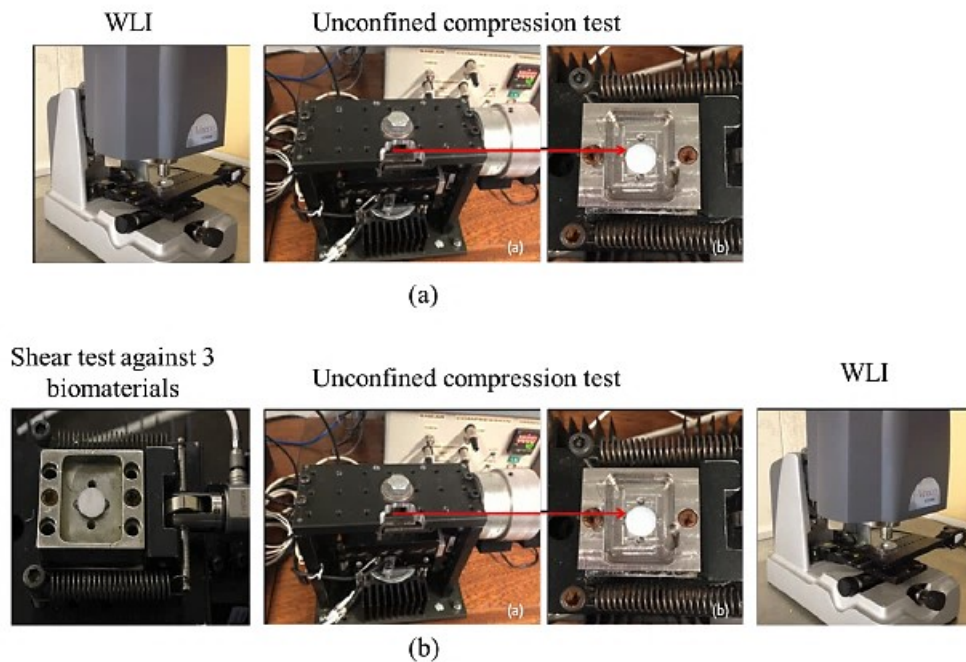


Figure 3-22 (a) Surface roughness measurements and characterisation of mechanical properties of human AC with various grades of OA, (b) evaluating the tribological performance of 3 biomaterials through shear test and friction measurements following with characterisation of the mechanical and surface properties of the tissue after the shear against biomaterials.

The second scenario of this research includes an animal study on whole joint. The initial surface roughness and tribological properties of healthy porcine glenoid cartilage were characterised (Figure 3-23(a) and (c)). In the next step, the damage was induced on the tissue artificially through enzymatic digestion in an attempt to stimulate OA (Figure 3-23(b)). After the damage, the friction test was carried out again in order to evaluate the tribological behaviour of tissue. Following this, articular cartilage plugs were extracted from the glenoid surface to investigate surface roughness with WLI and structural properties via histological techniques (Figure 3-23 (d)).

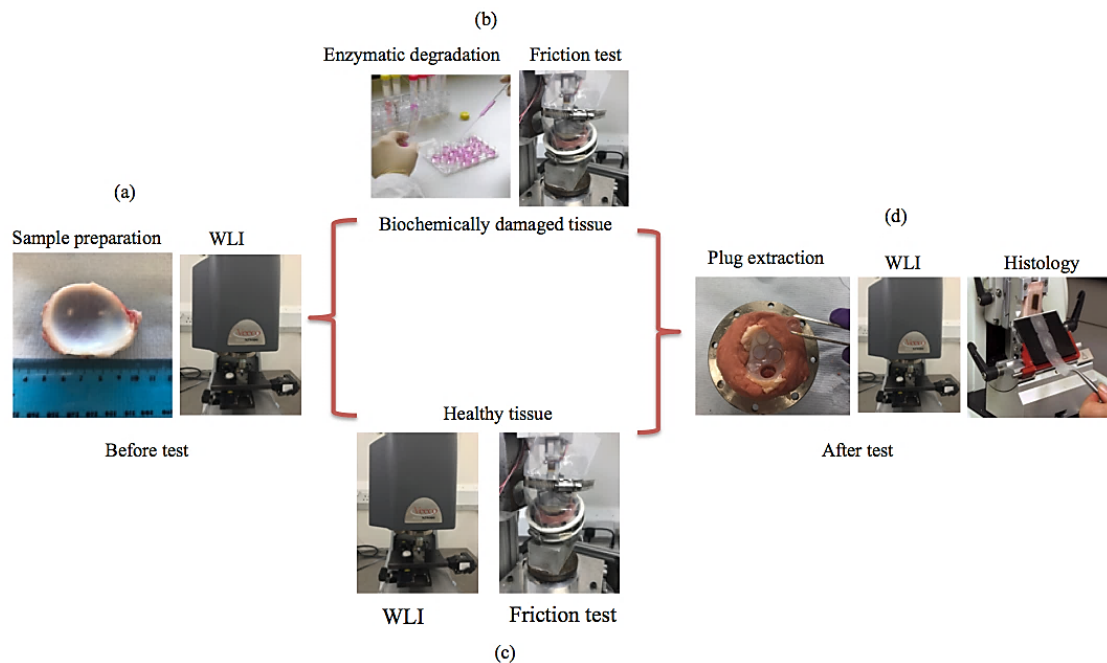


Figure 3-23(a) Initial surface roughness measurement and characterisation of mechanical properties before inducing damage, (b) Inducing biochemical degradation following with surface roughness measurement and friction test, (c) friction test on healthy tissue, (d) Articular cartilage plug extraction from the glenoid followed by surface roughness measurement and histology

The next chapter will explain the work that was carried out in collaboration with a previous PhD student (Ajdari, 2016). This will investigate and compare the performances of three common biomaterials, CoCr, Al₂O₃ and PCU, articulating against the various human samples characterized by different grades of OA.

4 THE EFFECT OF PROSTHETIC MATERIAL ON ARTICULAR CARTILAGE DAMAGE RELATED TO HEMIARTHROPLASTY

Disclaimer:

The content of this chapter can also partly be found in Ajdari's thesis (2016). The previous PhD student has conducted the experimental investigation (friction and shear test) on human cartilage samples. The development of the histology protocol was a significant work and was done as part of this PhD thesis.

4.1 Introduction

This chapter explains the mechanical and structural properties of non-OA and OA human cartilage. Moreover, OA-like AC was, for the first time, compared to human osteoarthritic tissue to investigate the role of mechanical degradation, as well as the role of proteolytic enzymes in the pathology. Finally, the performances of three common biomaterials, CoCr, Al₂O₃ and PCU, articulating against the various grades of OA, were compared.

Hemiarthroplasty (HA) is a replacement of half of a diarthrodial joint with an artificial bearing surface. Hemiarthroplasty has obvious advantages of a relatively simple surgical procedure, bone preservation and ease of revision. For the last seventy years, hemiarthroplasty of the hip has been the main stay for treatment of hip fracture (Cram et al., 2017; Gjertsen et al., 2014; Miller et al., 2013; Tol et al., 2017). However, it is the use of HA in the shoulder that is the most controversial. There are many and common indications for HA in the shoulder including primary shoulder arthritis (Boileau et al., 2006b; Gartsman et al., 2000; Smith and Matsen, 1998); osteonecrosis of humeral head (Barnes et al., 1991; Baumgarten et al., 2004; Grevula et al., 1995) and acute fracture dislocation of the shoulder or displaced fracture of the proximal humerus (Connor and D'Alessandro, 1995; Loew et al., 2006) or femoral neck (Blomfeldt et al., 2007; Cuckler and Tamarapalli, 1994; Rodríguez-Merchán, 2002). The use and proportion of HA relative to other replacement options in the shoulder remains substantial. In USA, a study on 7 million people reported 6336 shoulder arthroplasties from 2005 to 2013. Of these 2179 were hemiarthroplasties (34%), 3026 total shoulder arthroplasties (48%) and 940 reverse shoulder arthroplasties. Diagnoses were principally osteoarthritis (60%) and fractures (17%) (Dillon et al., 2015). In Germany, hemiarthroplasty was used in the shoulder in 5975 cases in 2012, total shoulder arthroplasty in 13329 cases and reverse shoulder arthroplasties in 8011 cases (Oppermann et al., 2016). In UK, the national registry (Porter, 2013) reported a total of 1968 primary shoulder replacements in 2012 of which 846 were hemiarthroplasties, 525 total shoulder arthroplasties and 597 reverse arthroplasties.

However, there are varying results after shoulder HA (Antuña et al., 2008; Robinson et al., 2003). Success of shoulder arthroplasty depends on multiples factors: proper height, retroversion and tuberosity healing (Bigliani et al., 1996; Boileau et al., 2006b) but the advantages are a simple procedure and avoiding the risk of glenoid component loosening.

Bad results are correlated to degree of glenoid wear (Levine et al., 1997). Patients' outcomes after currently use HA are sometimes shown to be less successful than with total arthroplasties (Dean et al., 2016; Ferrel et al., 2015; Sebastián-Forcada et al., 2014). Painful glenoid arthrosis is the most common indication for revision of HA (Ferrel et al., 2015; Gartsman et al., 2000; Sperling and Cofield, 1998). Rispoli et al. (Rispoli et al., 2006) showed that 18% of HA used primarily in treatment of shoulder osteoarthritis were revised for painful glenoid arthritis, 4% of revision of shoulder HA for fractures in Ferrel et al. study (Ferrel et al., 2015). There is general uncertainty about the cause of seemingly accelerated cartilage wear in hemiarthroplasties (Champion and McNally, 2004; Haidukewych et al., 2002; Hasan et al., 2002; Hedtmann and Werner, 2007; Parsons et al., 2004; Sperling et al., 2002). One of the main factors in determining the longevity of this type of reconstruction is the resulting damage and wear of the cartilage.

Due to the problems of cartilage damage and the resulting unreliable outcome of HA many surgeons prefer total shoulder arthroplasty despite the significant risk of glenoid component loosening. Other surgeons prefer reversed shoulder arthroplasties despite the limited clinical history and great difficulty of revision of this type of prosthesis. As a result, the choice between the three types of arthroplasties is very controversial. Much research and development has been aimed at addressing the problems of total shoulder arthroplasty and reversed shoulder arthroplasty. In contrast, solutions towards reducing the cartilage degeneration as relevant to the success of HA has received much less attention and it is this gap in knowledge this paper aims to address.

Many studies report on the breakdown of cartilage when articulated against a prosthetic material as related to hemiarthroplasty (Dombroski et al., 2009; Krawczyk et al., 2008). Most such studies report on metallic femoral or humeral prostheses articulating against the cartilage of the acetabulum or glenoid, respectively. With the increasing use of ceramic implants, a limited number of studies report on ceramic prostheses in HA (REFS). A few studies (Cook et al., 1989; Jung et al., 2008; Müller et al., 2004; Oungouljian et al., 2015b) have investigated the suggestion that ceramics or other material choices, including polymeric materials (Luo et al., 2010) may offer lower rates of cartilage wear and by extension improved reliability of HA. These latter studies all describe the behaviour when the prosthetic head is articulated against intact cartilage. However, in the shoulder primary OA is a common indication for HA. Even in a case

where the cartilage is initially intact, OA almost invariably develops postoperatively (Bülhoff et al., 2017b; Herschel et al., 2017; Kofoed and Kofod, 1983; Lizhang et al., 2011; Parsons et al., 2004; Sen et al., 2009; Yamagata et al., 1987). Thus, most hemiarthroplasties need to be able to function in the presence of tissue affected by OA. The wear and tear of cartilage caused by the femoral or humeral prosthesis in the various OA environments has never been investigated before and there is a lack of knowledge of the relative tribology of different prosthetic materials against arthritic cartilage as relevant to the HA joints.

The overall aim of this study was to provide information to help determine the most appropriate prosthetic material for HA; and how the severity of OA suffered by the patient might affect this selection. The objectives were to assess the damage of human cartilage when tested against three orthopaedic materials in a pin-on-disc test setup; and to carry out this assessment on cartilage with different degrees of OA. Specifically, Co-Cr alloy, alumina ceramic (Al_2O_3) and PCU were tested against five levels of OA varying from intact cartilage to severely OA degraded cartilage.

4.2 Materials and Methods

Pin-on-disk configurations have been the most commonly used in vitro setups to study cartilage tribology: higher degree of control on the experimental variables but lack biochemical and biomechanical synergies that are found in a synovial joint (Farizon et al., 1996; Saikko, 2014; Shi et al., 2011, 2012). In a pin-on-disk setup, variables such as the stroke length and sliding velocity control the friction properties of the system and the wear of cartilage surfaces. Synovial joints typically operate in a mixed lubrication regime and thus slow sliding (1-4 mm/s) velocities are generally adopted in these pin on plate to reproduce these conditions in vitro, while also avoiding non-physiological hydrodynamic lubrication between the surfaces. The output of this test is a curve of friction coefficient versus time which following the appropriate interpretations provide understanding of the tribological behaviour of the material.

Human femoral head samples were obtained from patients from Charing Cross and St Mary's hospitals during hip replacement surgery for fracture or OA. These samples were individually classified into 5 grades of OA by an orthopaedic surgeon according to the International Cartilage Repair Society (ICRS) grading system (Kleemann et al., 2005;

Mainil-Varlet et al., 2003) (Figure 4-1). The groups corresponding to the 5 grades OA were termed non-OA, OA1, OA2, OA3 and OA4 in increasing order of OA severity.

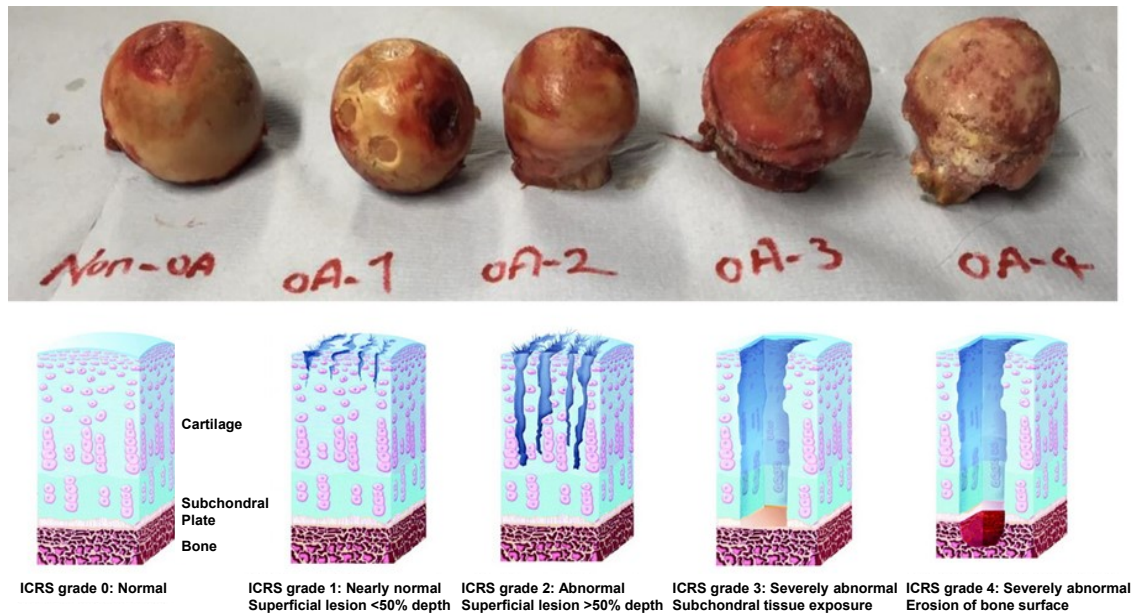


Figure 4-1 ICRS cartilage grading

Human femoral head articular cartilage plugs (Figure 4-2) were extracted from the femoral heads with a surgical coring device. Using a surgical scalpel, full thickness AC was carefully removed from the underlying subchondral bone resulting in cartilage discs of 10mm diameter. This size was judged acceptable based on the work by Obeid et al.,(1994) who reported that an 8mm diameter cartilage plug offered an acceptably flat surface and a low level of disruption of the collagen network. In total 45 samples were utilised, with 9 plugs taken from each OA grade of humeral head; three plugs were tested against each biomaterial. Discs of both Cobalt–chromium alloy (CoCr28Mo) and of ceramic (alumium-oxide bionit, ISO 6474) were obtained from Mathys Medical Company (Figure4-2). Discs of PCU were obtained from the PCU cushions of the Tribo Fit hip replacement manufactured by Joint Replacement Instrumentation Ltd (JRI). The mechanical and surface properties provided by the manufacturer are shown in Table 4-1. PCU is not currently used in HA but was chosen to represent the potential of polymeric materials for the HA application as these polymers have been suggested to replicate cartilage behaviour (Gabarre et al., 2014) and are in clinical use as meniscal replacement (NUsurf reference).

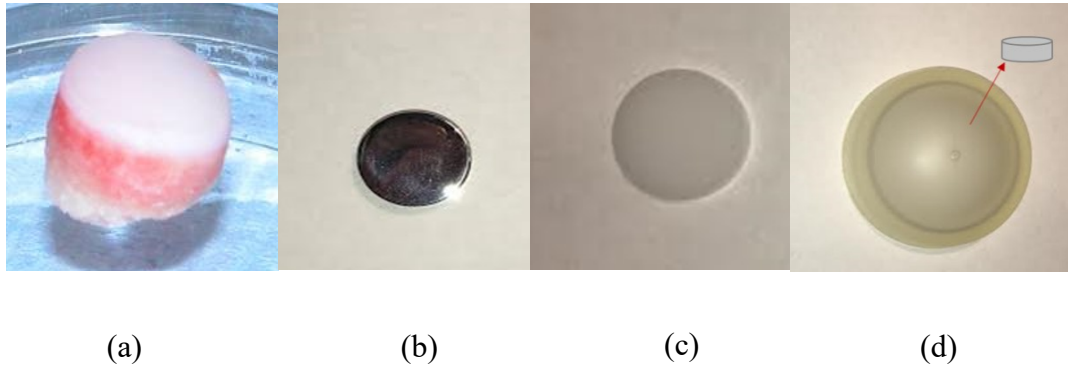


Figure 4-2 (a) A human cartilage sample, and the three materials: (b) CoCr, (c) Ceramic, (d) PCU

Table 4-1 Specifications of used biomaterials

Material	Supplier	Hardness	Young's modulus (MPa)	Surface roughness (R _a) (nm)
CoCr28Mo	Mathys Medical ("Startseite" 2017)	≥ 40 HRC – up to 46	241*10 ³	46
Bionit (Al ₂ O ₃)	Mathys Medical ("Startseite" 2017)	59 HRC	380*10 ³	35
PCU	JRI (Active Implants) ("The Case for the Use of Polycarbonate-Urethane in Orthopedic Implants MDDI Medical Device and Diagnostic Industry News Products and Suppliers" 2016)	80A-55D (durometer)	1.4-18.2	873

Combined compression and shear tests were performed using a multiaxial testing rig (MCSTR) (Figure 4-5) developed in previous work (Accardi et al., 2013). The AC specimen was placed in the sample holder and fully immersed in a bovine serum solution. The three types of biomaterials (Co-Cr alloy, ceramic and PCU) were fixed as the counter-facing specimen and compressed against the AC disc.

To investigate the performance of each of the three biomaterials the MCSTR test was performed with each of the biomaterials as the counter-face sliding against cartilage. The friction coefficient was measured during the MCSRT tests.

Unconfined compression tests (Jurvelin et al., 2003; Wei et al., 2008; Wu et al., 2004), carried out using the MCSTR test set-up without a shear component, measured Young's modulus, permeability and long-term relaxation time (τ_1) of the cartilage samples before and after MCSTR testing. Additionally, the surface roughness characteristics of the cartilage samples were investigated through white light interferometry (WLI) measurements and compared before and after MCSTR testing. Finally, histology of the cartilage samples was carried out after testing to provide a visual assessment of cartilage damage due to MCSTR testing.

A high friction coefficient, a decrease in cartilage Young's Modulus, an increase in cartilage permeability, a decrease in cartilage relaxation time, an increase in cartilage surface roughness or a disrupted appearance of the cartilage from histological images following MCSTR testing were all used as measures of cartilage damage. Superior biomaterial performance in the context of hemiarthroplasty was defined as the biomaterial that caused minimal damage to the cartilage during the MCSRT test.

4.2.1 Unconfined compression- stress relaxation test

As explained previously full thickness AC samples were removed from the 10mm osteochondral plugs using a scalpel and the thickness of the plugs were measured using Vernier calliper at 5 different locations around the sample's circumference and then an average was taken. The AC sample was placed in the sample holder and immersed with PBS. The sample holder was then gradually raised until contact with the AC sample and the fixed upper specimen was made. The upper specimens for the unconfined compression are the three different biomaterials (ceramic, metal, PCU). Contact between the tissue and the metal plate was associated with a small peak increase in the compressive reaction force measured by the load cell, which was of the order of around 0.1N or lower. Once the contact was established, the AC was left to equilibrate for 15 minutes and this was considered to be the "zero" displacement position. The MCSTR test conditions imposed a compressive strain of 10% of the sample thickness (resulting in a nominal pressure of 0.3MPa) with a ramp of time of 0.5s. These inputs were accurately chosen in the rig LabVIEW control software. The variation of reaction force was measured and recorded at intervals of 0.05s. Once the test was finished the sample was left to equilibrate in PBS for at least 1hour before retesting. The stress relaxation test was chosen as the preferred type of compression test due to the considerable amount of literature data

available for comparison and validation of the results obtained using the rig, as well as the relative simplicity of the test. The variation of reaction force overtime obtained using the unconfined compression stress relaxation technique curve fitted with the numerical and analytical model was used to obtain the relevant young's modulus data. Using MATLAB, the experimental curve was then fitted with the continuous reduced relaxation function and figure 4-3 is obtained. This analysis was not within the scope of this thesis and the details of this fitting can be found in (Accardi, 2012). Determining Young's modulus is done by dividing the relaxation force by the sample area multiplied by the strain (10%) as shown in the equation below:

$$E = \frac{F_{Relaxation}}{A * Strain} \quad 4.1$$

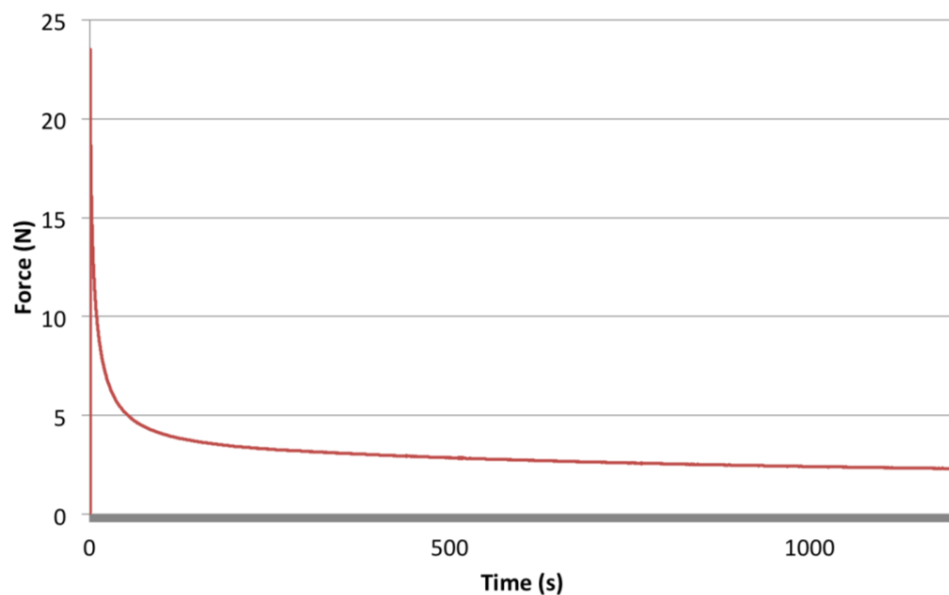


Figure 4-3 Representative average force against time graph

The relaxation force is the steady part of the curve. For this data, the relaxation force was determined by averaging the force over the last 600s of the test.

4.2.2 Shear test

A reciprocating shear motion was then introduced using a 4mm/s sliding speed and 2mm stroke length resulting in a frequency of 1Hz. A modified sample holder was utilized having a 10mm diameter and 3mm deep recess which was used to press fit a part of the sample in place and provide lateral constrain during shear. Once the stroke length and frequency and load had been chosen, the shear test was carried out by loading the AC

sample against the upper specimen and powering the horizontal solenoid which moved the tray in a reciprocating action using a sinusoidal output signal from the control software. The MCSTR setup measures the normal and shear forces and the resulting friction coefficient was averaged over 0.1s and written to a data file every second. An example of a representative AC shear test data file is shown in Table 4-2. The data represents a 10s portion of approximately 40s following the start of the test.

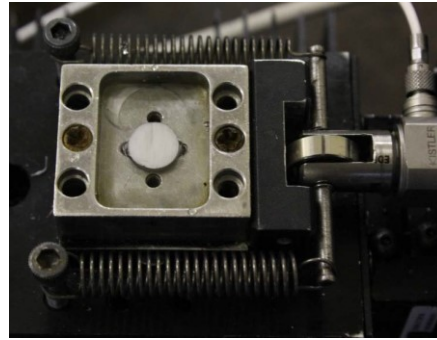


Figure 4-4 AC sample placed on a UHMWPE disc prior to being immersed with PBS

Table 4-2 Output data of a representative AC shear test

Time (s)	Horizontal Displacement (Amplitude) (V)	Horizontal Displacement (Average) (V)	Horizontal Force (Amplitude) (V)	Horizontal Force (Average) (V)	Vertical Displacement (Amplitude) (V)	Vertical Displacement (Average) (V)	Vertical Force (Amplitude) (V)	Vertical Force (Average) (V)
40.13	0.193	3.757	0.488	4.273	0.02	3.418	0.041	1.519
41.11	0.193	3.757	0.500	4.261	0.02	3.419	0.051	1.525
42.12	0.193	3.758	0.499	4.253	0.02	3.419	0.041	1.508
43.12	0.193	3.758	0.539	4.261	0.01	3.418	0.041	1.510
44.11	0.194	3.755	0.549	4.274	0.02	3.419	0.041	1.532
45.13	0.193	3.757	0.541	4.240	0.02	3.425	0.061	1.513
46.11	0.193	3.757	0.541	4.23	0.02	3.427	0.051	1.513
47.12	0.193	3.757	0.531	4.23	0.02	3.427	0.051	1.514
48.11	0.193	3.757	0.560	4.218	0.02	3.428	0.041	1.511
49.12	0.193	3.757	0.559	4.209	0.01	3.428	0.051	1.534
50.12	0.193	3.755	0.583	4.205	0.01	3.429	0.051	1.512

The data obtained from the MCSTR rig were recorded using the horizontal and vertical displacement and force transducers. The “average” and “amplitude” refer to the sinusoidal output signal. In order to extract the friction coefficient from the data, the “Vertical Force average” was converted into N by means of a simple (Volt/Newton) calibration which had been previously carried out for the rig. The weight of the

“horizontal slide” on the load cell was then subtracted in order to yield the exact applied constant vertical force on the sample. This was done in order to verify that the input vertical load originally prescribed had been accurately applied to the sample. The “Horizontal Force Amplitude” resulting from running the machine with no vertical load applied was recorded prior to commencing the shear test. This was done in order to obtain a measure of friction loss associated with the MCSTR. This value was then subtracted from the “Horizontal Force Amplitude” recorded during the test. This value was then divided by 2 to yield the semi-amplitude which was then converted into N. Finally equation 4.2 was then applied to every data line in order to obtain friction as a function of time for every second.

$$\mu = \frac{F_T}{F_N} \quad 4.2$$

Where F_T and F_N is the tangential and normal force to the surface respectively.

4.2.3 Surface roughness characterization

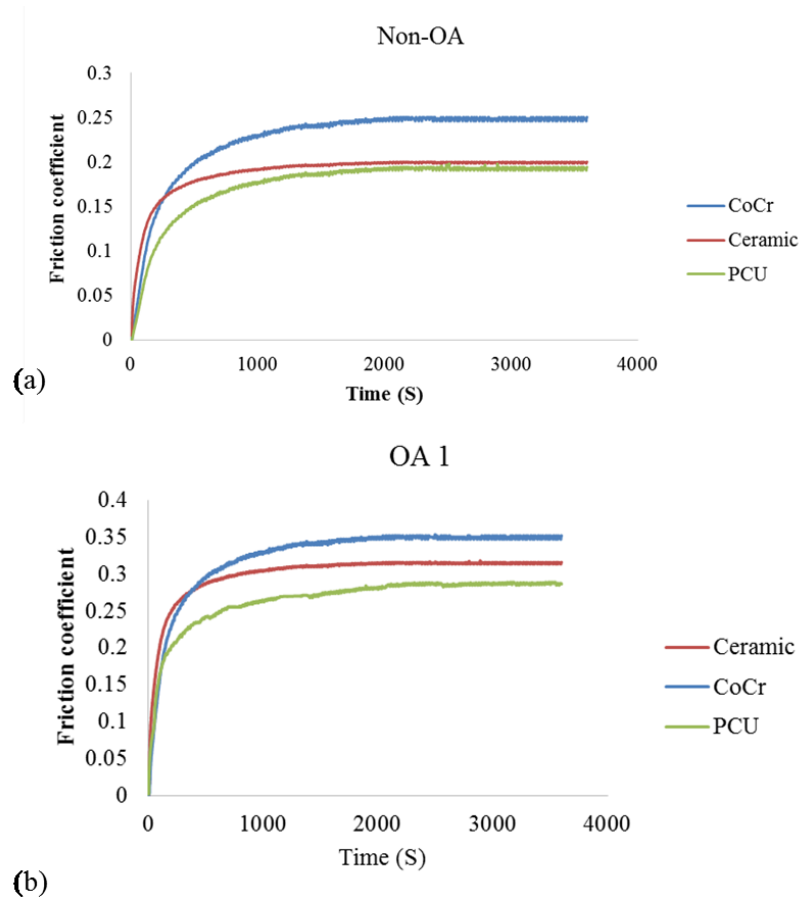
Surface roughness measurements were performed on the samples in order to quantify and visualise changes in surface topography due to OA and as a result of the testing. Five measurements were taken in adjacent areas of the tissue’s surface, and the obtained surface topography parameters were then averaged for each of the tested samples. Roughness and surface parameters were calculated automatically by the inbuilt analysis software.

4.2.4 Histology methods

Cartilage explants from the mechanically tested samples were fixed in 10% Natural Buffer Formalin (NBF) for 48 hours for histology. The samples were cut into halves to ensure proper fixation. Unworn cartilage was used as positive control. Following fixation the samples were dehydrated through a graded ethanol concentration (50% , 70%, 90%, and 100%), cleared using Histoclear, infiltrated and embedded in paraffin wax. Longitudinal five-micrometre-thick sections were cut using the microtome (Leica) and stained with Haematoxylin and eosin (H&E). Stained sections were visualised by light microscope (Zeiss, Germany).

4.3 Results

The frictional response from the MCSTR testing of the different biomaterials against cartilage of various grades of OA is shown in Figure 4-5. Only the results for non-OA, OA1 and OA3 are shown as the trend of the two less arthritic groups (OA1 and OA2) were very similar as were the trends from the more severely arthritic groups (OA3 and OA4). In all cases, the friction coefficient increased non-linearly, demonstrating a steeper rise at beginning of the test later stabilising to a constant value (the equilibrium friction coefficient) after a given number of cycles. The equilibrium friction coefficient for all the combinations of biomaterial and the degree of OA severity is shown in Figure 4-7. It is noteworthy from both Figure 4-7 and Figure 4-8 that the friction coefficients for lower grades of OA (OA1 and OA2) were higher than the non-OA samples while further increases in the severity of OA (OA3 and OA4) caused the friction coefficients to drop even to a level below that of the non-OA samples.



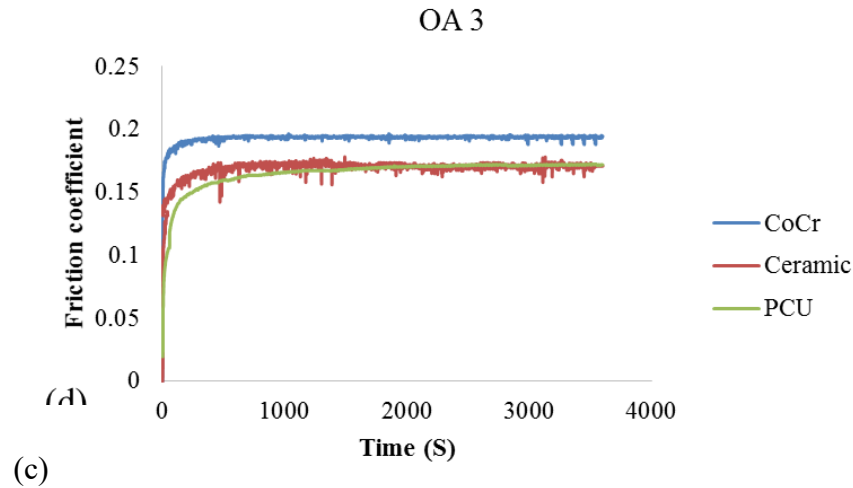


Figure 4-5 Representative frictional response curves of (a) Non-OA, (b) OA1 and (c) OA3 human cartilage tested against all three types of biomaterials.

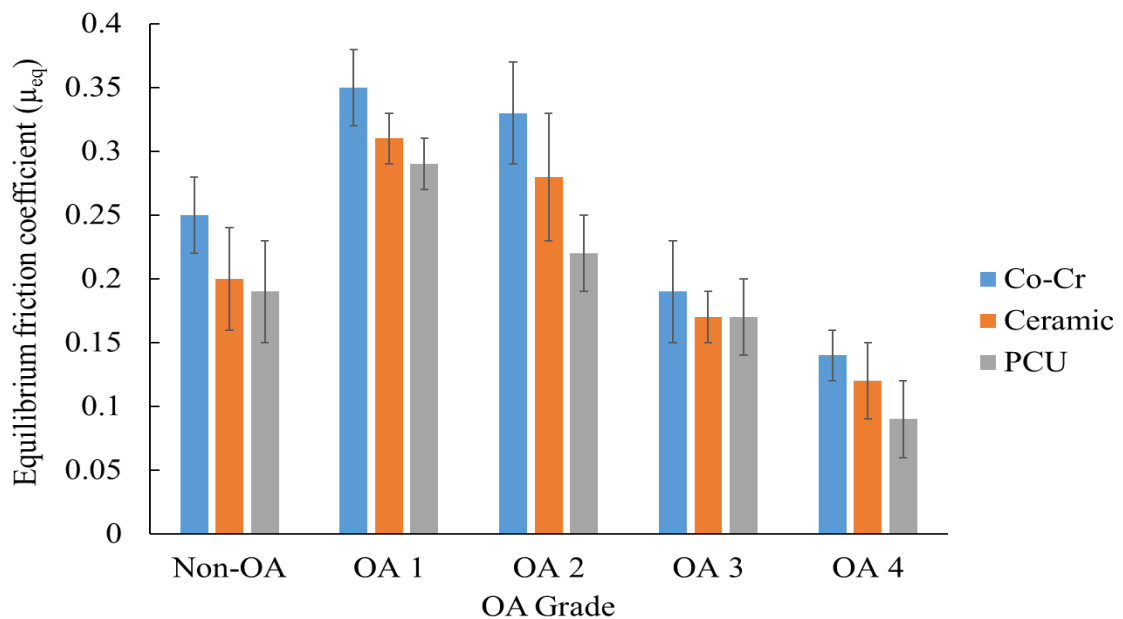


Figure 4-6 Equilibrium friction coefficient of various grades of human OA samples in the shear test against three materials.

For all grades of OA, Co-Cr generated significantly higher (worse) friction coefficients than both ceramic and PCU (Figure 4-5). The comparison between ceramic and PCU was more complicated with ceramic and PCU showing similar values when tested against non-OA cartilage as well as severely degraded cartilage (OA3) while for intermediate degrees of arthritis (OA1 and OA2) ceramics showed higher frictional values (Figure 4-5).

Figure 4-7 and Figure 4-8 shows the Young's Modulus, permeability and stress relaxation time, respectively, assessed from the confined compression tests that followed the MCSTR shear testing. Each of these figures demonstrates the effect of using different biomaterials and degrees of OA during the MCSTR testing on the respective mechanical properties. The confined compression test could not be performed reliably for OA4 samples, as the cartilage in the OA4 samples was so thin that the resulting viscoelastic behaviour was almost negligible and difficult to measure reliably. Hence, OA4 results are not shown in figures 6 to 8. In fact, this issue caused problems even for less arthritic samples (OA2 and OA3) when assessing the permeability and stress relaxation time (figures 4-6 and 4-7).

An overview of Figures 4-5 to 4-7 indicates that all three biomaterials led to a deterioration of the mechanical properties of the cartilage (relative to the cartilage properties before shear testing). However, Figure 4-5 shows that the Young's modulus of cartilage after testing against PCU was significantly higher than when tested against CoCr and ceramic. Similarly, Figure 4-6 and 4-7 show that the use of PCU resulted in relatively lower permeability and higher stress relaxation times, respectively, all suggesting that the integrity of the cartilage is relatively intact. Using CoCr generally resulted in slightly poorer mechanical property values relative to the use of the ceramic counter-face (Figures 4-5 to 4-7).

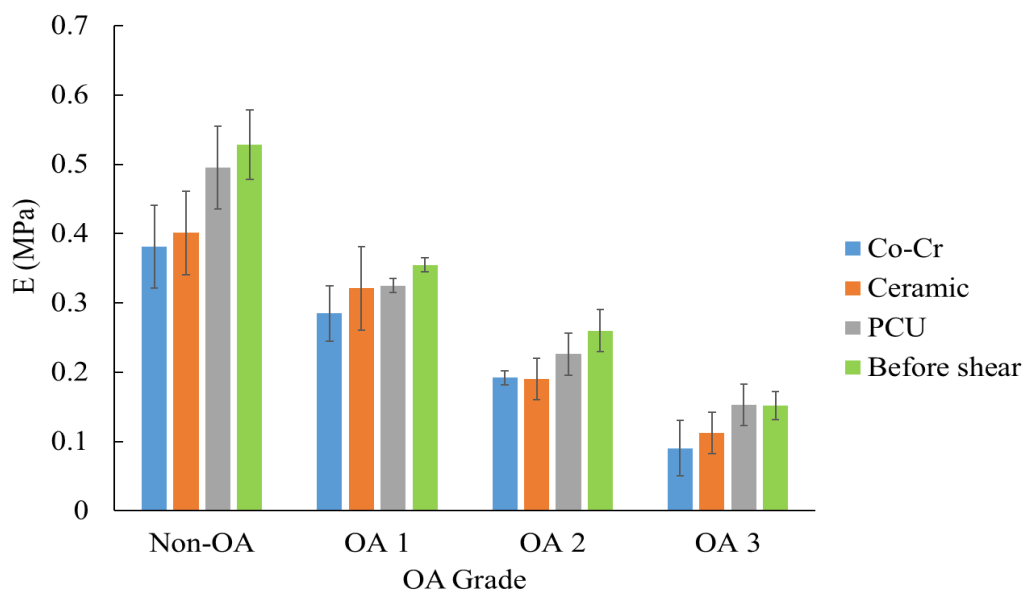


Figure 4-7 Young's modulus of OA cartilage before shear testing and after testing against different biomaterials.

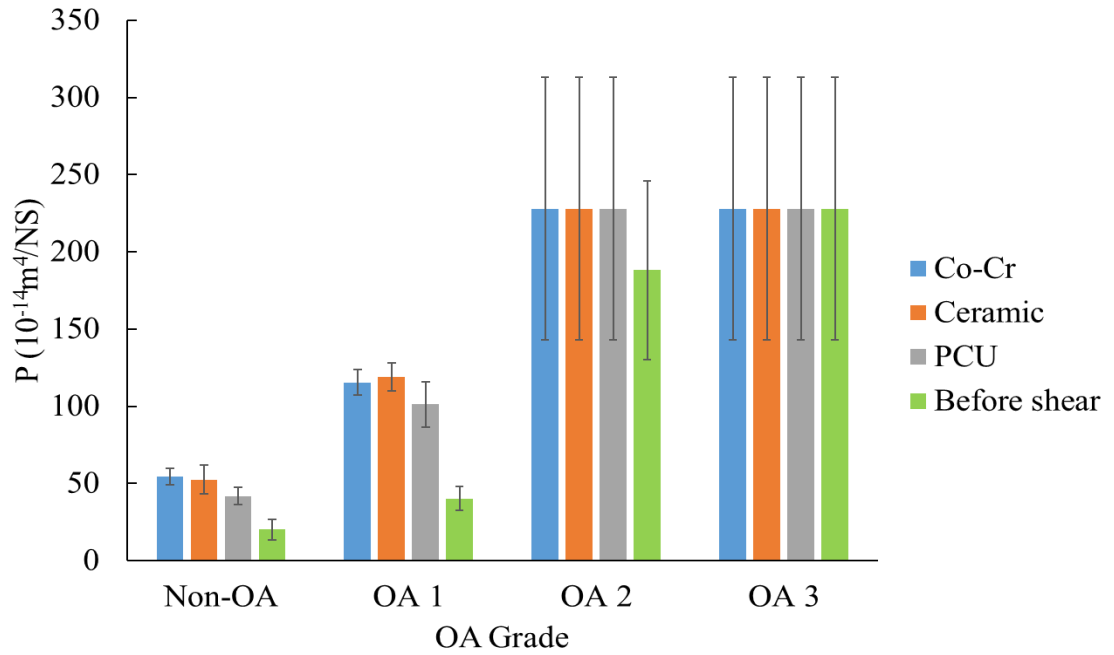


Figure 4-8 Permeability of OA cartilage before shear testing and after testing against different biomaterials.

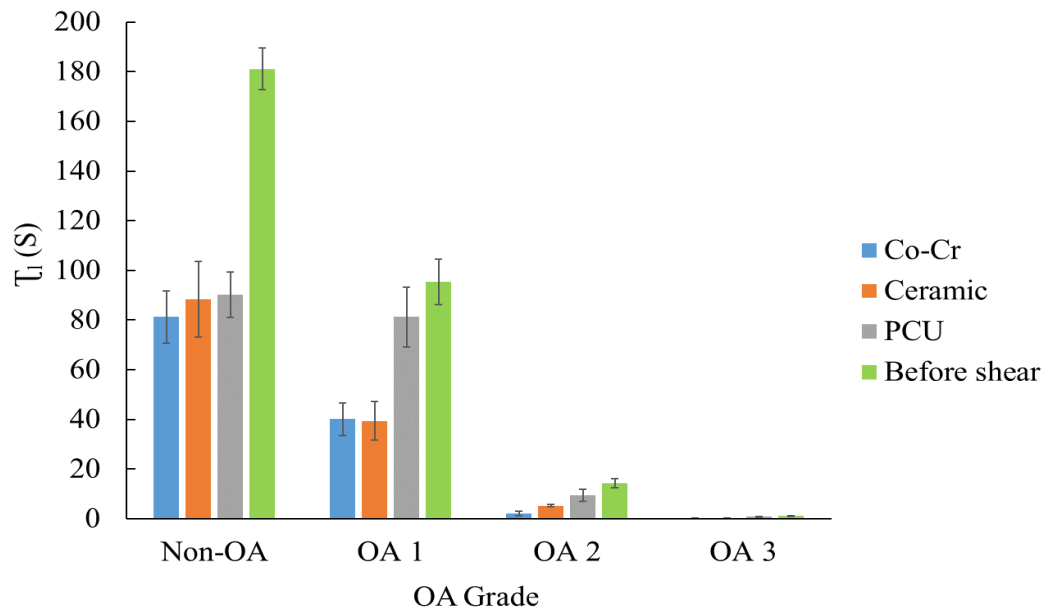


Figure 4-9 Long-term relaxation time, t_1 , of OA cartilage before shear testing and after testing against different biomaterials.

The surface roughness increased with the severity of OA (Figure 4-8). Shear testing against a biomaterial further increased the roughness. CO-Cr testing led to the largest (worst) increase in cartilage surface roughness while PCU testing led to the smallest increase.

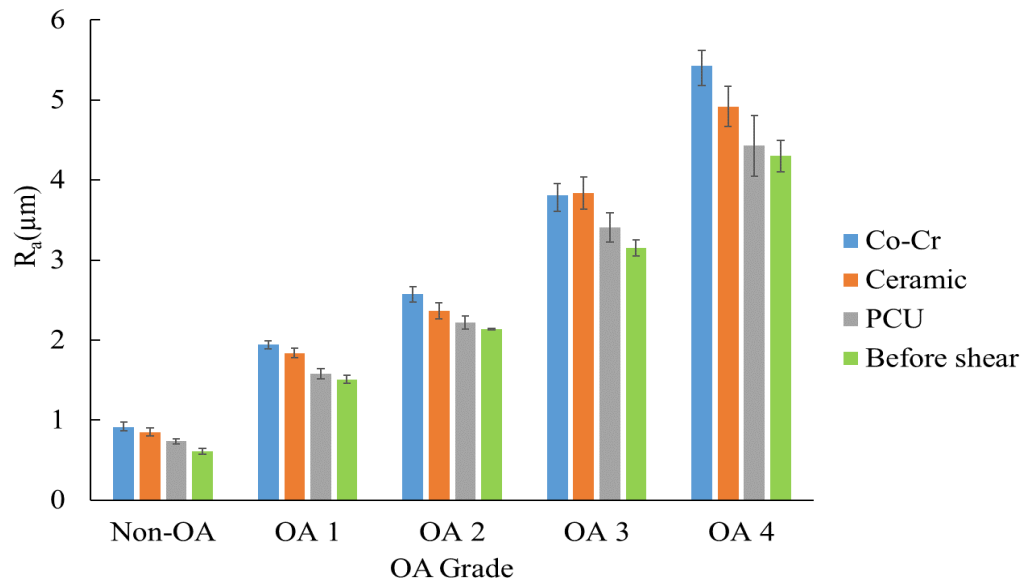


Figure 4-10 8 Surface roughness of OA cartilage before shear testing and after testing against different biomaterials.

Figure 4-9 shows representative through-thickness structural changes of Non-OA cartilage samples when tested against the three biomaterials. In the cartilage tested against the CoCr counterface, the surface was no longer smooth, and damage and irregularities extended deep below the surface. In the cartilage tested against the ceramic there was some damage with small fissures in the superficial zone but the damage did not extend as deep into the cartilage as when tested against CoCr. Finally, the PCU created the least damage in the cartilage compared to the two other materials.

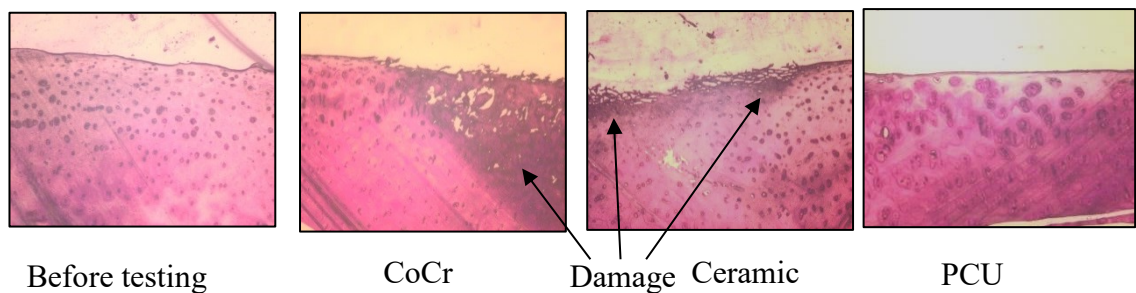


Figure 4-11 Images from histology demonstrating structural changes in cartilage following testing of Non-OA cartilage samples against a biomaterial. In order from left to right: Non-OA sample before testing, after testing against CoCr, after testing against the ceramic, after testing against the PCU (Images taken at x2.5 magnification).

4.4 Discussion and conclusion

This study found that all the biomaterials investigated damaged the cartilage as a result of shear testing; CoCr alloy caused the most damage followed by the Al_2O_3 ceramic while the PCU caused the least damage. While the degree of arthritis clearly had an effect on the measured parameters it did not change the finding that CoCr alloy performed slightly worse than the Al_2O_3 ceramic and that PCU performed the best of the three materials.

Cook et al., (1989) also investigated the effects of prosthetic materials in the context of hemiarthroplasty. Cook et al. implanted femoral heads into 45 canines and the degeneration of the acetabula cartilage was assessed 2 to 18 months postoperatively. Consistent with the results of our study, Cook et al. reported that cartilage articulating against ceramic implants (pyrolactic carbon) exhibited significantly lower levels of wear, fibrillation, eburnation glycosaminoglycan loss and subchondral bone changes than when articulating against metallic implants (a cobalt chromium alloy and a titanium alloy). In another animal study, Jung et al. (2008) implanted femoral components, made of two types of ceramic, ZrO_2 and pyrolactic carbon as well as CoCr alloy, into 27 rabbit knees and assessed the tibial cartilage 3 months postoperatively. In contrast to Cook et al., Jung et al. found that CoCr alloy caused less cartilage damage than the ceramics. There may be several explanations for these different findings. Differences in implant positioning and other details of the surgical procedure may have complicated the analysis. Also, the ceramic used by Jung et al. was a ZrO_2 which may phase transform possibly leading to increased surface roughness and inferior tribological properties. Jung et al. do not report the surface roughness of the implants used and differences in surface roughness between implants and between studies may affect the results.

In-vitro studies using joint simulators and pin-on-disc setups have also demonstrated that articulation against ceramics results in less cartilage damage and lower friction coefficients compared to metal bearings. Using a joint simulator and cadaveric human hip joints Müller et al. (2004) reported friction coefficients of 0.083 for ceramic (Al_2O_3) against human cartilage and 0.118 for metal (steel alloy) against human cartilage. Patel et al. (1997) reported 30% less cartilage wear and a lower friction coefficient, 0.015 versus 0.21, when articulating against ZrO_2 compared to CoCr alloy. Oungoulain et al. (2015) using a pin-on-disc setup and cartilage plugs from the bovine tibia also found less damage and lower friction coefficients when articulating against glass than against Cobalt

chromium alloy or steel reporting friction coefficients of ~ 0.12 vs ~ 0.23 and ~ 0.26 , respectively (assessed from Figure 2B in Oungoulia et al, 2005). The noticeable differences in reported friction coefficients both between previous studies and to our own study may be explained by different experimental methods (joint simulators versus pin-on-disc), test conditions and parameter settings as well the curvature of the cartilage, even when using cartilage plugs, as well as the different surface roughness of the biomaterial. However, the trend that ceramic materials result in reduced cartilage damage when compared to metals is consistent across studies.

In an in-vitro study using a pendulum friction simulator and the bovine medial compartment, Luo et al.,(2010) compared the status of the cartilage in a polyurethane articulation against a steel articulation. Luo et al. reported no significant difference in friction coefficients (both approximately 0.15) but significantly less cartilage wear in the polyurethane articulation (90mm^3 vs 190mm^3). Overall, Luo et al. concluded that the compliant polyurethane performed better which is consistent with the better performance of PCU found in our study.

In this study, the ceramic performed better than the metal which may be explained by the lower roughness (35nm versus 46nm, Table 1). This suggestion is supported by the findings of Oungoulia et al. (2005) who reported that CoCr alloy with a roughness of 27nm had a friction coefficient of 0.23 while CoCr alloy with the same roughness as glass (10nm) had similar levels of damage and friction coefficient as that of the glass (0.12). However, roughness may not be the only relevant factor. Oungoulia et al. also found that steel with the same roughness (10nm) as the CoCr alloy and the glass had higher levels of damage and a higher friction coefficient (0.26). Steel is more hydrophilic than CoCr alloy which may have had an influence on the lubrication resulting in the higher friction coefficient of steel. As ceramics are generally less hydrophilic than metals this may also provide an explanation for the better performance of the ceramic seen in our study. The better performance of PCU in our study can probably be explained by the more compliant material that will lead to lower contact stresses and possibly improved lubrication conditions.

A similar study performed by Chan et al. (2011) evaluated the frictional behaviour of ceramic, CoCr, stainless steel and UHMWPE when sliding against bovine AC. They utilised a pin-on-disc tribometer to measure friction. The details and parameters used in

this study are shown in table 4-3. Their findings were in agreement with the findings of this study. They reported that both ceramic and Co-Cr resulted in a higher coefficient of friction than UHMWPE (Chan et al., 20011).

Table 4-3 Comparison between the data in the present study and Chan et al., 2011

	Sample	Coefficient of friction	Sliding speed	Load	Stroke length	Duration
Present study	Human humeral head cartilage	CoCr=0.25±0.06 Al2O3=0.2±0.04 PCU=0.19±0.04	4mm/s	0.3Mpa	2mm	60 mins
Chan et al., 2011	AC from bovine stifle joint	CoCr=0.074-0.566 Al2O3 =0.134-0.569 PE=0.03-0.391	0.5mm/s	0.1Mpa	7.85mm	1-60 mins

The study had several limitations. It was an in-vitro study and the reciprocating shear testing was only run for about an hour to avoid biological cartilage degeneration. This is clearly different from the clinical or in-vivo situation where it may take months or years for the cartilage to degenerate following the hemiarthroplasty operation. Also, the pin-on-disc testing is arguably not physiological and will lead to tribological conditions different to the clinical situation. While these limitations will probably cause the reported values to be quantitatively inaccurate the trends observed in the study are more likely to identify trends important to understand the clinical situation. Probably the most important limitation was that the arthritic specimens, even grade OA4, by virtue of being small specimens could not represent many important characteristics of a whole arthritic joint such as osteophytes at the periphery, eburnated bone and cystic cavities within the joint. Such features are common in arthritic joints and make for a very harsh tribological environment that was not replicated in our study. Clearly, this limitation may affect our finding that the degree of arthritis did not change the relative performance of the three biomaterials.

Another limitation of this study was related to sample size; due to the low number of samples used per group, it was not possible to perform the statistical test and to detect clinically relevant differences and less conclusive results were obtained. In future studies, larger sample number must be used in order to deduce definite conclusions. Too small a sample size may prevent the findings from being extrapolated (Faber and Fonseca, 2014).

Also, the low sample size reduces the chance of detecting a true fact. However, in the work presented in this chapter, due to limitations related to human sample availability, it was not possible to test more samples. Many researchers consider six animals per group as adequate sample size, however, as part of future work appropriate sample size calculation needs to be done in order to obtain meaningful data.

Furthermore, one of the limitations of the ICRS grading technique, and in general Oa assessment techniques which base the progression of the pathology on morphological changes, is that biochemical and hence mechanical changes in the tissue could already exist in a morphological healthy (grade 0) tissue. This highlights the strong need for a technique and a device to evaluate the mechanical properties of AC in a clinical setting. By assessing the mechanical properties of osteoarthritic AC ideally through arthroscopy, it could allow an estimate of the structural damage of the tissue and a clearer understanding of the progression and development of the pathology. However, such a technique would have to be thoroughly investigated and validated across several different stages of osteoarthritic AC in order to establish consistency in the measurement. The results in this chapter show that future studies should involve experiments with higher contact pressure.

In respect to the clinical application, this study provides support that ceramic implants may be a better choice than metals and the articulating surface should be made as smooth as possible. While our results indicate that the degree of arthritis should not affect the choice of biomaterial this clinical implication needs to be further investigated using whole joints more representative of the key features of OA joints. The study would also seem to support the use of PCU for hemiarthroplasty applications. This may be appropriate for very early stages of osteoarthritis but in later stages where osteophytes and cysts may exist the relatively low strength of PCU may make it unsuitable for this application. Also, the recent clinical problems with PCU meniscal implants will need to be considered.

4.5 Chapter summary

This chapter explained the mechanical and structural properties of non-OA and OA human cartilage. Moreover, OA-like AC was, for the first time, compared to human osteoarthritic tissue to investigate the role of mechanical degradation, as well as the role of proteolytic enzymes in the pathology. Finally, the performances of three common biomaterials, CoCr, Al₂O₃ and PCU, articulating against the various grades of OA, were compared. The next two chapters of this thesis will focus on the second phase of this project, developing a joint simulator in order to validate the findings from this chapter in a more clinically relevant environment. Chapter 5 discusses the shoulder joint simulator development and design modifications.

5 DEVELOPMENT OF A FRICTION AND WEAR SHOULDER JOINT SIMULATOR

Disclaimer:

In this chapter the original simulator was developed for hip joints by Collinge et al. and Welham et al (this includes the mechanical and software development). This PhD project focused on modifying the rig to test shoulder joint implants which was within the scope of this PhD. Furthermore, as part of master's research project strain gauges were added to measure friction values. The assembly and calibration were done in collaboration with Gan, 2017.

5.1 Introduction

With the aim of testing femoral head implants which were based on ISO 14242-1, former research students from Imperial College conceptualised a custom-made, one-station simulator. The current chapter will feature a discussion of the final rig design that was used in order to test shoulder implants against cadaveric tissue. This will include an in-depth and accurate description, justification, and modification, along with an evaluation of its functioning. In addition, advice will be given with regards to how the device should be used and maintained, seeing as it needed further development over time. Both the mechanical and electrical components' structure as well as operation will also be detailed, so as to facilitate full comprehension of the device. Moreover, this section will explore the way in which an innovative mechanical test rig devised for testing shoulder humeral head implants against glenoid cartilage was designed as well as developed. Although commercial simulators are available, their function is to test prosthetic joints, meaning that they are not equipped to test cadaveric tissue; additionally, they are costly (Welham et al., 2014). A functional, single degree of freedom simulator was the origin of this portion of the PhD project; this simulator, which was produced by former project students, replicates the human flexion-extension gait cycle (Collinge et al., 2013; Welham et al., 2014). Moreover, it allows for femoral head implants to be removed without difficulty.

5.2 Available simulators

Given that hip hemiarthroplasties are being carried out on younger and more active people, it is crucial to decrease prosthetic implants' rate of wear, which can be done by acquiring information on their tribological wear properties (Wright and Goodman, 2001). Extreme wear can result from an implant's connection with native cartilage, therefore, information on the joint's tribological properties is a vital aspect of preventing negative effects on the joint's cartilage (Pawaskar et al., 2011). The importance of hip joint simulators lies in the fact that with them, products can be tested in-vitro before clinical trials occur; moreover, implants' lifespans can also be determined in this way, thereby making these simulators central to both the research and development areas of medical joint implants (Affatato et al., 2006). The tribological conditions of a human hip joint as well as gait cycle must be closely mirrored in vitro in order to ensure the reliability of the data acquired from a simulator test (Affatato et al., 2008).

However, it should be highlighted that the rate of an implant's wear varies depending on certain factors such as frequency of activity, bone quality and weight of patients (Saikko, 2005). Also, in vivo dynamic and tribological conditions are not fully duplicated in vitro (ASTM-WK451, 2008). Specifications such as number of degrees of freedom, ball-cup relative position, loading profiles and number of stations all vary depending on most progressive hip wear simulators (Affatato et al., 2008). These devices permit for multiple orientations of the ball-cup system to be used; however, the upside-down position, which is symmetrically inverted to the standard physiological orientation, prevents drying out as a result of air bubbles reaching the top of the joint, subsequently promoting efficient lubrication. Moreover, gravity causes a build-up of minute particles in the acetabular liner, which travel between the bearing surfaces. This describes the way in which synovial fluid travels around the joint capsule in vivo, rather than particles retracting from the contact interface (Affatato et al., 2008).

Affatato et al. have conducted an extensive examination of both older and more novel hip joint simulators, comparing use of lubricant, load data, the number of DOF, and recording pertinent information. The collected data points to a wide variation in wear data, which is a reflection of simulators' varying wear assessment procedures. This essentially renders a comparison of test data unachievable. Consequently, the BS ISO 14242-1 standard came to life; however, despite this standardisation of factors in the simulation procedure, a comparison between wear data produced by different simulator rigs, using the same prosthesis, is impossible. The only comparison which can yield results pointing to indications of wear rate, is that made between the same simulators (Affatato et al., 2008). Muller et al.'s literature review focuses on research looking at the tribological properties of materials which were used in hemiarthroplasties. This research also involved pin-on-disc setups and pendulum trials against cadaver acetabulum. The Johannes Gutenberg University Hospital saw the development of the Hemi- EndoProsthesis Flexion Extension (HEPFIEx) simulator, which is seen as the only device to successfully reproduce a flexion/extension movement of $+30^{\circ}/-18^{\circ}$ simultaneously to a sinusoidal force load with 2.5kN peaks on hemi-endoprostheses. The HEPFIEx was devised in order to facilitate the comparison between metal and ceramic hip hemiarthroplasties under dynamic loading conditions (Müller et al., 2004). It also uses a pneumatic actuator and has the same features as the total hip joint wear simulators which Affatato et al. explored, with the exception of the incorporation of different types of samples.

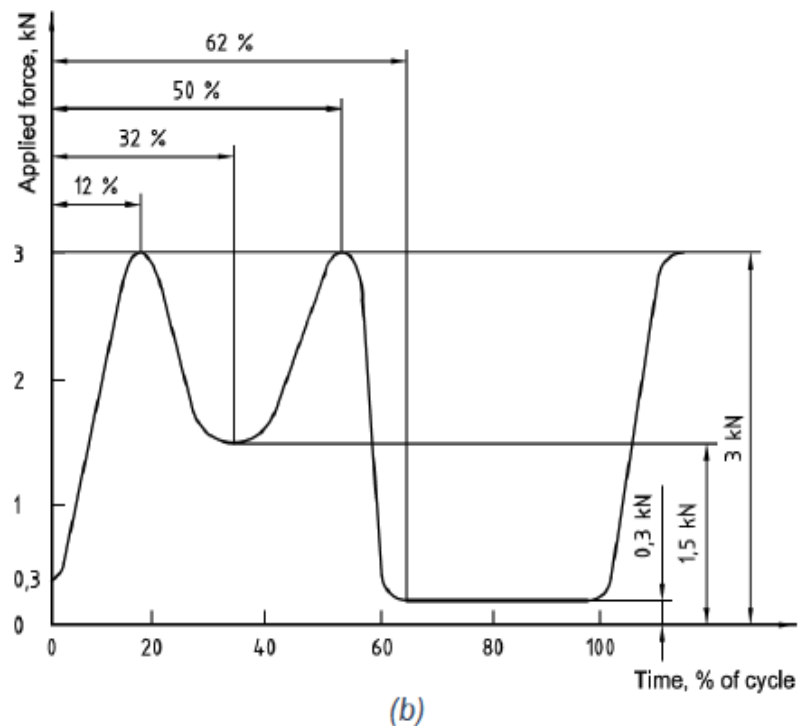
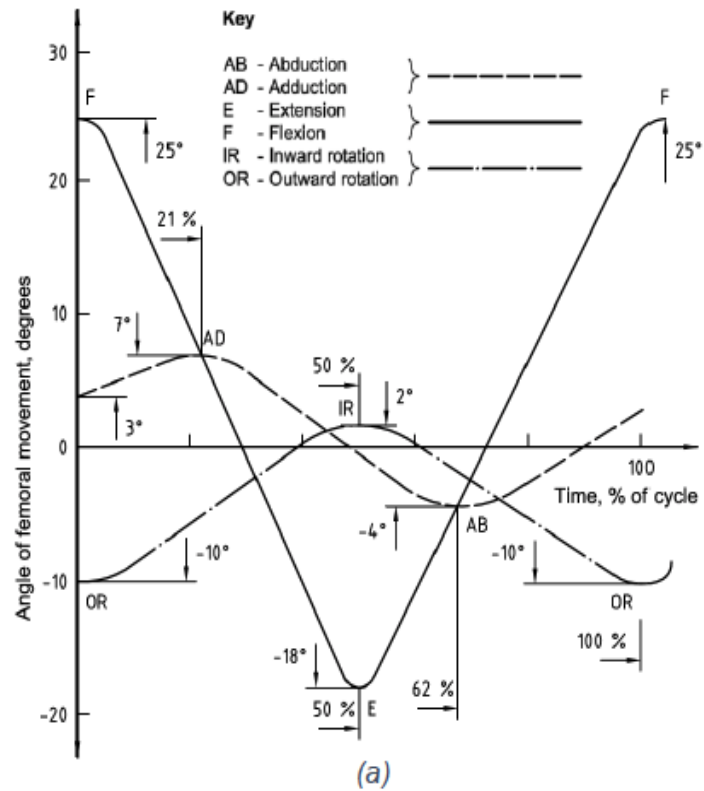


Figure 5-1 (a) angular position and (b) load cycle for the walking motion in accordance with BS ISO 14242-1 Adapted from (British Standards Institution, 2002)

5.3 Design specifications

The ISO 14242-1 standard offers guidance with regards to total hip joint prostheses, laying out loading and displacement specifications in order to assess machines' wear rate, along with relevant environmental conditions and motion cycles to recreate the motion of walking (British Standards Institution, 2002). This is the standard which was used when developing the imperial hip joint simulator; this was because of the lack of guidelines available for hemiarthroplasty implants. Using ISO 14242-1 facilitated the comparison of data gathered from various simulators. The first section of the ISO standard outlines the physical geometry and loading orientation for testing the femoral head and acetabular cup. Whilst the loading profile clarifies the amount of force which should be applied on the joint as a function of time, the motion profiles present the joint's degrees of freedom. The device's parts were already designed following ISO standards (Collinge et al., 2013; Welham et al., 2014). The simulator supplies the flexion extension part of the angular displacement cycle and the load cycle at a frequency of $1\pm0.1\text{HZ}$; the applied load is at 30° off the humeral neck axis (Figure 5-1).

The Imperial Simulator, which was developed by former master's research group followed the specifications outlined below (DMT-19, 2014):

- A novel vertical loading mechanism needs to be designed according to the loading cycle outlined in BS ISO 14242- 1:2002, and with the aim of being synchronised with all other motions. The desired cycle must include constant monitoring of the applied cycle so as to ensure that loads remain within $\pm 3\%$ of the target value during the flexion/extension motion profile.
- Motion control and loading cycles should occur at a constant cycle rate as much as is feasible for the duration of a test. In order to determine an average, a rate of $1.0\pm0.1\text{ Hz}$, as described in ISO14242, will be measured over a prolonged length of time
- A load cell (or an equivalent) must be used to keep track of the load cycle in real time, to guarantee that the load experienced by the joint matches the required output load. The load data should be gathered whilst testing is underway and verified against the anticipated response (new).

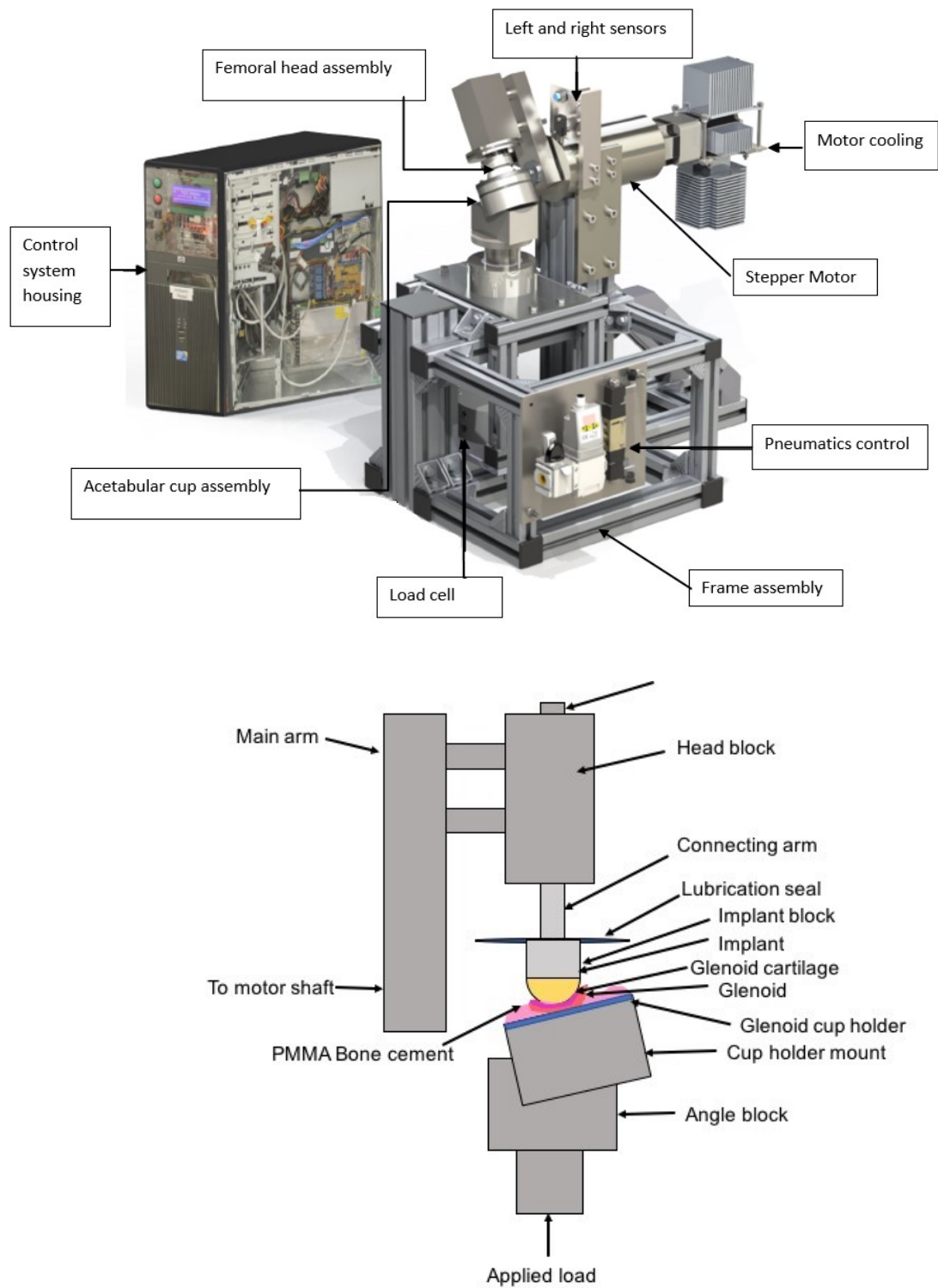


Figure 5-2 General assembly and schematic of simulator

5.4 General mechanical and control system assembly

5.4.1 Pneumatic system

To promote the reliability of a method of loading over long test periods, the development of a loading system within the rig was crucial. Although various loading systems, such as electro-mechanical, piezoelectric and hydraulic ones, were considered, it was concluded that the pneumatic system would provide the best performance (Welham et al., 2014). This choice was largely based on the fact that this system would decrease the simulator's dependency on mechanical parts, given that the device's life is estimated to be approximately 50 million cycles.

Since a pneumatic actuator is powered by air, it can utilize a compressor rather than a pressure vessel and pump; however, its position accuracy is greatly limited. Moreover, maintenance can be costly for this type of system, as pneumatic actuators are prone to gas leaks. As mentioned above, a simulator's life is estimated to be approximately 50 million cycles, meaning that the actuator's essential strength lies in its ability to decrease the simulator's dependency on mechanical parts. The system was developed with criteria adhering to the BS ISO 1219-1:2012 circuit diagram:

- A maximum of 3KN applied load
- Fully definable variable loading cycle
- Rise time of 120ms between 0.3-3KN
- Uses an electronic control interface

For the cylinder to successfully apply the 3KN maximum load necessary, the air supply must be continuous and of a minimum of 5 bar. The cylinder applies a load that is relative not only to the pressure applied, but also the piston's surface area. Given that it solely needs to make up for the deflection of the cup assembly which occurs under the sample's applied load and wear, a compact, double-acting cylinder with a minimised 5-inch stroke was selected. Bearing in mind its double-acting feature, a 5/2 directional control valve with 5 ports (1 inlet, 2 outlets, 2 exhausts) and 2 states (on both sides of the piston), is introduced before the cylinder, so as to determine to which end the air is applied. The state is switched with the use of solenoids regulated by a central controller once a 24V signal is across the input. Direction is changed once an experiment has been completed. The arrangement of the piston within the cradle is illustrated in Figure 5-3. Aiming to

identify both the fatigue and tensile properties along with the materials appropriate for the cradle, Welham et al., 2014 conducted numerous investigations.

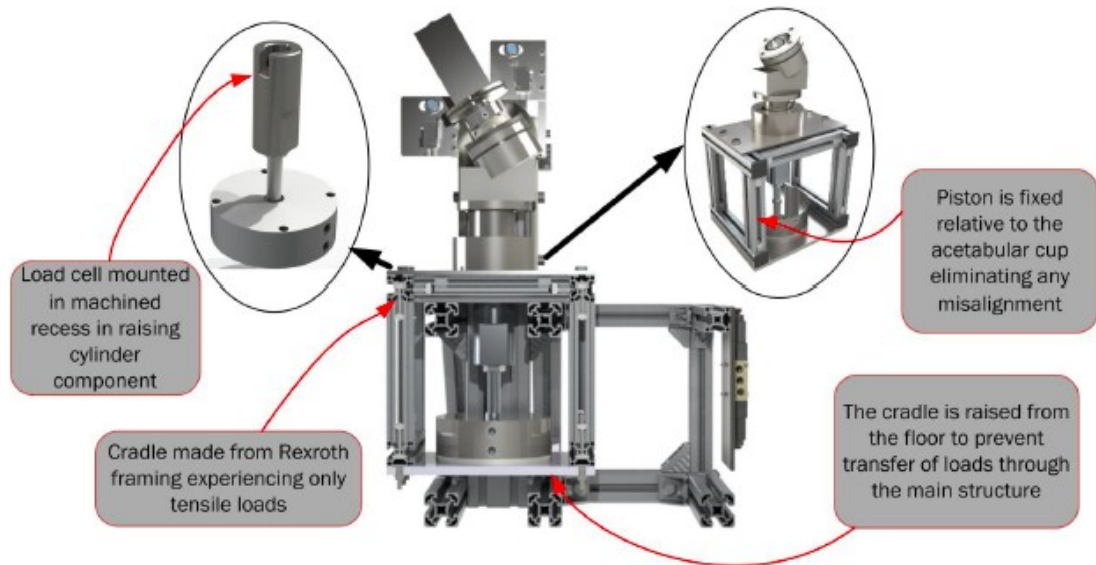


Figure 5-3 Layout of piston mounting within cradle

5.4.2 Electronic regulator

The electronic regulator is a central component of the pneumatic system, supplying pressure that is proportional to the voltage, and allowing for the control of the variable ISO loading cycle. In order to achieve the system's necessary performance, precise control of the electronic regulator is crucial; moreover, decreasing the number of tasks performed by the internal mechanisms as much as possible increases the intricate regulator's life. A 24V supply provides the regulator with its power, whilst a 0-10V DC control voltage controls the device; the outlet pressure is relative to the applied control voltage, with a range of 0-7 bar. At first, a 10 kHz, 10-bit pulse width modulation signal supplied control voltage from the Arduino. This employed an operational amplifier as well as a first order low-pass filter with the aim of smoothing and amplifying the signal to the necessary range of voltage.

5.4.3 Load cell and calibration

In order to successfully survey and adjust the loads applied by the microcontroller, a load cell was used. The key selection consisted of physical size, robustness and sensitivity. Welham et al. considered OMEGA LCM304- 5KN, given its suitability in terms of cost

as well as size with regards to mounting. A method for the rapid detachment of the load cell needed to be devised so as to facilitate the raising cylinder's rotation, which was accomplished with the use of a four pin XLR connector. The cell is found within a raising cylinder; this cylinder offsets any wear or vertical deflections, enabling the pneumatic piston to remain at minimum stroke for as long as possible. Figure 5-4 illustrates the load cell's internal configuration, including a Wheatstone bridge. Two parallel potential dividers are present; one holds the load cell's strain gauge along with a fixed resistor, whilst the second includes two fixed resistors. Any alterations in the strain of the cell's strain gauge (shown in blue, Figure 5-4), results in an alteration in resistance, subsequently leading to alterations in half of the bridge's voltage ratio. The voltage different between the midpoints of both potential dividers is measured as the output voltage of the circuit. It must be said that this change is measured (20mV per volt input). Therefore, when considering a 10V input to the load cell, the overall variation consists of only 200mV (Welham et al., 2014).

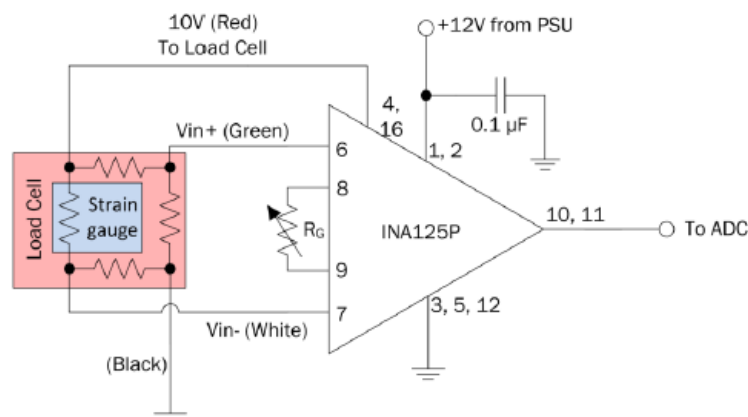


Figure 5-4 Diagram of a load cell circuit

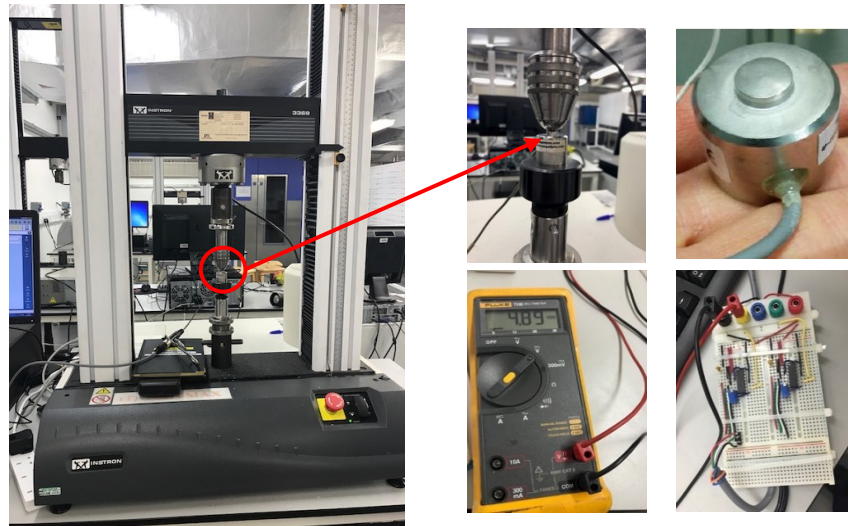


Figure 5-5 (a) Load cell mounted on to Instron 3369 machine, (b) Load cell placed under the indenter, ready for load application, (c) OMEGA LCM304 load cell , (d) Voltmeter showing voltage readings, (e) Load cell electrical circuit built onto a board

The Arduino controller needs the load cell readings to ensure that the applied load is situated in the appropriate range of error. The Arduino's built-in analogue-to-digital converter turns these readings into a digital signal and has an input voltage range of 0-5V. The load cell was calibrated so as to ascertain that it supplied correct readings. Therefore, to calibrate the cell's response with regards to voltage, an Instron 3369 mechanical testing was employed, with a 50KN load cell (Figure 5-5). Moreover, it was crucial for the load cell signal to fill the converter's entire 0-5 V range, in order to increase the system's sensitivity by as much as possible. An amplifier, the Texas Instruments INA125P, was used both to amplify the load cell signal as well as to supply the regulated voltage needed to provide power to the load cell's circuit (Figure5-4). The amplifier's gain was regulated by varying R_G and tuned with the application of a 5KN compressive force to the load cell in an Instron machine; the gain was increased up to the point where the amplifier's output measured 5V. Given that this surpasses the maximum force which the cell will undergo in the simulator, a buffer is provided, and the Arduino's input is kept from going above the 5V limit. Thereby, each of the converter's state represents a 4.89KN change. This accuracy level was seen as acceptable, seeing as $\pm 90N$ is the ISO requirement for loading accuracy. A linear correlation between voltage and load was found which confirmed the calibration of the load cell (Figure 5-6).

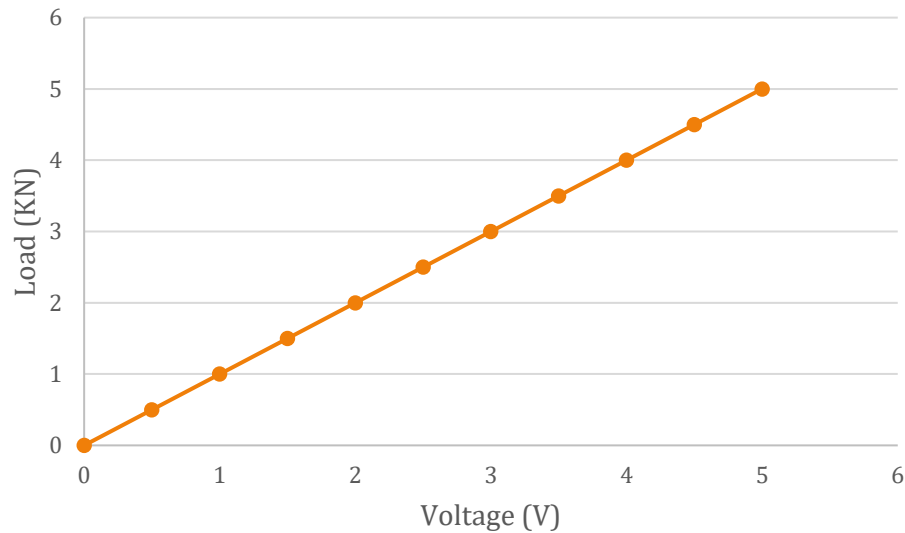


Figure 5-6 Correlation between load and voltage

5.4.4 Calibration Gauge

Keeping in mind this project's aims, the flexion extension motion takes place at 1 Hz, therefore, the stroke cycle value is 1. In terms of the range of motion outlined by the ISO, -18° to 25° was required. A calibration meter was put together to facilitate calibration, as illustrated in Figure 5-7. The inclusion of the tolerances on the range of motion enables straightforward positioning of the limit switches onto the outer tolerances of the -18° and $+25^\circ$ markings.

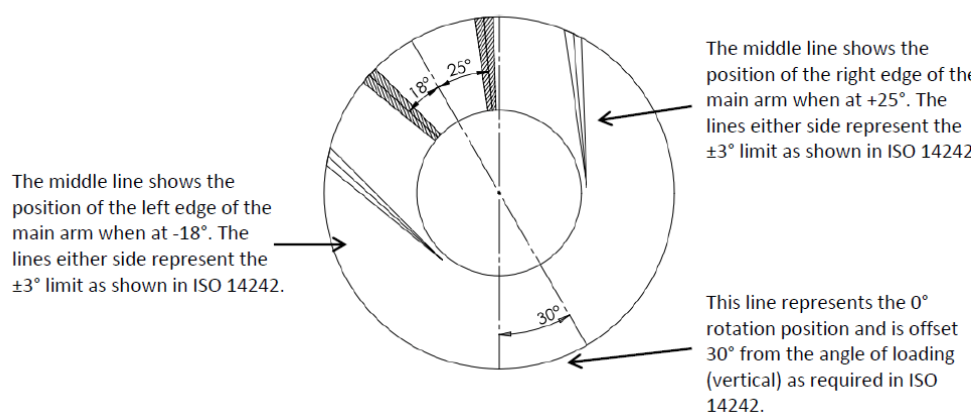


Figure 5-7 Description of the calibration gauge as seen on the simulator

As the stepper motor was set up to carry out a full range of motion from its initial position, the range of motion was calibrated by aligning the main arm to the lowest point (-18°). Following this, tests with varying frequency values of 1600, 1700, 1800, 1900 and 2000 Hz were carried out. The main arm's maximum displacement position was recorded via a marking on the calibration meter after every test. Moreover, in order to counter human error which might arise from judgement being made following visual observation, 5 runs at each frequency were carried out. Then, the average of the data collected from the calibration for each frequency values was determined.

5.4.5 Motor Cooling system

A group investigation conducted previously anticipated high surface temperature; as a result, heatsinks were used to dissipate the heat and decrease the motor's surface temperature. Thermal conductive tape was used to fit four heatsinks to the motor surfaces, so as to increase heat transfer between the two surfaces as much as possible. Additionally, a mounting plate was included to provide support to the two largest heatsinks (Figure 5-8).

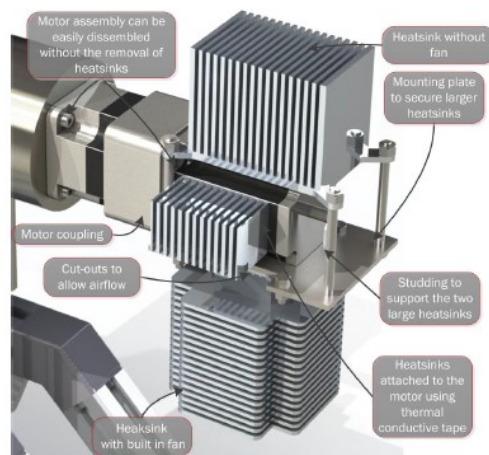


Figure 5-8 Arrangements of heatsinks on motor

5.4.6 Limit switch and sensors

Non-contact inductive sensors were connected to an input on the Arduino in such a way so that when the main arm is approximately 5mm away from a sensor's surface, their output voltage drops to 0V. This input tracks the sensor's state and prompts an 'interrupt' when an alteration in the signal is detected. This trigger should normally occur at the end of every half cycle in normal operation, thereby making sure that the full range of motion is being achieved. Hard limit sensors are wired to the Arduino in series, so that using the switch breaks the circuit. Given that any breaks in the circuit keeps the device from running, this serves as an additional precaution. In contrast, a fault in the circuit could remain undetected if instead, operating the switch completed the circuit. Two brackets accommodate sensors which detect the arm's position, see Figure 5-9; this was to calibrate and ascertain that the arm's motion is within the designated rotation limits. On each bracket were two kinds of sensors: a non-contact inductive proximity sensor and a contacting limit switch. The brackets themselves were laid out so that the proximity sensors detect the main arm's position as it arrives towards the rotation's limit, in this way enabling the control system to continually keep track of the position. As a safety measure, the hard limit switches are located at a wider angle, meaning that these are activated if the arm over-rotates as a result of the structure's large inertia or slack in the motor transmission. As a consequence, power is interrupted, thereby instantly bringing the test to a halt. This counters potential damage to the simulator as well as the sample that is being tested. Given that the sensors are arranged in horizontal slots, their positions can be changed during calibration, as well as for a new cycle with another angular range.

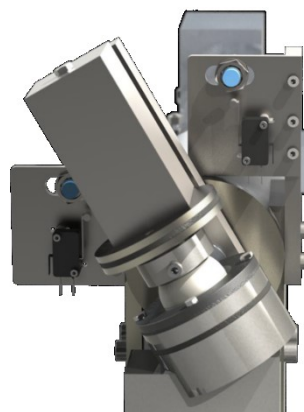


Figure 5-9 Sensor and limit switch assembly

5.4.7 Microcontroller

The control system microcontroller was chosen based on the number of pins it possesses, to which external elements like sensors and motors can connect, as well as access to support resources. The system needed approximately 30 pins, which is why Arduino models were looked at. Arduino Mega 2560 fulfilled the criteria and was the preferred option as it is greatly suited to the hardware and software packages which the project needs.

5.4.8 Stepper motor

A 3.1Nm Nema 23 stepper motor (CNC4you, product code: 60BYGH301B) was employed for the flexion/extension motion and supplied larger torque. This synchronous electric motor is able to convert digital pulses into mechanical shaft rotation. The motor is a digital input-output device, with the input pulse being relative to its rotation angle. The device is straightforward and unlike standard DC/AC motors, is easier to control, and supplies larger torques at lower speed. Moreover, it responds brilliantly to start and stop.

The CW8060 micro-stepping controller supplies 48V which powers the motor; this can also divide the motor's fixed step size into various, smaller angular step sizes and current settings, allowing for the torque to be changed. The motor runs via a 20:1 planetary gear box to the flexion extension arms, with the range of motion as 43 degrees, as outlined the ISO standard; consequently, that the arm's angle can be worked out, per step, for different micro-stepping settings. A half step micro-stepper was chosen, as it struck a balance between smooth motion and good torque performance (Figure 5-10); below can be seen the angular motion per step:

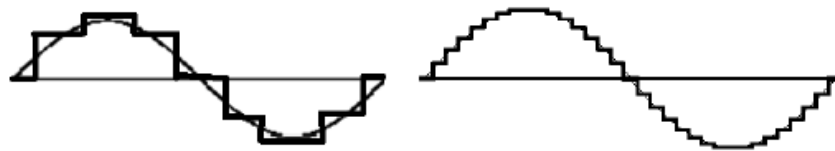


Figure 5-10 Effect of micro stepping (y-axis: displacement, x-axis: time)

$$\text{Angle per step} = \text{motor full stop} \times \text{micro-step reduction} \times \text{gearbox reduction}$$

$$= 1.8^\circ \times 0.5 \times 1/20 = 0.045^\circ/\text{step}$$

$$\text{Steps in ISO range} = \text{angular range}/\text{angle per step} = 43/0.045 = 956$$

A setting of 4.28A was chosen once tests were run on the existing rig. A HG07 breakout board connects the control system to the micro-stepper; the HG07 has been designed in order to electrically isolate and separate the controller from the remaining electrical system. This was done with two purposes in mind; the first is to ensure that any spurious voltage surges do not result in any sort of harm to the controller. The second is to allow the micro-stepping controller to separate any incoming control signals into the required signals. A D-type 24-pin connector connected to the HG07 breakout board was created to act as a custom wiring loom between the HG07 and the Arduino. This wiring can allow for the passing of control signals to the stepper motor circuit. Figure 5-11, shows the different control components.

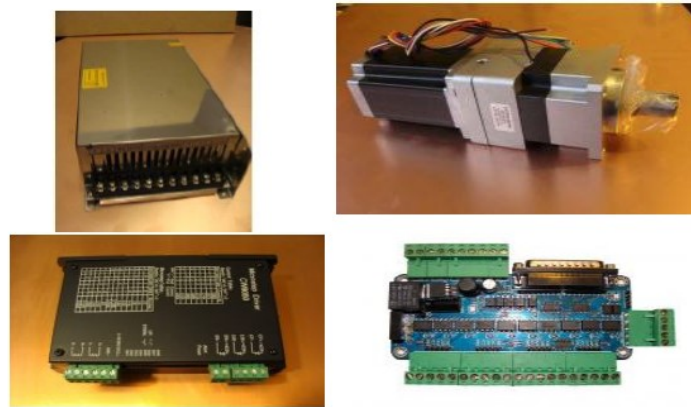


Figure 5-11 (a) Power supply, (b) Stepper motor, (c) Breakout board, (d) Micro-stepper

5.4.9 Software and graphical user interface

An Arduino code was developed by Master's students (Welham et al., 2014), in order to carry out periodic actions, for instance determining the load at different points in the cycle, the Arduino microcontroller employed timers. External code libraries were used, so as to take maximum advantage of the Arduino's functionality. These libraries are essentially prewritten sets of functions, which link low level complex microcontroller commands to higher level tasks, including making something appear on an LCD screen, and setting a timer. A graphical user interface (GUI) was written with the aim of enabling the connection of a PC to the port located at front of the simulator, as well as the selection of test parameters and initiation of the test without any understanding of the Arduino control system's inner functioning; see Figure 5-12. The GUI is straightforward to use, as its layout is uncomplicated. Test parameter options can be selected via drop down lists

as opposed to being manually typed, thereby reducing the occurrence of human error. The GUI application was made in the C# programming language, which is both modern as well as object-oriented, and relies on the .NET framework. Visual Studio Professional was used for the writing of the C# code; this is the compiler and debugging software. Moreover, the GUI was created with an open architecture, thereby, adaptations can be made to the code in order to supply additional modifications and variations to the loading cycle. Having said that, this would also mean that the Arduino code would have to be altered so as to reflect the modifications.

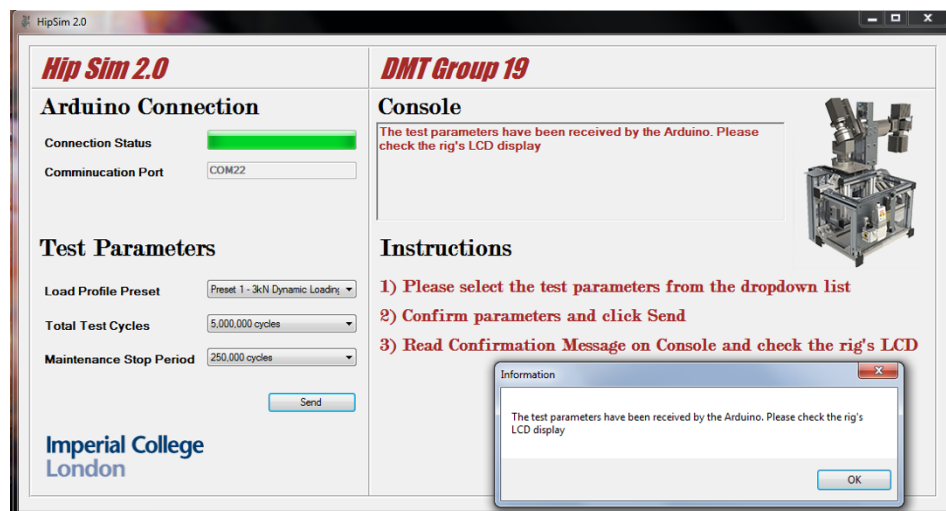


Figure 5-12 GUI displaying successful Arduino connection and transmission of test parameters

5.4.10 Front panel

The CD drive bay covers the PC housing had to be removed, and a front control panel was inserted in their place. This was created with the use of the original mountings in order to enable the LCD, buttons and Arduino to be mounted. With the use of nuts, the buttons' threaded shafts were fastened to the panel. Mounting the Arduino in this location not only facilitates access to the USB port for uploading new code, it also decreases electrical interference by keeping the Arduino away from the power supplies found at the back of the case. As demonstrated in Figure 5-13, the panel was cut from an acrylic sheet via the use of a laser, and a label for every button was engraved onto it with the cutter.

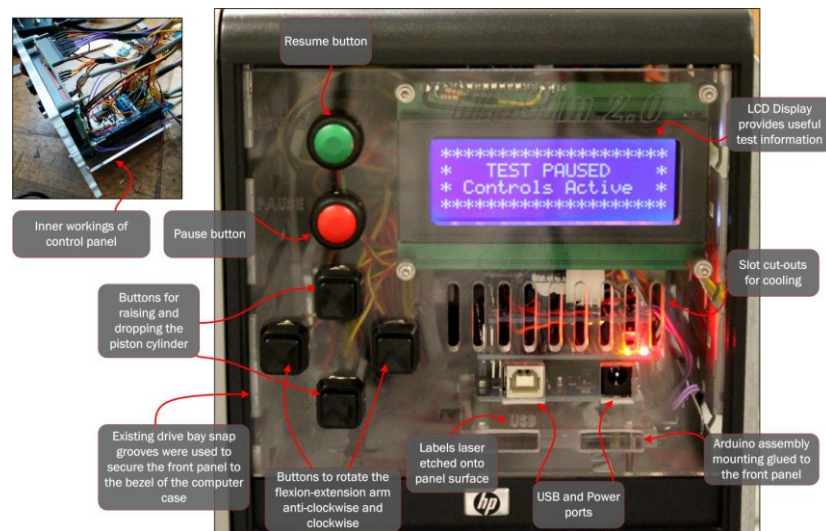
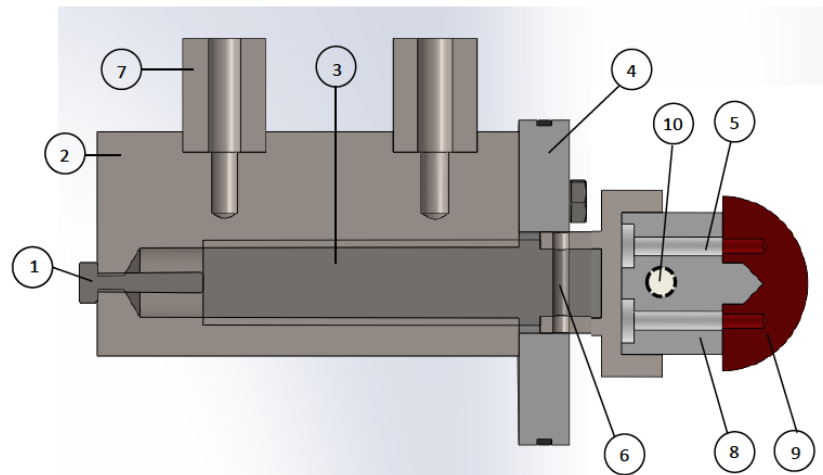


Figure 5-13 Front panel layout

5.4.11 Femoral head holder assembly – old design

The femoral head holder assembly has three objectives. The first is to tightly grip the femoral head sample. The second is to enable small alterations to be made to the bone's position, so that the centre of rotation shaft is successfully aligned to the femoral head's centre. Lastly, the third is to supply a sturdy link between the bone and the motion arm. Assuming a femoral head is perfectly spherical, when split in half into a hemisphere, the centre of rotation invariably lies upon the hemisphere's flat edge. The subassembly and components are shown in Figure 5-14. Moreover, attaching the hemisphere to a flat surface in order to provide support would be straightforward. Though, this was specifically designed for femoral head previously, and a biological femoral head is not perfectly spherical, and it is improbable that it could be accurately cut in half. However, grinding methods (using sand paper) can result in a high degree of accuracy. Given that bovine serum will be touching the femoral head, the elements around it must be able to resist the resulting corrosion. It was therefore decided to create the mounting rod with Stainless steel T316, as it fulfils the above-mentioned requirement. Having said that, intricate machining processes are needed to thread the 20 mm diameter mounting rod. To overcome this obstacle, instead, the head of an M20 stainless steel screw was detached and the remaining piece was included in the design. An O-ring groove supplied by a seal flange allows for the placement of a rubber seal. Additionally, this is what the upper hose clip will be strongly clamped to.



Part No.	Part Name	Description
1	M6 Locating Screw	This M6 screw prevents any rotation in the rod during operation, fixing the axial location of the femoral head.
2	Head Block	The head block locates and connects to the support rods via recesses and locates the screws to connect to the seal flange and mounting rod.
3	Mounting Rod	The mounting rod is threaded and allows the femoral head to be adjusted in the vertical direction prior to operation. When a satisfactory position is attained, the M6 screw (as explained), locks it into position.
4	Seal Flange	The seal flange contains an o-ring groove for a rubber seal to be seated preventing leakage.
5	Nylon Screw	Two nylon screws are used to connect the femoral head to the head attachment. Made from UHMWPE to allow use in MRI.
6	Spring Pin	A spring pin is pushed through the support rod and mounting rod to connect them and prevent rotation of both parts relative to one another.
7	Support Rod	Two support rods connect the head block to the main arm.
8	Head Attachment	The head attachment is used to hold the femoral head ensuring consistency of its positioning, easy disassembly, and use in MRI. It also has a central extrusion to align to the centre of the test sample, and to support shear loading during operation.
9	Femoral Head	The load is directly applied to the femoral head or test sample, and its holes are prepared in the femoral head jig
10	Connecting Bolt	A single connecting bolt mounts the head attachment to the mounting rod to allow for easy disassembly.

Figure 5-14 Head holder assembly and components (old-design)

5.4.12 Cup holder assembly

The cup holder assembly can firmly hold a variety of femoral cup sizes and, in accordance with ISO-14242 standards, angles the cup at 30°, simultaneously enabling vertical adjustment. Moreover, the assembly translates the load acquired from the loading screw straight onto the cup, as well as enables the application of any future Inward/Outward rotation; however, in this situation, it restricts it. The cup holder assembly was created to ensure that its rotation axis corresponds with the femoral head's centre of rotation, thereby enabling subsequent groups to apply inward/outward rotation to the entire component. As

the cup holder assembly needed the ability to move upwards as well as downwards for location relative to the femoral head, a bearing became crucial in order to offer support for this whilst also enabling it to slide up and down. An Oilite flanged plane surface bearing was selected after having considered the rotation that would be applied later. This enables axial movement and rotation about the axis; the flange supplies a surface to effortlessly constrain the bearing, which was very inexpensive (suitable for a potentially temporary part). However, it must be noted that Oilite bushings may not be suited to linear motion. Having said that, the resulting effects of, for instance, the load being marginally off-centre, would most probably be inconsequential. As of yet, the simulator rig does not have an inward/outward rotation; the cup holder assembly's rotation is made impossible by a pin that can be removed without difficulty. This hinders rotation at any elevation of the cup holder assembly, as is illustrated in **Error! Reference source not found..**

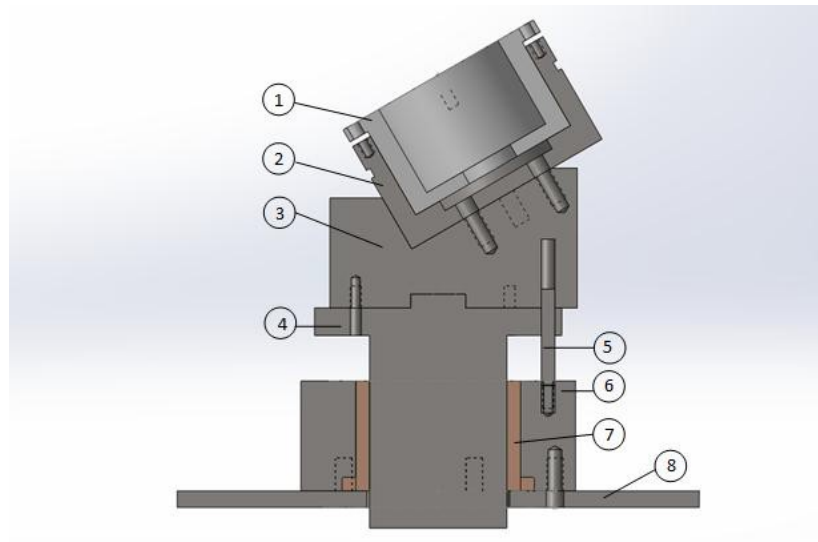


Figure 5-15 Cup holder assembly and components

Part No.	Part Name	Description
1	Cup Insert	The cup insert contains the acetabular cup. It varies according to the acetabular cup being used, since its internal diameter matches the outer diameter of the cup. It is filled with bone cement from the inlet gap at its base. A gasket prevents leakage into the connections between this and the SS cup holder.
2	Cup Holder	The cup holder contains the cup insert, has an o-ring groove for the lower lubricant seal.
3	Angled Block	The angled block allows the cup to be angled at 30° as specified in the ISO standards. It is attached to the cup holder slider. It allows the cup holder and cup holder slider to be located easily via concentricity.
4	Cup Holder Slider	The cup holder slider allows this subassembly to be displaced in the vertical direction. Such displacements are required since when the loading is applied, the loading screw would push up against the base of the cup holder slider. The slider also ensures that there is a full conformal contact between the cup and the test sample.
5	Pin	A pin is slotted in between the cup holder bush, angled block and cup holder slider. It restricts rotation of the cup, which might arise due to the flexion-extension motion.
6	Cup Holder Bush	The cup holder bush constrains the oilite bearing in all degrees of freedom
7	Oilite Bearing	The oilite bearing reduces the friction coefficient between the sliding cup holder slider surface and the bearing itself.
8	Plate	The plate connects the cup holder subassembly to the Rexroth frame and also contains the oilite bearing.

5.5 Modifications and improvements

Considering that the shoulder joint is more intricate than a hip, and that many daily activities can be defined (ADL), there are, as of yet, no ISO standards for the shoulder joint wear testing (Smith et al., 2015; Wirth et al., 2009). Additionally, not many in-vitro shoulder wear studies populate the literature, regardless of the fact that shoulder joint replacement is not only a well-known practice, but also of the awareness that wear is an obstacle hindering the long-term survival of patients (Smith et al., 2015). Shoulder joints undergo various ADL activities, where ranging loads and displacement patterns are not only different but also extensive (Kohut et al., 2012). Most simulators which have tested shoulder prostheses involved modified hip and knee and single station simulators; moreover, complete shoulder physiological loading and motions were not applied. Newcastle University saw the development of a shoulder wear simulator (Figure 5-16) which implemented the angular position and load cycles for the mug to mouth ADL (Figure 5-17). As shown in Figure 5-17, at 30% of the cycle time the shoulder load cycle rises from 180N to 250N and falls back to 180N at 90% of the cycle time. This loading cycle is distinct from that of the imperial hip simulator's gait cycles (Smith et al., 2015). Anglin et al.'s research is mentioned in the ASTM standard F1378-12 shoulder prosthesis

specification, proposing that with regards to in vitro shoulder joint simulator studies, reaction forces of approximately 750N or 1-2 times body weight should be employed (Anglin et al., 2000a, 2000b). This study was the first to successfully completely recreate the physiological motion and loading of a typical shoulder ADL with a shoulder simulator. Moreover, although conventional Polyethylene total shoulder replacements has been largely explored and studied, the same cannot be said for ceramic and metal shoulder hemiarthroplasty implants, as far as we are aware. Clinical data for shoulder hemiarthroplasties are limited and basic scientific evidence examining the wear characteristics of shoulder hemiarthroplasties under physiological loading is lacking (Klawitter et al., 2018; Kohut et al., 2012).

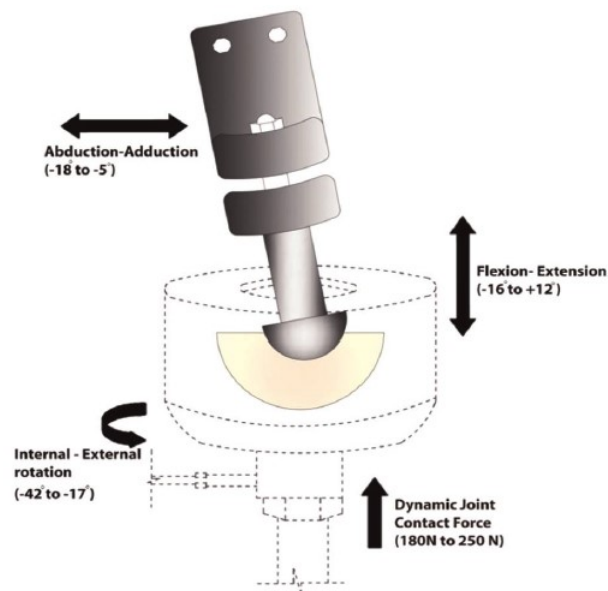


Figure 5-16 Schematic of the Newcastle shoulder simulator (Image adapted from Smith et al., 2015)

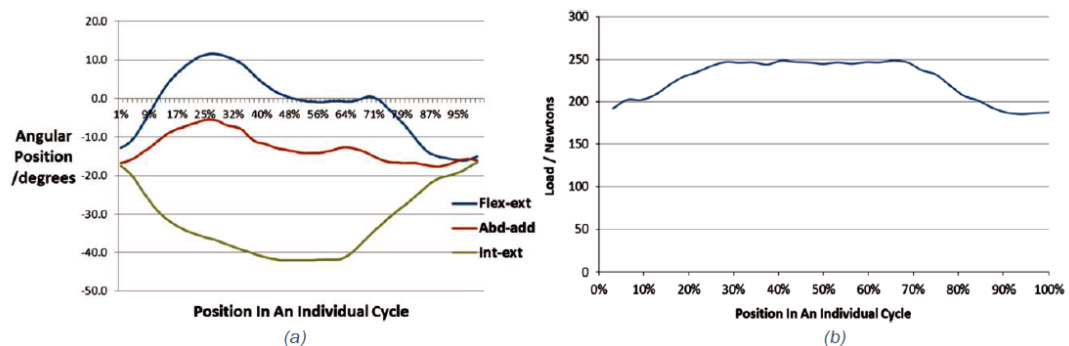


Figure 5-17 (a) Angular position and (b) load cycle for the mug-to-mouth ADL (Image adapted from Smith et al., 2015)

The sample holder design was altered to be able to hold humeral heads of differing dimensions. This was done in order to enhance the shoulder implants testing rig. In addition to putting into effect the shoulder loading mechanism so as to more accurately meet the specifications outlined in the ASTM standard. As previously mentioned, to date there are no ISO testing standards outlining information about simulating shoulder joint motion, given that the shoulder joint is more complicated than the hip, and numerous day-to-day activities can be defined (ADL) (Smith et al., 2015; Wirth et al., 2009). The research of Anglin et al., provides the direction of contact force for various ADLs, as shown in Figure 5-18.

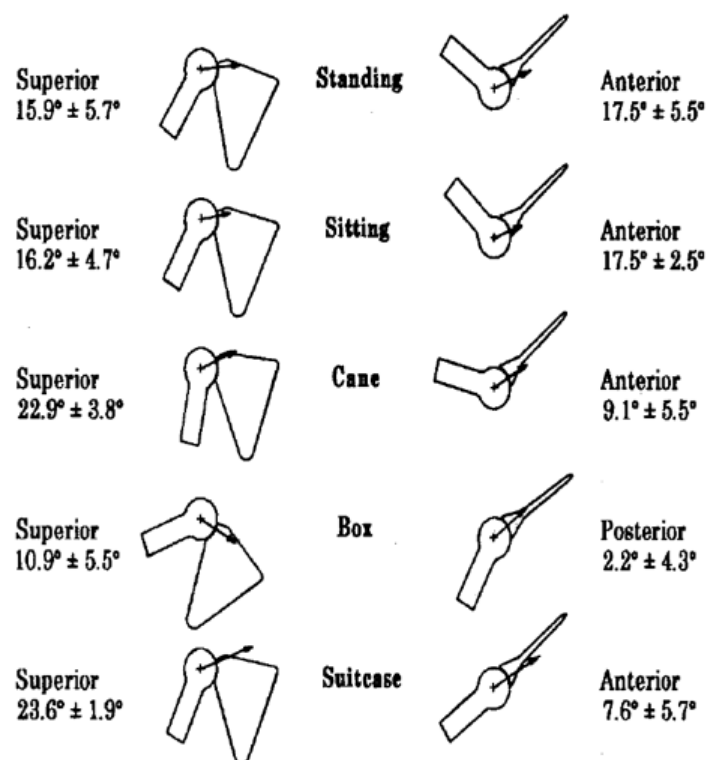


Figure 5-18 Direction of shoulder joint reaction force for various ADLs (Anglin et al., 2000b)

5.5.1 Implant holder modifications

The previous design for the rig allowed for femoral heads to be securely mounted on the head holder. Moreover, this head holder enabled slight alterations to be made to the implant's position, so as to accurately align the centre of rotation shaft to the femoral head's centre of rotation. Additionally, it supplied a solid link between the implant and motion arm (Figure 5-19). In previous design UHMWPE nylon screws attach the femoral head to the head attachment. The lubricating seal flange with an O-ring groove to accommodate a rubber seal with the aim of countering leakage (Collinge et al., 2013).

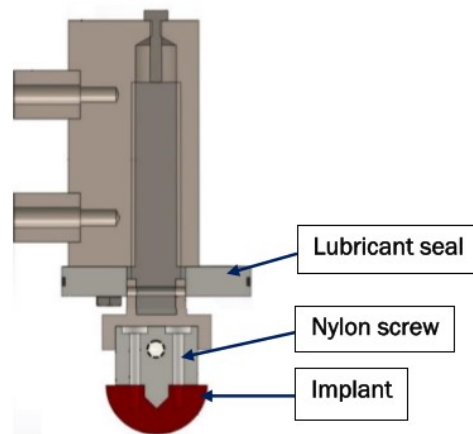


Figure 5-19 Incumbent design of the main arm

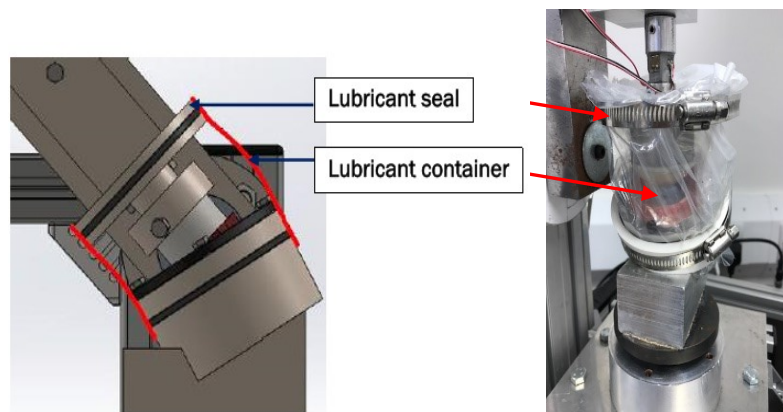


Figure 5-20 Method used to contain joint lubricant in the incumbent design

Modifications as well as adaptations were made to this hip simulator, to make it suitable for the testing of humeral component implants against cadaver glenoid. However, challenges arose from the device's design. Firstly, nylon screws as illustrated in Figure 5-19 will cause damage to the implants, as the humeral head implants are 13.33-15.65mm deep. Secondly, attaching strain gauges close to the implant whilst avoiding the lubricant proves a challenge, due to the placement of the seal and gaiters, which are there to hold in joint lubrication, as demonstrated in Figure 5-20.

5.5.2 Main Arm and Head Block

The design of the simulator's motion arm, which includes the components after the motor shaft up to the implant, was reviewed and revised in order to overcome these obstacles. Figure 5-21 outlines the revised aspects of the motion arm. It must be noted that the $\pm 25^\circ$ / $\pm 18^\circ$ rotational limits and 30° orientation of the acetabular/glenoid cup, as shown in Figure 5-22 were not revised. Nevertheless, there is potential to altering these so as to correlate

the angular position cycles and joint loading directions for numerous ADLs. However, in this instance it was decided that the completion of a full working simulator and friction measurement system was more important. It was necessary to ensure that the humeral head could be removed in a straightforward manner, as well as accurately and reproducibly substitutable. As outlined in Figure 5-21, the main arm was made wider, from 25mm to 28mm, so that as the arm moves, stiffness is increased against bending. Moreover, in order to adapt to a longer implant holder, the arm's connection point to the head block was brought upwards. In an effort to reduce mass as well as the assembly's moment of inertia, the 6082-T6 aluminium head block was made shorter from 100mm, as illustrated in Figure 5-21. This not only reduces bending in the main arm, but also the torque that is necessary to prompt motion.

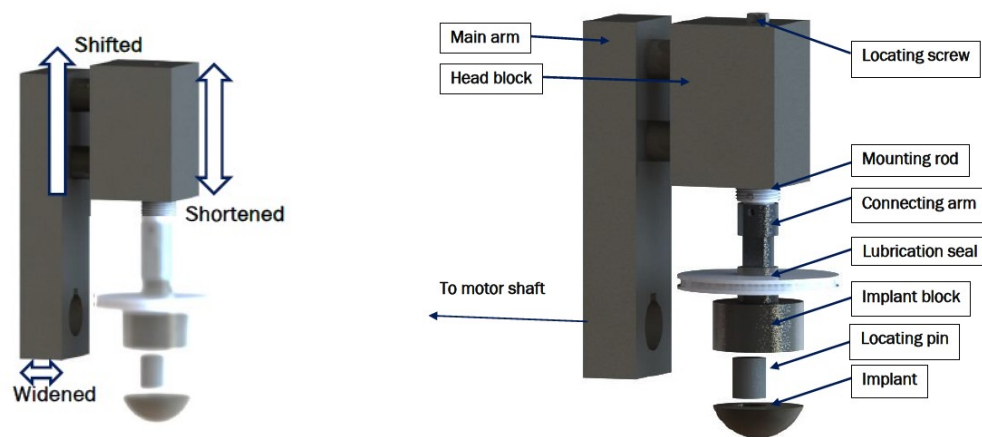


Figure 5-21 Modifications to the main arm and head block

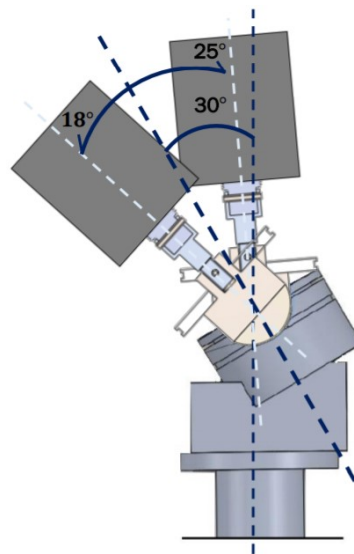


Figure 5-22 +25°/-18° limits of motion about the 30° orientation of cup

5.5.3 Connecting Arm

A threaded mounting rod which was from the original simulator design brings the connecting arm, implant block, locating pin and implant together with the head block. The rod enables for the vertical adjustment of the implant, which is needed to guarantee that the centre of curvature corresponds with the motor shaft's rotation axis. Two flat surfaces are placed on either side of the connecting arm, so as to easily locate the strain gauges as well as link the mounting rod and implant block, as can be seen in Figure 5-23. The connecting arm consists of Aluminium 6982-T6 and is thinner and less stiff than the remainder of the motion arm, emphasizing strain that is recorded at the location. Moreover, it is 12mm wide between the flat surfaces, with a second moment of area of $2.18 \times 10^{-9} \text{m}^4$. Given that there are 69.15mm between the strain gauges and the implant's centre, the safety factor is of 2.36 against yielding under vertical loading of 750N at the leftmost limit of rotation.

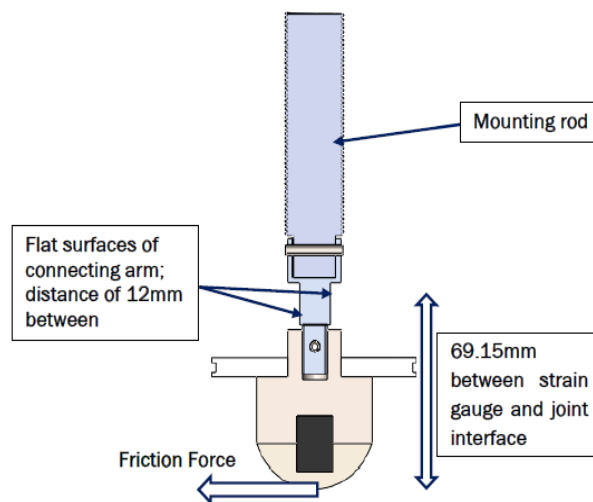


Figure 5-23 Section view of mounting rod, connecting arm, lubricant seal, implant block, locating pin and implant

5.5.4 Implant block and locating pin

The finished design for the implant block and locating pin emerged from an earlier concept involving the implant being contained in a cup; this can be seen in Figure 5-25. Although this design has the potential to be used again following testing, the edge of the cup shown in Figure 5-25 might encroach on the glenoid. Therefore, the implant block has been designed as a component that is adhesively bonded to new implants with Loctite EA9466 epoxy. EA9466 was selected due to the fact that it is very strong as well as

compatible with metals, ceramics, and plastics. A thin layer of glue was applied on to the humeral head and the head holder and left for 1 minute before the head was placed on top of the head holder. Once this was done the excess glue around the edges was removed with a plastic knife. This combination was left to set for 48 hours using a clam standing in a vertical position (see Figure 5-24). The implant block's geometry can be altered to suit implants of different diameters. Additionally, as illustrated in Figure 5-26, a locating pin can be found between the implant block and the hole in the implant which can be fixed to the bone. This facilitates the transfer of loads between the implant and block.

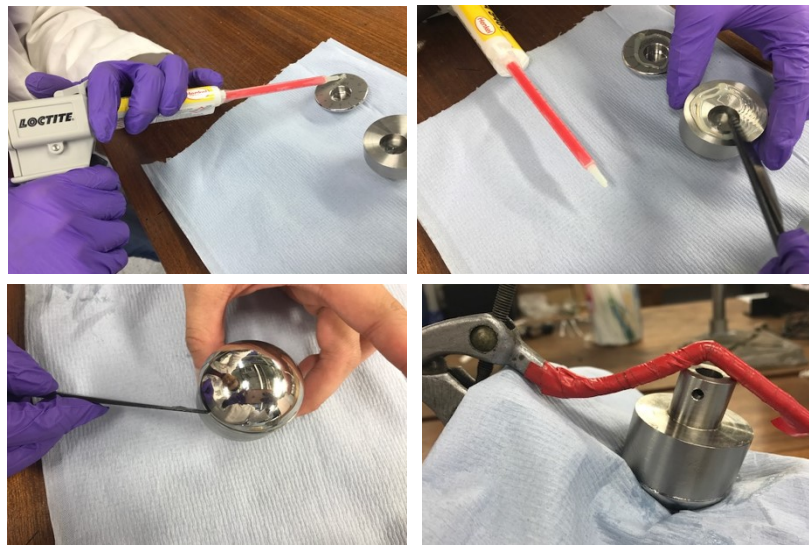


Figure 5-24 Steps taken to mount the humeral head on to the head holder with epoxy glue

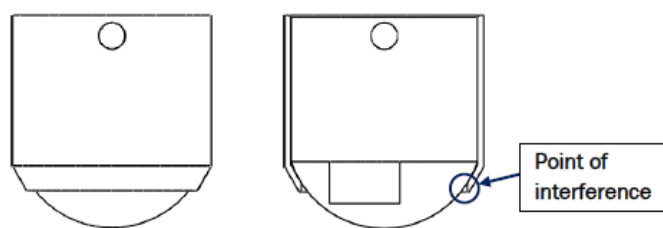


Figure 5-25 Design concept of a cup for mounting the implant, full view and section view (left to right)

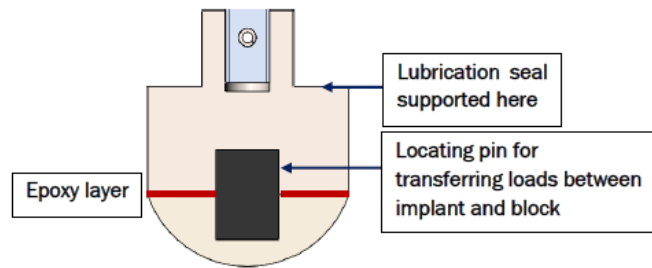


Figure 5-26 Section view of the implant block and implant showing the locating pin and epoxy layer

5.5.5 Lubrication seal

For joint simulator studies according to ISO standard 14242-1, use of a lubricant with similar properties to synovial fluid, such as $(25\% \pm 2\%)$ bovine calf serum is recommended (Bortel et al., 2015). With regards to the current study, a sealed food grade transparent bag is the most suited to accommodate the lubrication. This is due to its flexibility, as well as the fact that despite the arm's constant movement, it will not tear nor leak. Moreover, the bag is transparent, thereby facilitating any necessary alterations of the glenoid's position against the humeral head, if needed. With a syringe and a 3mm flexible tube, the lubricant was poured into a clear plastic casing; in the event of any unseen leakage, more liquid was added. Otherwise, a syringe and needle were used to remove the liquid and replace it with the new lubricant, with minimal spillage (Figure 5-27). The sealed bag's two extremities were cut off. Also, to avoid any tension and possible splitting, the bag's length had to exceed the distance between the O-ring, so as to ensure that it buckles. Given that the strain gauges were situated above the lubrication seal, it had to be placed in a way so that the gauges could not come into contact with the fluid.

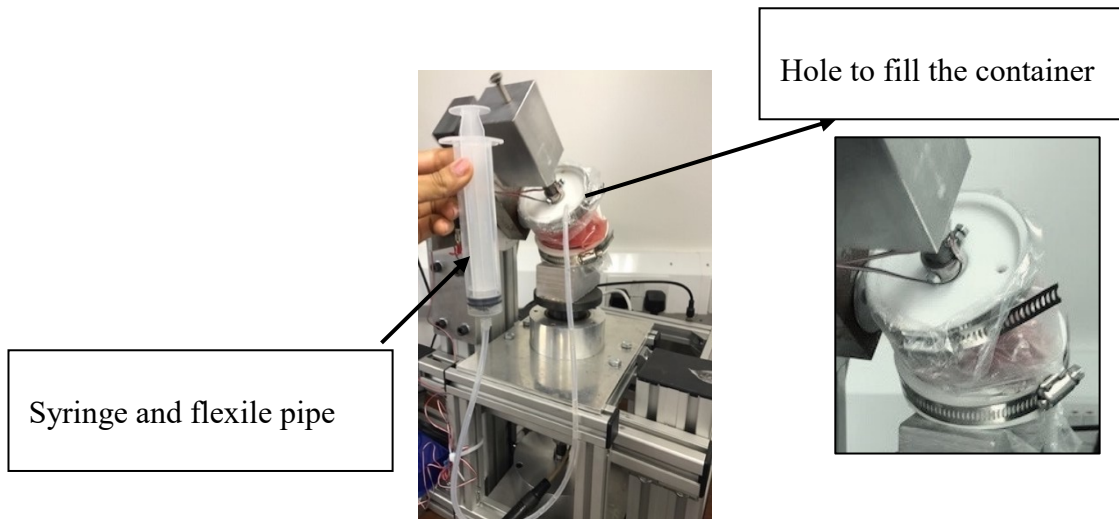


Figure 5-27 Lubrication system setup

5.5.6 Cup holder modification

The cup holder assembly was altered so as to be able to secure glenoid of different sizes. The angled block's curved centric surface allows the holder, which is attached by screws, to remain positioned. This assembly is positioned on a plate screwed onto the frame. In order to enable the adjustment of the implant and joint, the base plate was altered; the holder was redesigned for larger cadaveric tissue use and PMMA bone cement (Figure 5-28). The cup holder's design allows for its axis of rotation to match with the tissue or implant's centre of rotation and for upwards as well as downwards movement relative to the tissue. So as to avoid the cup rotating while the test is taking place, a pin was placed between the cup holder and the cup holder brush. The redesigned sample holder featured a hole which was added to the bottom of the holder with the aim of making it easier to remove any bone cement once the test finishes. The holder consists of stainless steel 316 material and is therefore reusable. Additionally, the holder's diameter was made bigger, thereby allowing for more bone cement to fill the inner cup holder, and for the tissue to be supported more tightly.

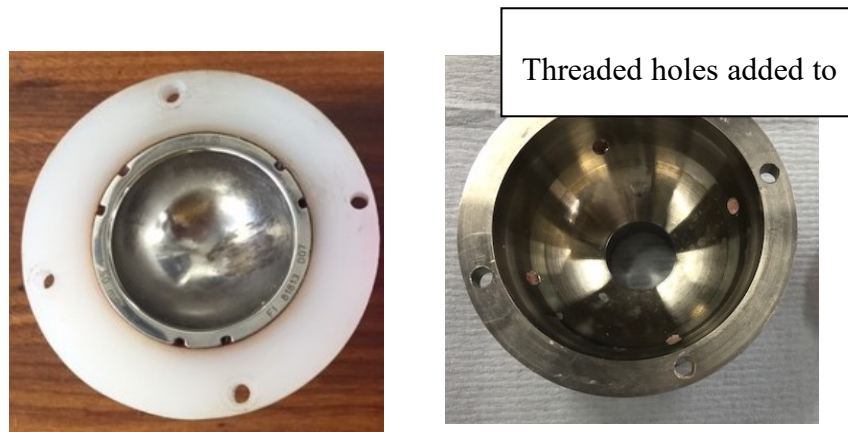


Figure 5-28 Former and altered sample holder design

5.6 Friction measurement system

As part of this study's main aims, it looked to develop and implement a friction system onto the rig developed at Imperial College. Ways to determine friction as well as coefficient of friction have been developed in hip simulators; this could assist in the design and implementation of a friction measurement system in the joint simulator. Muller et al. and Saikko employed a torque transducer on their hip simulators' motor shaft to determine friction values in the joint interface (Müller et al., 2004; Saikko, 1992). The torque transducer determined the value of torque resulting from friction in the joint interface, among other torques needed to overcome torsional inertia, keeping in mind friction and incorrect alignment of the femoral head. In the software, these other torques are removed, with only the frictional torque remaining. At the Johannes Gutenberg Hospital, Müller et al. observed this technique only yielded approximate results, given that the measurement of frictional torque is influenced by the size and dimension or local irregularities in the joint (Müller et al., 2004). As demonstrated in Figure 5-28, friction forces at contact surfaces close to the centre of rotation deliver less friction torque than at surfaces that are further away from the centre. Moreover, seeing as the exact pressure distribution within the contact is uncertain, one can only arrive at an approximate coefficient friction. Lastly, it should be highlighted that the joint interfaces are in mixed lubrication and using friction coefficient to define lubricated joint is not wholly accurate. For this reason, values reflecting friction forces or frictional coefficient in the joint interface should be used to compare friction attributes between materials. Moreover, according to Müller et al. it is not possible to replicate in-vivo physiological conditions

with in vitro simulator testing given that a precise establishment of the wear rate of prostheses and cartilage cannot be reached (Müller et al., 2004).

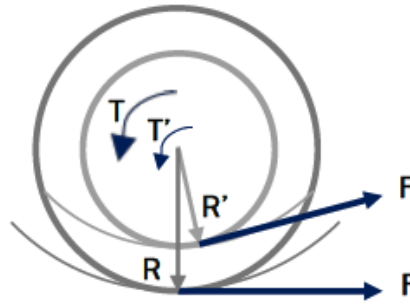


Figure 5-29 Frictional torque is lower if friction force is closer to the centre of rotation

5.6.1 Mechanics

A vertical force F as well as a horizontal force P (the two components of the resultant force) are applied on the motion arm by the static load in the joint interface. Presumably, the loads are applied at the implant's lowest point. Although this also constitutes an out-of-plane force, it is not seen as the arm motion and the friction forces are believed to remain in plane (Figure 5-29).

The resultant force applied to the joint can also be considered schematically as the sum of a normal force acting along the axis of the arm labelled as N , and a tangential force that is perpendicular to it, which in the static system initially balances the system. Once the arm is in motion, the sliding between the implant and the glenoid's articular cartilage leads to a friction force whereby μ is the coefficient of friction:

$$F_{friction} = \mu N \quad (1)$$

Strain gauges are placed on either side of the arm, at the locations shown in Figure 5-32 and not only they measure bending strains but simultaneously remove axial strain when used in the half bridge arrangement. Direct tangential force and friction are what cause the bending in the arm.

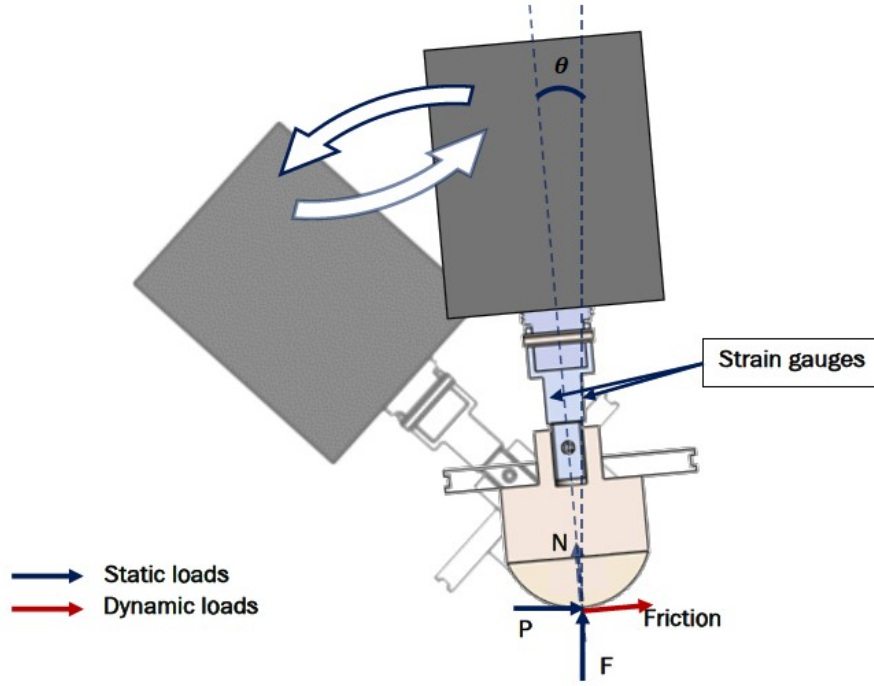


Figure 5-30 Free body diagram of the static and dynamic loads on the arm

Equation 2 illustrates bending moment, which is a result of direct loading, where L_s represents the distance from the contact to the strain gauge and θ represents the angle of the main arm from the vertical. Equation 3 illustrates strain resulting from direct loading, where E is the Young's Modulus, I is the second moment of area and y is the radius of the arm where the strain gauges are affixed.

$$M_{direct} = FL_s \sin \theta + PL_s \cos \theta \quad (2)$$

$$\varepsilon_{direct} = \frac{\sigma_{direct}}{E} = \frac{M_{direct} y}{E I} \quad (3)$$

As demonstrated in Equation 4, bending strain as a result of friction can be determined by eliminating bending strain resulting from direct loading from strain measurement. Equation 5 illustrates bending moment as a result of friction. When divided by the moment arm, the friction force is determined in Equation 6, where normal force N is expressed in Equation 7.

$$\varepsilon_{friction} = \varepsilon_{measured} - \varepsilon_{direct} \quad (4)$$

$$M_{friction} = \frac{\sigma_{friction} I}{y} = \frac{\varepsilon_{friction} E I}{y} \quad (5)$$

$$F_{friction} = \frac{M_{friction}}{L_s} = \mu N \quad (6)$$

$$N = F \cos \theta - P \sin \theta \quad (7)$$

Figure 5-30 outlines the vertical force F in the joint interface as the applied physiological load. A pneumatic loading system applies the force load, while a load cell located in the Imperial simulator measures it. Having said that, the simulator cannot directly measure the horizontal force P at the joint interface. Welham et al. have in the past employed Castigliano's Energy Theorem and finite element analysis (FEA) (this is described in further details in Appendix A) to ascertain the horizontal force. The horizontal force determined at the leftmost limit, this being $\theta = 48^\circ$, for a much larger load corresponding to hip loading in humans, is displayed in Table 5-1 with a percentage difference of 0.81% between them (Welham et al., 2014). This is, however, based on important assumptions about the configuration and stiffness of the system and will be put to the test later in the thesis. In particular, the assumptions made in Appendix A may provide an overestimation of P given that in reality the joint has one compliant component (the glenoid) and one much stiffer part (the implant).

Table 5-1 Horizontal force at leftmost limit $\theta = 48^\circ$ (Welham et al., 2014)

Energy method	FEA	%difference
2.42KN	2.44KN	0.81%

5.6.2 Angular position measurement

The arm's motion is determined by the number of micro-steps between the two limits along with the time delay that exists after each step. Once a cycle is completed, the time delay is updated in order to guarantee that the frequency is $1 \pm 0.1\text{Hz}$. With a 1/16 step size, the motion arm begins with a $250\mu\text{s}$ delay, and the speed is increased by lowering the amount of delay by $2\mu\text{s}$ following each step; this is done until a regular delay is established. Once a few tests were conducted, it was found that a regular delay of $40\mu\text{s}$ gave the desired cycle length. This in turn results in the angular position θ which is

illustrated in Figure 5-31. A correlation between the angular position of the main arm and the strain measurements can be achieved by noting down the number of micro-steps that occur between the two limits and the time delay; following this, the horizontal force P and friction coefficient can be determined.

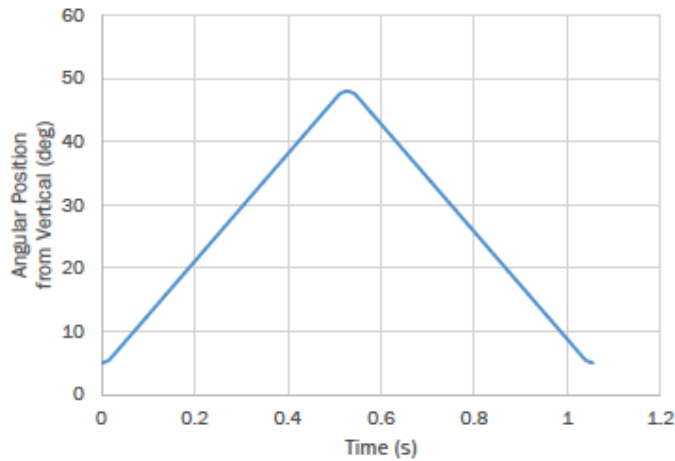


Figure 5-31 Graph of angular position from vertical θ with time

5.6.3 Strain measurements

On both sides of the motion arm can be found strain gauges of gauge factor 2.14 which are bonded lengthwise. This was done with epoxy, as it is stronger and lasts longer than the cyanoacrylate that is usually used. There are flat surfaces included on the main arm so as to facilitate the application of the strain gauges, as can be seen in Figure 5-32. A National Instruments NI 9237 bridge completion module connects to the strain gauges in the half-bridge ii mode, as illustrated in Figure 5-35 and Figure 5-36 for the purpose of recording onto LabVIEW on the computer. This configuration solely allows for the bending strain to be measured, rejecting axial strain. At first, the design of the motion arm meant that one end had two different radii. However, this resulted in higher bending stress at the thinnest sections, ultimately leading to a collapse of the arm following a few tests (Figure 5-33). The design was then altered so that the lower part of the arm consisted of one piece, thereby preventing fractures as a result of high bending stress (Figure 5-34).



Figure 5-32 Initial design; a section of the motion arm with flat surfaces for strain gauges application



Figure 5-33 The collapsed connector

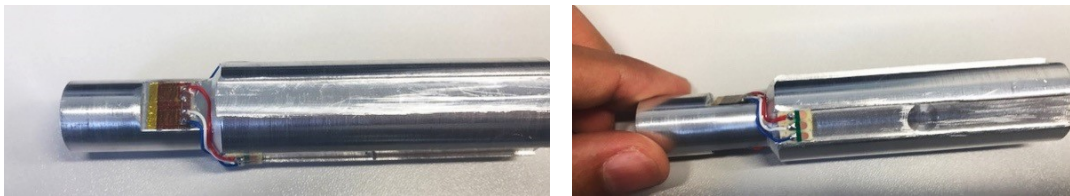


Figure 5-34 Modified motion arm connector with strain gauges attached on the flat surfaces

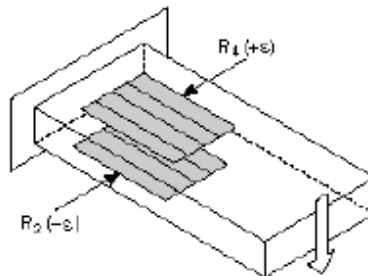


Figure 5-35 Half-Bridge ii configuration

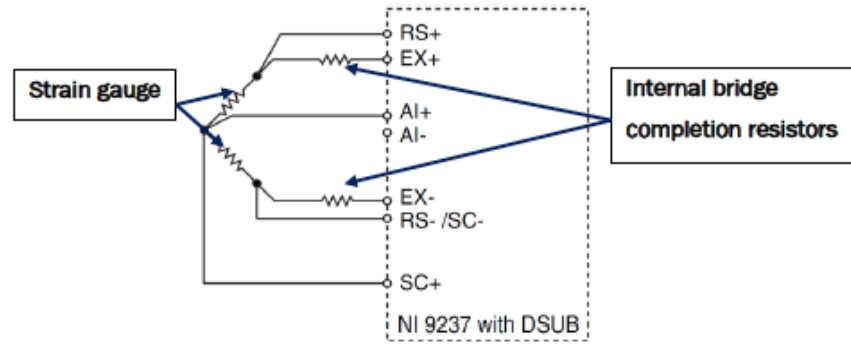


Figure 5-36 Half-bridge wiring diagram for NI 9237 and D-subminiature (D-sub) breakout board

Given its ability to record quarter-, half- and full bridge measurements, the NI 9237 module was selected. Its input range is of $\pm 25\text{mV/V}$ with 24-bit resolution. Equation 8 displays the calculation of the quarter-bridge strain resolution with a strain gauge factor of 2.14; this being 1.39ne . Strain resolution does not present a challenge when half-bridge resolution is halved to 0.70ne .

$$\text{Resolution} = \frac{50 \times 10^{-3}}{2^{24} \times 2.14} = 1.39 \text{ ne} \quad (8)$$

Although the NI 9237 has an accuracy of 0.0375mV/V , for half-bridge configuration this changes to $8.76\mu\text{e}$, as demonstrated in Equation 9. How this affects the updates which will be carried on the simulator design were explored in Section 5.5.3.

$$\text{Accuracy} = \frac{0.0375 \times 10^{-3}}{2.14 \times 2} = 8.76 \mu\text{e} \quad (9)$$

The strain was recorded on a modified continuous strain input programme from the LabVIEW library. Given that the resistance of a 41mm length lead wire is 0.3Ω , the effect of lead wire resistance can be determined accordingly; consequently, the resistance of a 1,914mm lead wire is 14Ω . The potential divider in Figure 5-37, with excitation voltage V_{in} , can be used to ascertain the effect of this resistance on output voltage V_{out} . Upon the application of a strain ϵ to the strain gauge shown as R_1 , its resistance rises by $\Delta R = GR\epsilon$ where G is the gauge factor. Equation 10 illustrates how an expression for V_{out} can be derived. Given that considering a strain of $1000\mu\text{e}$, the voltage output ratio both with and without taking lead wire resistance into account is 0.99994, it can be said that the lead wire length should not greatly influence strain measurement. Lastly, a 3D-printed

polylactic acid (PLA) tray supports the DSub breakout board of the NI 9237 on the frame of the joint simulator, and has a cover for protection, as demonstrated in Figure 5-38.

$$V_{out} = \frac{R_w + (R + \Delta R)}{2R_w + 2R + \Delta R} V_{in} = \frac{R_w + (R + GR_\varepsilon)}{2R_w + 2R + GR_\varepsilon} V_{in} \quad (10)$$

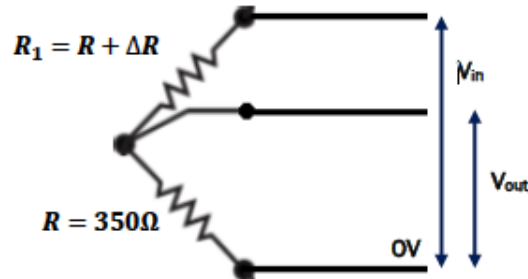


Figure 5-37 Output voltage for applied strain

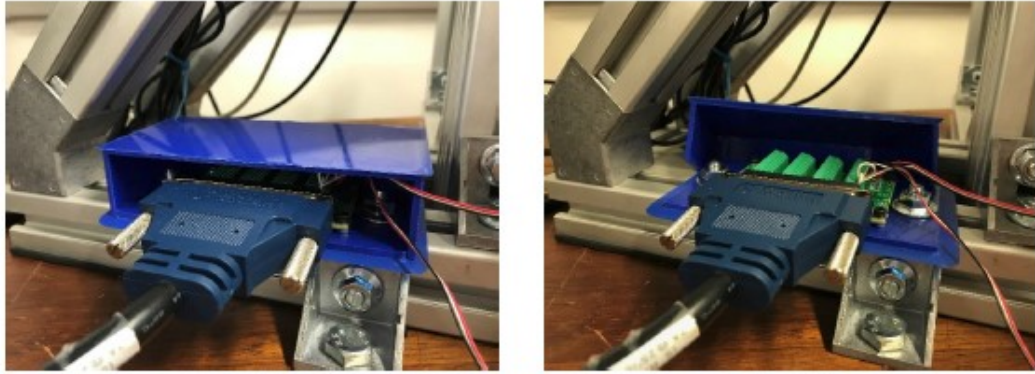


Figure 5-38 Polylactic Acid (PLA) casting for D-subminiature (D-sub) breakout board with cover on and cover off (left to right)

5.6.4 Strain gauge calibration

In order to calibrate the strain gauges, masses were positioned on the motion arm at a distance of $L = 25.5\text{mm}$ from the strain gauge, as demonstrated in Figure 5-39. Equation 11 can be used to determine theoretical strain with beam theory, where the distance from the surface to the neutral axis $y = 0.006\text{m}$, the second moment of area $I = 2.18 \times 10^{-9}\text{m}^4$, Young's modulus of the aluminium part $E = 70\text{GPa}$ and gravitational acceleration $g = 9.81\text{ms}^{-2}$.

$$\varepsilon = \frac{\sigma}{E} = \frac{My}{EI} = \frac{mgLy}{EI} \quad (11)$$

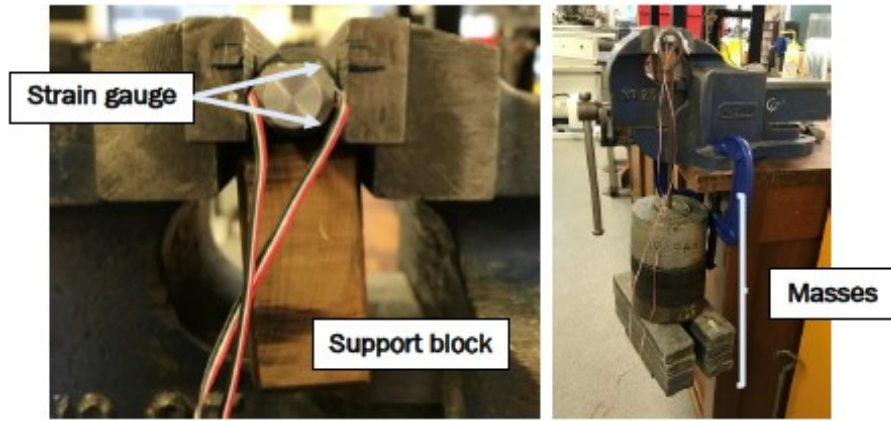


Figure 5-39 (a) securing and ensuring the motion arm is horizontal, (b) Calibration with free weights

A clamp grips the motion arm as displayed in Figure 5-39. The arm is held up by a wooden block, and markings have been made on the clamp's side in order to locate it and to make sure that the strain gauges are parallel to the ground. To ensure the position's accuracy, a spirit level was used. Before the arm is loaded, the masses were determined. The highest possible mass which could be loaded on the arm was 63.657kg, considering the height of the hanger. Each mass was deposited on the hanger, after which the strain which was measured and displayed on the LabVIEW interface was recorded, once it had settled. This procedure was repeated for subsequent masses, and overall was carried out three times. The average from the resulting data was then calculated. As illustrated in Figure 5-40, a linear correlation was established between calculated strain ϵ_e and averaged measured strain ϵ_m . Equation 12 depicts the relationship, and this can then be utilised to correct the measured strains for friction measurement.

$$\sigma_m = 1.1189\sigma_e - 3.1539 \quad (12)$$

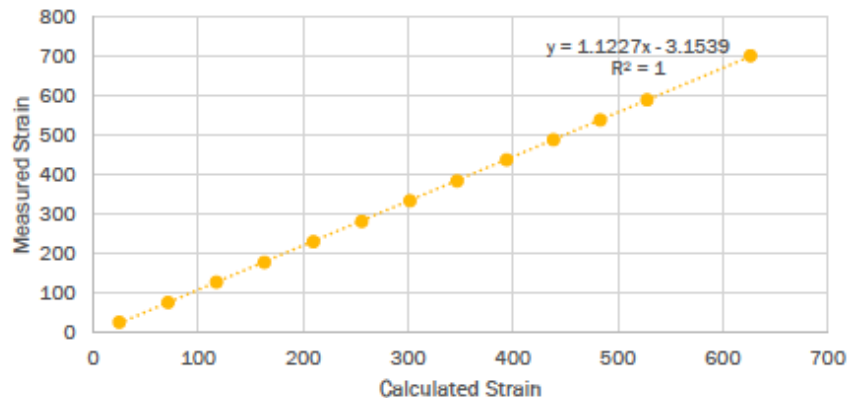


Figure 5-40 Correlation between measured and calculated strain

Ensuring that hands and feet remain at a distance from the test setup whenever possible whilst calibration was underway was necessary to avoid injury as the masses could fall. Moreover, appropriate posture was used whilst carrying heavy loads, and gloves were worn to avoid suffering cuts from rusty weights.

5.6.5 Data Collection

To collect data, a USB data acquisition board model (OM-USB-140FS, 14-bit Multifunction, Omega Engineering, Figure 5-41) was selected, and information was logged into the computer with a LabVIEW interface. Arduino provided the signals for the board. The values for direction, load, angle, and the Vout were supplied on LabVIEW in real time. Moreover, the change of angle was also displayed, meaning that the test could be brought to a halt in the occurrence of any errors or an angle change to a very high value. With the purpose of gathering data, the OMEGA board was connected with a USB to National Instrument NI cDAQ-9171, and different pins were used for input and outputs. 100 data points were collected per second to increase accuracy.



Figure 5-41 OMEGA data acquisition board

5.7 Full system test

Certain assumptions are made by the mechanical model outlined in Section 5.6.1 for measuring friction. Kinematics of the joint consist of pure sliding. Having said that, rolling may take place if the friction coefficient is high, as illustrated in Figure 5-42.

1. The calculation of the horizontal force in the joint can be done by representing it as a pin-joint and minimising the strain energy.
2. Throughout the entire duration of the rotation cycle, the point of contact in the joint interface is at the centre of the implant surface.

It was necessary to ascertain whether friction and wear in the joint can be determined and whether the mechanical model's assumptions for friction are true. For this reason, a complete test of the joint simulator's altered mechanical system along with the implemented friction measurement system with an alumina ceramic implant against porcine glenoid was conducted.

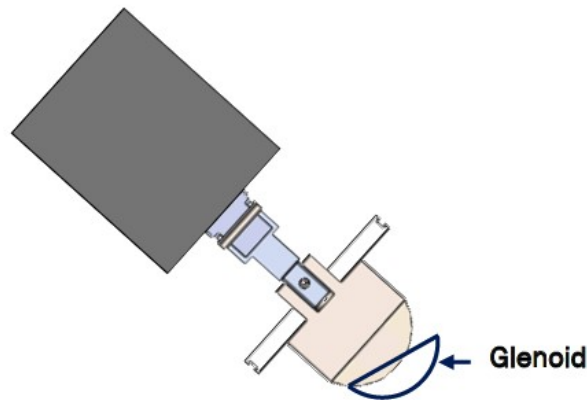


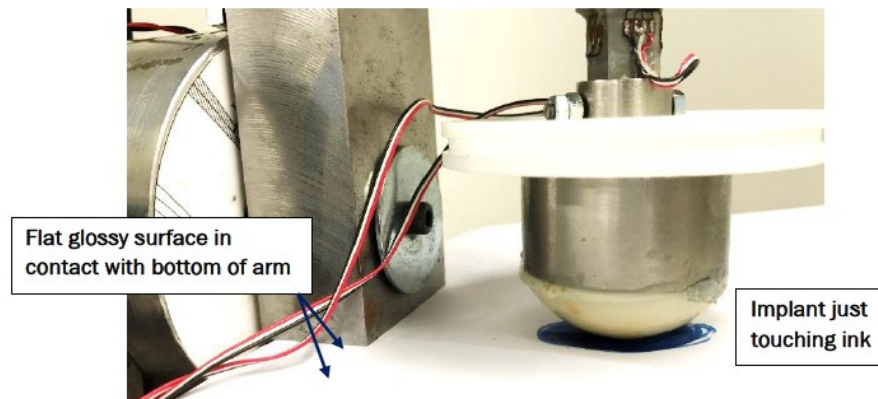
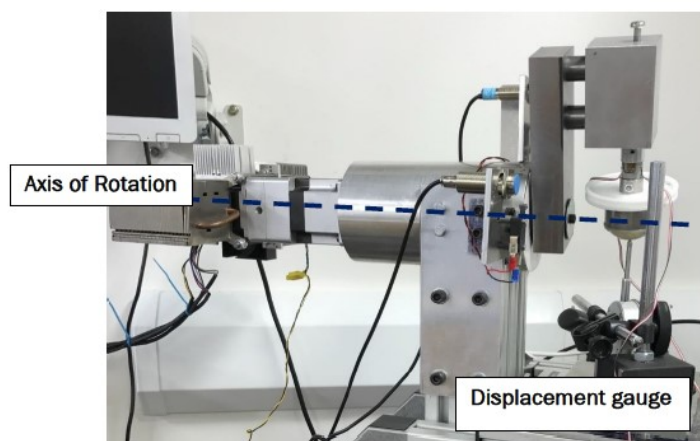
Figure 5-42 Rolling out of the joint at the left limit

5.7.1 Method

The lengths of each part had to be measured for energy method calculations, this was calculated by (Gan, 2017), before assembling the simulator, following the HipSim 2.0 operating procedures laid out by Welham et al. The calculations can be found in Appendix A. As demonstrated in Figure 5-43, the implant's centre point was demarcated with ink on a glossy surface, after which the implant was lowered until it made first contact with the surface. The inked surface must be flush to the main arm's bottom surface, thereby resulting in a small ink mark located at the centre of the implant surface. To prevent the vertical displacement of the implant by the rotation of the arm, a displacement gauge was situated at the mark, as demonstrated in Figure 5-44, allowing for the implant's height to be altered. This enables the alignment of the implant's centre of curvature and the axis of rotation of the motor. However, as shown in Figure 5-45, due to rotation, in order to measure bending strain the strain gauges have to be aligned. Therefore, the implant height cannot be altered to fully prevent vertical displacement of the implant. According to measurements, the lowermost point moves $1.86 \pm 0.05\text{mm}$ vertically.

Table 5-2 Vertical displacement of the implant

Measurement		1	2	3	Average
Vertical displacement (mm)		1.94	1.79	1.86	1.86 ± 0.05

*Figure 5-43 Marking the centre of the implant**Figure 5-44 Using a displacement gauge to make sure centre of curvature of implant matches axis of rotation*

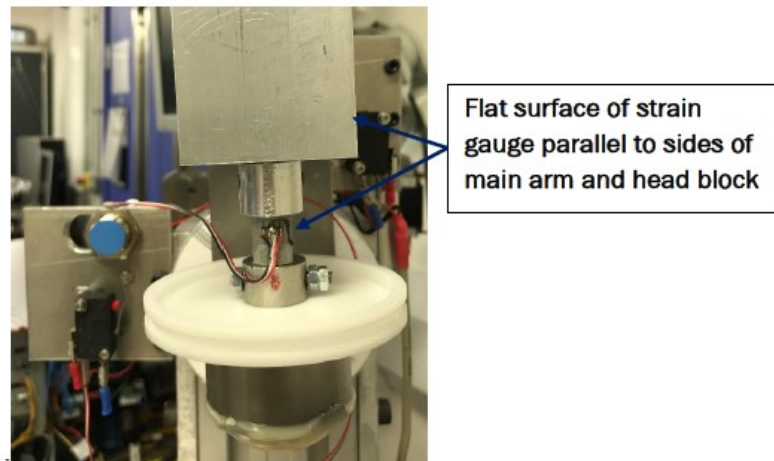


Figure 5-45 Strain gauges aligned to measure bending due to rotation

From this point on, set up and calibration can be achieved by following the normal procedure. The limit switches are prepared so that they trigger at the limits of rotation, the glenoid is mounted and the pneumatic cylinder is raised in such a way as for the glenoid to make contact with the implant. The load cell is connected, and the air supply switched on. Although in a full experiment, setting up the lubrication jar before the glenoid is mounted is the easier option, in this system test, the joint kinematics needed to be observed well, therefore this was not done. The 750N load cycle is used for the duration of 100 cycles, including a maintenance pause which took place after 50 cycles. Whilst the angular positions were recorded over serial, the vertical force were recorded at 100Hz. Additionally, the LabVIEW programme records bending strain at 1612.9Hz, which is the minimum sampling frequency attainable on the NI 9237. Moreover, the time duration for the completion of 50 cycles was recorded independently, to check against the measurements.

5.8 Preliminary results for 50 cycles

The system test was well carried out. The altered simulator successfully simulated motion of the joint. Figure 5-46 displays the applied vertical load in the test's second cycle. This load increases to approximately 800N at 0.12s and stays mostly constant until 0.78s, at which point it drops once more to zero. The applied load imitates the shoulder loads which the elderly experience during their day-to-day activities and demonstrates that the updated simulator is able to replicate the physiological loads in the shoulder joint. The photos included in Figure 5-47 illustrate the kinematics of the joint at the rightmost, central and

leftmost points in the cycle, demonstrating that these mainly consists of sliding between the implant and glenoid; thereby this is an assumption which the mechanical model can make.

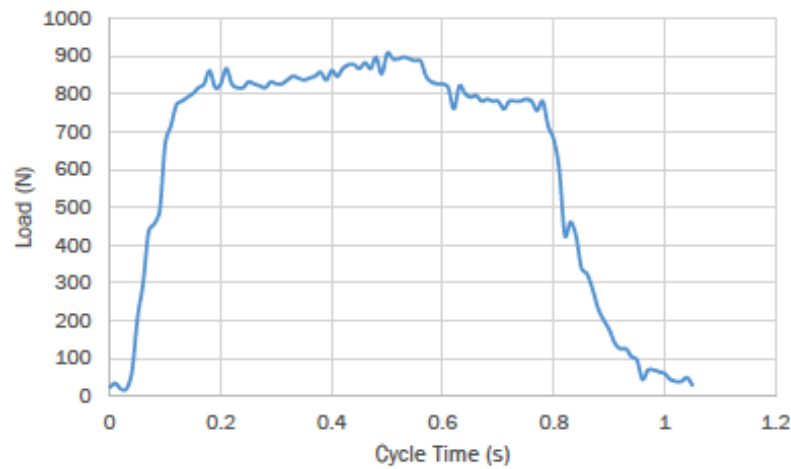


Figure 5-46 Applied vertical load in the second cycle

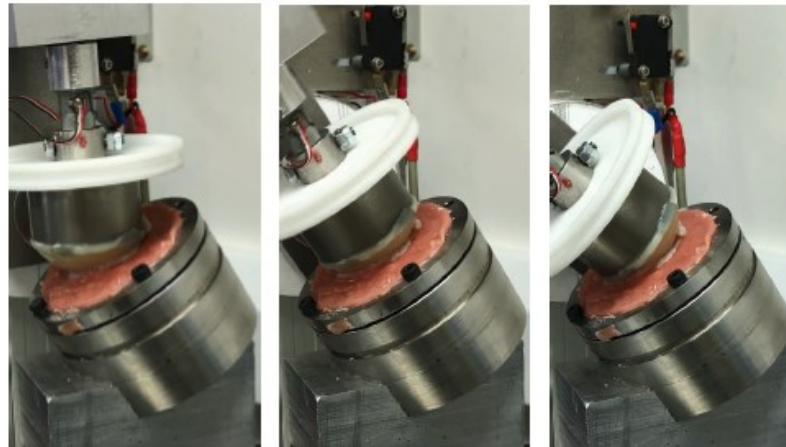


Figure 5-47 Joint at rightmost, central and leftmost points in the cycles (left to right)

5.8.1 Strain

Figure 5-48 includes the strain which was recorded during the first 50 cycles; these were corrected for calibration. Figure 5-49 displays the direction of positive moment and strain. At the beginning of the cycle, the strain is zero, and increases to a peak of approximately $2000\mu\epsilon$ just before the leftmost limit. When looking at the strain and angular position cycles for the initial 20s, one can observe that the cycles shift in relation with each other with time. This is explained by the fact that on one hand, the strain data has a period of 1.055s, whereas on the other hand, the load and angular position data has a period of

1.05s, given that load is measured at time intervals of 0.01s. Consequently, the strain data will no longer match the load and angular position data in future cycles. As a result, the remaining analyses will only take into account the first 5 cycles.

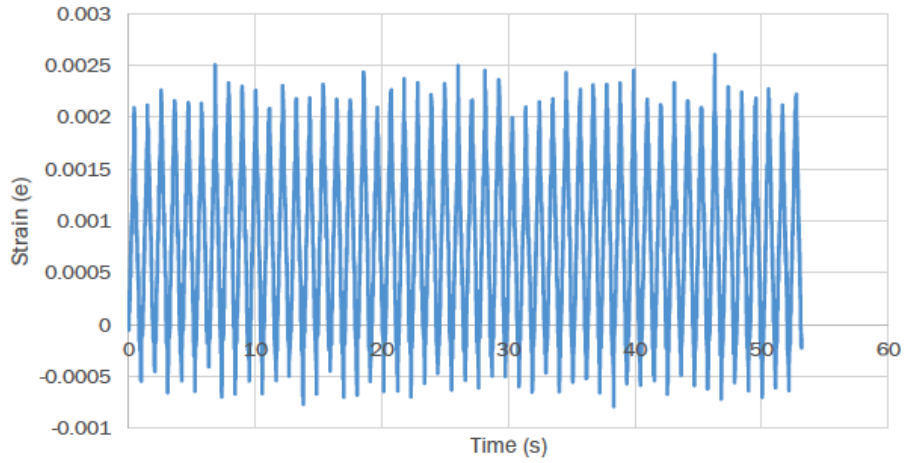


Figure 5-48 Strain, corrected for calibration, for first 50 cycles

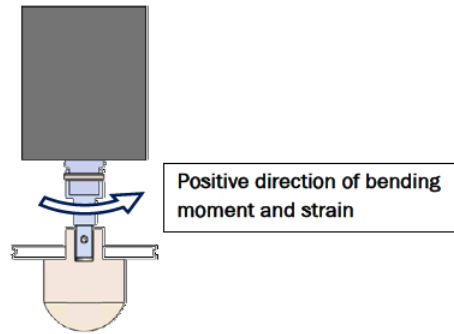


Figure 5-49 Direction of positive bending moment and strain

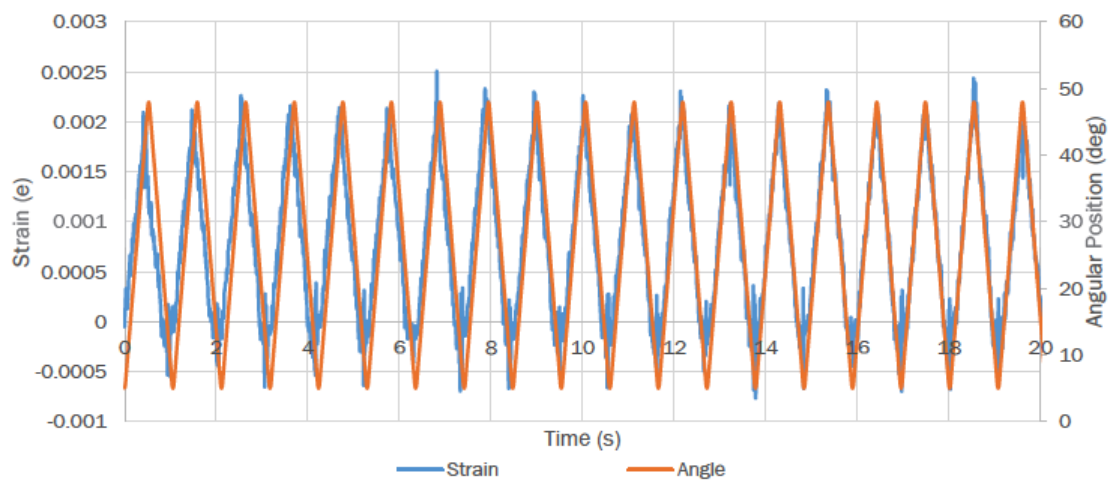


Figure 5-50 Comparison between strain and angular position

5.8.2 Friction Analysis

The model outlined in Section 5.6.1 was used to determine the values for friction force and coefficient; this is demonstrated in Figure 5-51 for the first 5 cycles. This simply plotted as the ratio between the tangential force and the normal force (hence it can have both positive and negative values in this and the following plots-however, the absolute values of the friction coefficient will be used to look at the results when both part of the cycles are considered to find the average friction. The friction coefficient peaks mid-cycle at the left limit, otherwise fluctuating towards the end of the cycle. Sizeable spikes in friction coefficient can be seen to occur between cycles, this is most likely due to the amplified noise caused by low values of normal and friction forces in this area. Consequently, the loaded section of the cycles between 12-75% of cycle time should be examined. Given that the direction of rotation shifts between the cycle's two halves, a sign reversal is anticipated between friction and the friction coefficient. Despite this, the friction coefficient stays positive during the loaded part of the cycles. This potentially denies the validity of the assumption that horizontal force in the joint can be determined with the minimum strain energy method. This is put to the test by taking away the horizontal force from the mechanical friction model and recalculating the friction force and coefficient of friction in the revised model. This model is explained in details in section 5.8.3 and is computed by previous Imperial Master's student.

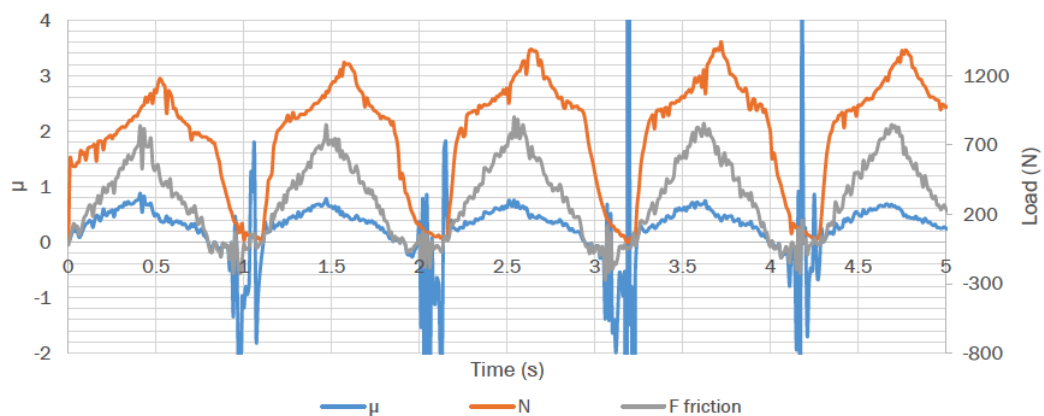


Figure 5-51 Friction (grey), coefficient of friction (blue) and Normal force N (Orange), x-axis indicates time and y-axis indicates coefficient of friction and load

5.8.3 Revised friction model

As explained previously, the static load in the joint interface exerts a vertical force F and horizontal force P on the motion arm. Initially, angular position of the arm to measure the horizontal force was not known from the simulator and the imperial joint simulator is unable to determine the horizontal force at the joint interface, therefore Castiglioni's minimum strain energy method was adopted by Welham et al. (2014) to approximate this force. After obtaining the results, it was found that the assumption that horizontal force in the joint can be calculated using minimum strain energy method is not valid (as shown in Figure 5-50) and it was decided to assume the horizontal force was negligible as it was not captured by the calculations in Appendix A. This was tested by removing the horizontal force from the mechanical model which was initially calculated and recalculating the frictional force in order to create a shift in frictional forces and generate Figure 5-51. Friction force and coefficient of friction reach a peak just before the mid-cycle, which is when the arm slows down before coming to a halt and changing direction. The higher friction coefficient in this instance could be due to static friction being higher than dynamic friction. Normal force N drops mid-cycle, an unusual occurrence given that normal force should increase at the limits of motion, as a result of impingement with the glenoid rim. This therefore points to a need to improve the mechanical model's accuracy.

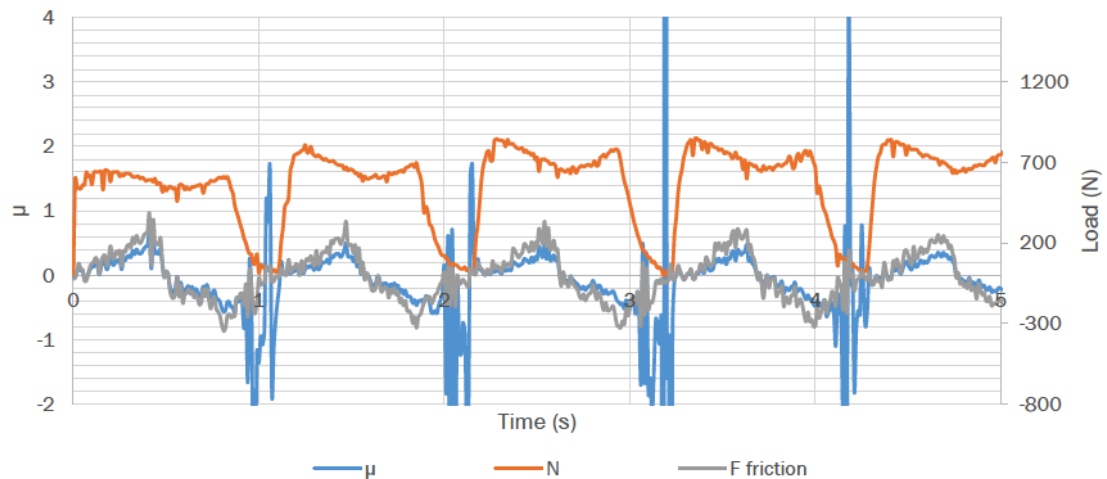


Figure 5-52 Illustrates the friction force and coefficient of friction reversing signs in the middle of the cycle, which was achieved with the removal of the horizontal force to create a shift

Additional improvements to the mechanical model can be identified by verifying the assumption that the point of contact in the joint stays stationary at the centre of the implant. Figure 5-53 shows an approximation denoting that the point of contact is shifted

by an angle α which can vary linearly from $\alpha = 25^\circ$ at the rightmost limit to $\alpha = -18^\circ$ at the leftmost limit.

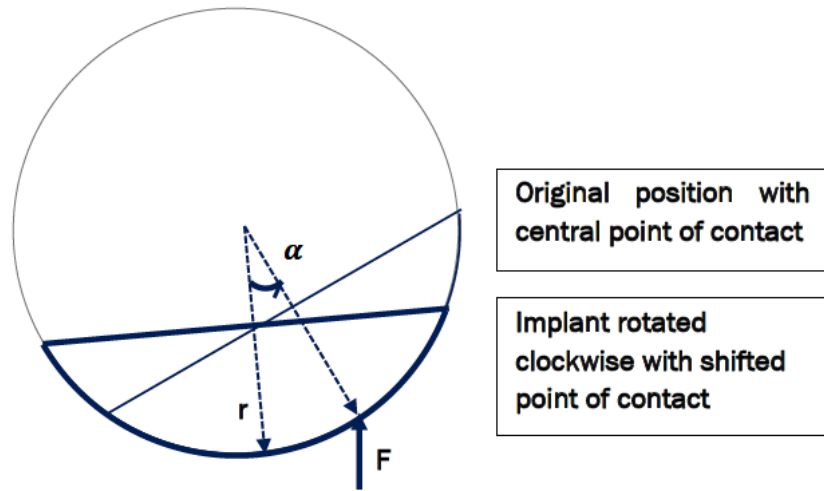


Figure 5-53 Shift in point of contact relative to the central position

As a result, the offset vertical force leads to alterations to the moment arms and normal force, which can be worked out in Equations 13-15.

$$M_{direct} = F(L_s \sin \theta + r \sin \alpha \cos \theta - r(1 - \cos \alpha) \sin \theta) \quad (13)$$

$$M_{friction} = F \cos \alpha (L_s - r + r \cos \alpha) + Fr \sin^2 \alpha \quad (14)$$

$$N = F \cos (\theta + \alpha) \quad (15)$$

This yields the result which can be seen in Figure 5-54, where normal force remains approximately the same in the loaded part of the cycle. It must be noted that there is a small rise in the normal force mid-cycle, which can be explained by the implant's downwards movement of 1.86mm when rotating from the right to left limit. As demonstrated in Figure 5-55, when taking the moving point of contact into consideration, a slightly lower coefficient of friction can be observed.

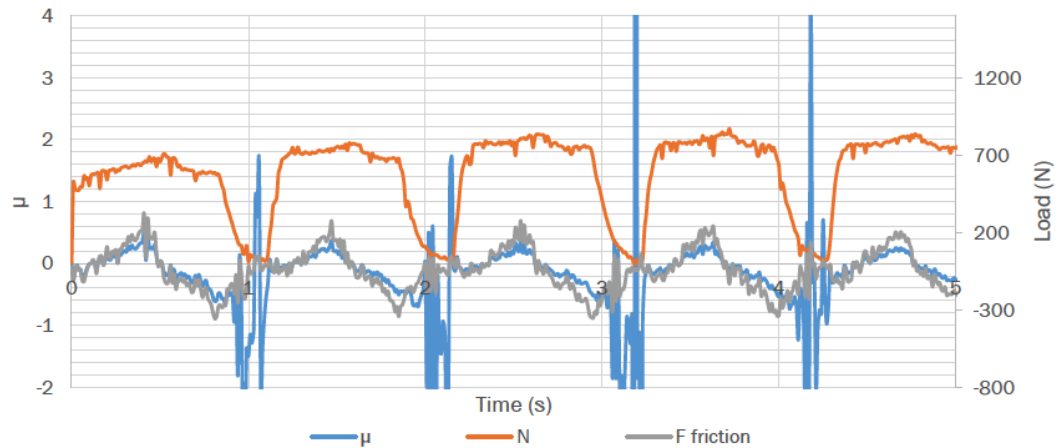


Figure 5-54 Friction, coefficient of friction and normal force N accounting for moving point of contact

As explained previously, only a portion of the data were taken into consideration (shown in Figure 5-54). At the start and the end of each cycle the data were ignored as the data was spiked and were scattered due to nonhomogeneous surface of the samples and non-centric centre of rotation.

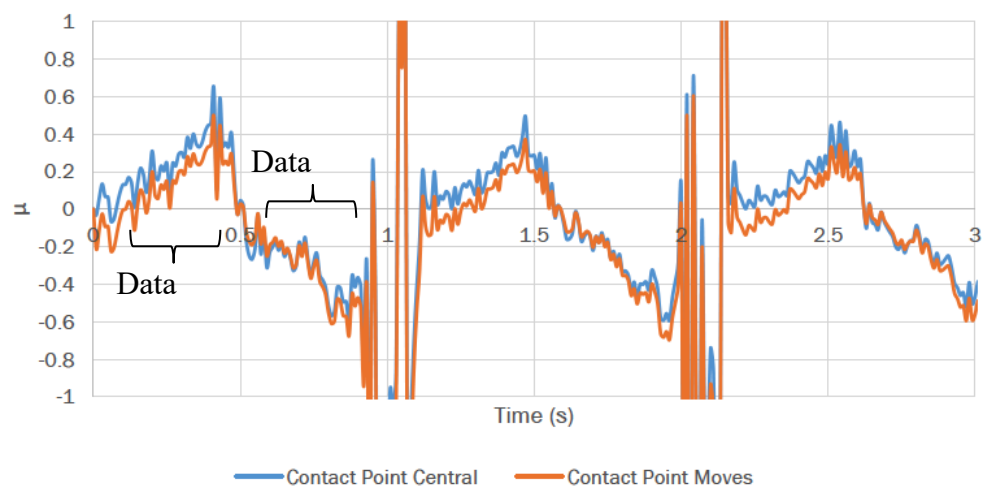


Figure 5-55 Comparison of friction coefficient for models with central and moving contact point

Figure 5-56 illustrates a snapshot of the second cycle with absolute value of friction coefficient in the loaded region. Beyond the limits of rotation, the arm is able to rotate at a steady pace and given that the normal force is more or less constant, the friction coefficient should likely level off in this region. However, this is not the case in Figure 5-56 potentially due to the noise in the data and uneven contact area (hence sliding progressively extending to different zones in the contact area). Nevertheless, an indication

of friction coefficient is attainable from the mean of the absolute friction coefficients, which was worked out for cycles 2-5 and displayed in Table 5-3.

Table 5-3 Average absolute friction in the loaded time intervals

Cycle	Time	Average Coefficient friction
2	1.2-1.85	0.16
3	2.3-2.95	0.17
4	3.4-4.05	0.21
5	4.5-5.15	0.22
Average		0.19±0.02

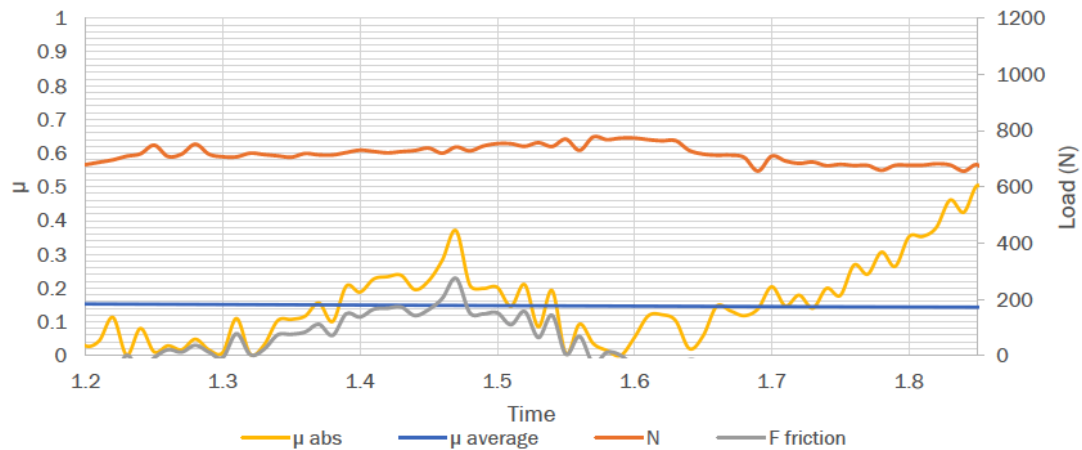


Figure 5-56 Friction, absolute coefficient of friction and normal force in the loaded part of second cycle

5.9 Discussion

In this chapter, a single station hip joint simulator was modified and optimised for testing of shoulder joints. A friction measurement system consisting of strain gauges attached to the sides of the motion arm and connected to a National Instrument card has been designed, implemented and calibrated for use. All the mechanical and electrical components of the joint simulator are explained thoroughly. A preliminary full system test was developed and carried out in dry contact against the ceramic implant head to ensure the strain gauges function properly. The Imperial shoulder simulator is a simple simulator device that is capable of testing native shoulder joints against humeral head

implants. This simulator is easily adaptable to various scenarios such as studying total shoulder or reverse shoulder arthroplasty with various ADL loading regimes.

The shoulder simulator could be significant in several ways. Firstly, it could allow weaknesses in current hemiarthroplasty designs to be pinpointed and fed back to the designers and manufacturers so that the implant can be improved. Secondly, the performance of different designs of shoulder implants could be compared in the simulator and this data shared with interested scientists/clinicians/patients and engineers. Thirdly, the simulator will permit novel designs shoulder prosthesis to be tested in the laboratory prior to implantation in human subjects. All these advantages offer opportunities to improve artificial shoulder joints for the increasing number of patients requiring such implants (Smith et al., 2015).

Most simulators in the literature tested total shoulder replacement or reverse shoulder replacement as they are the most commonly performed surgeries on the shoulder (Langhor et al., 2016; Smith et al., 2015; Kohut et al., 2012). In comparison to other simulators, there are other joint simulators that tested shoulder joints, but they used hip, this simulator is capable of testing shoulder joint under loading regimes that are found in daily activities. Jones et al. (2015), conducted a study on the whole shoulder joint in order to obtain the frictional response of the glenohumeral joints during 24h of reciprocal loading in a pendulum testing device at moderate (0.2mm/s) and low sliding (0.02mm/s) speeds under 200N load. Their study showed that the initial COF response of 0.0015 and final response was 0.0046, which shows the COF remains extremely low for shoulder joints under 24h loading. As part of the friction data validation, as this can be used as literature data for a whole shoulder joint, would be essential to test the porcine glenoid against the humeral head to ensure whether the same data is provided as stated in Jones et al.

There were limitations associated with an experimental set-up which impacted the accuracy of the data obtained. The simulator rig was designed to test the femoral head under hip joint physiological loading and motion. Therefore, testing shoulder joints require improvement on the motion which needs a more degree of freedom and motion compared to hip. But as this was a preliminary work this was sufficient for comparison. It was not possible to have low loads on the system due to low resolution and low accuracy of the load cell. Therefore, higher loads such as 700N were chosen. The system suffered

from excessive mechanical vibration. Optimising the rig in which fewer bolts and screws are involved would be necessary.

A further limitation was that the test was carried at room temperature in dry contact instead of lubricated at 37°C. In the next chapter all the tests were carried out at room temperature in a lubricated environment. Another limitation of this chapter is associated with the small number of tests performed using the ceramic humeral head in a dry condition, hence a more rigorous study using both metal and ceramic implant's is needed in order to draw conclusions on the outcome of this preliminary work. In order to more accurately correlate the frictional response of cartilage with the material used. This will be studied further in the next chapter. It is also helpful, in order to reduce the extra noise in the data, to transfer the control of various systems of the simulator from Arduino to LabVIEW. The present simulator is not capable of producing flexion/extension and rotational motions, in order to add these motions, the simulator mechanics and drive system has to be modified. The data obtained in this chapter were preliminary and were part of the protocol development, more meaningful data will be discussed in chapter 6.

5.10 Chapter summary

This chapter detailed how the Imperial joint simulator was successfully updated to replicate the physiological loads and motion of the shoulder joint, whilst adhering to ISO-14242 standards. The simulator completed 7200 cycles over period of 2 hours. Moreover, the development, calibration of a friction measurement system as well as developing a mechanical model for the friction forces, was achieved. The preliminary test which was outlined in this chapter was conducted in collaboration with the Master's student (Gan, 2017) A mean friction coefficient of 0.19 ± 0.02 was established following a system test conducted between a ceramic humeral implant and porcine glenoid in dry contact and is in agreement with the friction coefficient determined in past pin-on plate studies, which was 0.20 ± 0.04 . Currently, the joint simulator and friction measurement systems can be used to determine the relative friction and wear of shoulder hemiarthroplasty with implants ranging in materials, which constitutes this research's next stage. The developed simulator protocol and the strategic considerations expressed to provide a useful first step in developing a protocol for shoulder hemiarthroplasty. The next chapter will provide a more detailed evaluation as well as preliminary results for tests conducted with the addition of a lubrication environment (bovine serum).

6 THE EFFECT OF HEAD MATERIAL ON ARTICULAR CARTILAGE TRIBOLOGY IN HEMIARTHROPLASTY

6.1 Introduction

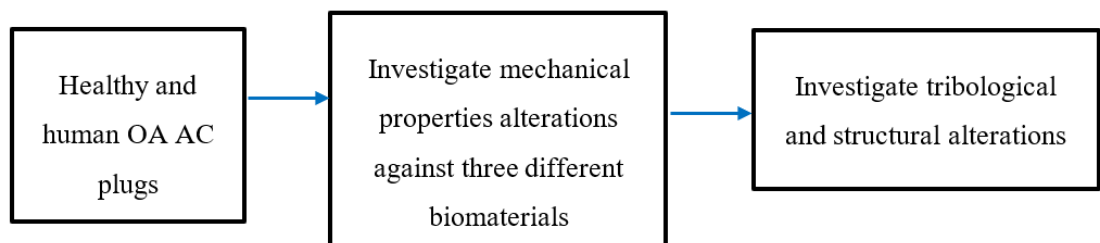
Understanding changes early in the development of OA are crucial since these changes may still be reversible, and therefore preventative treatment could be initiated to inhibit further progression. OA has been considered to affect the entire joint (Man and Mologhianu, 2014). In research, due to AC superior soft-tissue contacts, advanced MRI techniques have been developed to detect and quantify the early physiological changes that precede the morphological changes of the cartilage (Schrauth et al., 2016). The loss and morphological changes of AC during OA are due to variations in mechanical properties which are in turn due to changes in the structural and biochemical, biological and enzymatic properties of tissue (Pelletier and Pelletier, 2010).

In this respect, changes in biochemical properties, and therefore mechanical properties, represent one of the earliest indications of OA. The *in vivo* measurements of AC deformation is essential to understand how mechanical stresses transmitted between the cells of healthy tissue and change over time in the pathologic joint. However, the quantification of these changes *in vivo* is extremely challenging and constitutes on-going research (Chan et al., 2016). To successfully assess whether AC is affected by OA, detailed information about the biomechanical behaviour of the cartilage is required. This will enable the prediction of the effects of mechanical manipulation of the joints in the process of prevention or treatment of joint disorders. Furthermore, the information gained can be indispensable for diagnosis and understand the onset and progression of OA at different stages which can be valuable in the development of tissue-engineered cartilage and orthopaedic joint replacements (Kuroda et al., 2009). Non-biological materials are commonly used in contact with native AC to restore load-bearing functions to joints for a variety of orthopaedic conditions. In the clinical routine, the materials used for HA surfaces include cobalt-chromium alloy, various ceramics such as Zirconium (ZrO_2) and aluminium-oxide (Al_2O_3), and polymer implants. One of the objectives of this study was to investigate the friction and wear of cartilage against different hemiarthroplasty materials using a more realistic joint simulator that simulates physiological loads and motion of a shoulder joint.

Therefore, the scope of this chapter is to (as outlined in Figure 6-1):

- 1- Correlate different forms of structural damage to the frictional response of the tissue to better understand the impact of ECM degradation on the mechanical response and wear resistance of the tissue
- 2- Compare the frictional and structural response of healthy and digested (OA-like damage) cartilage samples to shed lights on possible similarities between them and the possible origins of the pathology
- 3- Establish a complete structure-function map relating biochemical and structural variations to changes in mechanical properties, tribological and damage in tissue.
- 4- To set out a protocol using the updated simulator system and investigate the effect of hemiarthroplasty material *in vitro* on cartilage tribology and structure.

Step 1- Chapter 4



Step 2-Chapter 6

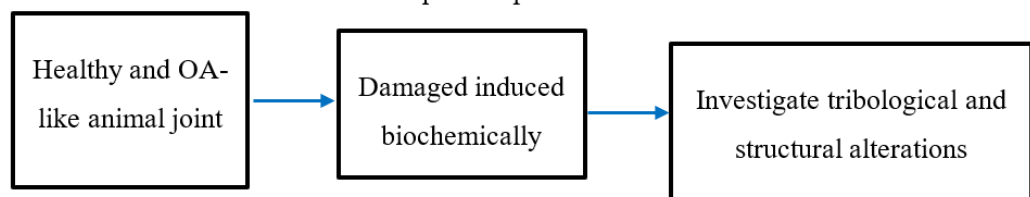


Figure 6-1 Research outline

6.2 Materials and Methods

6.2.1 Specimen preparation

Sixteen porcine shoulder joints were obtained within 2 hours of slaughter (5-6 months old). The joints were separated into two different groups. One group was for testing the healthy samples against the implants and the other for digested cartilage samples against the implants.

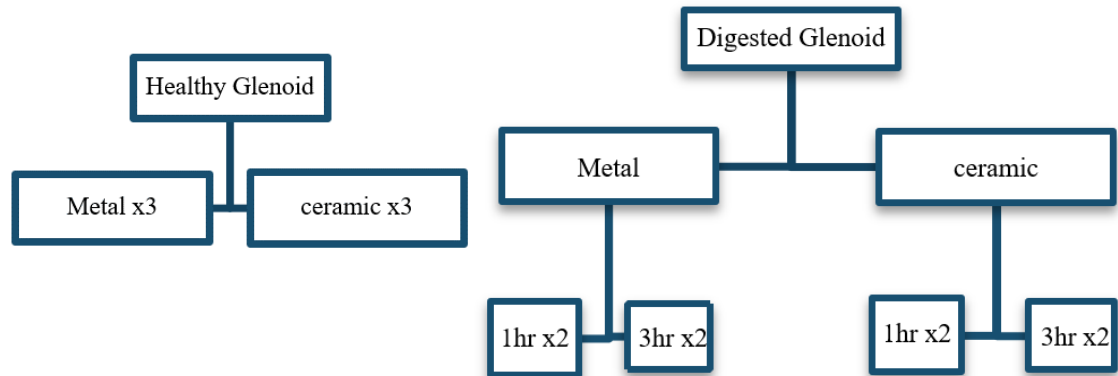


Figure 6-2 Breakdown of samples used throughout this chapter

The joints were dissected, and glenoid were obtained using the methodology described in section 3.3.3. After the dissection, the glenoid was placed in the sample holder, and it was filled with PMM bone cement, and the glenoid were covered with a gauzed soaked in PBS to avoid dehydration as shown in Figure 6-3.

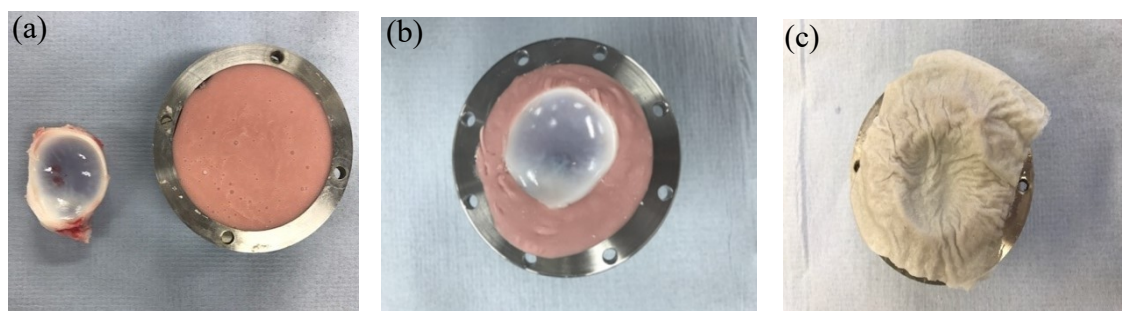


Figure 6-3 (a) Dissected glenoid and holder filled with PMMA cement, (b) glenoid positioned in the cement and (C) glenoid covered with PBS soaked gauze

6.2.2 Tribological testing

The glenoids were tested after being fixed in PMMA bone cement in the sample holder within 16 hours, and the friction simulator was set-up as explained in chapter 5. This was fitted onto the friction simulator, and the centring rod was used to establish that the centre of rotation (COR) of the bearing was in the correct location. A dynamic load of 750N at 1Hz was applied to the glenoid by the pneumatic load cell with a flexion/extension of $\pm 30^\circ$ for 2 hours (7200 cycles) at room temperature.

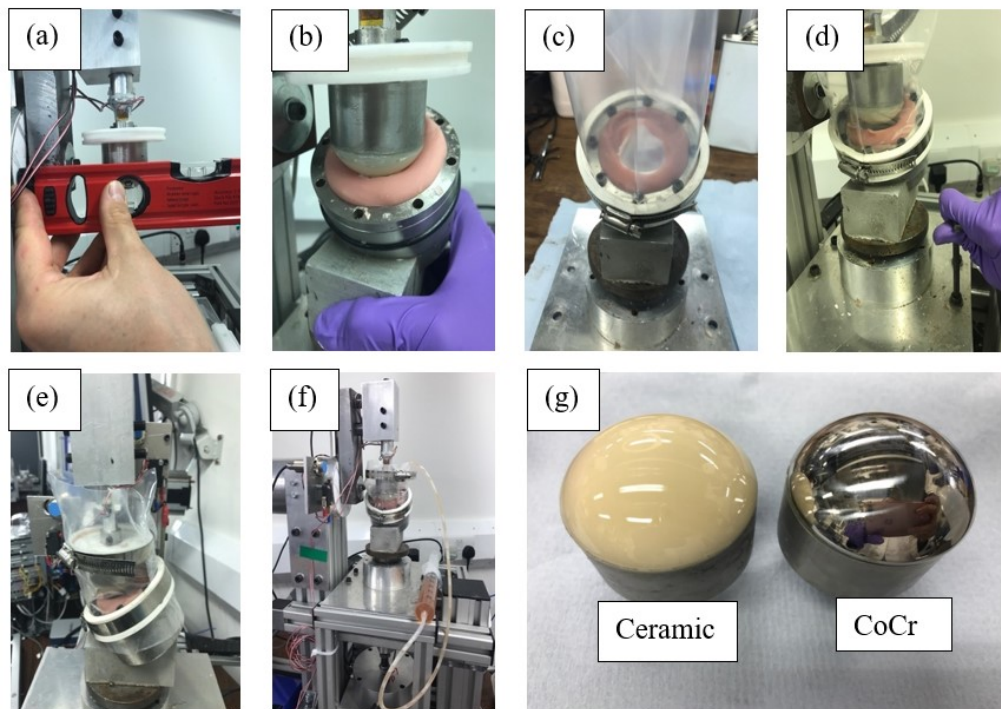


Figure 6-4 Friction simulator test set-up: (a) the centre of rotation of the implant was adjusted, (b) While the bone cement is dough like the position of the glenoid is adjusted in respect to implant position, (c) The sample holder is secured using the screws and the lubrication plastic is secured tightly around the implant to avoid leakage, (d) The sample holder plate is fixed tightly with screws on to the rig, (e) The gaiter clamps on top and bottom were secured and tightened, (f) Bovine serum was added to the joint using a syringe and flexible clear PCU pipes (1m), (g) 45mm radius of curvature humeral head CoCr and Ceramic implants fixed on to the implant holder.

This was repeated three times for both ceramic and metal implant material. The lubrication casing was filled with 25% bovine calf serum. If there were leakage from the casing, the lubrication bag was filled with more serum, and it was ensured the liquid covered the glenoid at all times. During the test, the data for friction, load value, the angle of the arm, were recorded on the LabVIEW software. Before each test, the glenoid surface roughness was measured using WLI. Post-testing the sample holder was taken out of the

rig carefully and five plugs were taken out of the glenoid for further structural analysis testing. Once again, the surface roughness of the plugs was measured with WLI and HIROX microscope and histology. Throughout the tribological test, parameters such as load, and frictional force were measured, and the results were analysed after to obtain the COF for each biomaterial. Figure 6-4 shows the friction simulator test set up and various steps during the test.

6.2.3 Contact area

Before commencing a wear and friction experiment, the contact area between porcine glenoid and humeral head implant material was measured using extra-low-pressure (4LW) sensitive Fujifilm (Fuji Photo Film Co. Ltd., Tokyo, Japan). This was done to ensure that the implant had the maximum possible contact with the glenoid. The counterface material was glenoid surface and implants (Ceramic and Metal). The Fujifilm was composed of an A-film and c-film. The A-film was coated with the microencapsulated colour forming material while the C-film was coated with the colour developing material. As the pressure was applied, the microcapsules were ruptured, and the colour forming material reacts with the colour developing material. Red patches appear on the film. The two Pre-scale films were cut separately. The rough surfaces were placed to face each other, and the film was inserted between the implant and the glenoid. The surface of the glenoid was dried gently with a lint-free tissue. Next, the strips of A- and c-films were compressed between the implant and the cartilage surface. The surface of the film and sample holder was covered with a Clingfilm to avoid slipping and movement of the film. A static load of 750N with no motion was applied. After unloading, the C-film was coloured to a certain intensity depending on the applied pressure, and this coloured red patch was designated as the contact area between the bearing surfaces. The film was taken out, and pressure distribution was checked (Figure 6-5) Both the ruler and the film was pictured at a set distance and imported into the ImageJ processing software to calculate the actual contact area. This was done on five different samples, and from the measurements all had very similar values, indicating, regardless of the differences in the samples the pressure distribution was consistent throughout the samples. As it can be from the Figure 6-5 (b), the pressure distribution is not uniform and the contact area is also formed by isolated contact patches, which results in variation of the response during sliding motion.



Figure 6-5 Illustrations of (a) fujifilm position between the implant and glenoid sample, and (b) the contact area measuring using Fujifilm

6.2.4 Enzymatic induced in articular cartilage

In total, eight porcine glenoid samples in total were used, two samples for each material for two different digestion periods. Two levels of enzymatic digestion were used solely to quantify the level of degradation of the ECM components, namely PGs and collagen. One hour to give minimum damage and 3 hours for maximum damage. All the samples were kept at 37°C incubator for the entire duration of digestion. After the digestion samples were tribologically tested, two samples per implant from each degradation duration. The surface condition of the samples was characterized by WLI and histology. Figure 6-6 shows the schematic of samples used for both tribological and histological characterizations using enzymatic digestion.

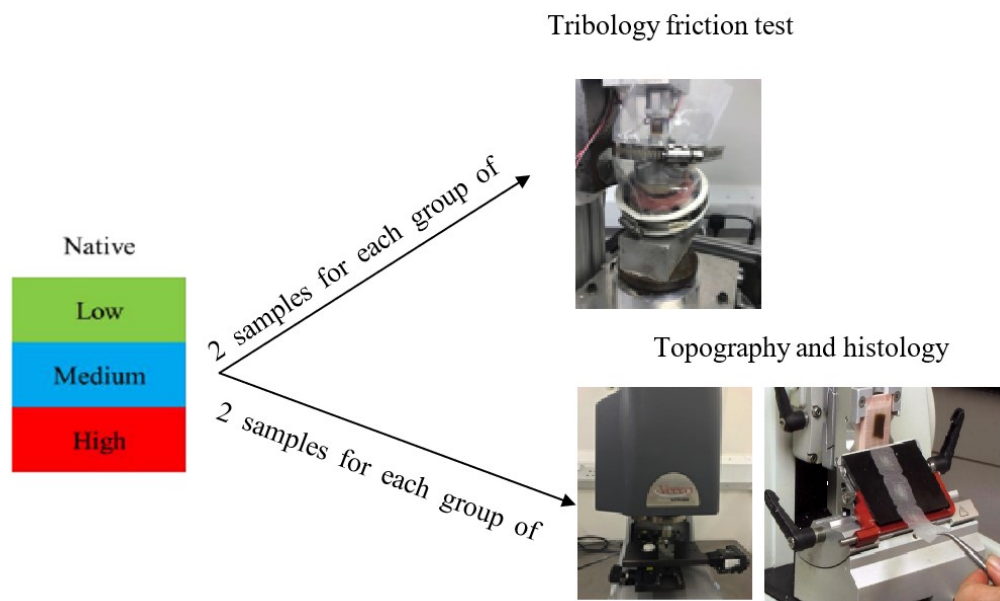


Figure 6-6 Schematic of tribological and surface characterisation damage of AC after enzymatic digestion

6.2.5 Surface characterization

After tribological testing for 2 hours, the cartilage surface was inspected for wear. The surface properties and damage of porcine cartilage samples were characterised before and after friction test using WLI. A WLI microscope was used for the non-contact surface topography measurements of glenoid and cartilage plugs. Before the friction test, the glenoid was taken, and the surface was dried thoroughly with lint-free paper and placed under the microscope. Due to the irregular shape of the glenoid, it was necessary to ensure that the sample was parallel to the lens and this was adjusted using the two-axis knob. Ten different positions along the surface of glenoid were chosen and imaged. Post friction test; five 10mm cartilage plugs were taken off the surface of the glenoid and the plugs were imaged with WLI. Once again, it was necessary to ensure the cartilage surface was dry; five different scans were taken from the cartilage surface to achieve an average roughness (Figure 6-7). Before the friction testing the potted glenoid was taken and placed under the microscope and tilted in a way that the lens is parallel to the surface of cartilage. Images from 10 different location across the surface of glenoid were taken at low and high magnifications. Post-testing, once the AC plugs were taken out, they were secured with a blue tag on a V-shape sample holder. Extra care was taken not to touch the surface and images were taken as quickly as possible to avoid dehydration of the samples. Once the images were taken, the plugs were placed in 10% formalin fixative for histological analysis which will be described in the next section.

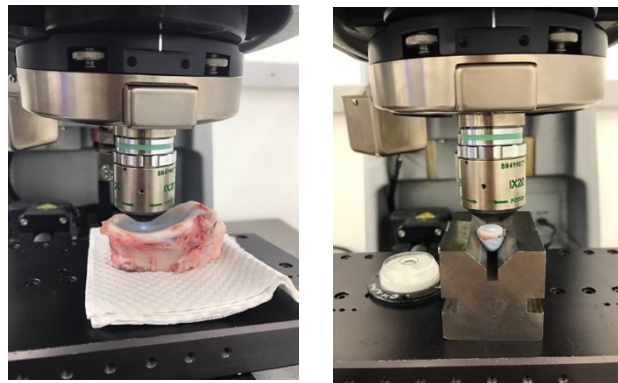


Figure 6-7 Positioning of the porcine glenoid and porcine cartilage plugs under the WLI for surface characterisation

6.2.6 Histology

Then micro-architecture and micro-morphology of the cartilage was also analysed after tribology tests with use of histology. The osteochondral plugs were removed from the surface of tested glenoid, and after WLI surface characterisation they were fixed in 10%NBF for 48 hours and decalcified with 10% formic acid for seven days. After decalcification, the round plugs were halved, and dehydrated, cleared, infiltrated and embedded in paraffin wax as described in section 3.9. The wax blocks were then sliced into 5 μm thick sections and placed on glass slides and oven dried ready for staining. To visualise the general micro-architecture and micro-morphology of the cartilage, Toluidine blue staining was used. The slides were then observed using a Zeiss optical microscope.

6.3 Results

6.3.1 Tribological characterization - Wear simulator

Figure 6-8 shows the LabVIEW interface for the joint simulator. In this configuration, the data were collected from the Arduino and transferred onto LabVIEW via the OMEGA board the board picked up the pulses, and the proximity sensors turned on and off every time the arm passed the sensors, the data were collected at 100HZ. Friction force and coefficient were calculated using the model explained in equations 5.21, 5.22, 5.23 in chapter 5. The full system test was concluded successfully with the updated simulator capable of simulating the motion of the joint. Friction coefficient was measured over 2-hour duration. Representative raw results for applied load and coefficient of friction for zoomed in one cycle and entire 7200 cycles directly from the LabVIEW are shown in Figure 6-9. As it can be seen, there are slightly higher peaks due to noise generated by the movement of the mechanical rig. Raw data were collected from the load cell at a rate of roughly 100Hz using a National instrument Omega board which collected the data from Arduino to allow a high rate of data collection. Antialiasing filtering was applied to the load data to remove any unwanted noise from the load cell.

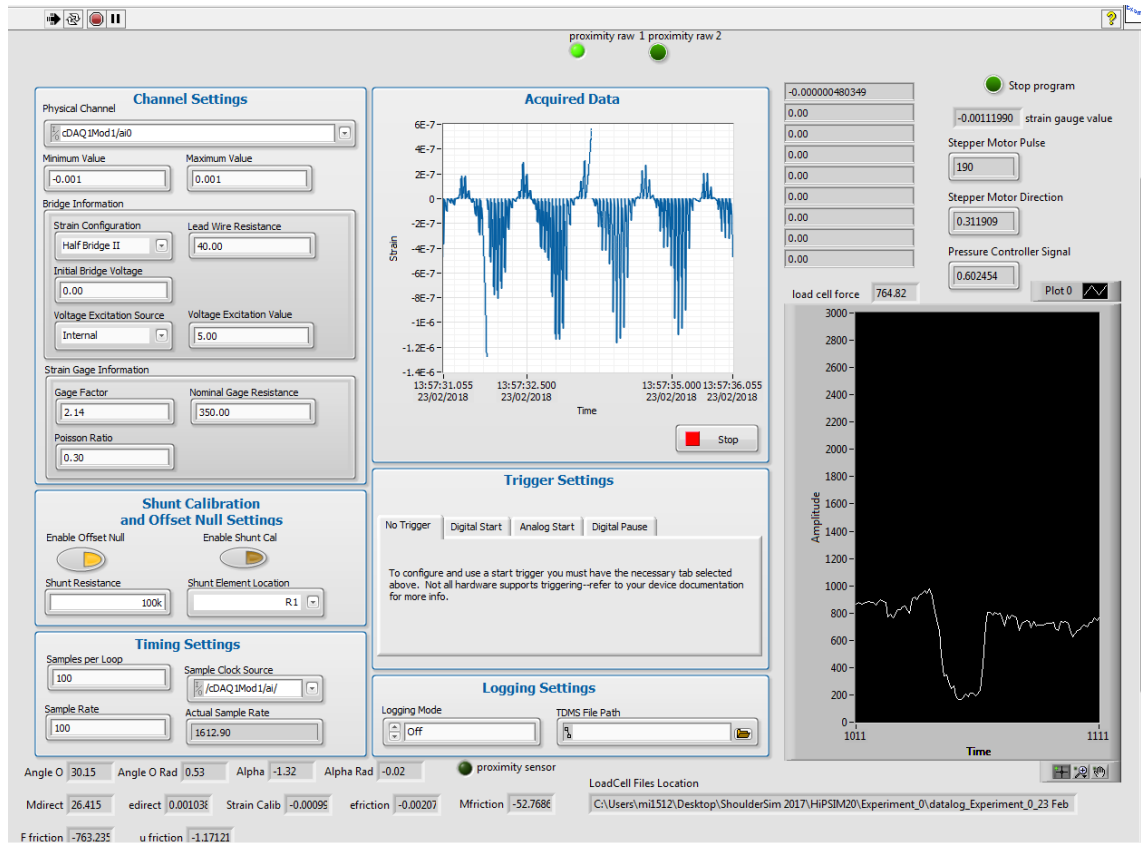


Figure 6-8 Example of LabVIEW interface for one typical test

Initially, to remove this noise, the data were reduced from 100 Hz to 10Hz, but that affected the real COF data as it was averaged which is not an accurate way of measuring COF. To measure COF more accurately, the results were initially checked for the first 5-10 consecutive cycles around the randomly chosen area in the graph. Once it was confirmed that the evolution of one cycle is representative of the larger set of cycles, one random cycle was chosen from each 1000 cycle, and the data were analysed for that specific cycle. In Figure 6-10 C vertical load rises to around 850N at 0.12s (10% of the cycle) and it remains roughly constant until 0.78s (90% of the cycle) when it returns to zero. This applied load is representative of the shoulder loads experienced by elderly people in their daily activities and shows that the updated simulator is successful in simulating the physiological loads in the shoulder joint as well. Significant spikes in friction coefficient are observed between cycles, which is probably due to the low values of normal and friction forces amplifying noise in this region. Therefore, it is helpful to consider the loaded part of the cycle which is not affected by these issues, hence between 12-75% of cycle time.

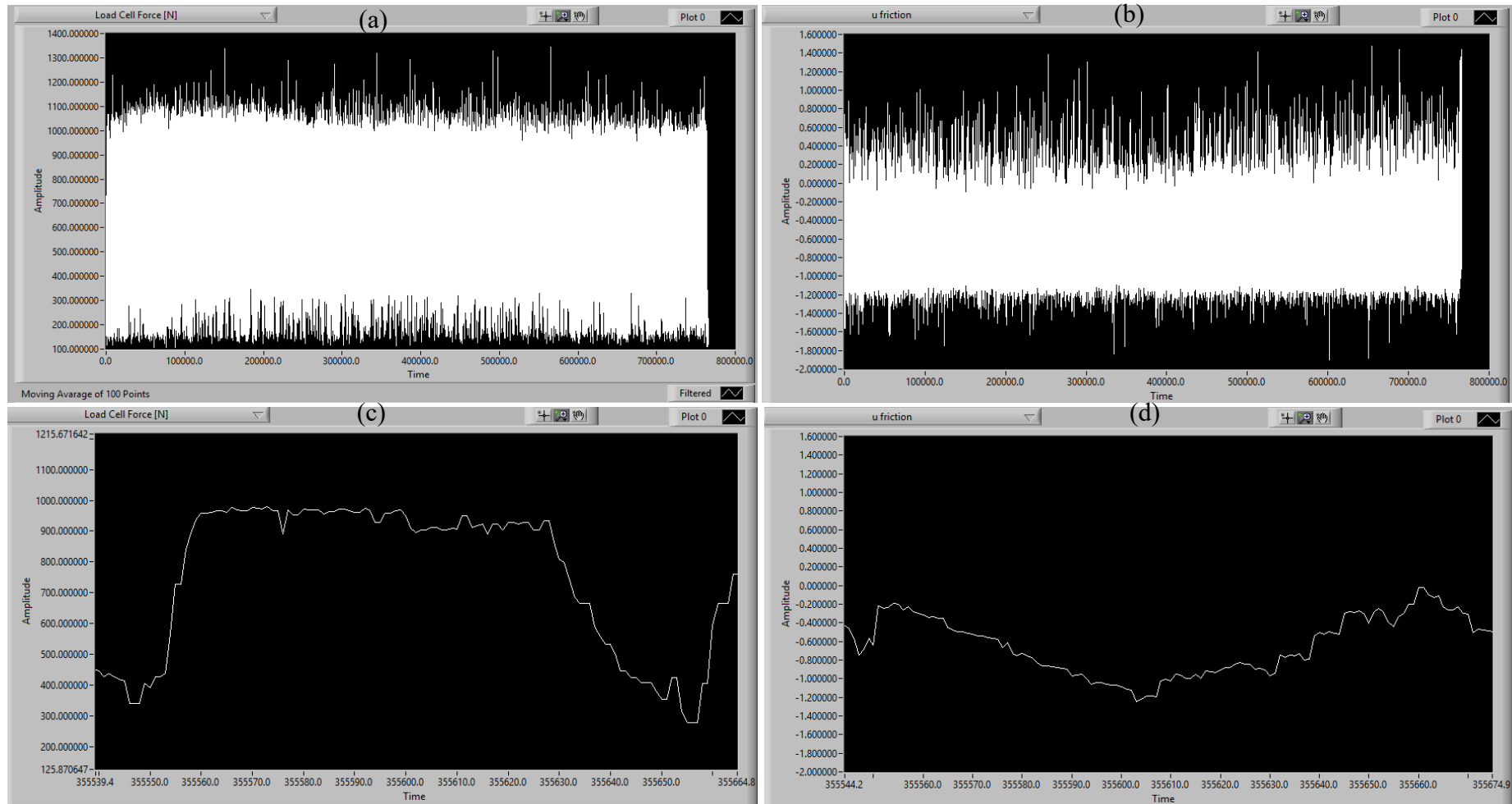


Figure 6-9 (A) Example of applied load raw data from the LabVIEW for one sample for 2-hour cycle (B) Zoomed in load data for one random cycle, (C)) Example of applied friction raw data from the LabVIEW for one sample for 2-hour cycle,(D) Zoomed in friction data for one random cycle

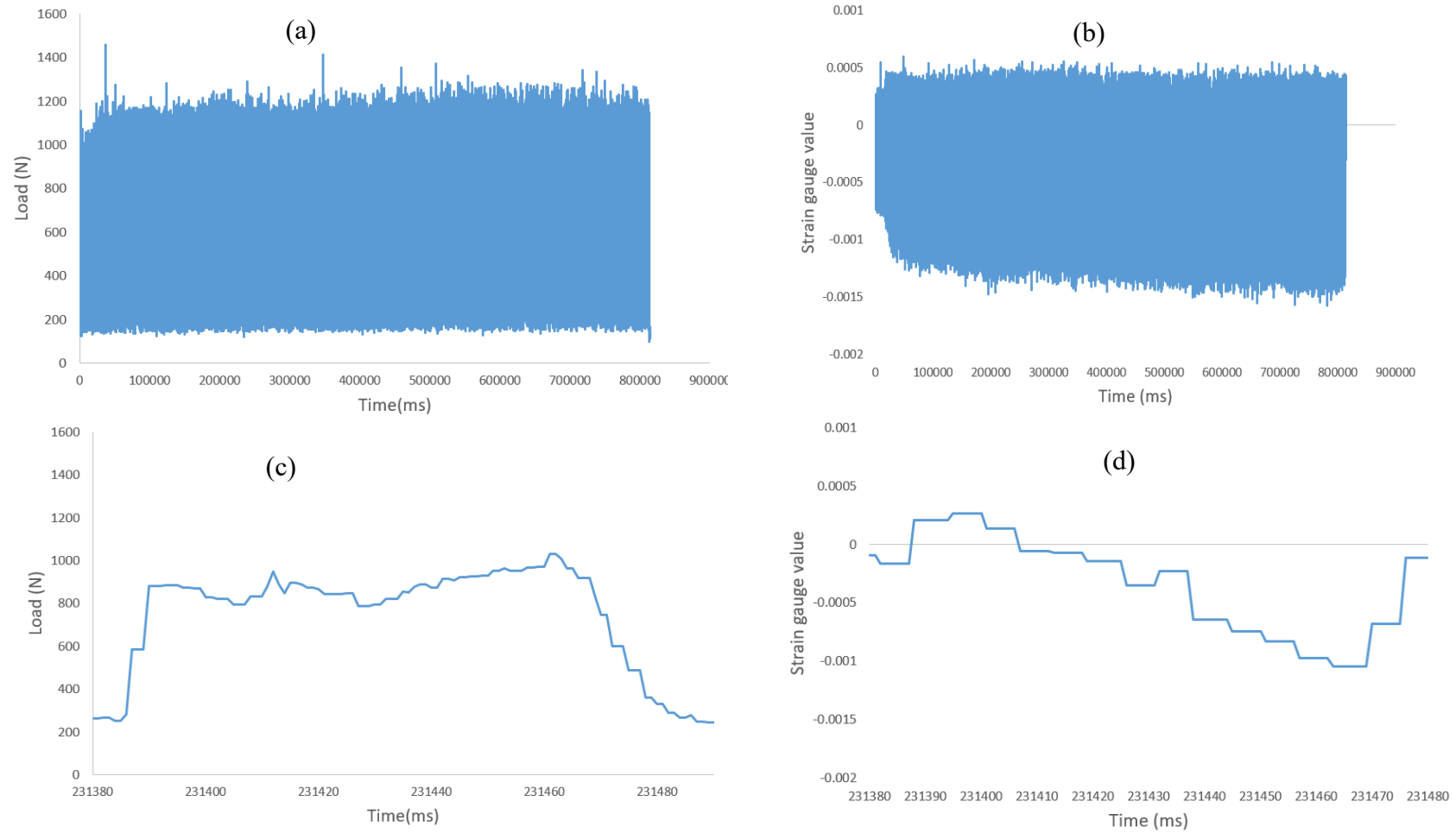


Figure 6-10 (A) Example of applied load raw data from the LabVIEW for one sample for 2-hour cycle (B) Zoomed in load data for one random cycle, (C)) Example of applied friction raw data from the LabVIEW for one sample for 2-hour cycle, (D) Zoomed in friction data for one random cycle

6.3.2 Revised and Modified friction data

The load and COF data for one cycle in every 1000 cycle were averaged, and they were reduced by the average value. The averages were taken from five different joints. Figure 6-11 demonstrates a representative average result for one of the samples. As explained previously, from every test result, averages of eight random, 1000 representative cycles were taken. It can be seen from all eight curves that the variation for each 1000 cycle within 30-50s of the first half cycle lies with the same coefficient of friction range of (0.1-0.3). It can also be noticed that the response of the joint gets high at the beginning and at the end of the cycle and this could be due to non-homogenous geometry and centring of the glenoid. It is worth mentioning again, that the absolute values for the coefficient of friction were taken into account, negative COF simply means the change in frictional force direction.

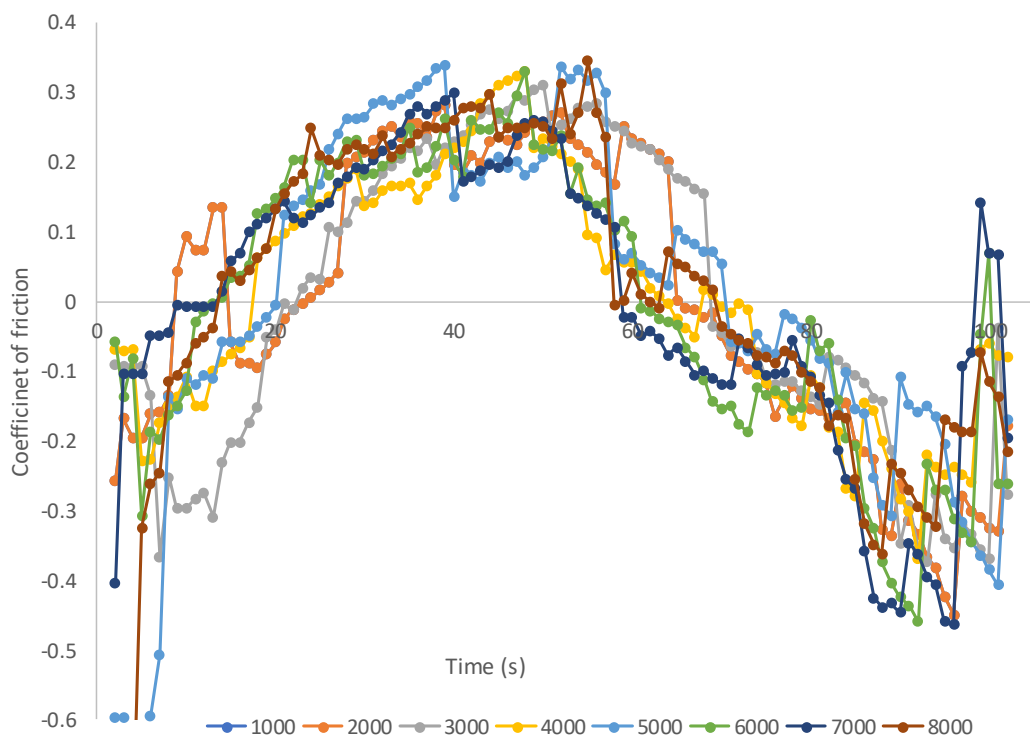


Figure 6-11 Average COF data for every 1000 random cycles for one representative sample (1-hour ceramic)

Figure 6-12 and Figure 6-13 Figure 6-15 show average COF data for a total of 4 healthy ceramic and metal implants. Figure 6-12 Average Coefficient of friction for the healthy cartilage against ceramic (average $\pm$ SD) average from five joints. The averages were taken from five different joints.

Figure 6-14 shows the method which was used to extract right COF values from the curve. To estimate the value of COF, averaging the values obtained for the entire cycle would not be the right procedure as this would account for values that do not correspond to dull sliding between the implant material and the glenoid. From the data shown both in Chapter 5 and here, it can be seen that the joint is in full sliding contact for only a portion (approximately 40-50%) of the cycle. As it can be seen from Figure 6-11, the data shows clearly that friction varies within the cycle and certainly we cannot assume sliding near the reversal point (in the middle of the cycle) and at the edges as also the normal load is varying; therefore it was decided to ignore values in the area in which (as also demonstrated by the continuous variation of friction coefficient in these areas) between approximately 0-15% , 40-50% and 85-100% of the cycle. These limits were adjusted to check their sensitivity and more work may be required to better define the region over which the averages are calculated, The above was done to make sure that the average data was computed where the implant was in full sliding contact with the glenoid .To avoid considering values of friction corresponding the non-sliding conditions, which are obviously are much less easy to interpret and cannot be considered if Coulomb's law is applied to study the frictional response of the joint. It should also be noted that the signal when the load is changed normally and at the point where motion is reversed is intrinsically noisy and therefore data in these regions are less trustworthy.

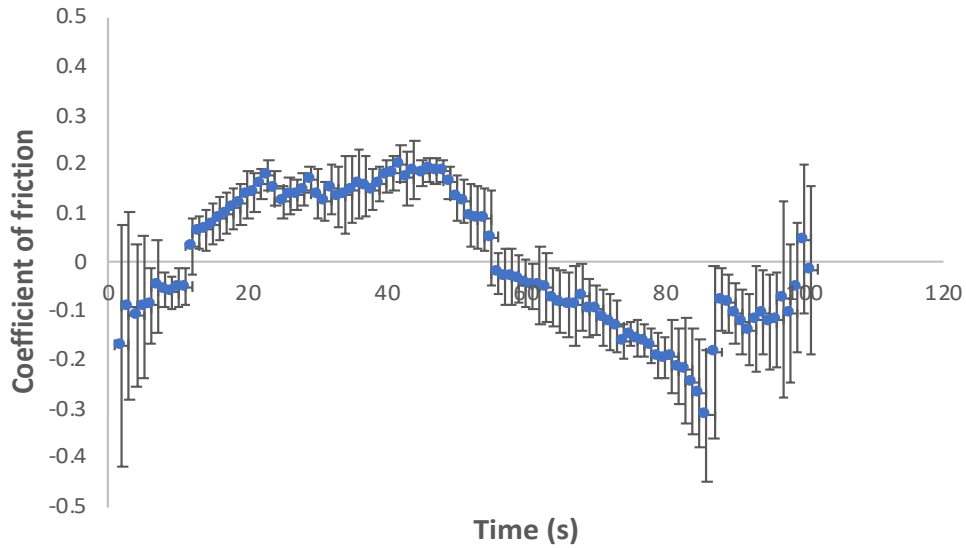


Figure 6-12 Average Coefficient of friction for the healthy cartilage against ceramic (average $\pm$ SD) average from five joints

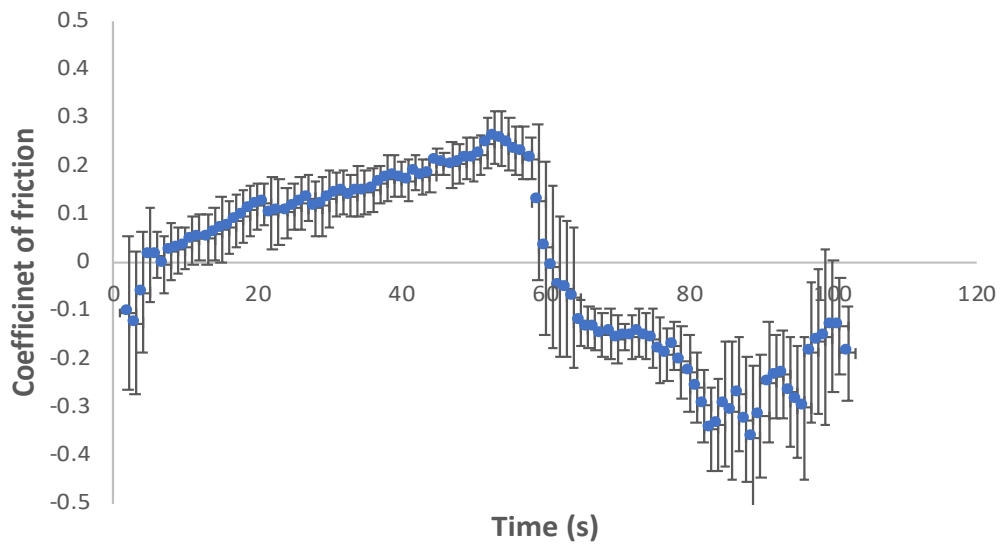


Figure 6-13 Average Coefficient of friction for healthy cartilage against metal implant (mean 95%), average taken from five joints

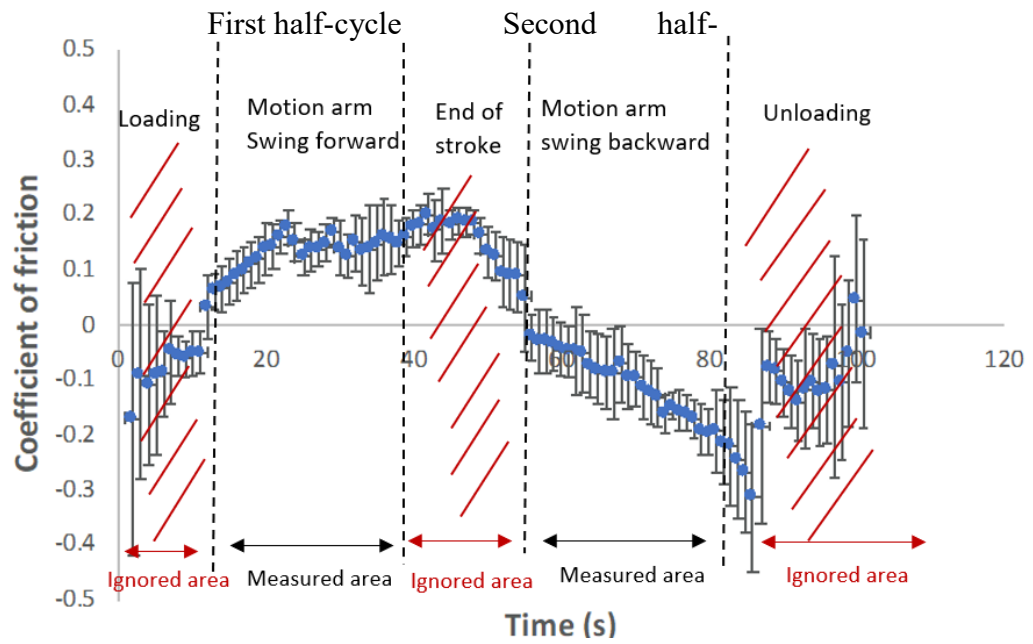


Figure 6-14 Demonstrating the areas which COF data were utilised for the results and areas which were ignored due to scattered data during sliding motion

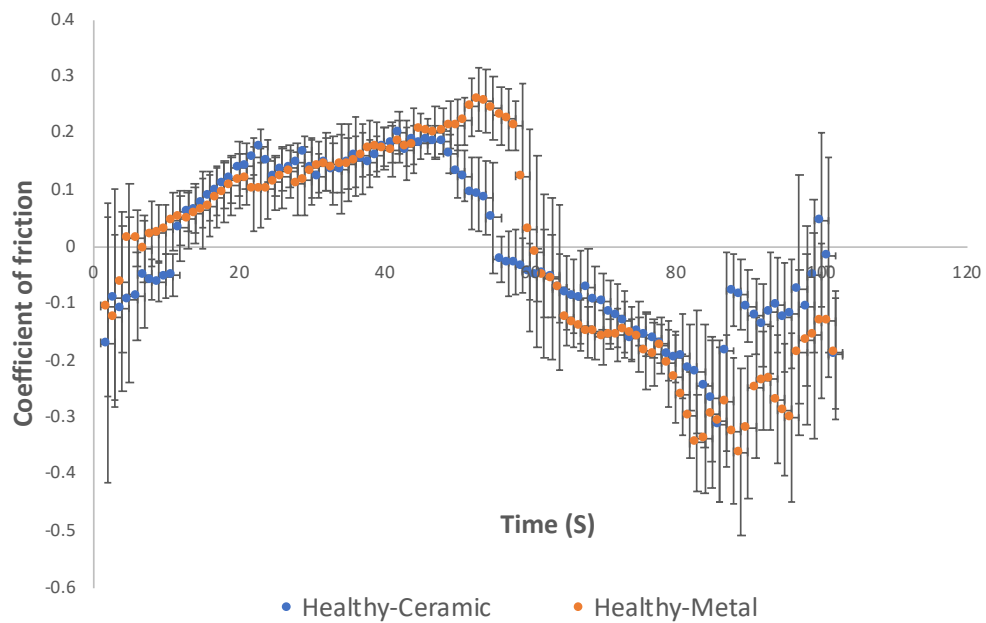


Figure 6-15 COF graph for native cartilage against ceramic and metal implants

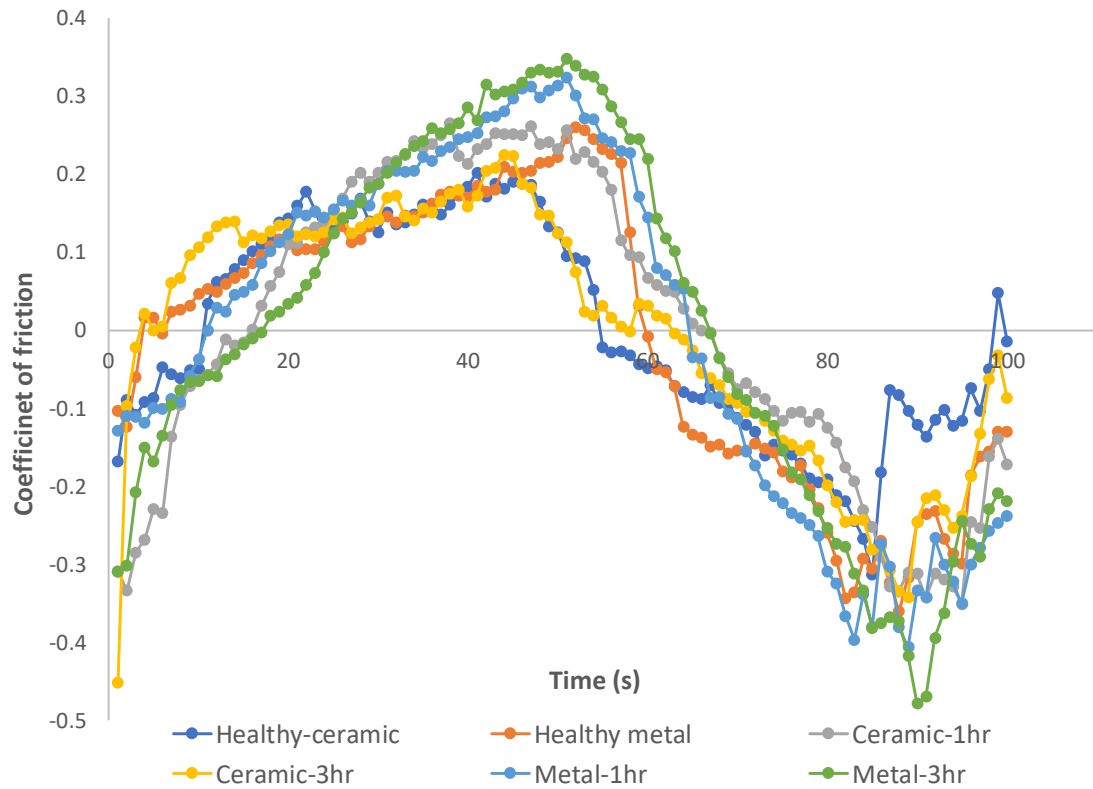


Figure 6-16 Coefficient of friction results for all the healthy and digested sample

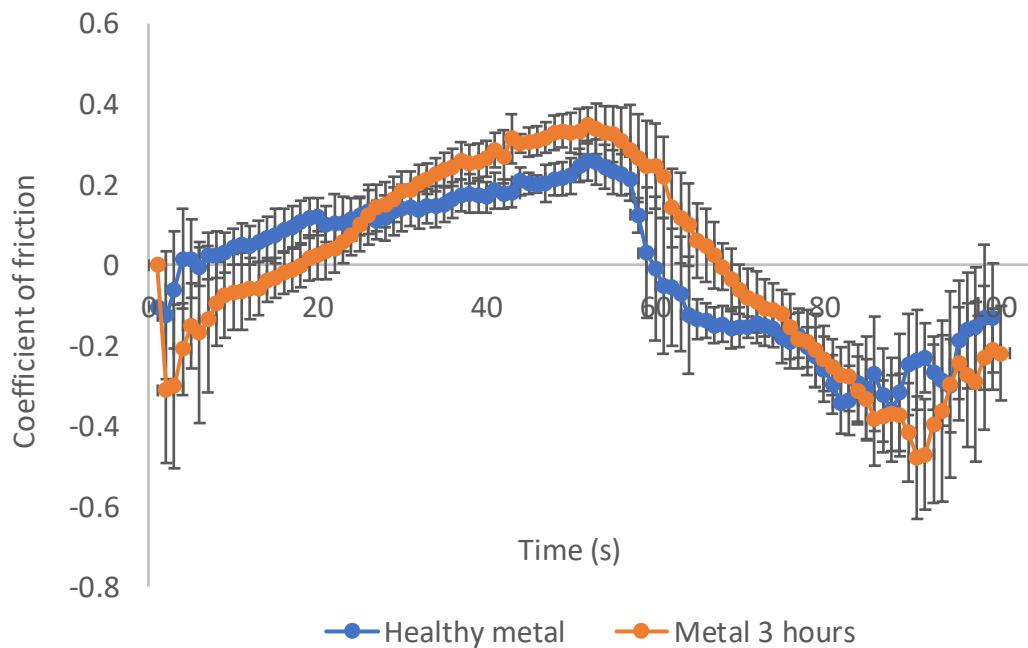


Figure 6-17 Example of COF data Comparison between healthy cartilage against metal implant and 3hours digested cartilage against metal implant

Table 6-1 demonstrates the averaged (mean $\pm$ STD) first and second half cycles for all the samples used in this project. Since the direction of rotation changes between two

halves of the cycle, friction forces should be expected to reverse signs. Although friction coefficient is by definition positive, here the value shown is the ratio between tangential and normal forces, hence Figures 6-11 to 6-17 show negative values for the COFs. This is simply due to the fact that the tangential force is changing sign at around mid-stroke and absolute values of the average of the two-cycles are considered when calculating the COF- see Table 6-1 and Figure 6-18.

Table 6-1 Summarised Coefficient of friction data for healthy and digested glenoid (mean $\pm$ SD)

Implant type	Ceramic	Metal	Ceramic	Ceramic	Metal	Metal
Digestion time	Healthy	Healthy	1hr	3hr	1hr	3hr
First-half cycle (μ)	0.13 $\pm$ 0.02	0.15 $\pm$ 0.02	0.17 $\pm$ 0.05	0.19 $\pm$ 0.05	0.22 $\pm$ 0.05	0.23 $\pm$ 0.09
Second-half cycle (μ)	0.13 $\pm$ 0.11	0.16 $\pm$ 0.06	0.17 $\pm$ 0.10	0.23 $\pm$ 0.07	0.27 $\pm$ 0.07	0.26 $\pm$ 0.11

Figure 6-18 shows the bar chart for the frictional response of the two half cycles for healthy and OA-like samples. As shown, the values of COF increase as the digestion time increases and these values are higher for the metal implants compared to ceramic.

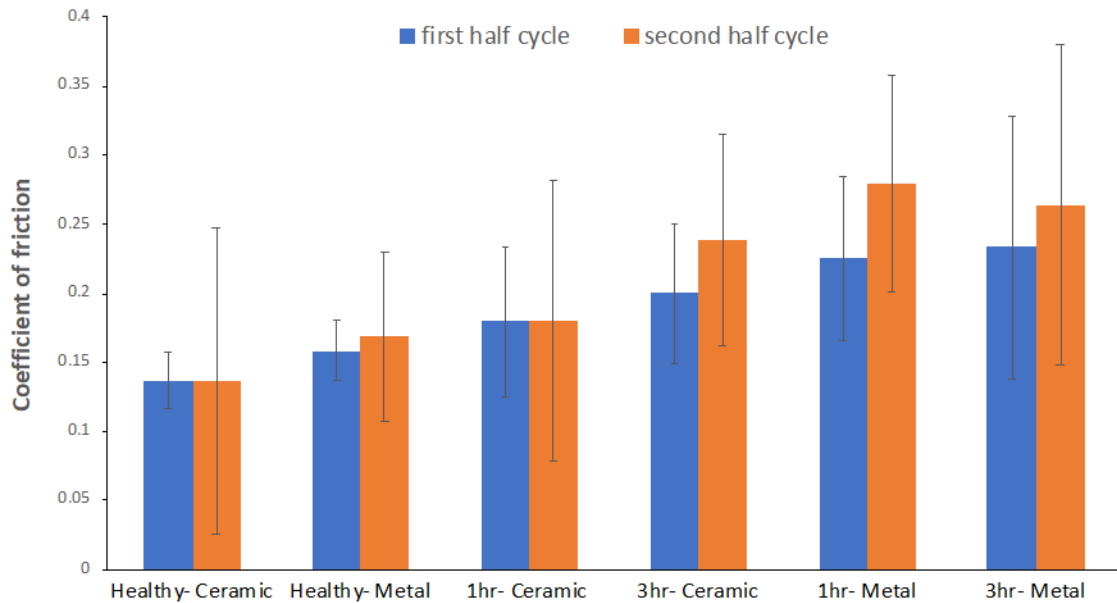


Figure 6-18 Average data for healthy and digested cartilage for first half cycle and second half cycle

6.3.3 Wear and surface characterization

6.3.3.1 Optical microscopy

The worn/damaged articular cartilage surfaces were observed with optical microscopy (Hirox RH-2000 with the MXB-2500REZ objective). The topography of worn surfaces was also examined using white light interferometry (Myko NT9300, Veeco Metrology, USA) with a height resolution of 0.5nm. Figure 6-19 (a)-(d) show the non-damaged cartilage surface for a representative sample before the friction test. Wear tracks were formed on the cartilage surface (see Figure 6-20 (a)-(d)). Surface fibrillations were not very evident on the cartilage samples through gross examination but wear tracks was seen under the microscope. Wear damage preliminary starts by fatigue failure of the extracellular matrix in a subsurface region, therefore leading to delamination, rather than abrasive wear of cartilage surface. No bone exposure and damage was observed in the peripheral cartilage region, which suggests longer test duration is required in order to see visible surface damages. Scratches were mainly present in the centre of the glenoid running in the direction of flexion/extension motion during the tribological test. Light wear was observed in the central and at the edge of the glenoid.

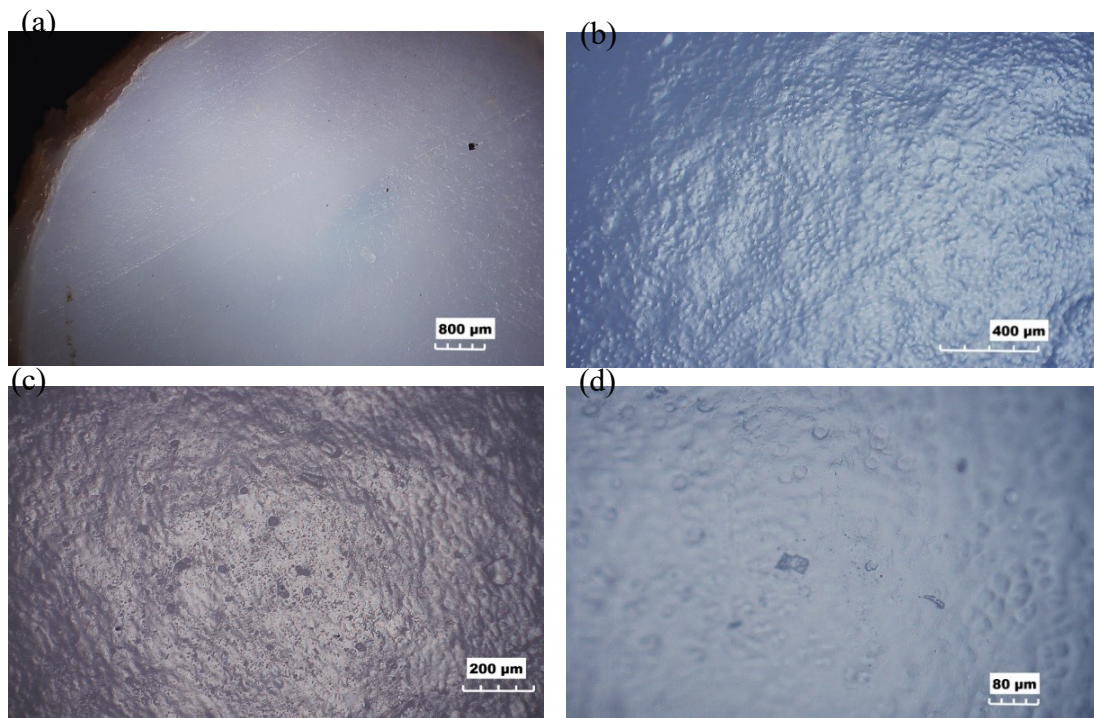


Figure 6-19 Hirox microscope images before the friction test at 800, 400, 200, and 80 μm magnification, showing unworn areas of the cartilage

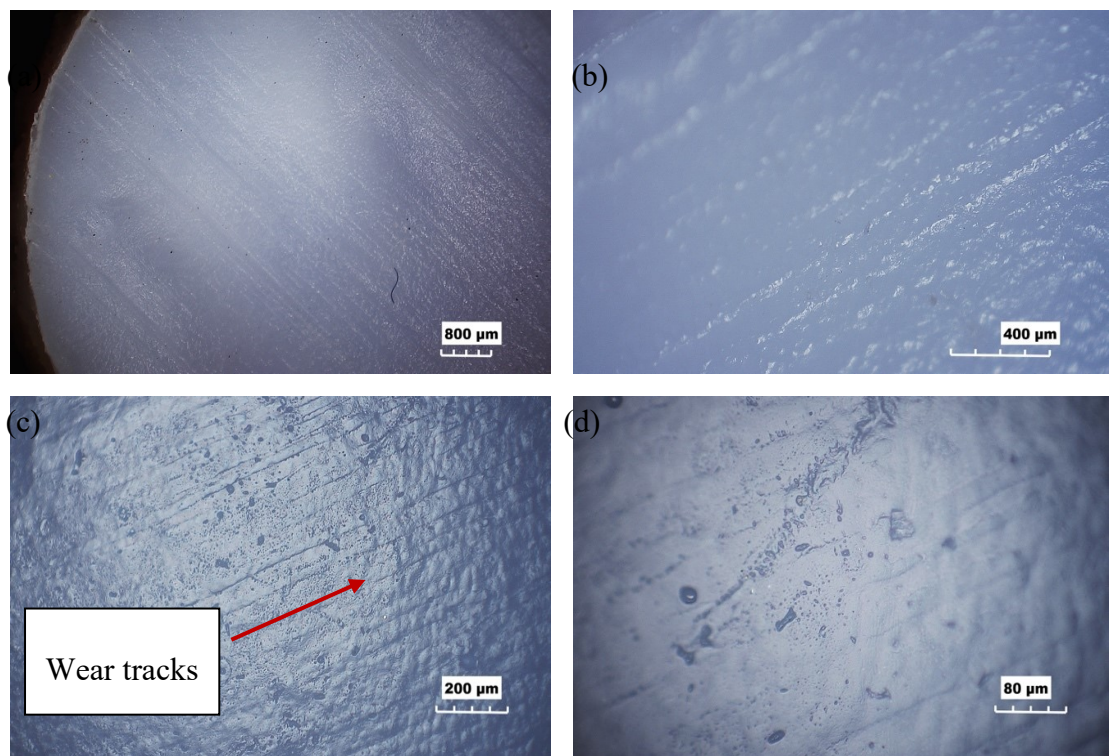


Figure 6-20 Example of Hirox microscope images for one sample after friction test, wear tracks and worn areas can be seen at 800, 400, 200, and 80 μm magnifications

6.3.3.2 Macroscopic evaluation- staining with India Ink

Quink inks are dye based and contain organic solvents. India ink is very fine soot, traditionally derived from lampblack, mixed with water to form a liquid. Hence, it is a suspension of particulate carbon. More recently, it is used for studying cartilage erosion and fibrillation. Because India ink is inert and not a stain, it does not alter the tissue and it can be washed off the tissue (Aspden, 2011). The use of India ink on the AC surface can facilitate quantifying the depth of cartilage loss in the macroscopic scoring process (Schmitz et al., 2010). As explained by Richardson et al., the cartilage surface is painted for 15s, with 20% (v/v) dilution of blue Indian ink (Parker, Quink) in Phosphate buffer saline. Any extra ink is blotted off with a ball of cotton wool.

This is an effective, quick and inexpensive method, already used by many researchers to look at the macroscopic wear on cartilage surface. Because Indian ink has a high affinity for fibrillation in AC, it can be used to indicate the extent and severity of fibrillation on the cartilage surface (McGann et al., 2012). This process has been adopted in previous studies to visualise cartilage damage (Meachim, 1972). As can be seen from the images below, no noticeable wear was visualised using this method and this is may be due to the low number of cycles that the tests were performed.

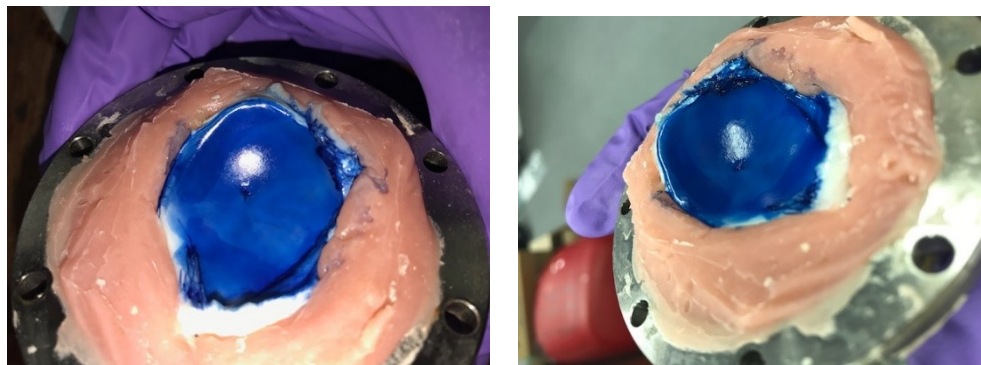


Figure 6-21 Macroscopic visualisation of cartilage surface with India Ink stain, no major damage was visualised using this technique

6.3.3.3 *White Light Interferometry*

White light Interferometry (WLI) measurements on each plug were taken on the areas that the cartilage was subjected to load. Figure 6-22, shows representative images of the surface topography of AC before (a) and after (b) the friction test against the two biomaterials for healthy and digested samples. It was found the surface roughness increased with increase in test duration. The surface topography of native cartilage consists of several humps and pits or bowl-shaped depression, these are clearer from 2D images (Figure 6-22 (a-native)). This layer is more evident after a latex glove finger is gently rubbed over the surface to remove the surface amorphous layer (SAL). It is known that SAL covers cartilage pits and humps. SAL is a superficial layer extending from the superficial zone (800 nm-2 μ m) thick in porcine AC. The reasons for these depressions on the cartilage surface is not fully understood, and the composition of this layer has not been intensively studied, but it is thought that it contains glycoprotein or proteins, chondroitin/keratan sulphates and proteoglycans, phospholipids, and hyaluronic acid (Graindorge et al., 2006; Jay et al., 1992).

Furthermore, these depressions have been postulated to be related to the underlying cell lacunae (Clarke, 1971). It is worth noting that for AC following friction test, the measurements were made on the damaged area of the sample which had been subjected to loading. Table 6-2 (a) and (b) summarises the average roughness and surface parameters obtained using WLI before and after friction test; the parameters were obtained from 10 cartilage plugs taken from different joints per level of enzymatic damage, as previously described. The parameters were calculated by in-built analysis software. All the data are shown for 2 hours of friction test under lubricated environment. It is worth mentioning that, although the values of surface roughness parameters are theoretically only valid for 2D profiles, the inbuilt software automatically computes the average of the roughness for the entire surface. Surface roughness parameters have slightly higher values following friction test (Table 6-2 (b)), also deeper depressions and pits on the surface can be seen as shown in Figure 6-22.

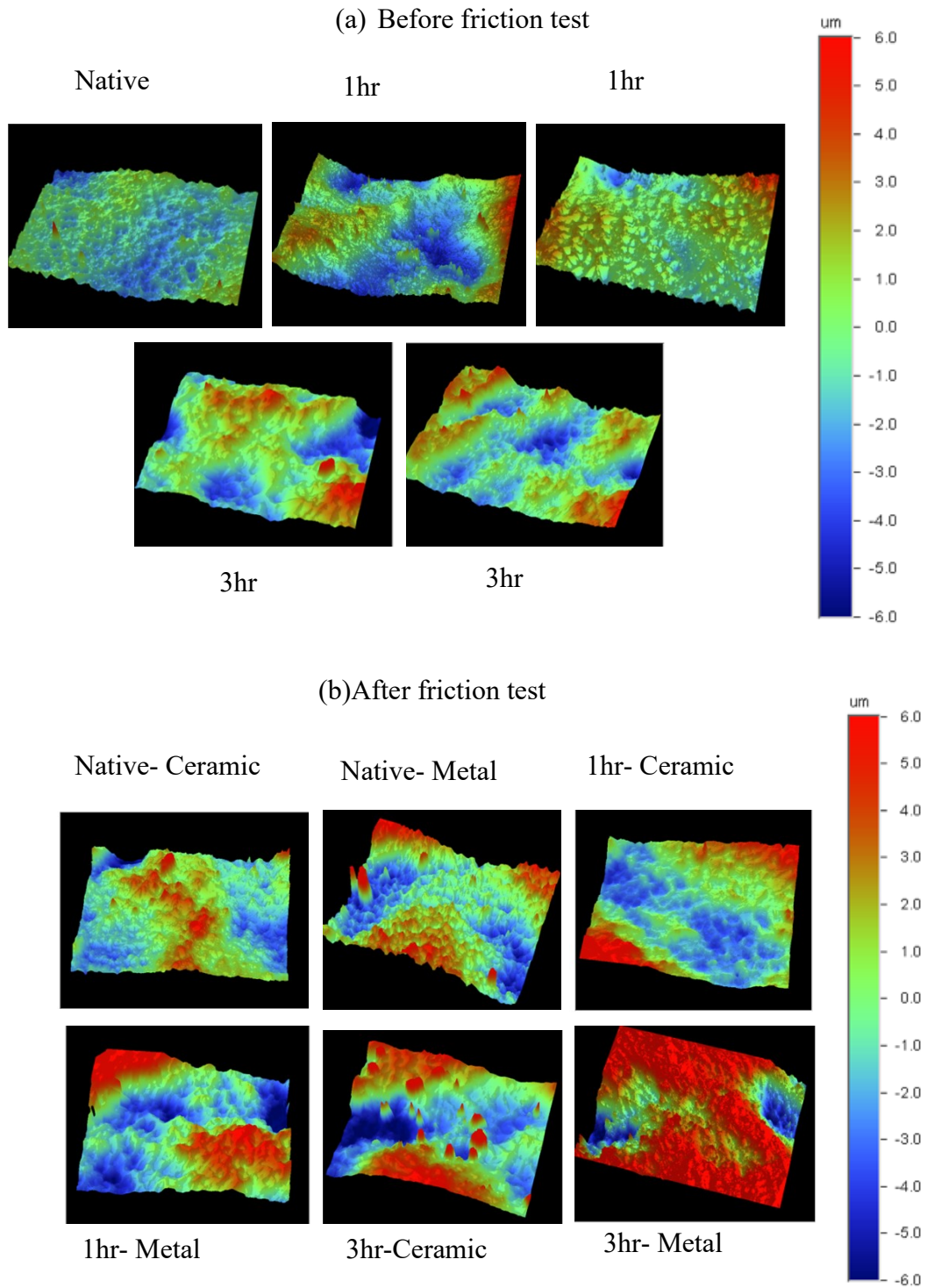


Figure 6-22 Representative WLI images before and after subjecting native and enzymatically induced OA-like cartilage to friction test for 2 hours

Table 6-2 Surface parameters of native and enzymatically damaged OA-like cartilage (a) before and (b) after friction test

Enzymatic degradation	Surface parameters (before friction test)					
	$R_a(\mu\text{m})$	$R_q(\mu\text{m})$	$R_s(\mu\text{m})$	$R_t(\mu\text{m})$	$S_{sk}(\mu\text{m})$	$S_{ku}(\mu\text{m})$
Native	0.81 ± 0.16	1.03 ± 0.22	6.02 ± 1.8	9.21 ± 0.52	0.05 ± 0.16	2.46 ± 0.8
Ceramic-1hour	1.51 ± 0.20	1.95 ± 0.33	12.54 ± 4.6	18.12 ± 7.69	0.33 ± 0.18	2.36 ± 0.9
Metal-1hour	1.71 ± 0.30	2.11 ± 0.35	13.43 ± 1.27	14.77 ± 1.63	0.28 ± 0.29	3.1 ± 1.04
Ceramic-3hour	2.23 ± 0.5	3.06 ± 0.24	16.45 ± 5.07	17.65 ± 7.89	0.35 ± 0.15	3.17 ± 1.74
Metal-3hour	2.63 ± 0.33	3.29 ± 0.28	20.17 ± 4.20	20.19 ± 4.57	0.43 ± 0.32	3.14 ± 1.30

(a)

Enzymatic degradation	Surface parameters (After friction test)					
	$R_a(\mu\text{m})$	$R_q(\mu\text{m})$	$R_s(\mu\text{m})$	$R_t(\mu\text{m})$	$S_{sk}(\mu\text{m})$	$S_{ku}(\mu\text{m})$
Native-Ceramic	1.30 ± 0.28	1.66 ± 0.33	8.35 ± 2.35	13.92 ± 2.47	0.05 ± 0.48	2.52 ± 0.34
Native-Metal	1.91 ± 0.27	2.39 ± 0.31	15.02 ± 2.30	16.29 ± 1.53	0.18 ± 0.06	3.22 ± 1.20
Ceramic-1hour	2.05 ± 0.67	2.46 ± 0.77	16.61 ± 3.74	18.03 ± 3.98	0.24 ± 0.08	3.39 ± 0.83
Metal-1hour	2.12 ± 0.44	2.63 ± 0.55	18.16 ± 3.66	22.27 ± 8.85	0.42 ± 0.30	3.47 ± 1.63
Ceramic-3hour	2.57 ± 0.48	3.23 ± 0.58	19.73 ± 6.97	22.59 ± 6.45	0.50 ± 0.2	3.54 ± 1.56
Metal-3hour	3.10 ± 1.47	3.75 ± 1.72	21.39 ± 3.97	23.22 ± 4.57	0.63 ± 0.59	3.85 ± 0.74

(b)

6.3.4 Histology results

The structural alterations of mechanically damaged AC samples were investigated histologically for a more in-depth evaluation of the effect of frictional damage on AC. As explained previously, articular cartilage was enzymatically digested in order to create OA-like damage. As digestion of the entire glenoid cartilage joint has not been done previously in the literature, it was necessary to determine the right Trypsin concentration and digestion time to obtain relevant concentration and time. This was achieved by submerging cartilage plugs from glenoid into the various concentration of trypsin and analysing the level of damage via histology. Initially, as preliminary work, 25% porcine pancreas trypsin was used to digest the cartilage at different durations (1, 2, 3 hours). As the histological results demonstrate in Figure 6-23, this concentration appeared to be high and resulted in discolouration and digestion of the entire cartilage; therefore, It was decided to reduce the concentration of Trypsin. The new concentrations of Trypsin were chosen according to a study done by Moody et al. 2006.

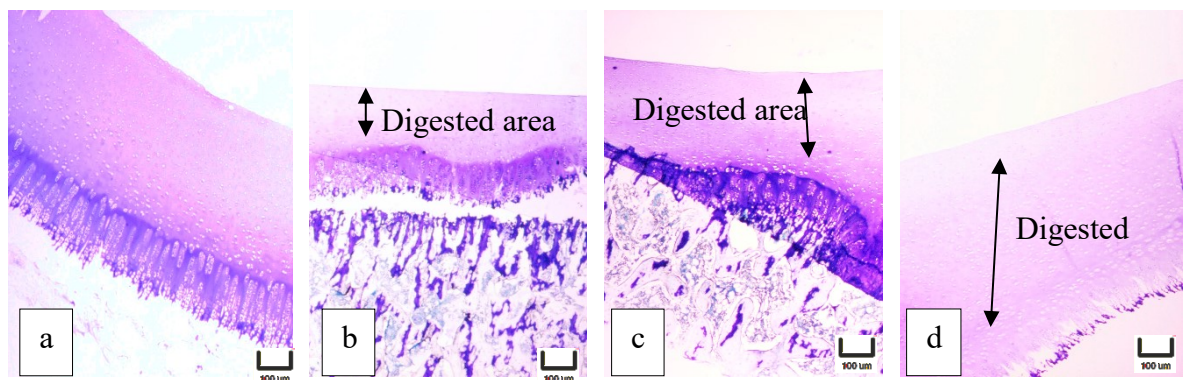


Figure 6-23 Toluidine blue staining of digested cartilage with 25% Trypsin (a) Healthy-not treated (b) Trypsin digested-1hour (c) Trypsin digested- 1.45 hours (d) Trypsin digested-2.30 hours. All images taken at x2.5 magnification with Zeiss Axioskop infinity

Following 25% trypsin concentration, three lower concentrations with various durations were chosen and analysed. 0.1, 0.5, and 1 mg/ml. Cartilage specimens treated with trypsin in PBS solution appeared to degrade proteoglycans in a wavefront penetration action throughout the entire depth of the cartilage for three different periods of digestion (Figure 6-24), increasing in PG loss with increasing exposure time. The complete loss of staining was achieved with 1mg/ml trypsin concentration at four h digestion time. As it can be seen, the control group showed no loss of staining, indicating that depletion of PG was due to the action of trypsin alone.

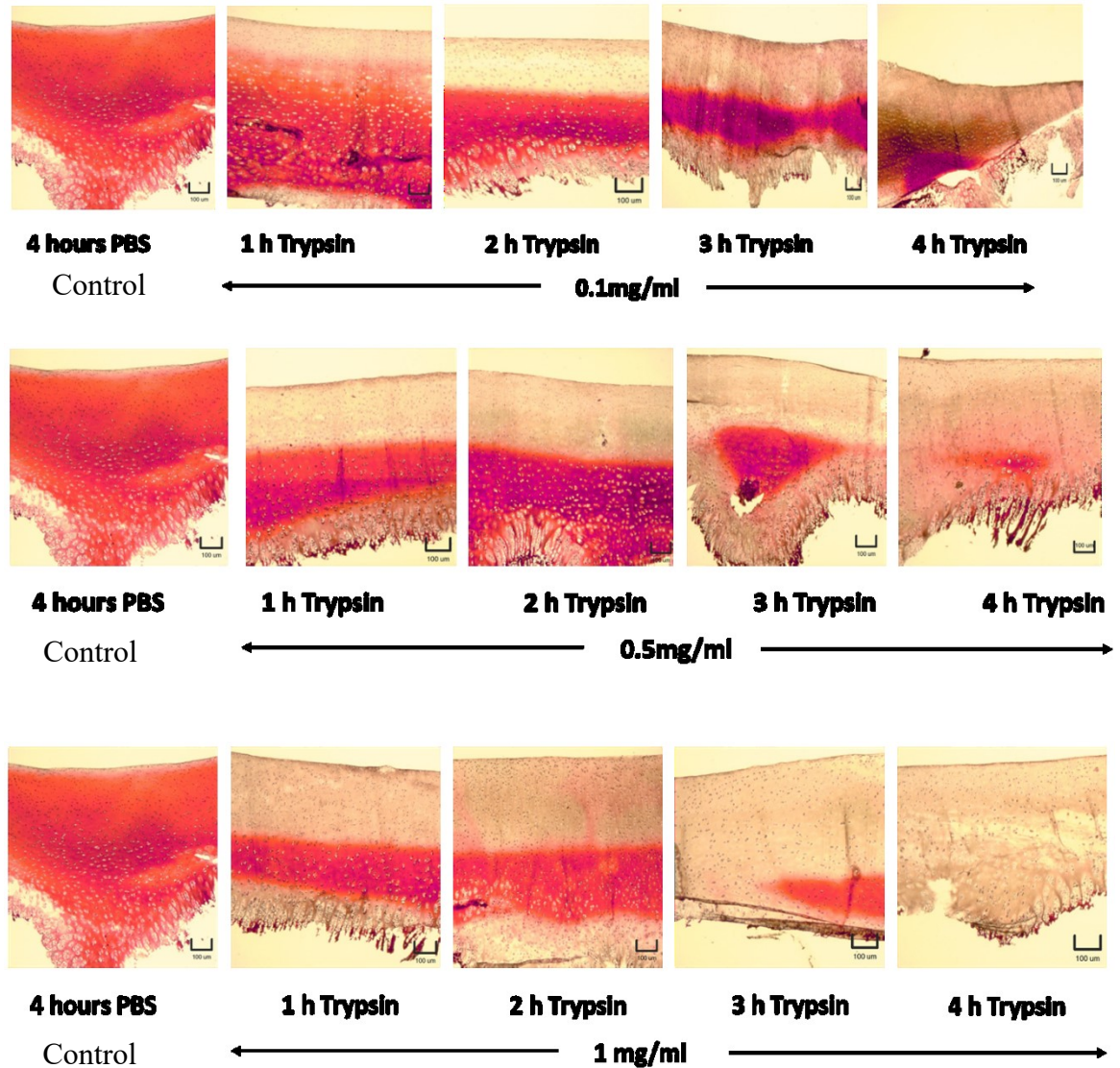


Figure 6-24 Safranin-O and fast green stained sections of biopsies taken from the trypsin digested cartilage. Each row of sections displayed here shows stained section for each digestion time (1h-4h) with different trypsin concentration (0.1,0.5,1mg/ml) with reference to the control section (PBS). The comparison here shows the trypsin is responsible for an active and progressive wave front proteoglycan digestion for up to 4 hours depending on trypsin concentration.

For each histology image, the thickness of lost PG (discoloured sections) were measured three times using Image J software. The results indicate as the exposure time increased the thickness of areas with PG loss also increased. These results are shown in Table 6-3.

Table 6-3 Average digested cartilage thickness for each trypsin concentration

Trypsin concentration	Digested Articular Cartilage thickness (μm)			
	1 h	2 h	3 h	4 h
Low-0.1mg/ml	174.42 $\pm$ 2.10	200.06 $\pm$ 1.70	269.06 $\pm$ 1.89	289.70 $\pm$ 2.17
Medium-0.5mg/ml	250.51 $\pm$ 1.64	366.89 $\pm$ 0.85	449.06 $\pm$ 0.79	565.01 $\pm$ 1.17
High-1mg/ml	345.73 $\pm$ 0.96	416.10 $\pm$ 2.35	581.54 $\pm$ 1.35	656.69 $\pm$ 0.72

Figure 6-25 demonstrates the histology results for enzymatically digested glenoid. The healthy, 1 h, and 2 h digested glenoid were tested against both ceramic and metal humeral head implants for 2 hours pendulum reciprocation. As it can be seen, the glenoids were digested consistently, but no significant damage occurred after the friction test. This could be due to many factors such as a low number of cycles; the humeral head may not have been in full contact with the cartilage while the test was running. Even though the surface roughness changed throughout the test, no macroscopic changes occurred that could be seen via histology.

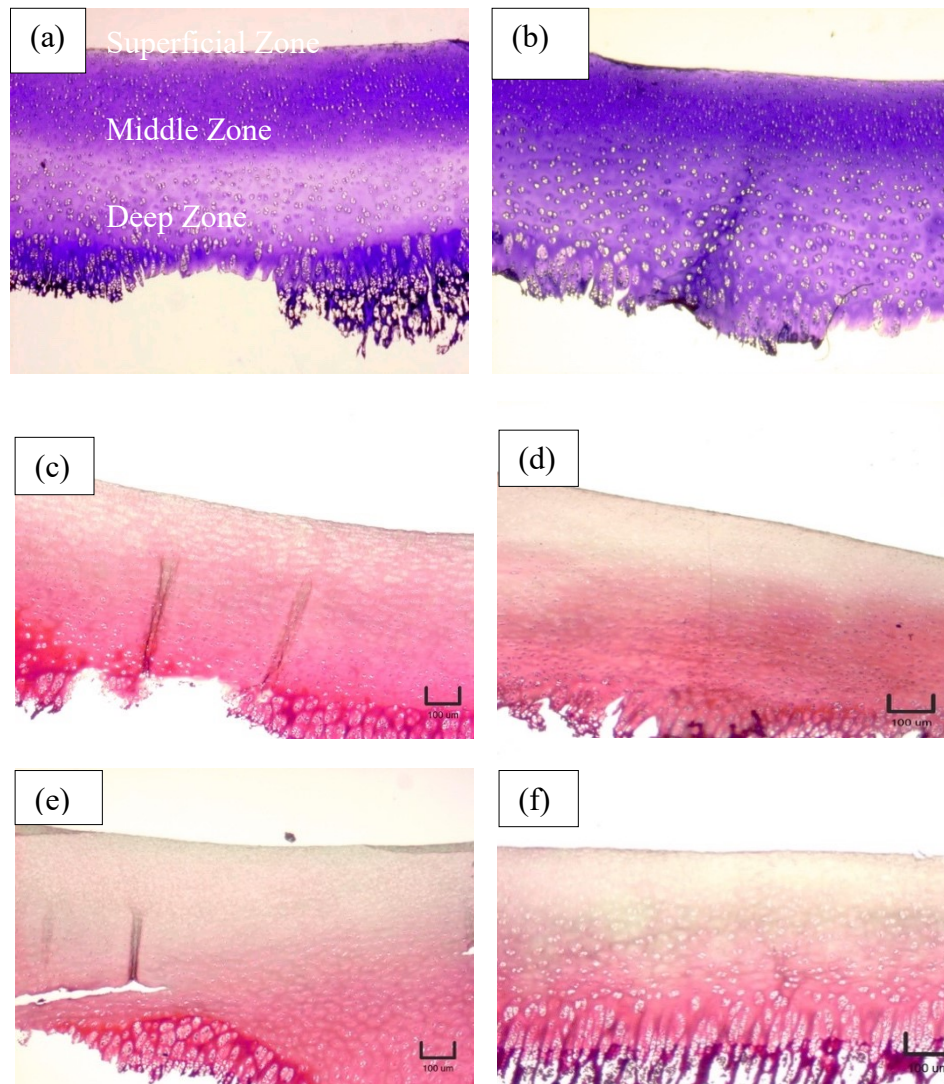


Figure 6-25 Examples of stained native and digested articular cartilage sections after friction test. (a) Various zones within cartilage, (a&b) sections stained with Toluidine blue, (c-f) sections stained with Safranin O and Fast green. (a) Native AC against ceramic, (b) Native AC against CoCr., (c) Enzymatically digested AC (1 hour) against ceramic, (d) Enzymatically digested AC (1 hour) CoCr., (e) Enzymatically digested (3 hours) against ceramic, (f) Enzymatically digested (3 hours) against CoCr. All images were taken with All images taken at x2.5 magnification with Zeiss Axioskop infinity 2opticalt microscope.

6.4 Discussion

In this study, selective degradation of AC tissue was used in order to reveal the effect of PG damage on the frictional response. A COF comparison between healthy and digested cartilage against two different implant materials was made, and structural damage was estimated. The main aim of this work was to lay the foundation for a protocol relating enzymatic degradation and frictional response and structural changes to better understand the effect of degradation on the properties of cartilage. The work is done in this project a preliminary comparison of tribological properties of native and OA-like cartilage. However, a more thorough test programme is required to shed light on differences between the effects of two implants on frictional properties of AC. This will establish the objective for future research projects.

6.4.1 Evaluation of frictional data

Friction coefficient was measured during friction testing for periods of two hours. The two hours period was chosen as the previous pin-on-plate shear test was carried out for 2 hours as short-term testing. Also, as this was a preliminary test and due to lack of time and nature of cartilage, it was decided to run short term. As it was shown in Figure 6-12 COF values of cartilage for the first half cycle (20-40s) increased gradually through the cycle. The reason for the increase in friction values is that there is a gradual loss of fluid within cartilage over time. Hence, less of the load is supported by the fluid phase of the cartilage and more is supported by the solid phase, therefore the friction between articulating surfaces increases. As shown in chapter 4 and also by (Accardi, 2012; Ajdari, 2016), the change in frictional response of AC has been associated with a loss of compressive stiffness due to loss of interstitial fluid pressurisation and the loss of the tightly packed PG structure which is responsible for supporting compressive load (Musumeci, 2016). Regarding frictional response, for 1 hour enzymatically digested cartilage (low PG loss) and 3hours digestion (high PG loss) against the ceramic implant, COF value was 0.17 ± 0.05 and 0.19 ± 0.05 respectively. As it can be seen the PG depletion had a significant effect on the frictional response of AC. For metal implant, the values for 1 hour and 3 hours digestion time were 0.22 ± 0.05 and 0.23 ± 0.09 respectively. The increase in the COF following PG depletion is due to variations of the ECM's composition in the superficial layer. It is thought that the digestion of GAGs on the AC surface causes a decrease in the lubricating action of the surface, therefore affecting the

fractional response (Basalo et al., 2005). The COF values presented in this study for healthy cartilage against ceramic (COF value = 0.13 ± 0.02) found to be similar compared to values obtained in a study conducted by Chan's group (COF value = 0.13) (Chan et al., 2011).

During friction test, significant spikes were observed between each cycle, which was probably due to the low values of normal and friction amplifying noise in the region. This could be due to vibration in the glenoid cup as well as the entire rig during the experiment. One way to minimise this was to ensure that the bolts in the rig are sufficiently tightened, additionally the entire rig was bolted to a wooden bench to reduce any micro movement and the step size in the motor was reduced from 1/2 to 1/16. Therefore, it was helpful to consider the data between approximately 15-75% of the cycle time. Since the direction of motion arm rotation changes between each cycle, friction reverses sign, however, COF remains positive throughout the loaded part of the cycle.

A study conducted in 1997 looked at the tribological performance of CoCr sliding against cartilage in a pin-on-disc model. The COF was found to be 0.02 (Patel and Spector, 1997). According to Chan et al., (2011) CoCr alloy implant would produce the highest wear rate when compared to Al₂O₃ (1.42 vs 0.81) in a pin-on-plate model. The friction coefficient of AC has been shown to vary across a relatively wide range (from as low as 0.002 to as high as 0.5), depending on the loading configuration (Forster and Fisher, 1999). However, based on prior studies, it has been shown that the friction coefficient can remain very low (between 0.002 and 0.01), as long as the interstitial fluid load support within the cartilage remains elevated (Caligaris and Ateshian, 2008).

The lower friction results of ceramic compared to cobalt chrome is possibly due to the better wettability of ceramic compared to cobalt chrome (Meftah et al., 2013). Enzymatically induced OA-like AC samples with a lower level of damage followed the same trend in general. With PG depletion, the COF values were found to be strongly affected; There is a reason to believe that the protease in the lower digestion time (1 hour) have mainly degraded the superficial zone since not enough time has been given for the enzymes to penetrate in the deeper zone of the AC. When the results compared to Müller et al. (2004) study, different test variables are observed such as a number of cycles and load applied test temperature (Müller et al., 2004). The values in this study were higher for both ceramic and metal, and this may be due to variation in temperature and also cycle

length. In this study, only a portion of the data was taken into account (first half cycle between 20-40s), where the joint was in full sliding motion, whereas in Muller study the friction data from the entire cycle were taken into account. Also, in the Müller study combination of newborn calf serum and Ringer's acetate was used, which gives similar properties as synovial fluid, whereas in this study bovine serum was used for all the tests. The friction coefficient measurements in Müller study were an approximate and not accurate and was measured using $M = \mu * F * r$ (where m is Torque, F is Normal force, r is the Radius of the femoral head) as precise pressure distribution in the joint and contact area were unknown. Furthermore, Müller studied 20 samples whereas in the present study only 12 samples were used (two samples per implant) therefore definite conclusions cannot be postulated with the minimum amount of data obtained. This demonstrates that it is very difficult to reproduce the same exact physiological conditions in in-vitro studies compared to in-vivo. However, given that the test configuration and the lubrication are meant to mimic the most salient features of the joint mechanics, this can be used as a screening test for comparison between different solutions and biomaterials. The data obtained from these two studies concerns comparing the performance of different biomaterials running against the cartilage.

Table 6-4 Results comparison from Müller et al. and the present study

Test	(Müller et al., 2004)	Present study
Dynamic loading	Double peak	Single peak
Peak load	2500	800
Temperature(°C)	37	Room temp
Swivel angle (°)	+30/-18	+25/-18
Tissue	Porcine acetabula	Porcine glenoid
Implant type	Metal and ceramic femoral head	Metal and ceramic humeral head
Cycle length	900	7200
COF (healthy porcine)	Ceramic: 0.082, Metal: 0.101	Ceramic:0.13, Metal: 0.15

The friction tests in this study were conducted in bovine serum. In a physiological situation, since synovial fluid contains boundary lubricant that reduces the friction coefficient further, the onset of damage would occur at a later time. Synovial fluid contains proteins and other biological molecules that increase fluid viscosity and lower the coefficient of friction between articulating surfaces (McGann et al., 2012). While the

saline solution used was not physiological it allowed for the comparison between different biomaterials under identical testing conditions. Another difference from physiological conditions was that the test was performed at room temperature rather than human body temperature. Finally, the tests performed did not exactly replicate various shoulder motions, in the shoulder joint the physiological motions are in flexion/extension, rotation and abduction/adduction directions. In spite of all the potential differences between the testing conditions and the physiological loading encountered, all the tests were performed under identical conditions in order to compare the differences between each biomaterial.

6.4.2 Effect of head materials on cartilage surface roughness

Damage because of both tribological degradation and enzymatic digestion was assessed using WLI. The parameters were obtained from AC samples originating from twelve different porcine joints in total used for both inducing tribological damage and enzymatic degradation for both metal and ceramic implants. Due to the lack of samples, two joints per level of digestion per implant was used. From each joint, five cartilage plug samples were taken, and five measurements of surface parameters were made on each of the samples before and after the friction test with the joint simulator. The average across the various measurements and samples was then calculated.

For AC samples following frictional loading, measurements were made of the damaged area of the sample; this area was visible to the naked eye. The disadvantage of this technique is that it was not possible to image the same location before and after friction test, therefore, when imaging native cartilage samples, particularly close attention was given to imaging the areas where the implant was in full contact with the glenoid. Figure 6-20 shows representative WLI surface images of healthy and OA-like enzymatically digested articular cartilage before and after friction test. The surface roughness parameters obtained by the authors for native AC fall within the range of values obtained by other studies where WLI has been used (Graindorge et al., 2006; Shekhawat et al., 2008). Each of the tribological and enzymatic degradation (before the test) has a noticeable effect on the tissue's surface, causing a significant change in surface parameters and a rise in surface roughness. This superior wettability of ceramic implant could also be the main factor that results in significantly lower surface roughness compared to cobalt chrome.

6.4.3 Effect of enzymatic cartilage on cartilage

The patterns demonstrated by the samples treated in trypsin-PBS reveal that there was consistent PG depletion, regardless of the concentration of trypsin. However, it should be noted that the overall effect of trypsin may have been influenced by a continuation of its action once the sample is removed from the solution and moved to a different container filled with PBS. This residual action is slower than when it is in the enzyme environment (Moody et al., 2006a). Despite this, we expect this effect was consistent throughout the samples; therefore, producing the same effect. Also, the results of this study are affected by the intrinsic characteristics of the cartilage sample. From the histology results (Figure 6-23) it can be observed that different samples have different cartilage thickness. Therefore there is a significant variation in the level of PG damage. Older animals have thicker cartilage with higher PG content which requires a higher digestion time. Thus, when choosing the samples, it is necessary to select animals within the same age to reduce the variation in the results. Also, there is a consistency of PG distribution and concentration across the depth of cartilage, but the concentration and distribution of PG from the surface through to the bone is unique to each sample and is non-linear. Perhaps, this is the main reason for the variation in the level of digestion for each sample. If all the samples contained the same amount of PGs in each cartilage zones, it may be expected that the penetration rate of trypsin in all the samples would be constant.

6.4.4 Effect of friction on cartilage structure

To fully understand the effect of tribological study on macroscopic properties of cartilage, histological analysis was carried out. The cartilage sections for native and enzymatically digested cartilage were stained and imaged with an optical microscope. Toluidine blue and Safranin-O/fast green staining protocols as mentioned in chapter 3 were used for staining the microscopic slides. Safranin-O and TB are cationic dyes that stain proteoglycans as well as glycosaminoglycans. TB has been reported to provide more intense staining because it has a higher affinity for the sulphur in cartilage compared to Safranin O. Safranin-O is proportional to PG content in normal cartilage (Schmitz et al., 2010). To visualise the general tissue components of AC and the structural damage due to friction test, this is a relatively simple stain and quick staining process to perform. The different zones of the cartilage structure can be seen in Figure 6-25 (a) through variation in the intensity of the TB stain. Bone exposure is a very important category of wear and

must be used to compare between healthy and damaged cartilage. Histology data from previous in-vivo studies using CoCr femoral heads in the canine model exhibited more degradation, fibrillation and bony changes. According to Chan et al. (2011) friction test at low periods of the cycle can cause superficial zone protein (SZP) removal, during sliding and the macroscale damage cannot be seen. SZP is a key boundary lubricant, which can be removed during the sliding motion. They showed that CoCr implants created a higher loss of total protein and SZP compare to Ceramic (Figure 6-26). These results correspond to the macroscale friction coefficient patterns of biomaterials against cartilage biomaterials against cartilage.

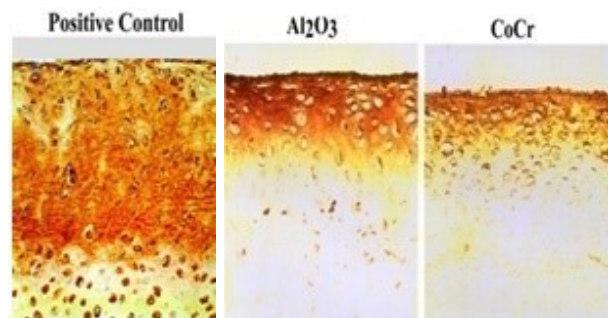


Figure 6-26 Immunohistochemistry image from Chan et al. (2011) showed lower SZP content at the cartilage surface sliding against CoCr, and higher SZP surface content sliding for 60 mins against Al₂O₃ (Ceramic).

Zheng et al. carried out a study to digest the bovine patella cartilage with 1mg/ml trypsin concentration for 1h and 2h. They measured the thickness and material properties of the digested and undigested cartilage specimen using ultrasound without damaging the surface (Zheng et al., 2001). Comparing the ultrasound data with histology showed that the digestion time was not proportional to digestion depth in the tissue. Furthermore, the elastic properties of the cartilage solid matrix decreased massively after trypsin digestion. This method can ultimately be used for OA diagnosis following the development of a probe used with arthroscopes. Furthermore, studies have demonstrated that PG depletion can result in the reduction of cartilage stiffness (Guterl et al., 2010). Preliminary validations of the simulator proved that reproducible motion and loading profile could be applied to fully lubricated test components for periods of up to 2 hours. Single station wear simulators have obvious limitations. One would be that in this study the simulator only applied one axis of motion of motion flexion/extension. The simplification of motion to only one axis, as oppose to three-axis can fundamentally change wear of implant and produce different results. Most simulator studies to date are on hip or knee prosthesis and

the loading used were non-physiological or do not reflect the exact ADL motions. Moreover, cementing the glenoid using the PMMA bone cement, is an exothermic process and it also has the potential to damage the tissue. In future studies the use of synovial fluid would be beneficial, it has been shown that SF can reduce friction by a factor of ~2 over other salines (Jones et al., 2015).

The additions made to the simulator have focused on changing the loading pattern to around 750N, the head holder and cup holder assembly, and introducing strain gauges as a friction measurement system. This has highlighted certain critical issues for the future performance of the rig. Below are some suggestions for possible rig improvements for future iterations:

- a) In order to find out the source of vibration in the test rig, it may be helpful to attach accelerometers onto the test rig. These areas can then be stiffened to reduce vibration. The glenoid cup holder should also be stiffened to reduce vibration of the glenoid. This could be done by adding more pins to the cup holder.
- b) An improved method of locating the implant on the head block which allows it to be adjusted vertically while allowing the strain gauges to be in the correct plane should be designed. This would allow the center of curvature to coincide with the axis of rotation. A method of measuring horizontal force in the joint to improve the accuracy of the mechanical model should also be designed.
- c) The main arm was large and heavy, which meant that it created large moments. This moment can be reduced by changing the material of the arm in order to reduce the weight and move the centre of gravity closer to the shaft.
- d) As well as extending the length of testing, the entire motions of the shoulder including abduction/adduction and internal/external rotation could also be factored in. This will produce more clinically relevant results compared to the results in Chapter 6 that only applied for flexion/extension due to the limitation of the friction simulator.
- e) Finally, with the benefit of more time, the structure of the simulator may be further modified to reflect the geometry of the shoulder joint and incorporate the loading directions of the various ADLs from Anglin et al.'s (2000) research.

6.5 Conclusion

The primary focus of this study was to develop a preliminary methodology to investigate the effect of two different implant head on cartilage tribological properties and to determine the biomaterial/cartilage interface with the lowest coefficient of friction/ least wear. In shoulder hemiarthroplasty, the material used affects the tribological properties of cartilage. Amongst the tested biomaterials, CoCr demonstrated the least desirable tribological properties, producing the largest increase in COF through the 2 hours duration of sliding. The effects of the humeral head material on cartilage friction, deformation, degeneration, for 2 hours pendulum reciprocation was as follows:

1. Average COF values obtained for Ceramic humeral head (0.17 ± 0.05) were lower than the values obtained for CoCr humeral heads (0.19 ± 0.05) using Fetal Bovine Serum (FBS) as the lubricant.
2. When the ceramic humeral head is articulated against porcine glenoid, it produced slightly lower surface roughness values than CoCr humeral heads.
3. Proteoglycan degradation in cartilage accelerated with an increase in trypsin enzyme concentration and digestion time. This method can be used to create the OA-like model of AC for future studies.
4. The ceramic material may be recommended for the humeral head in shoulder hemiarthroplasty due to the lower friction and surface roughness values examined in-vitro.

Significant physiological factors that affect cartilage wear including inflammatory responses and cellular activity could not be simulated by this study. However, since this study was mainly a proof of concept for the rig and was performed to compare different implant materials, it can be considered acceptable as a screening protocol for potential hemiarthroplasty implant materials. As a result, the present study was successful proof of concept in terms of being able to test different biomaterials against cartilage using a one station joint simulator. However, due to lack of sample availability and implant heads, it was not feasible to carry out many friction tests, therefore no definite conclusions can be postulated in terms of friction values. Therefore, as part of future studies, longer test duration is required to be carried out in order to assess the damage more thoroughly. Moreover, a thorough investigation of the effect of different biomaterials on wear and tribology of Articular Cartilage using the simulator is required. Further investigation will

focus on varying test parameters such as duration, implant radius of curvature, simulator range of motion, enzymatic digestion time and contact stress and measuring cartilage wear and mechanics using a variety of techniques. The development of this joint simulator is a significant step in the pre-clinical testing of shoulder implants in hemiarthroplasty, which will be used to investigate the tribology of the whole shoulder joint in its healthy and diseased state.

6.6 Chapter Summary

This chapter included a comprehensive study of the frictional behaviour of native and OA-like enzymatically digested porcine glenoid against the humeral head implants of two different biomaterials: CoCr and ceramic. Following this, surface topography and histology measurements were performed to assess the AC structure after the friction test. The following chapter will discuss the main results and findings from each chapter in more details along with limitations associated with each study. To conclude, recommendations for future work will also be given.

7 CONCLUSION AND FUTURE WORK

7.1 Introduction

In this thesis, the reader will have acknowledged that for a successful detailed understanding of AC and OA pathogenesis and progression as well as for design and development of an in-vitro joint simulators, inevitably necessities bridging the gap between medical, biological and engineering world. The primary aim of this thesis was to analyse cartilage performance during hemiarthroplasty using different techniques, approaches and experimental models; this is ultimately aimed at being able to achieve early diagnosis of the pathology using biomechanical, biochemical and tribological approaches, as well as improving the performance of biomaterials commonly used in hemiarthroplasty, to improve the outcome of surgery in cases where operation essential. The studies conducted in this thesis helped to understand the performance of three different implant biomaterials articulating against human cartilage affected by various grades of OA (Chapter 4), update and validate the Imperial in-vitro joint simulator (chapter 5), the effect of implant material on healthy and OA-like cartilage friction during shoulder hemiarthroplasty (chapter 6). Investigating these aspects of the in-vitro tribological model allowed the limitations to be highlighted which could influence the results. These limitations discovered from previous chapters and possible improvement for this project are discussed further in this chapter.

7.2 Comparing the performance of three biomaterials (Co-Cr), (Al₂O₃) and (PCU) against human non-OA as well as all four grades of OA articular cartilage

Tribological and mechanical performance of different grades of human OA-AC against three commonly used orthopaedic biomaterials were investigated, in order to gain a thorough understanding of the cartilage-biomaterial response and to aid enhance the performance of hemiarthroplasties in the future. This study utilised various techniques to assess the structural, topography and mechanical properties of AC before and after the shear test. The results indicated that PCU has the most favourable properties amongst all three biomaterials investigated when tested against cartilage, while CoCr alloy would produce the highest coefficient of friction and creates more damage to the tissue. When compared to CoCr, ceramic demonstrated a lower level of COF and produced less tissue damage. The results of the present study suggest that expanding the use of Ceramics and

PCU and other polymers in orthopaedic applications where cartilage has been replaced by an engineered biomaterial is worth exploring.

7.3 The effect of enzymatically induced damage on tribological properties of articular cartilage

It is thought that during OA, proteolytic enzymes such as MMP13 are involved in the degradation of the matrix and decrease the mechanical properties of AC. This leads to softening of the tissue and ultimately wear and loss of AC. Variations in mechanical and biochemical properties of AC during OA occur before any visible morphological changes (Buckwalter and Mankin, 1998a). While studies have explored the structure-function relationship of the tissue (Rieppo et al., 2003b; Silver et al., 2001), up until now, there have been no comprehensive studies evaluating the mechanical, frictional, and wear response of AC at different levels of PG and collagen (structural) degradation. Understanding this is important as it could strongly help to detect earlier signs of OA and affect the treatment options used for various grades of OA.

In chapter 6, a proteolytic enzyme, named Trypsin was used, due to its inexpensiveness and availability compared to MMP1, to degrade the PG of the AC samples. This was done to mimic early to late OA by inducing PG depletion. In previous studies in our research group (Accardi et al., 2013), low PG depletion, showed to decrease the stiffness of tissue and increase the stress relaxation rate while increasing its permeability. In the present study low degradation (1h) showed to have an effect on the COF indicating some variation to the boundary lubricating properties of tissue. This stage is similar to early stage OA. In the early-stage of AC disease, homeostasis may be disrupted, and the matrix begins to break down through an imbalance in the secretion of proteinases and inhibitors. As a result, in the early stage of OA, the depletion of PG and the increase of water content can occur primarily in the top layer of the tissue near the surface (Buckwalter and Mankin, 1997). In-vitro, researchers use enzymes with similar properties to those found in-vivo, attempting to recreate the disease processes. Increase in PG depletion, result in induced mechanical properties of AC considerably and correlating to this study, the rise in digestion time increased the COF of AC noticeably. It is also believed that, since AC is inhomogeneous, damage to its surface which is responsible for the mechanical response of the tissue, can create significant variation in mechanical properties. This is due to PG and collagen fibres in the superficial zone are known to greatly influence the mechanical

response of the tissue. Therefore, this proposes, during in-vivo studies, that mechanically induced damage, as well as enzymatic degradation, could play an important role in the degradation of AC. During high level of enzymatic damage, COF is increased this is due to the accelerated diminishing of interstitial fluid from the AC during the tribological testing. At this stage, damage to the tissue is irreversible, highlighting the need to diagnose OA prior to this stage, when the tissue's wear properties are strongly compromised. The correlation found from this study and previous studies performed in our research group, in terms of the permeability, stiffness and frictional response of the tissue and the degree of OA. These provide valuable information that can be used to develop new methodologies for direct patient assessment, potentially opening new avenues for the production of new devices for direct implementation in the medical environment.

7.4 Comparing the tribological and structural performance of two biomaterials (Co-Cr) and (Al_2O_3) shoulder hemiarthroplasty against healthy and OA-like porcine glenoid

From a practical point of view, the experimental results from this study suggest that CoCr implants when compared to ceramic, should not be used for shoulder hemiarthroplasty due to excess wear and producing a higher coefficient of friction against cartilage. Ceramics have gained popularity due to having great scratch resistance properties, less surface roughness and a lower coefficient of friction compared with classic orthopaedics implant materials (Vanlommel et al., 2017). The better COF results for Ceramic implant maybe due to its better friction and wear characteristics compared with CoCr, especially its better wettability, which leads to lower COF values. On this basis, articulating ceramic against native cartilage would create less damage to cartilage (Vanlommel et al., 2017). In previous studies, the increase in friction was the result of the loss of fluid support and increased direct solid-to-solid contact due to unique biphasic nature of AC (McCann et al., 2008). Therefore, wear increased as a result of direct solid-to-solid contacts. In this study, a rise in friction was observed with an increase in test duration, caused by high contact stress, the breakdown of AC constituents and a loss of fluid pressurisation.

7.5 Clinical importance

It has been well documented that one of the primary complications after the implantation of shoulder hemiarthroplasty is glenoid erosion (Ohl et al., 2010). Glenoid wear due to friction from the metal component is confirmed by glenohumeral joint space narrowing and by an increase in glenoid depth. This causes pain in most patients after hemiarthroplasty surgery. Even though there have been studies that have investigated the tribological and mechanical properties of cartilage against biomaterials, to our knowledge there hasn't been any studies investigating the mechanical and surface properties of human OA A (grades non-OA to OA-4). Furthermore, this investigation can aid the surgeons in choosing the optimum biomaterial depending on OA grades for the patients who require Hemiarthroplasty. In respect to the clinical application, this study provides support that ceramic implants may be a better choice than metals and the articulating surface should be made as smooth as possible. While our results indicate that the degree of arthritis should not affect the choice of biomaterial this clinical implication needs to be further investigated using whole joints more representative of the key features of OA joints. The study would also seem to support the use of PCU for hemiarthroplasty applications. This may be appropriate for very early stages of osteoarthritis but in later stages where osteophytes and cysts may exist the relatively low strength of PCU may make it unsuitable for this application. Also, the recent clinical problems with PCU meniscal implants will need to be considered.

The shoulder simulator could be significant in several ways. Firstly, it could allow weaknesses in current hemiarthroplasty designs to be pinpointed and fed back to the designers and manufacturers so that the implant can be improved. Secondly, the performance of different designs of shoulder implants could be compared in the simulator and this data shared with interested scientists/clinicians/patients and engineers. Thirdly, the simulator will permit novel designs shoulder prosthesis to be tested in the laboratory prior to implantation in human subjects. All these advantages offer opportunities to improve artificial shoulder joints for the increasing number of patients requiring such implants (Smith et al., 2015).

7.6 Future work

Although maximum work was done to ensure that this study shed light on some of the most crucial areas of AC and OA research, the reader will have appreciated the complications associated with this project which require further research and developments. This thesis provided a foundation for moving towards the testing of full shoulder joint against materials that are commonly used in hemiarthroplasty in order to increase our knowledge of their performance in terms of wear and friction. As well as the suggestions made in section 5.9 related to rig improvement as part of future work, below are further suggestions for future work recommended by the author, which will help to better understand OA, as well as improving its diagnosis and the discovery of potential treatments as well as choosing the optimum biomaterial for hemiarthroplasty.

- a) Due to lack of time and sample availability, the tests were performed for two hours, and only two samples per biomaterials were tested. For future studies, in order to obtain statistically significant data, a minimum of six samples is required per each test group (healthy and enzymatically digested). Also, it would be beneficial to see the effect of friction on cartilage for longer test durations (i.e. minimum 1 million cycles) and assess the structural changes using histological methods. Moreover, for future long-term testing studies, cartilage recovery is important for its tribological properties and should be considered. With continuous testing, the COF is increased to a high level that causes major cartilage degradation. By including recovery time in future in-vitro testing, it allows the experiments to be more reflective of reality and physiological situation, as recovery period often occurs during the day. Although this will increase the length of the tests, it is useful to study the effect of various recovery periods.
- b) Another important study would be the using synovial fluid instead of bovine serum and quantification of protein absorption that takes place on the surface of different biomaterials in the presence of synovial fluid. Of particular interest will be investigating the nature of the boundary film forming at the cartilage/biomaterial interface and the rate at which the protein layer is disrupted and reforms as a result of articulation. The analysis of different biomaterials can provide further evidence to enable a more comprehensive classification and ranking of the biomaterial to be used in hemiarthroplasty. Superficial zone protein

is an important boundary lubricant that is likely to be constituent in the wear debris. Quantification of SZP may explain the differences seen between the materials in friction coefficient but not in total protein wear.

- c) Mechanical properties of porcine cartilage from knee and hip joints have been studied extensively in the past, whereas this is not the case for cartilage from porcine glenoid. This is due to relatively smaller cartilage thickness compared to knee and hip. Therefore, as part of future work, it would be beneficial to find a method such as AFM or nanoindentation to measure the mechanical properties of porcine glenoid cartilage plugs. Lavoie et al. developed a technique to measure mechanical properties over the cartilage surface on entire mouse knee using 3-axis Biomomentum Mach-1 mechanical tester (Lavoie et al., 2015). This will produce structural stiffness data before and after the friction test, which can ultimately provide more information regarding mechanical changes of cartilage under frictional loads as well as changes in cartilage stiffness with loading location. This technique can also be used to measure the cartilage stiffness before and after enzymatic degradation.
- d) An interesting further study would be investigating the frictional properties of different stages of human osteoarthritic glenoid against different shoulder hemiarthroplasty biomaterials using the simulator, in order to understand how the pathology affects the frictional response of tissue and also compare the frictional response of OA AC to AO-like AC.

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9 APPENDIX

9.1 Appendix A

Castigliano's minimum strain energy method was calculated by previous Master's research group at Imperial College London. Castigliano's minimum strain energy method makes use of the simplified model in Figure 9-1, which models the joint interface as a pin joint, with the motion arm built in at the main block and the acetabular/glenoid cup holder constrained to move only vertically. The strain energy is calculated by Welham et al. using Equations 1-4, where axial force in beam 2 is ignored (Welham et al., 2014). That the two methods yield similar results indicates that either may be used to approximate the horizontal force P .

$$U = \int_0^{L_1} \frac{M_1}{2E_1I_1} dx_1 + \frac{T_1^2 L_1}{2E_1A_1} + \int_0^{L_2} \frac{M_2}{2E_2I_2} dx_2 \quad (1)$$

$$M_{arm} = Fx_{arm} \sin \theta + Px_{arm} \cos \theta \quad (2)$$

$$T_{arm} = P \sin \theta - F \cos \theta \quad (3)$$

$$M_{cup} = -Px_{cup} \quad (4)$$

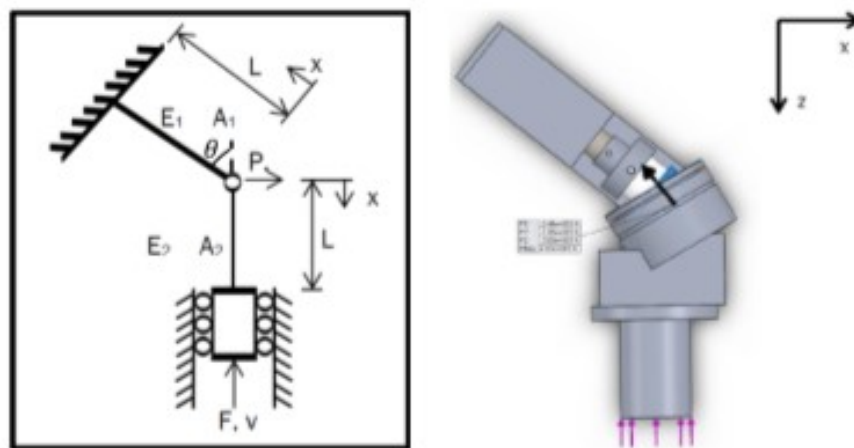


Figure 9-1 Simplified model of implant-joint interface (Welham et al., 2014)

Since the motion arm and cup holder are modelled as two beams of uniform Young's Modulus and cross-sectional area in the energy method, it can be improved by incorporating geometry and material properties in further detail. The expression for strain energy in Equation 1 can be updated to Equation 5 to account for the n components in the main arm and components A and B in the cup holder shown in Figure 9-2. For the system with minimum strain energy, $\frac{\partial U}{\partial P} = 0$ and horizontal force P for can be found.

$$U = \int_0^{L_1} \frac{M_{arm}}{2E_1I_1} dx_{arm} + \int_{L_1}^{L_2} \frac{M_{arm}}{2E_2I_2} dx_{arm} + \dots + \int_{L_{n-1}}^{L_n} \frac{M_{arm}}{2E_nI_n} dx_{arm} + \frac{T_{arm}^2}{2} \left(\frac{L_1}{E_1A_1} + \frac{L_2}{E_2A_2} + \dots + \frac{L_n}{E_nA_n} \right) + \int_0^{L_A} \frac{M_{cup}}{2E_AI_A} dx_{cup} + \int_{L_A}^{L_B} \frac{M_{cup}}{2E_BI_B} dx_{cup} \quad (5)$$

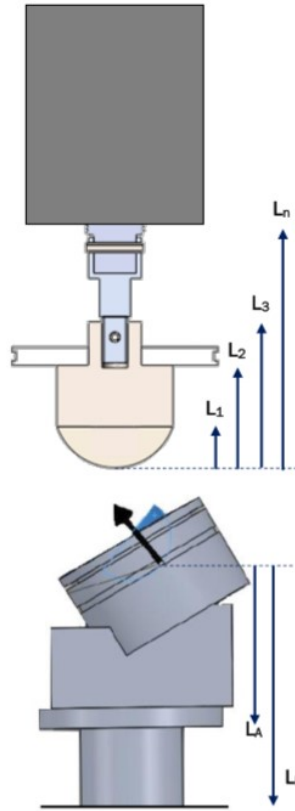


Figure 9-2 Components of the motion arm and cup holder

Evidently, the friction coefficient and horizontal load P are functions of the angle Θ that the main arm makes to the vertical. Therefore, apart from measuring strain, the angular position of the main arm has to be measured as well.