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Mechanical Properties of Retrieved Highly Cross-linked Polyethylene Acetabular Liners in Total Hip Arthroplasty

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Abstract

Highly crosslinked polyethylene (HXLPE) has replaced the conventional ultra-high-molecular-weight-polyethylene (UHMWPE) as the gold standard bearing surface in total hip arthroplasty (THA) due to superior wear characteristics and survivorship. However, HXLPE has demonstrated poorer mechanical properties, in vivo oxidation, and concerns of rim fractures. The purpose of this project was to study the mechanical properties at the rim of retrieved HXLPE acetabular liners.

We developed a simple technique for measurement of hardness at the rim of irradiated, remelted, HXLPE liners of a specific design. The effect of shelf time on mechanical properties of retrieved liners was determined and showed no correlation between hardness with shelf time. Furthermore, hardness testing of retrieved samples showed no correlation between hardness and time in vivo. This suggests that rim fractures in this design of liners are likely not a result of in vivo decline of mechanical properties.

Keywords

Total hip arthroplasty, Highly crosslinked polyethylene, Mechanical properties, Indentation testing, Oxidation, Rim fractures.

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List of Abbreviations

DSI – Depth-sensing indentation

EtO – Ethylene oxide

FTIR - Fourier transform infrared spectroscopy

gf – Gram-force

Gpa – Gigapascals

HXLPE - Highly crosslinked polyethylene

kgf – Kilogram-force

MRad – Megarads

NSAIDs - Nonsteroidal anti-inflammatory drugs

OA – Osteoarthritis

OI – Oxidation index

PTFE – Polytetrafluoroethylene

THA – Total hip arthroplasty

THR – Total hip replacement

UHMWPE - Ultra-high-molecular-weight polyethylene

VH – Vickers hardness

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Chapter 1

1 Hip, Total Hip Arthroplasty and Polyethylene

1.1 Hip Anatomy

The bony hip joint is the articulation of the femoral head into the acetabulum of the pelvis, and is a ball and socket joint. The weight of the head, thorax and upper extremities is transmitted via lumbar spine, sacrum, and ilium to the hip joint[1]. The hip balances these gravitational forces of body weight and the ground reaction forces of the lower extremity throughout a large range of positions. The bony anatomy (Figure 1-1), static (ligaments) (Figure 1-2) and dynamic (muscles) (Figure 1-3) stabilizers around the hip joint help accomplish this task, while preventing dislocation and maintaining efficiency.

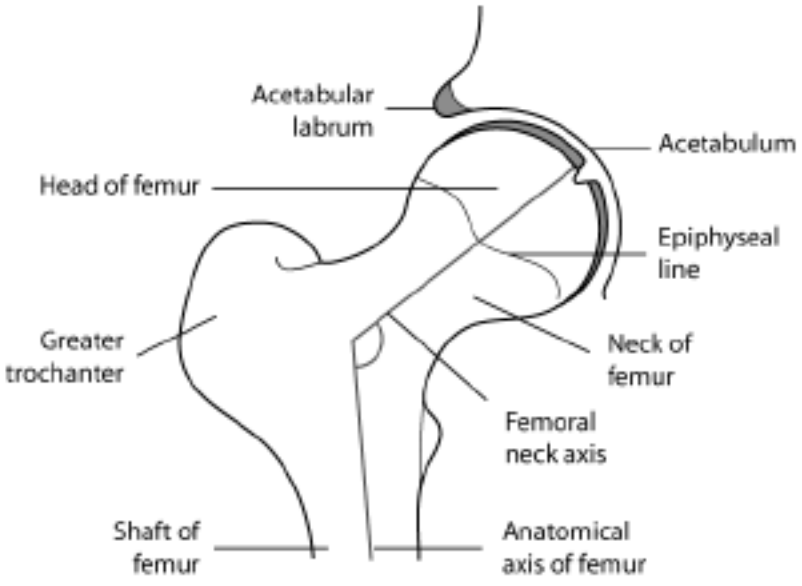

Figure 1-1 - The cross-sectional anatomy of the hip. (Permission from Byrne DP, Mulhall KJ, Baker JF. Anatomy & Biomechanics of the Hip. Open Sport Med J 2010;4:51–7.)

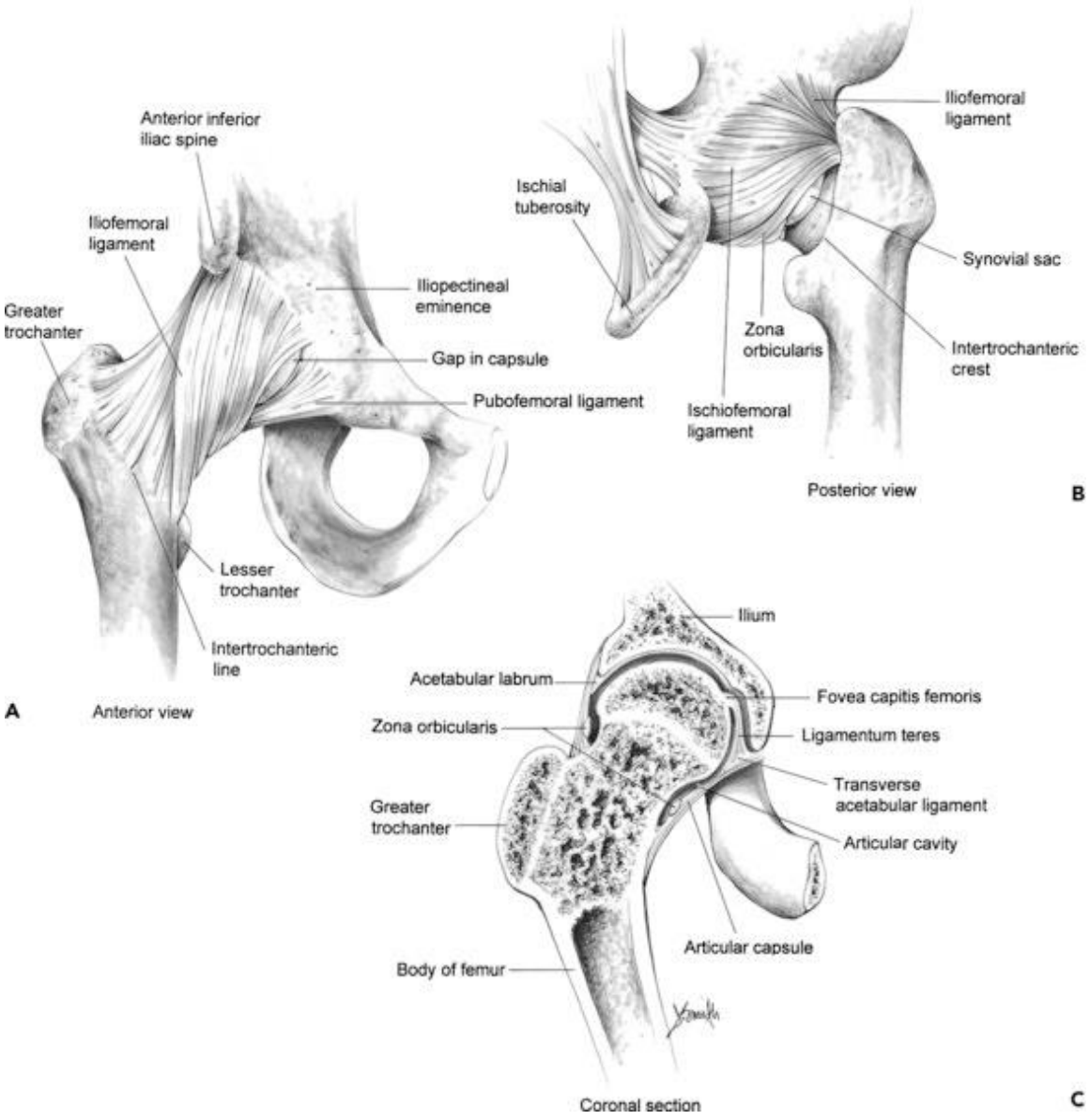

Figure 1-2 - A) Anterior view B) Posterior view C) Coronal section (Permission from Callaghan JJ, Rosenberg AG, Rubash HE, Clohisy J, Beaule P, DellaValle C. The Adult Hip: Hip Arthroplasty Surgery. Wolters Kluwer Health; 2015.)

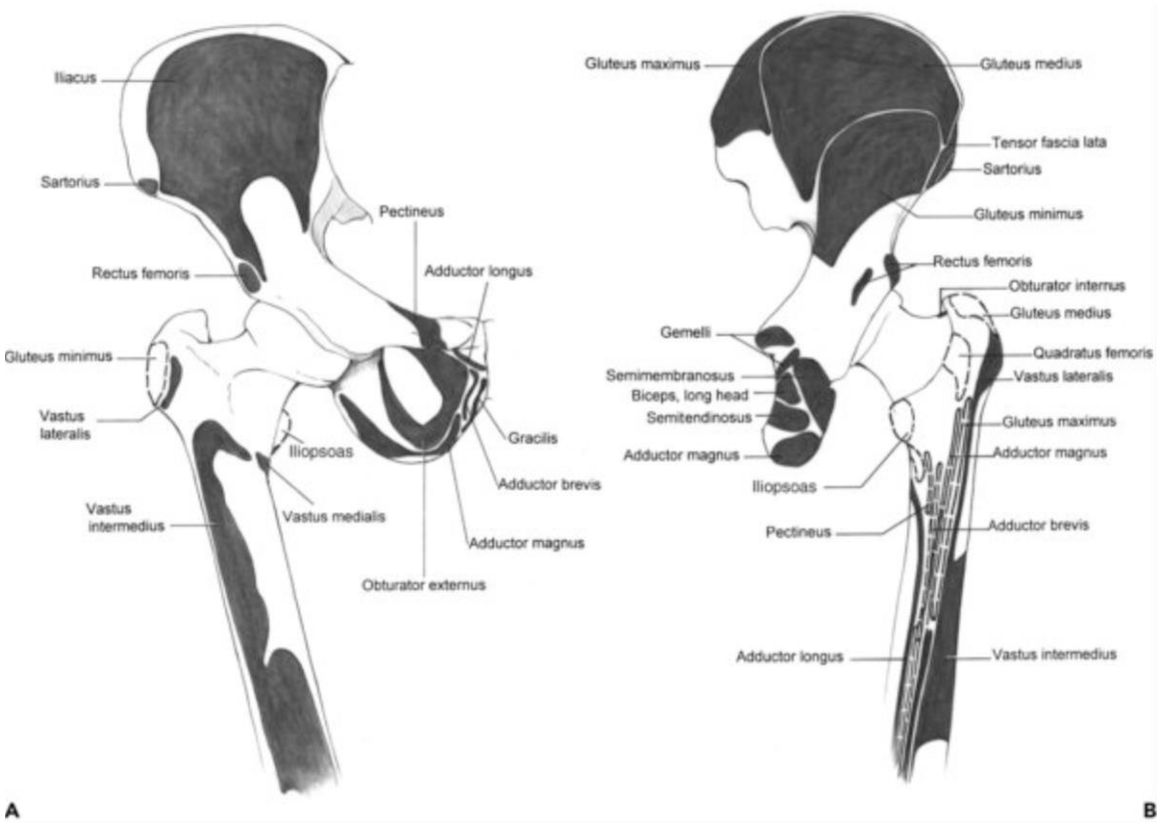

Figure 1-3 - Muscles or dynamic stabilizers around the hip joint A) Intrapelvic and anterior proximal femur B) Extra pelvic and posterior proximal femur (Permission from Callaghan JJ, Rosenberg AG, Rubash HE, Clohisy J, Beaule P, DellaValle C. The Adult Hip: Hip Arthroplasty Surgery. Wolters Kluwer Health; 2015.)

The acetabulum is hemispherical in shape and accommodates a nearly spherical femoral head. Acetabulum has an abduction (inclination) angle (Figure 1-4) of approximately 38 degrees in males and 40 degrees in females in the anterior posterior plane. This allows for abduction of the hip, while limiting its adduction[2]. Moreover, the acetabulum has an approximate anteversion of 16 degrees in men and 19 degrees in women to allow for flexion and to provide posterior coverage preventing dislocation in a flexed position. Furthermore, the ligaments, capsule, labrum and muscles surrounding the hip joint play a substantial role on maintaining stability of the hip joint. During a single leg stance or stance phase of the gait cycle, the hip experiences a downward force exerted by the body weight and the abductors (Figure 1-5). The resultant joint reaction force keeps the pelvis

level and depends on the magnitude of force due to the body weight and the pull of the abductors, and hip center - which can alter the lever arm of each force.

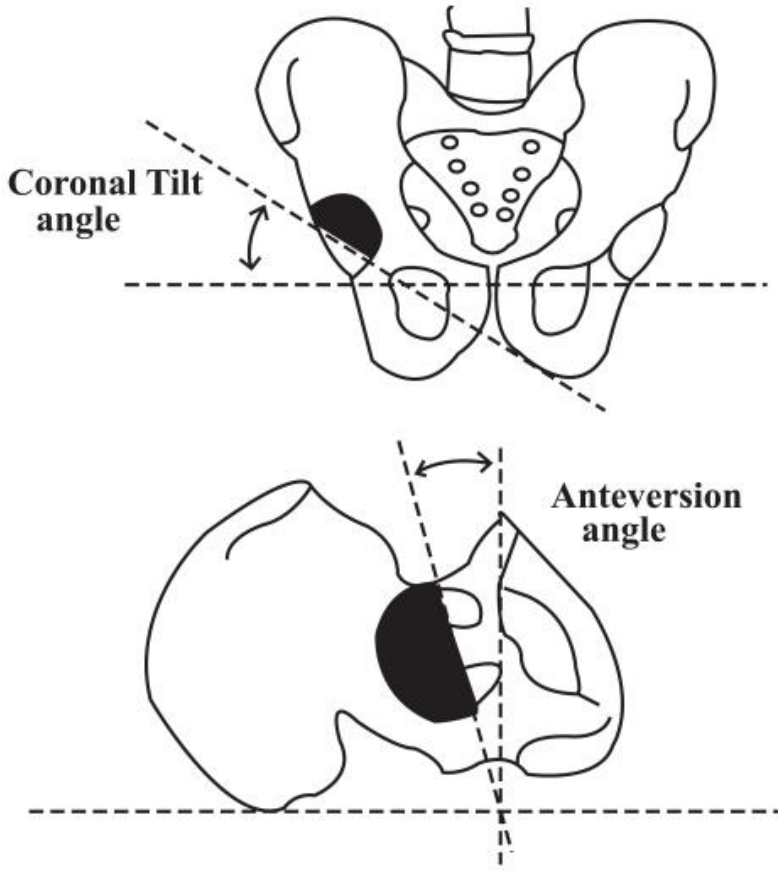

Figure 1-4 - Inclination, abduction or coronal tilt angle demonstrated on the anterior posterior illustration of the pelvis. Anteversion angle demonstrated on the lateral/sagittal illustration of the pelvis. (Permission from Mirza SB, Dunlop DG, Panesar SS, Naqvi SG, Gangoo S, Salih S. Basic science considerations in primary total hip replacement arthroplasty. Open Orthop J 2010.)

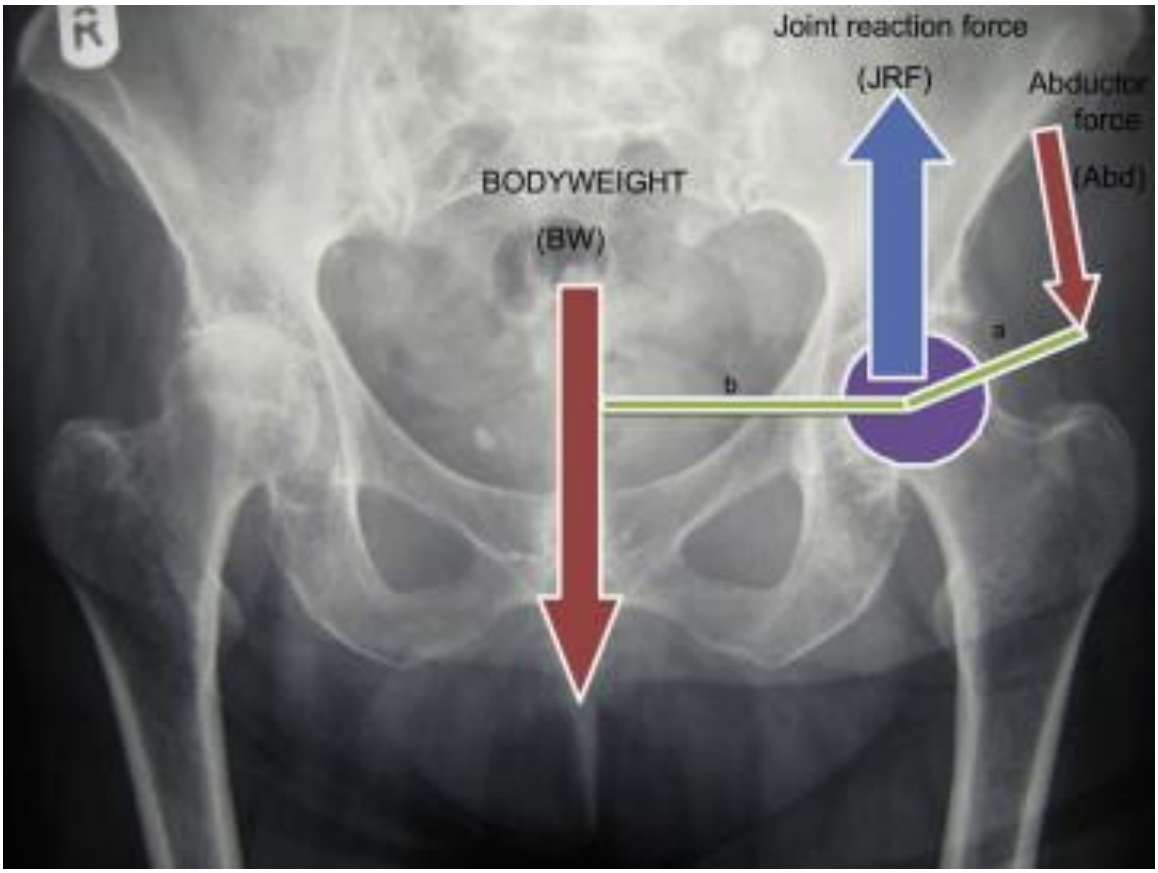

Figure 1-5 - Demonstrated above are the forces of body weight and abductor pull (red arrows) and their direction. Joint reaction force (blue arrow) is the net force experienced by the hip joint and can be influenced by the lever arms a and b depending on the hip/femoral head center. (Permission from Sariali E, Veysi V, Stewart T. MINI-SYMPOSIUM: ESSENTIAL BIOMECHANICS OF HIP REPLACEMENT (i) Biomechanics of the human hip e consequences for total hip replacement. Curr Orthop n.d.;22:371–5. doi:10.1016/j.cuor.2008.10.005.)

1.2 Osteoarthritis

Osteoarthritis (OA) is a disorder of a joint, involving the cartilage, bone, synovium and capsule[1]. Damage to focal areas of the articular cartilage, resulting in loss of volume of cartilage is the hallmark of OA. OA is the most common cause of musculoskeletal pain and disability surrounding the hip. The main risk factor for development of hip OA is age[3]. The treatment of hip OA includes non-surgical and surgical management options[4]. Non-surgical management includes activity modification/physical therapy,

nonsteroidal anti-inflammatory medications (NSAIDs) and intra-articular corticosteroids. Failure of non-surgical management is the prime indicator for surgical intervention in the setting of painful and debilitating OA. Total hip arthroplasty (THA) is the operation of choice for the treatment of hip OA in most of the patients.

1.3 Total Hip Arthroplasty

Low Friction total hip arthroplasty (THA) was first performed by Sir John Charnley in 1962 for treatment of arthritic conditions of the hip[5]. The indications for THA, as reported by Charnley, included primarily advanced osteoarthritis and rheumatoid arthritis, and secondarily ankylosing spondylitis, femoral neck fractures and Paget's disease of the bone[5]. The goals of the surgery involve improvement of pain and function while restoring normal anatomy, biomechanics and kinematics of the hip joint.

Metal femoral head on ultra-high-molecular-weight-polyethylene (UHMWPE) acetabular liner has been the most common bearing surface in THA (Figure 1-6). In THA, the acetabular cartilage is replaced with a hemispherical metal acetabular shell which fits into the patient's acetabulum. A UHWMPE polyethylene liner is locked into the acetabular metal shell. On the femoral side, the native head is removed and a metal stem is inserted into the intramedullary canal of the femur. A metal head is placed on to the neck portion of the stem. The modularity in the modern components gives multiple options to match the patient's anatomy and restore function. From a fixation standpoint, cementless and cemented fixation options exist for the acetabular shell and the femoral stem. Cementless fixation is preferred for young patients with good bone quality, while cemented fixation is used for older patients with osteopenic/osteoporotic bone.

The placement of the components in the proper orientation, restoration of leg length and offset of the hip has implications in restoring function and determining longevity of the hip replacement. The considerations in component placement on the acetabular side and the femoral side and their impact are discussed below.

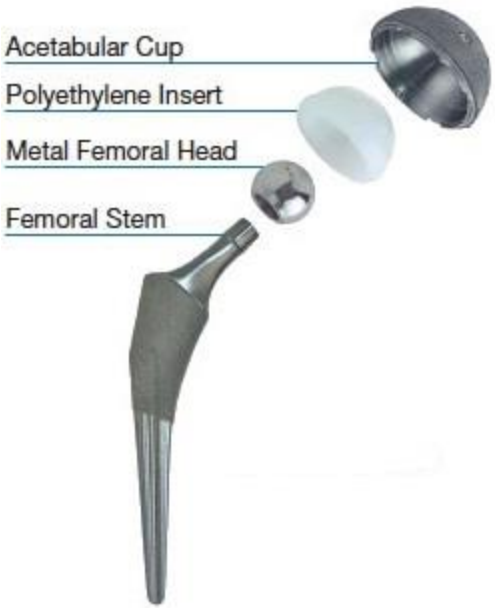

Figure 1-6 - Metal on polyethylene total hip replacement. (Permission from Total Hip Arthroplasty (THA). OrthopaedicsOne Clerkship. In: OrthopaedicsOne - The Orthopaedic Knowledge Network. Created Dec 13, 2010 21:12. Last modified Dec 14, 2010 09:10 ver.3. Retrieved 2017-06-01, from http://www.orthopaedicsone.com/x/-oDYAg.)

1.3.1 **Acetabulum**

The acetabular component position can influence center of rotation of the articulating femoral head. The center of rotation of the femoral head should be restored to its pre-disease position, usually by medial positioning of acetabular shell. This effectively increases the lever arm of the abductors, decreasing joint reactive forces, ultimately resulting in decreased wear of the UHMWPE liner. The abduction angle is chosen to match the patient's anatomy of around 40 degrees to maximize the range of motion. The more vertical placement or increased abduction angles can result in edge loading of the acetabular component and decreased range of motion before impingement (Figure 1-7). Excessive anteversion can result in impingement of the prosthetic neck on the posterior side of the acetabular rim during extension and external rotation, resulting in anterior dislocation (Figure 1-7). Conversely, inadequate restoration of anteversion of the

acetabular component leads to neck impingement on the anterior acetabular rim during flexion and can result in posterior dislocation.

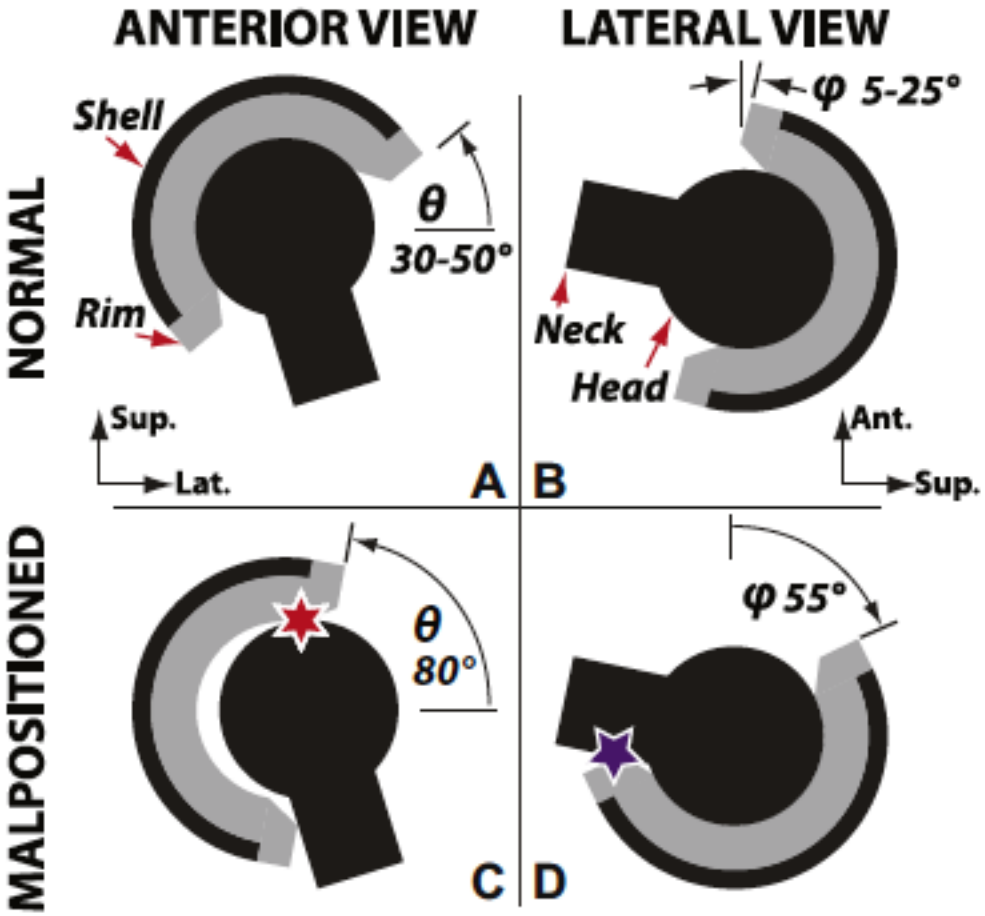

Figure 1-7 - A and B show an acetabular component with normal abduction and anteversion angle respectively. C and D show an excessively abducted and anteverted acetabular component. (Permission from Furmanski J, Anderson M, Bal S, et al. Clinical fracture of cross-linked UHMWPE acetabular liners. Biomaterials. 2009;30(29):5572-5582.)

1.3.2 **Femur**

Femoral neck anteversion, which is the rotation of the neck about the femoral shaft, must be considered and restored. This preserves the flexion and internal rotation of the hip prior to impingement of the prosthetic neck on the acetabular rim. A relative retroversion

can result in impingement of the neck with the anterior acetabular rim and result in posterior dislocation of the femoral head from the acetabulum. Conversely, a relative excessive anteversion can lead to impingement of the prosthetic neck with posterior acetabular shell during extension and external rotation of the hip resulting in an anterior dislocation.

Femoral offset is defined as the distance between the center of the femoral head and the long axis of the femur. Restoration of offset is important in hip biomechanics by appropriate tensioning of the abductor muscles (Figure 1-8).

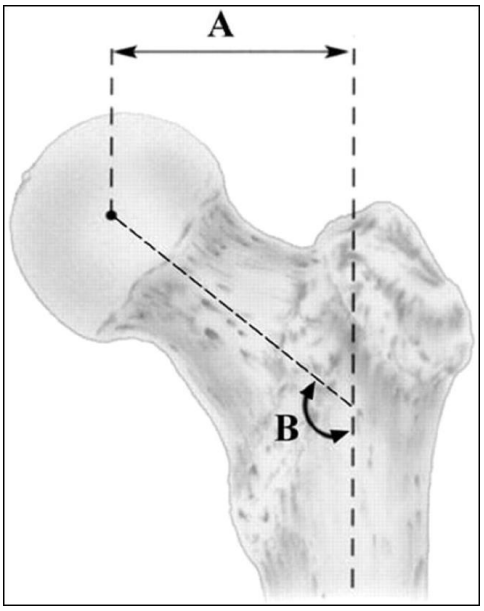

Figure 1-8 - Femoral offset is represented by the perpendicular distance "A" from the center of the femoral head to the long axis of the femur. The neck-shaft angle is represented by angle "B," which subtends the long axis of the femoral neck and the long axis of the femoral shaft. (Permission from Charles M, Bourne R. Soft-tissue balancing of the hip. J Bone Jt Surg 2004;86:1078–88. doi:10.1054/arth.2002.33263.)

The head to neck ratio, which is the ratio between the diameter of the prosthetic head and neck, is another important factor to consider. The increase in head diameter relative to the neck increases the jump distance before dislocation, reducing the incidence of dislocation (Figure 1-9). However, this comes at the expense of increasing volumetric wear of UHMWPE with increased head surface area articulating against the acetabular liner.

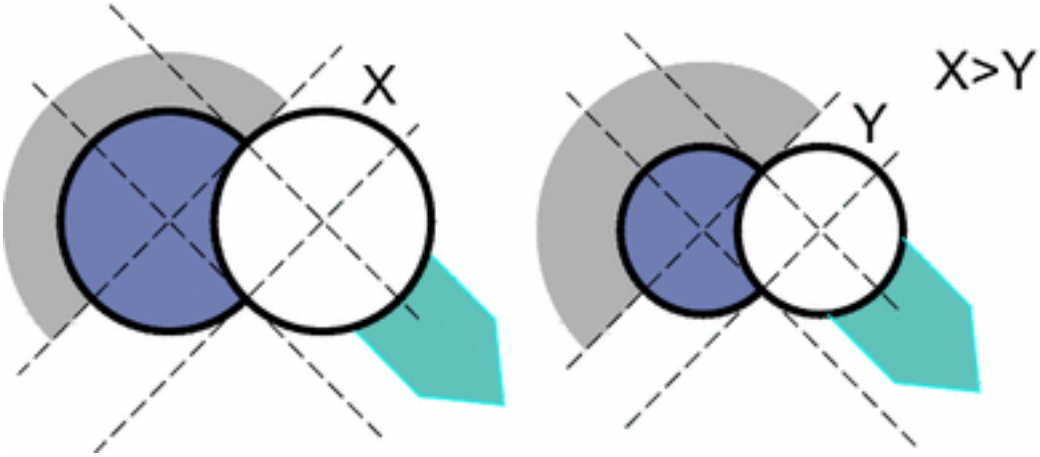

Figure 1-9 - Demonstrated above is the increase in jump distance with an increase in femoral head size. (Permission from Veitch SW, Jones SA. (v) Prevention of dislocation in hip arthroplasty. Orthopaedics and Trauma 2009 200902;23(1):35-39.)

While THA has been extremely successful clinically in improving quality of life and function[6–9], the revision THA burden has continued to rise[10–13]. The clinical failure of THA, and thus the increased need for revision THA, has been a result of surgery in younger patients, active population, and issues with implant longevity[13]. Despite the established cost effectiveness of performing THA[14], the increasing number of revisions is placing a tremendous clinical and economic burden on the healthcare system[10,13,15]. The most common causes for revision surgery has been reported as aseptic loosening, instability/dislocation and infection[10,16,17]. Registry data from Europe has suggested that aseptic loosening, bearing surface wear and osteolysis comprise the majority of the reasons for revision[18].

Wear of conventional UHMWPE and the reactivity of the generated wear particles in vivo has been the major player in osteolysis and aseptic loosening in THA[19,20]. The polyethylene debris generated because of wear leads to macrophage induced osteolysis via a complex inflammatory cascade. Osteolysis results in aseptic loosening of the hip implants from implant bone interface, leading to revision THA.

In an effort to reduce wear and osteolysis, highly cross-linked UHMWPE (HXLPE) was developed in 1990s[21]. Since the inception of HXLPE, the wear rates and incidence of osteolysis have significantly decreased[22–25]. Furthermore, the revision THA rates with HXLPE are lower than the conventional UHMWPE[23,26,27].

Development of HXLPE and the lower wear rates comes with a compromise of mechanical properties of polyethylene[21,28]. Formation of cross-linking requires irradiation of UHMWPE, thereby reducing its mechanical strength to failure[28]. In addition, concerns have developed regarding further degradation of mechanical properties with time in vivo, as a result of oxidation[29–32]. Numerous case reports have been published reporting fractures of the polyethylene at the rim of the polyethylene liners[16,33–35] (Figure 1-10). Increasing head sizes, to minimize dislocation, and subsequent use of thinner HXLPE acetabular liners has been named a contributing factor. Furthermore, increased susceptibility to in vivo degradation of HXLPE liners, and further compromise of mechanical properties raises significant concerns of implant longevity in THA[29–32].

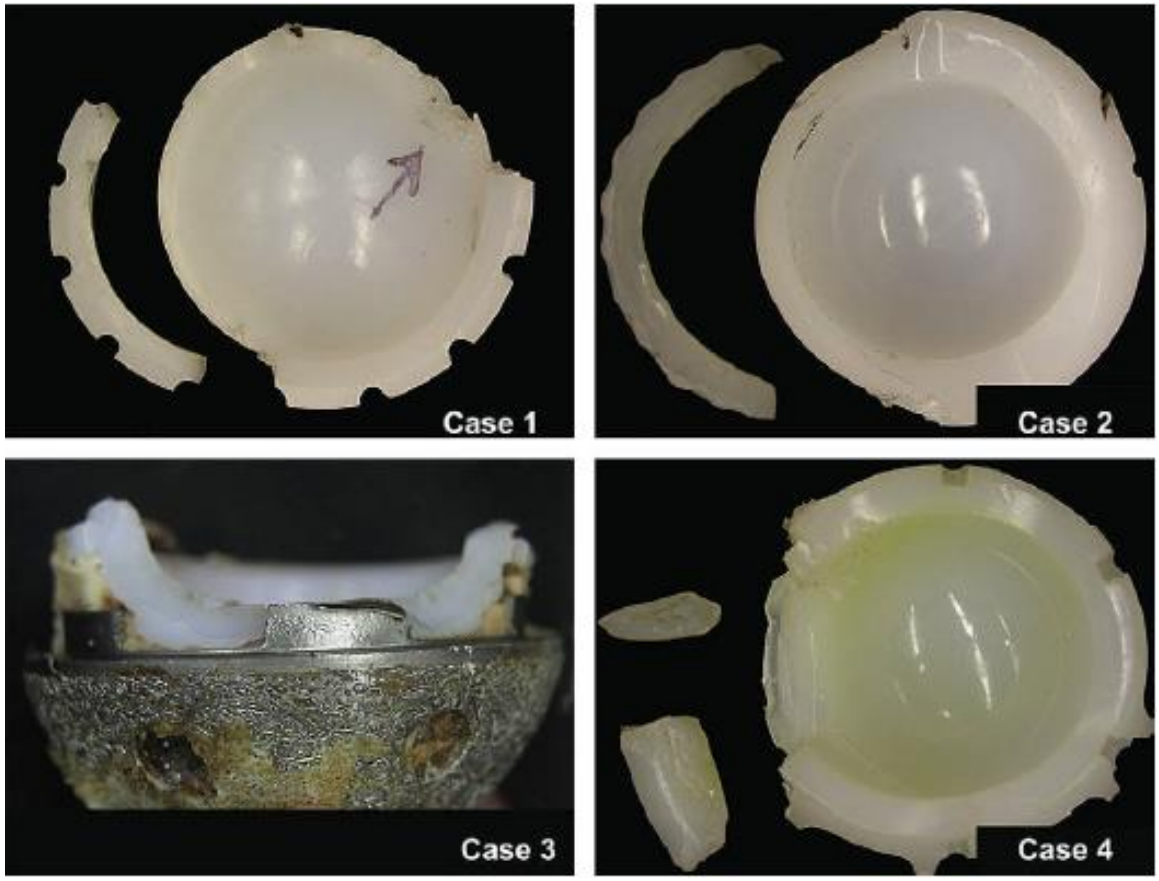

Figure 1-10 - Demonstrated above are the fractures at the rim of HXLPE liners. (Permission from Furmanski J, Anderson M, Bal S, et al. Clinical fracture of cross-linked UHMWPE acetabular liners. Biomaterials. 2009;30(29):5572-5582.)

1.4 Research Objectives and Impact

With the overall aging population, maximizing implant longevity in THA is especially important. OA accounts for 93% of the THA procedures[36], with the main risk factor for development of OA being age[37]. Globally, the number of persons aged 60 and above is expected to more than double by 2050 and more than triple by 2100, increasing from 901 million in 2015 to 2.1 billion in 2050 and 3.2 billion in 2100[38].

This will result in an increasing incidence of OA and a higher need for THA[39–41]. Over 1 million THA are performed worldwide and this number is expected to double in the next two decades[36]. In the United States, the number of THA is projected at 572,000/yr by 2030[12]. Per the Canadian joint registry data there has been a 19%

increase in the number of THA performed as compared to 5 years ago[42]. Additional implant retrieval studies, to understand the impact of in vivo degradation of HXLPE, are necessary to improve implant longevity, as the number of THAs performed continues to rise.

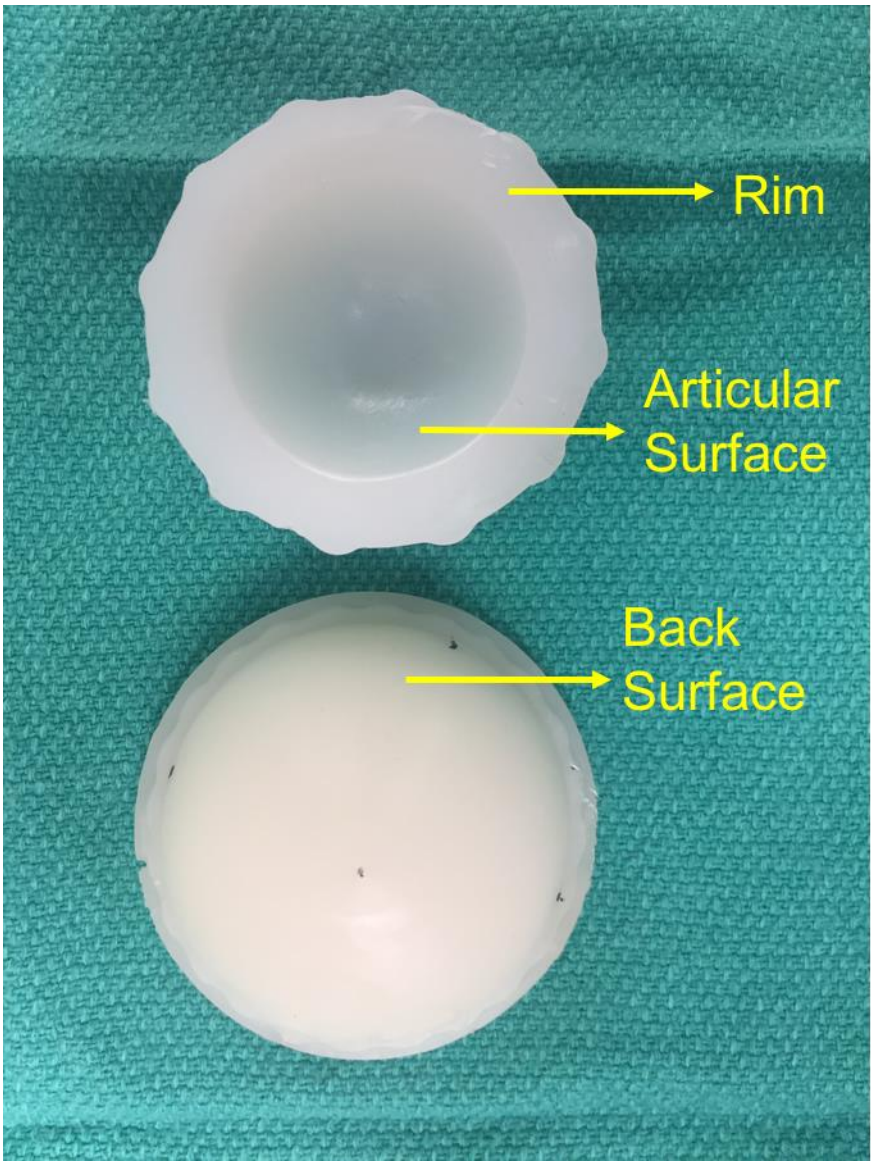

Figure 1-11 - Different regions of the polyethylene liner are labeled.

The objective of this masters is to better our understanding of the fractures at the rim (Figure 1-11) of the HXLPE liners. Implant retrieval analysis have shown clear evidence of oxidation at the rim of HXLPE acetabular liners with increasing time in vivo.

However, no studies have investigated the mechanical properties at the rim of the HXLPE after time in vivo. Some retrieval studies have reported on preservation of mechanical properties at the articular surface and backside of the HXLPE liners with increasing in vivo time. In this masters, we will develop a way of testing mechanical properties at the rim of the HXLPE liners. Furthermore, we will test the mechanical properties of retrieved HXLPE acetabular liners with varying in vivo times to investigate the impact of in vivo time on mechanical properties. This will help with the understanding of mechanical failures of HXLPE acetabular liners at the rim.

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Chapter 2

2 Clinical performance of highly cross-linked polyethylene in total hip arthroplasty, a literature review

2.1 Introduction

Total hip arthroplasty (THA) has been termed "The operation of the century" for its excellent improvement in pain and function of patients with end-stage arthritis[1]. An ultra-high-molecular-weight polyethylene (UHMWPE) liner articulating against a metal femoral head has been the predominant bearing surface in THA. Despite the clinical success, the longevity of THA using conventional UHMWPE is limited due to polyethylene wear, and the resultant osteolysis and aseptic loosening[2]. This led to the development of a highly cross-linked polyethylene (HXLPE) [3]. Since the adoption of HXLPE for THA in the early 2000s, a significant decline in polyethylene wear, osteolysis and wear related revisions has been reported[4–8]. However, irradiation and thermal treatment utilized in manufacturing of HXLPE leads to reduced mechanical properties of polyethylene [3,9]. In addition, presence of free radicals in irradiated annealed HXLPE predispose it to oxidation, further compromising its mechanical properties[10]. With case reports of fractures at the rim of the polyethylene liners, concerns related to mechanical properties and oxidation of first-generation (irradiated melted and annealed) HXLPE liners led to the development of second-generation (sequentially annealed, mechanically annealed, and vitamin-E containing) HXLPE [10–13].

The projected increase in demand of primary and revision THA warrants continued efforts to improve implant longevity[14] – especially since the number of younger and active patients undergoing THA is increasing[15]. Furthermore, revision THA poses a significant clinical and economic burden [16]. In this review, we will discuss the evolution of polyethylene, manufacturing processes, mechanical properties and clinical performance of HXLPE to date.

2.2 Methods

We performed a comprehensive literature search using PubMed and Medline. The keywords “hip”, “arthroplasty”, “crosslinked”, “polyethylene”. The terms/phrases “wear”, “osteolysis”, “revision”, “oxidation”, “mechanical properties. Studies from 2000 to 2016 were included. Study titles and abstracts were reviewed to ensure relevant and high-quality literature was included. Articles prior to 2000 were included if they provided relevant background information. Furthermore, “UHMWPE Biomaterials Handbook”, 3rd edition, by Kurtz was utilized for background information[17].

2.3 Conventional UHMWPE

2.3.1 Introduction

Contemporary THA, as started by Charnley, used metal on polyethylene as the bearing surface. Charnley initially (1958-1962) picked polytetrafluoroethylene (PTFE) as the bearing surface on the acetabular side due to its general chemical inertness and its low coefficient of friction[18]. PTFE acetabular cups failed early in 1-2 years secondary to low resistance to creep deformation of the PTFE resins and relatively poor abrasive properties[18,19]. Poor wear characteristics and clinical failure of PTFE led to use of alternative materials[19,20]. In 1962, UHMWPE was introduced to Charnley’s technician Craven, who tested the material in a self-designed wear tester with encouraging results[19,21]. The first hip made of UHMWPE was implanted in November 196219. As Charnley reported his outcomes in 1975, measurable wear rates up to 0.18 mm/year were reported in the first five years, and 0.10 mm/year for the next 5-10 years of implantation[18].

2.3.2 Evolution of polyethylene

In an effort to reduce wear, attempts were made to replace UHMWPE. Between 1970 and 1986, two new materials, polyacetal and Poly Two, were the most clinically relevant materials used to make acetabular cups[19,20]. However, due to early failure, the use of these was abandoned shortly after introduction[19,20]. Hylamer, a polyethylene with increased crystallinity, was introduced in 1990s with improved mechanical properties by

Depuy Orthopaedics[19]. Only 2 years after implantation, the wear rates in vivo were found to be unacceptable in THA, and it was discontinued[21].

Meanwhile, it was not until the 1990s that osteolysis was identified as a direct result of macrophage induced process from exposure to UHMWPE wear particles[22]. This led to increased efforts to understand the process of UHMWPE manufacturing[23]. Through these efforts, the deleterious effects of oxidation of UHMWPE from gamma sterilization in air were discovered[24], and led to the introduction of sterilization using ethylene oxide, gas plasma and gamma irradiation in an inert environment . In vitro studies demonstrated increased wear rates in conventional UHMWPE that were sterilized using ethylene oxide and gas plasma, as the cross-linking induced by sterilization in gamma irradiation in air was lost[25,26]. This led to the development of HXLPE in the late 1990s.

2.4 HXLPE

2.4.1 Introduction

The inception of HXLPE in THA in the late 1990s has led to a considerable decline in wear rates. Revision rates of THA when comparing conventional UHMWPE and HXLPE has shown a clear advantage since the routine use of the latter. Sterilization of conventional UHMWPE required 2.5-4.0 megarads (MRad) of gamma irradiation. However, cross-linking is induced in HXLPE using an irradiation dose between 5-10 MRad, which compromises its mechanical properties (discussed later). Moreover, formation of reactive species or free radicals increased the susceptibility of the HXLPE to oxidation after exposure to the environment or in vivo bodily fluids, with further deterioration of mechanical properties. Thermal processing was developed as a step in HXLPE production to reduce or remove the free radicals by annealing or remelting the irradiated HXLPE, respectively. Thermal processing led to further degradation of mechanical properties by inducing alterations in the microstructure of polyethylene. This led to the development of antioxidant stabilized, mechanically annealed, and sequentially annealed, second generation HXLPE – which will be discussed in further detail later. While case reports from mechanical failure of first generation HXLPE have been

published, this has largely been postulated to be a multifactorial problem. No reports of mechanical failure of second generation HXLPE have been published since its inception in 2005.

2.4.2 **Manufacturing**

2.4.2.1 **Overview**

To fully understand the chemical, mechanical and, thus clinical behavior of the polyethylene, one must understand the manufacturing process of UHMWPE. UHMWPE is a linear, semi crystalline polymer (45-65% crystallinity) with a molecular weight in the range of 4-6 million g/mol, and exist in crystalline and amorphous states[17](Figure 2-1). Its chemical inertness, lubricity, impact resistance, and abrasion resistance make it an excellent choice for use in total hip arthroplasty. Manufacturing of a finished UHMWPE implant requires three steps, which are generally carried out by three different highly specialized processes. First, UHMWPE powder or resin is polymerized from ethylene gas by polymer resin producers. Second, the powder is consolidated into a sheet, rod, or near-shape of the implant. Third, implant is machined into its final shape [27]. The overview of manufacturing process of conventional and various HXLPE is shown in Figure 2-2.

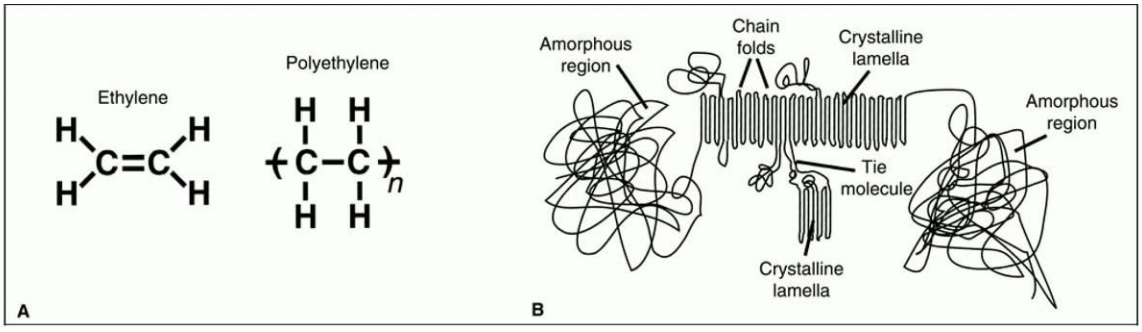


Figure 2-1 - A. Molecular structure of the monomer ethylene; B. The structure of UHMWPE, showing the crystalline and amorphous states, and crystalline lamellae. (Permission from Kurtz SM, 1 - A Primer on UHMWPE, In UHMWPE Biomaterials Handbook (Third Edition), William Andrew Publishing, Oxford, 2016, Pages 1-6.)

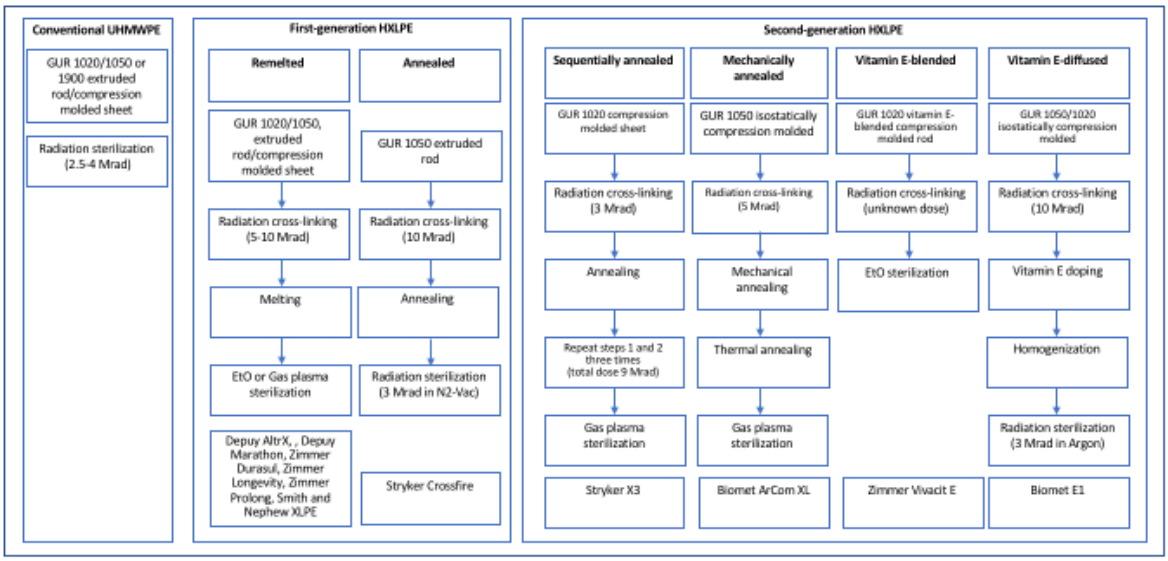


Figure 2-2 - Schematic depiction of manufacturing of UHMWPE in THA. (Modified with permission from Oral E, Muratoglu OK. Vitamin E diffused, highly crosslinked UHMWPE: a review. Int Orthop 2011; 35: 215–23.)

2.4.2.2 Resins

HXLPE implants used currently are fabricated out of three resins – GUR 1020, GUR 1050 and 1900H – which differ based upon their molecular weight and producer[27]. The condensed UHMWPE contains amorphous and crystalline regions, and the percentage and distribution of each can influence its properties and this can be affected by its resin type[28]. 1900H resin is no longer produced but stocks of this resin has been stored by some manufacturers and this may continue to be used[27,28]. Although variations in mechanical properties exist in terms of resin type used to manufacture an implant, no consensus is present as to which resin type is superior in terms of clinical performance[27].

2.4.2.3 Conversion from resin to bar or sheet

The resin is first converted into a molded-sheet, ram extruded bar or a preliminary implant with direct compression molding. The mechanical properties of the product can

vary based on the temperature, pressure and cooling rate used in this process[28]. Based on a survey conducted of commercial suppliers, differences in conversion method were found to influence impact strength and the tensile mechanical properties when comparing implants made out of GUR 1050 and 1020 resins[27].

2.4.2.4 First-generation HXLPE

In the production of HXLPE implants, the converted preliminary product undergoes irradiation treatment with either gamma radiation or electron beam with various doses ranging from 5-10 MRad depending on the manufacturers. The details of this process much like other manufacturing processes are largely proprietary. The amount of irradiation dose increases the amount of cross-linking and improves wear resistance, but the amount of cross-linking plateaus around 10 MRad to maintain tensile strength and fatigue properties[3]. Both gamma and electron beam irradiation have been accepted techniques and do not show relevant differences in wear rates[29].

The gamma irradiation process is slow but easily accomplished, the dose is expected to be uniform throughout the thickness of the polyethylene. Conversely, electron beam requires much shorter duration, but the depth of penetration is limited and sectioning of the material may be necessary. A much higher dose is typically necessary for electron beam irradiation and results in considerable heating of polyethylene. Therefore, the steps of cross-linking by electron beam irradiation and thermal processing (annealing or remelting) can be performed simultaneously[30].

Thermal processing of the irradiated material is then carried out to extinguish free radicals by mobilizing them through the cross-linked regions of the polyethylene[3]. Heating of the irradiated polyethylene below the melting temperature (~137°C) is known as annealing whereas above that is known as remelting. The choice of thermal processing affects the crystallinity, mechanical properties, radical content, resistance to in vivo oxidation[29].

Machining of the cups is then performed followed by terminal sterilization. Terminal sterilization can be carried out chemically using gas plasma or ethylene oxide (EtO), or

using gamma irradiation in an inert environment. Chemical sterilization produces no detectable free radicals whereas gamma irradiation can reintroduce free radicals and increase susceptibility to oxidative damage[31].

2.4.2.5 Second-generation HXLPE

Second-generation HXLPEs include mechanically annealed, sequentially annealed and antioxidant-stabilized liners, and were developed to improve the oxidation resistance and mechanical properties of the first generation HXLPE. Stryker Inc. introduced sequentially irradiated and annealed HXLPE called X3, which was cleared in 2005 for use by the FDA. GUR 1020 compression molded sheet was chosen for its production. Irradiation and annealing is performed in three repeating steps, in which 3 MRad of radiation is used for irradiation followed by annealing for 8h at 130 C, resulting in cumulative dose of 9 MRad. The three steps were shown to provide a desired balance between cross-linking and material properties. Following the sequential irradiation and annealing, the components are machined, and packaged for gas plasma sterilization[32].

ArCom XL Polyethylene is the only mechanically annealed second generation HXLPE which was introduced in 2005 for application in THA by Biomet Inc. Mechanical deformation is used to enhance mechanical properties during the manufacturing process. Isostatically molded compression molded GUR 1050 rods are used as the starting stock material. Cross-linking is performed at room temperature using 5 MRad of gamma irradiation. Mechanical deformation is performed by heating just below the melting point to 130 C, and followed by ram extrusion with diametral compression ratio of 1.5. The rod is heated again to annealing temperature to relieve residual stresses. Final machining into components is carried out, followed by gas plasma sterilization[33].

Vitamin-E stabilized HXLPE was introduced to provide oxidation resistance without compromising the fatigue strength, as a result of oxidation in annealed liners and decreased crystallinity in melted liners[34]. Vitamin E can be introduced in HXLPE in two ways.

Vitamin E-blended HXLPE is produced by mixing the liquid antioxidant with the UHMWPE resin and consolidating the mixture by compression molding, followed by irradiation of the consolidated blend. However, vitamin E acts as a radical scavenger and decreases the cross-linking efficiency of UHMWPE. This limits the vitamin E concentration that can be used, and increases the radiation dose required for effective cross-linking. Vivacit-E, introduced by Zimmer in 2012, is produced by blending GUR 1020 resin with vitamin E followed by compression molding. Warm e-beam irradiation is then performed for cross-linking with an undisclosed amount of dose. No thermal processing is performed. The molded sheets are then machined into components, followed by packaging and ethylene oxide sterilization[35].

The second approach of introducing vitamin E involves diffusion into an already irradiated and cross-linked UHMWPE, circumventing the issues of vitamin E dose that can be used and the cross-linking efficiency. E1 polyethylene, introduced by Biomet in 2007, is produced by this method. Crosslinking of GUR 1050/1020 resin is carried out with approximately 10 MRad of gamma irradiation. This is followed by diffusion of vitamin E by soaking the irradiated HXLPE in a vitamin E at an elevated temperature below the melting point with subsequent homogenization at an elevated temperature below the melting point – both performed in an inert environment. A high temperature during the diffusion and homogenization has a secondary effect on decrease of free radical concentration in the material[36]. Sterilization is performed with gamma irradiation in Argon with a 3 MRad dose[36].

2.4.3 **Clinical Performance**

2.4.3.1 **Wear Rates**

Numerous reports have shown significant decrease in wear rates with metal on first generation HXLPE as the bearing surface compared to UHMWPE [6,37–47]. Kurtz et al[39], in a systematic review of 28 studies, showed that at minimum 5-year follow-up, HXLPE was consistently reported to have lower wear rates and an 87% lower risk of osteolysis. A meta-analysis of 1038 total hip replacements (THR) from 12 randomized controlled trials by Kuzyk et al[40], at a mean follow up of 5.1 years (Range 2.3 – 8

years) showed decreased linear and volumetric wear rate in patients with HXLPE versus conventional UHMWPE. In a double blind randomized controlled trial, Thomas et al[43] showed that, at a minimum of 7 years postoperatively, the mean total femoral head penetration was significantly lower in HXLPE group than UHMWPE (0.33 mm versus 0.55 mm). The mean steady-state wear rate of HXLPE was 0.005 mm/yr, compared with 0.037 mm/yr for conventional UHMWPE. There were no patients in the HXLPE group that had a wear rate above the osteolysis threshold of 0.1 mm/yr, whereas 9% of patients were above this threshold in the conventional group. Glyn-Jones et al[6] showed, in a double randomized controlled trial, that the volumetric femoral head penetration from 1-10 years for the UHMWPE was 98 mm3 compared with 14 mm3 for HXLPE (p=0.01). Bragdon et al[45], in a multicenter retrospective analysis of 2991 THRs, showed that at minimum 7-10 year follow up HXLPE continued to demonstrate low femoral head penetration rate/yr as opposed to historical controls of UHMWPE, which demonstrated increased wear/yr with in vivo time.

2.4.3.2 **Osteolysis**

Osteolysis is a result of a complex inflammatory cascade, resulting from activation of macrophages in presence of wear particles, with the resultant bone resorption leading to aseptic loosening[22,48]. Although it has been established that as increased wear rates are associated with higher incidence of osteolysis[49,50], given the complex mechanism, the association of wear rate of HXLPE and osteolysis may not be as clear. While the wear rates in hips with HXLPE are much lower, there is a concern that the smaller wear particles produced from HXLPE might be biologically more active and may result in a higher incidence of osteolysis[51,52]. Thus, the lower wear rate may not correlate with decreased osteolysis, and ultimately reduced incidence of failure due to aseptic loosening. Despite these theoretical and in vitro concerns, a decreased incidence of osteolysis has been reported since the introduction of HXLPE in multiple studies [4,5,40–42,45,46].

2.4.3.3 **Revision Rate**

Despite the established benefits demonstrated in revision rates due to wear rates and osteolysis with HXLPE, the improvements in overall revision rates are not as clear. The

Austrailian Joint Replacement Registry demonstrated a reduced revision rate with HXLPE[53]. Paxton et al[7], using the data from Kaiser Permanente's Joint Registry showed that, at 7 years follow up, metal-on-conventional UHMWPE had an incidence of 5.4% as opposed to 2.8% for metal-on-HXLPE. Lachiewicz et al[4] reported on a single surgeon, and single implant experience, at minimum 10 year follow up, decreased reoperation risk with HXLPE compared with conventional UHMWPE (1% vs 13%, p =0.03). More recently, Hanna et al[54] showed that at minimum 13 year follow up, for patients aged 45-65 years, with revision for polyethylene wear as the end point, an implant survivorship of 86% for conventional UHMWPE as opposed to 100% for HXLPE. In contrast, in a meta-analysis report of combined results of six international registries in patients with cementless fixation, and ages 45-64 years, it was reported that metal-on-HXLPE does not reduce the risk of revision compared to metal on conventional UHMWPE for this subgroup of patients[8]. Inconclusive evidence on revision rates, in combination with case reports of rim fractures and degradation of HXLPE in vivo, further raises concerns about future performance of HXLPE as a bearing surface in THA.

2.4.3.4 Reports on Mechanical Failure

Multiple reports have been published in peer-reviewed journals showing impending or complete fractures resulting in failures of HXLPE liners near the rim[11–13,55–58] (Figure 2-3). Tower et al[11] examined four Longevity (Zimmer) acetabular liners retrievals after 7-27 months in vivo and noted cracking or rim failure at the superior aspect along the groove in the polyethylene that engages the locking ring of the shell. They concluded that failure was due to thin polyethylene at the cup rim, relatively vertical cup alignment, and the diminished material properties of HXLPE. Furmanski et al[13] reported on nine Longevity retrieved liners retrievals and observed six out of the nine liners had initiated cracks at the root of the rim notches, and postulated the loading of the unsupported and notched rim put these implants at a higher risk of crack propagation. Decreased resistance to fatigue crack propagation of HXLPE, implant design factors such as notches, locking mechanisms and unsupported rim, as well as edge loading and impingement have been postulated to factors resulting in these failures[58].

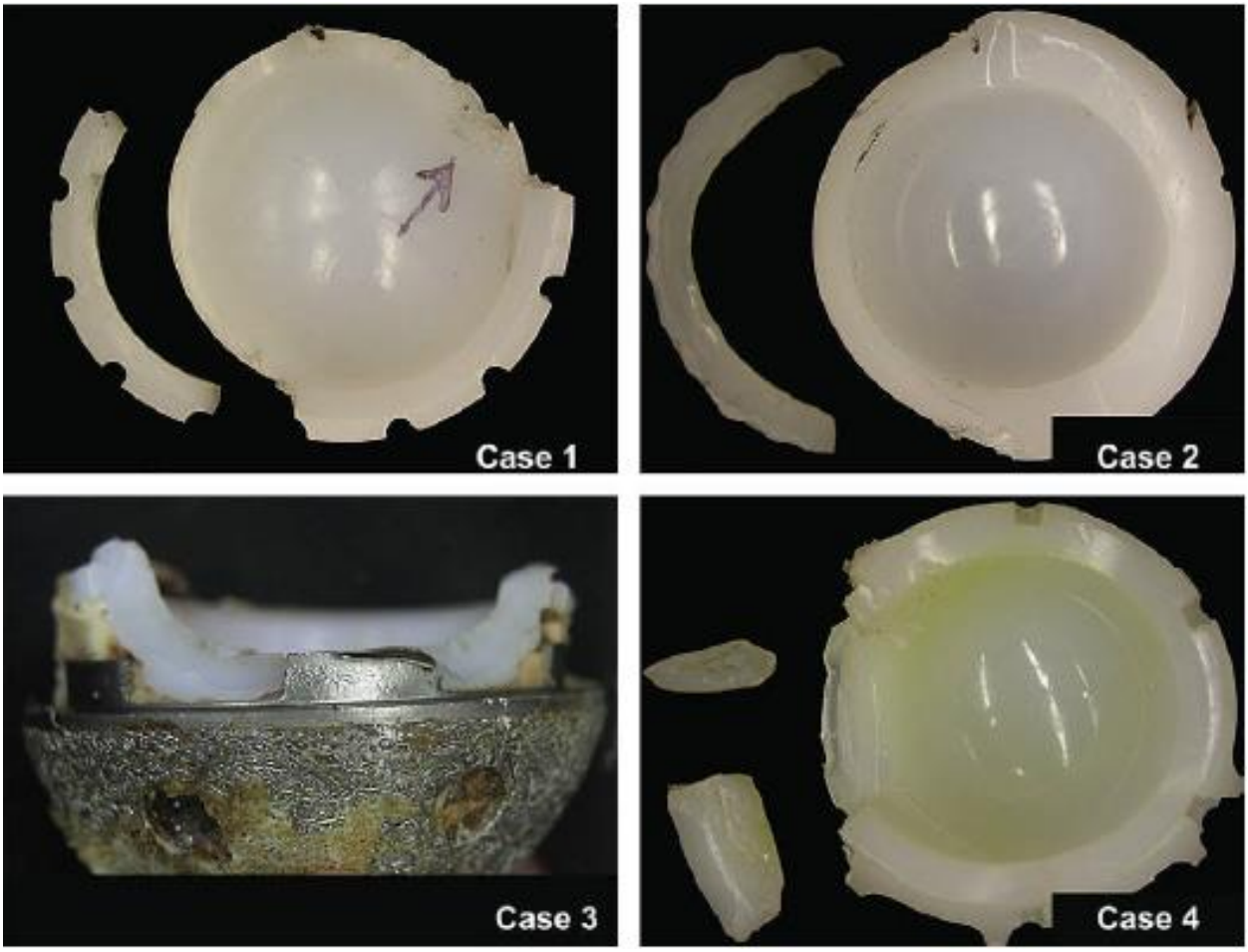


Figure 2-3 - Pictures demonstrating fractures of HXLPE liners (Permission from Furmanski J, Anderson M, Bal S, et al. Clinical fracture of cross-linked UHMWPE acetabular liners. Biomaterials. 2009;30(29):5572-5582.)

2.5 Oxidation

2.5.1 Overview

The chemical and physical effects of oxidation on UHMWPE have been studied before the advent of HXLPE. Oxidation is a chemical process, which results in cleavage or chain scission, leading to fragmentation of the large polymer into lower molecular weight units, and also the introduction of oxygen-containing groups into the UHMWPE[19]. The energy required for breakage of bonds can be provided by different forms, including UV/visible light, heat, mechanical stress, or radiation[59]. The issues with wear,

osteolysis and subsequent revisions led to the understanding of the process of oxidation induced by gamma radiation sterilization in presence of air[19]. The first step after radiation involves the formation of macroradicals, which in the presence of oxygen, can convert to peroxyradicals. These radicals are reactive species that stimulate further chemical changes after irradiation, although the rate declines[59]. The cleavage of chemical bonds due to the presence of reactive species results in degradation of mechanical properties. This includes increased hardness or embrittlement, decreased fatigue strength and ultimate tensile strength[60]. Although the development of irradiation in an inert environment minimized oxidation during the sterilization, oxidation in air permeable packaging on shelf continued to be an issue[23]. Furthermore, exposure to oxygen of UHMWPE/HXLPE during implantation and in vivo through synovial fluid is unavoidable.

2.5.2 **Resin, consolidation method, and oxidation**

In considering oxidation of HXLPE in vivo, it is important to determine the resin and the consolidation method used to manufacture the product. Studies have shown that the amount of oxidation during shelf aging differs between GUR and 1900 resins [61]. The significance of these variations on in vivo oxidation and clinical performance remains unknown.

2.5.3 **Irradiation and Oxidation**

Gamma irradiation in air had been the most common method for UHMWPE sterilization until the late 1990s for THA, until the oxidative degradation of UHMWPE was identified[23]. Oxidation during and after irradiation depends on the dose and type of irradiation, the gaseous environment, and the temperature. These variables differ between manufacturers. Increasing dose of irradiation produces a higher number of reactive radicals, which can result in a higher degree of crosslinking in the amorphous phase, but free radicals in the crystalline phase become trapped[62]. The free radicals in the crystalline regions are long-lived and can cause oxidation whenever they migrate to the interface between amorphous and crystalline phases[63]. Without an appropriate thermal (melting versus annealing) or chemical (antioxidants) treatment post-irradiation, the

oxidation process initiated can continue during shelf storage and implantation, with the rate of this process depending on the surrounding temperature and the amount of available oxygen.

2.5.4 **Thermal processing and oxidation**

To prevent oxidative degradation of irradiated UHMWPE, melting after irradiation was introduced to decrease free radicals to undetectable levels[64]. However, in vivo retrieval studies have recently shown presence of some oxidation in irradiated and melted HXLPE[65]. It was also noted that irradiated and melted retrievals oxidized on shelf ex vivo even after short periods of implantation[66], suggesting that initiation of in vivo oxidation via an unknown mechanism. Cyclical loading and aging in vitro has now been shown to promote oxidation in irradiated and melted polyethylene despite initially undetectable free radicals[67]. Furthermore, in vitro studies have shown that even small amount of oxidation can result in deterioration of mechanical properties in irradiated remelted HXLPE liners[68].

Another method developed to reduce oxidation of the irradiated polyethylene was annealing. Annealing heats the irradiated material just under the melting point, which reduces the number of free radicals, but does not eliminate them completely[69]. A number of retrieval studies have clearly shown increasing oxidation as in vivo time increases, particularly affecting the rim surface[70–72]. It has been postulated that the articular surface is protected by the femoral head, backside is protected by the shell, while the rim remains exposed to oxygen in bodily fluids. Sequential annealing was introduced in 2005 to reduce the likelihood of oxidation by performing irradiation and annealing process three times sequentially, in an effort to eliminate the free radicals more effectively[14]. Despite this, sequentially annealed HXLPE liners show evidence of in vivo oxidation, although to a lesser extent in comparison to single annealed HXLPE liners[73].

2.5.5 **Sterilization, packaging and oxidation**

As mentioned previously, gamma irradiation in air was identified as a culprit in oxidative degradation of UHMWPE in the 1990s. It was soon identified that UHMWPE that was

gamma sterilized in air-permeable packaging continued to undergo oxidative degradation due to the presence of macro radicals that persisted for years after irradiation[74,75]. Concerns related to this degradation on shelf led to the development of chemical sterilization methods including gas plasma and ethylene oxide (EtO), and gamma irradiation sterilization in an inert environment[23]. The chemical sterilization methods are effective sterilization method and yield no free radicals that can subsequently oxidize. McKellop et al[25] reported on the wear performance of UHMWPE sterilized with chemical and irradiation techniques, and found that the wear rates were significantly lower in UHMWPE sterilized by gamma irradiation as opposed to gas plasma and EtO. The protective effect of the irradiation on wear rates from cross-linking had a greater effect than the deleterious effect of oxidation mechanical properties. However, after the inception of HXLPE, the use of the chemical sterilization method continued since cross-linking was obtained using a much higher dose (7.5-10 MRad) prior to sterilization. A variety of packaging methods and sterilization techniques are employed by various manufacturers during production of HXLPE [33]. The packaging methods are proprietary for each manufacturer but barrier packaging is employed for gamma sterilization in inert environment, to prevent the problem of oxidation on shelf, while gas-permeable packaging techniques are used for EtO and gas plasma sterilized components[31]. There is a paucity of literature concerning oxidation on shelf prior to implantation.

2.5.6 **In Vivo time and oxidation**

In vivo oxidation of HXLPE depends on the total irradiation dose from cross-linking and sterilization, and the resultant free radical content after thermal sterilization[61]. Therefore, first generation irradiated and melted HXLPE should be relatively oxidative stable as compared to the irradiated and annealed HXLPE liners.

However, recent retrieval analysis of irradiated and melted HXLPE liners question the notion of oxidative stability in vivo[65,66] – although more long term retrievals are necessary. Oxidation measurement as recorded by Fourier transform infrared spectroscopy (FTIR) showed measurable oxidation in 22% of retrieved melted HXLPE liners and inserts after an average of two years in vivo[65]. In contrast to melted liners, annealed and gamma inert sterilized liners have measurable levels of free radicals, which

possess the potential to oxidize upon exposure to oxygen. Retrieval analysis of annealed and gamma inert sterilized HXLPE components demonstrated that oxidation occurs preferentially at the rim of the liner, perhaps due to the greater exposure to oxygen containing body fluids at the rim[70,76] (Figure 2-4). Clinical significance of in vivo oxidation of the liners remains open to debate, as no THA failures have been reported secondary to oxidation alone. The degree of oxidation has been related to degradation in mechanical properties (Figure 2-5). A threshold of oxidation index (OI) level of 1.0 to 1.5 has been shown to correlate with sufficient lost in mechanical strength such that it falls 60% below ASTM minimum standards for implantable polyethylene[77]. Other literature suggests an OI > 3 as a threshold where the ability to withstand mechanical loading in vivo has been compromised[61]. More recently, Oral et al[68] showed that even small OI of 0.1, can have detrimental effects on the mechanical properties and wear rate of irradiated melted HXLPE.

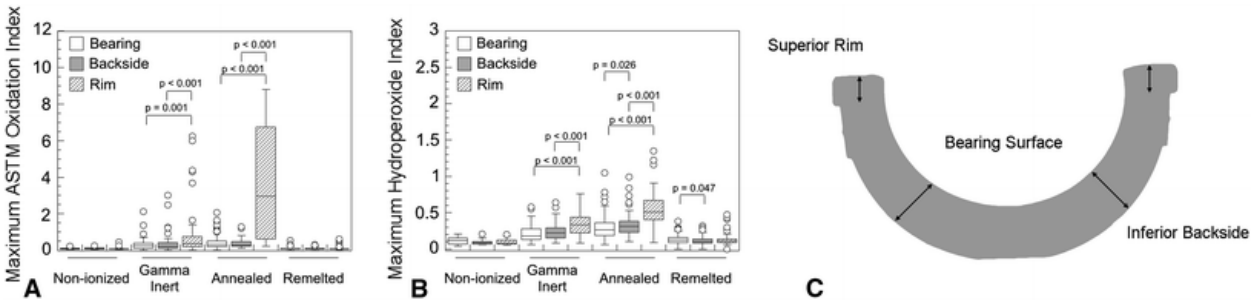


Figure 2-4 A. Oxidation index and B. Hydroperoxide index (a measure of oxidation potential) of retrieved samples of conventional (listed as non-ionized, gamma inert sterilized above), annealed (first-generation HXLPE), remelted (first-generation HXLPE) liners. The relative oxidation of annealed liners can be seen. Also, the regional variations with preferential rim oxidation can be noticed. C. Illustrates the sampling locations for testing at the rim, bearing surface and backside of the liners. (Permission from MacDonald D, Sakona A, Ianuzzi A, Do first-generation highly crosslinked polyethylenes oxidize in vivo? In: Clinical Orthopaedics and Related Research. Vol 469. Springer; 2011:2278-2285.)

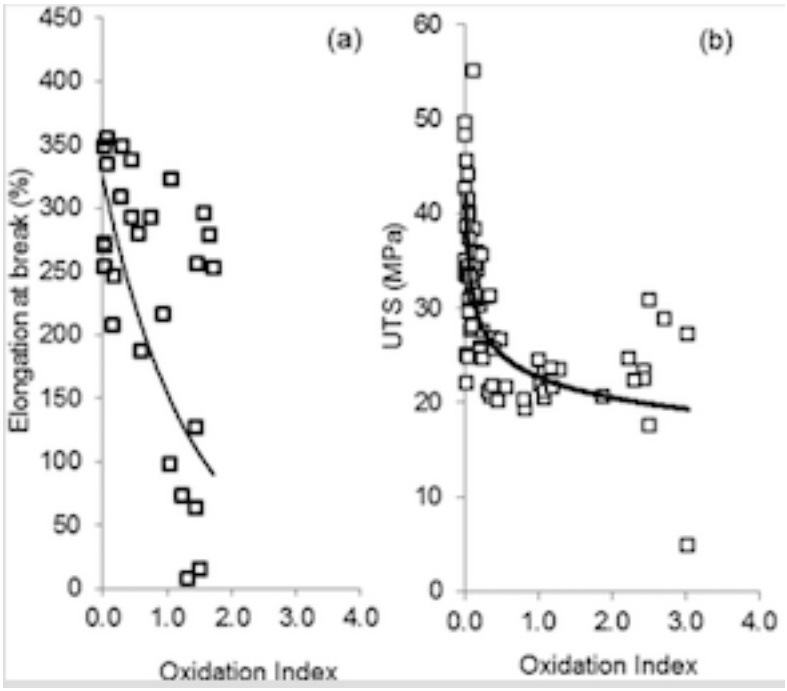


Figure 2-5 (a) The elongation at break and (b) ultimate tensile strength decrease as oxidation increases in irradiated melted HXLPE with in vitro thermo-oxidative aging. (Permission from Oral E, Neils AL, Doshi BN, et al. Effects of simulated oxidation on the in vitro wear and mechanical properties of irradiated and melted highly crosslinked UHMWPE. J Biomed Mater Res B Appl Biomater 2016; 104: 316–322.)

As mentioned previously, second generation HXLPE liners were developed to prevent mechanical degradation due to in vivo oxidation and to retain mechanical properties lost due to melting. Retrieval analysis on sequentially annealed (X3), second generation, HXLPE liners have decreased but detectable oxidation levels in comparison to annealed (Crossfire) liners[73]. Meanwhile, Vitamin E-diffused (E1, Biomet) components have shown relative resistance to oxidation in comparison to sequentially annealed and irradiated melted retrieved liners in short term retrievals[78].

2.6 Mechanical Properties

2.6.1 Overview

The concern related to polyethylene wear and osteolysis has largely disappeared since HXLPE was introduced. With reports of mechanical failure at the rim, the study of mechanical properties particularly, fatigue and fracture properties is becoming more important[11–13,55,56].

The microstructural variations that result from the molecular weight of UHMWPE, percent crystallinity, lamellar thickness, cross-linking can influence the mechanical properties[79]. Various manufacturing processes, including the consolidation method, irradiation, thermal stabilization, and sterilization can affect the microstructure and alter the mechanical properties. In addition, as discussed previously oxidation during implantation and biomechanical cyclic stresses may play a role in degradation of mechanical properties in vivo.

2.6.2 Mechanical Testing

The FDA requires testing of ultimate tensile strength, yield strength, young's modulus, Poisson's ratio and percent elongation as part of stage 1 testing of a new UHMWPE material submission. If stage 1 testing reveals properties identical to another material on the market, no further testing maybe necessary. If differences exist, stage 2 testing includes fatigue, crack propagation and J-integral testing. In addition to the testing on the resin, the manufacturers must test the finished components for clinical failure modes under the in vivo loading conditions to ensure the material will perform adequately[80]. Tensile testing is the most common mechanical test conducted on UHMWPE. A dog bone or dumbbell shaped specimen is machined or punched out and loads are applied at a constant speed until specimen failure, and the load and axial displacement are observed. Stress and strain are calculated, followed by determination Young's modulus, yield stress, ultimate tensile stress and elongation at failure from the stress/strain curve. Small punch testing is a method that makes use of the biaxial deformation of small disks by indentation by a hemispherical punch, thereby creating tension in the material. This test was adapted by Kurtz et al[81] for use in UHMWPE retrievals to test samples from the

components as opposed to the generic UHMWPE materials. Gilbert et al[82] pioneered hardness testing of polyethylene using micro indentation to study the surface mechanical properties of UHMWPE, as it relates to wear resistance and oxidation.

2.6.3 **Resin and Consolidation**

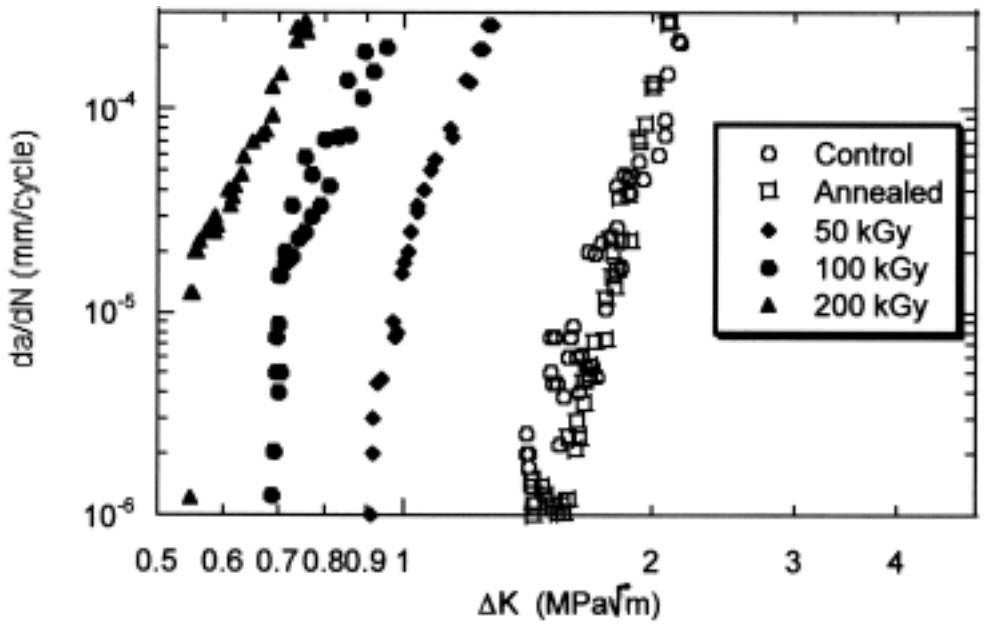
As demonstrated in Table 2-1, the resin type and consolidation method influence mechanical properties. Although statistically different, these differences do not appear to be clinically substantial at this stage, but must be considered when testing retrievals.

Table 2-1 Demonstrated are the variations in mechanical properties of yield strength, ultimate tensile strength, elongation at break (%) and Izod impact of UHMWPE based on resins, consolidation method, and irradiation dose.(Modified with permission from 1. Greer KW, King RS, Chan FW. The Effects of Raw Material, Irradiation Dose, and Irradiation Source on Crosslinking of UHMWPE. J ASTM Int. 2004;1(1). 2. Sobieraj MC, Rimnac CM. Ultra high molecular weight polyethylene: Mechanics, morphology, and clinical behavior. J Mech Behav Biomed Mater. 2008;2:433-443.)

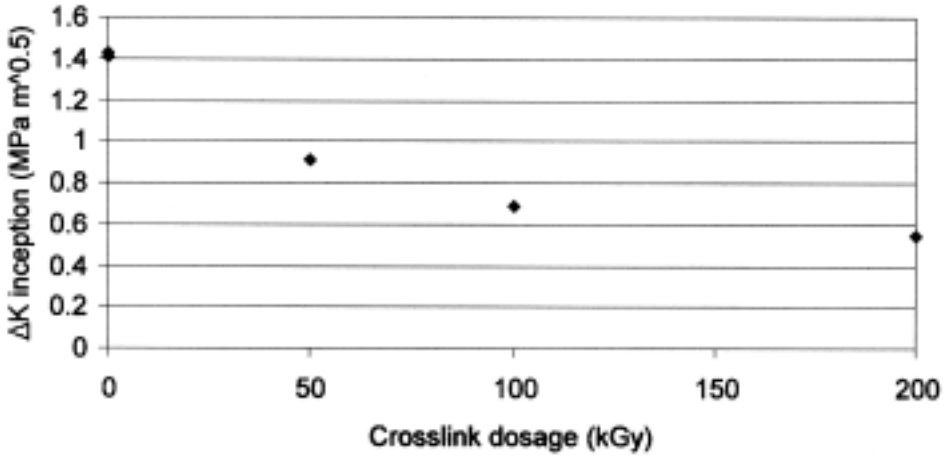
Dose (Mrad)	Irradiation	GUR resin	Sheet or bar	Yield strength (MPa)	Ultimate tensile stress (MPa)	Elongation at break (%)	Izod impact (kJ /m2)
0	None	1020	Sheet	23.6±0.1	42.1±2.7	396±20	161.3±1.9
			Bar	23.6±0.1	37.2±6.4	376±52	139.5±1.4
		1050	Sheet	22.5±0.1	43.8±3.5	358±20	93.7±3.4
			Bar	22.3±0.4	40.0±5.0	353±33	97.9±2.9
3	e-beam	1050	Sheet	20.4±0.1	36.7±5.8	284±49	90.1±1.2
			Bar	21.0±0.1	43.6±6.8	340±32	86.8±1.0
6	e-beam	1020	Sheet	21.3±0.0	41.6±3.7	315±18	87.4±3.6
			Bar	23.5±0.2	45.3±5.0	335±24	88.1±3.2
	gamma	1020	Sheet	23.1±0.1	36.7±0.7	270±5	74.6±2.0
			Bar	23.1±0.2	35.4±0.8	278±8	74.3±1.0
	e-beam	1050	Sheet	20.4±0.1	36.9±3.8	264±15	73.3±1.2
			Bar	21.2±0.2	39.5±3.1	275±21	70.6±1.5
	gamma	1050	Sheet	20.1±0.1	33.2±1.2	247±5	73.0±1.6
			Bar	20.6±0.1	31.6±1.0	243±8	72.0±0.4
12	gamma	1020	Sheet	21.4±0.1	33.3±1.7	212±7	56.7±0.2
			Bar	21.3±0.3	31.1±2.1	215±9	59.6±1.2
	e-beam	1050	Sheet	20.6±0.2	34.1±4.0	209±15	60.9±2.0
			Bar	21.2±0.2	36.6±3.2	227±14	57.5±2.1
	gamma	1050	Sheet	20.0±0.1	30.2±1.6	188±7	49.9±1.7
			Bar	21.0±0.1	29.2±1.0	185±5	51.4±0.6

2.6.4 **Cross-linking**

While high level of cross-linking improves adhesive and abrasive wear, it diminishes the mechanical properties such as ultimate strength, ductility, fracture toughness and fatigue crack propagation[83,84]. Irradiation with doses of 5-10 Mrad results in cross-linking of long chains in the amorphous regions, limiting molecular chain mobility in the amorphous region, decreasing creep and ultimately increasing resistance to wear debris release from contact surface[85]. However, this results in decreased plastic deformation, manifesting as a reduced resistance to fatigue crack propagation, rendering components more susceptibility to fatigue fracture[12,58]. As irradiation dose increases fatigue crack propagation and fracture toughness of UHMWPE decreases[9,84–87] (Figure 2-6).



(a)



(b)

Figure 2-6 (a) Fatigue crack propagation of five groups of polyethylene (b) Fatigue crack propagation inception values as radiation dose increases (Permission from Baker D a, Bellare a, Pruitt L. The effects of degree of crosslinking on the fatigue crack initiation and propagation resistance of orthopedic-grade polyethylene. J Biomed Mater Res A. 2003;66:146-154.)

2.6.5 **Thermal Processing**

Oxidation embrittlement has been an issue long-established, especially in an irradiated UHMWPE[88]. Thermal processing decreases susceptibility to oxidation by removal of free radicals. However, it also alters the microstructure of the HXLPE by decreasing its crystallinity[89]. Annealing preserves much of the UHMWPE crystallinity, thereby maintaining mechanical properties. Conversely, melting treatment reduces crystallinity significantly resulting in decreased resistance to fatigue crack propagation and fracture toughness[58].

2.6.6 **Sterilization**

Gamma irradiation in air sterilization was abandoned in the 1990s after oxidative degradation of UHMWPE was identified as a problem. Chemical sterilization methods with EtO or gas plasma have been shown to preserve the microstructure on UHMWPE thereby preserving its mechanical properties[31]. Gamma-inert sterilization continues to be used as a contemporary method, which would be expected to further decrease the mechanical properties and increase the susceptibility to oxidation embrittlement by the production of macroradicals produced by irradiation.

2.6.7 **In Vivo Time**

With decreased fatigue and fracture properties of HXLPE, along with evidence of in vivo oxidation at the rim, the mechanical testing of retrievals has become more important. Kurtz et al[76] demonstrated on first generation HXLPE annealed retrievals that after intermediate implantation time, no significant deterioration of ultimate tensile strength is noticed at the bearing surface, as measured by small punch testing. Of note, bearing surface was shown to be protected from in vivo oxidation in comparison to the rim of liners and no mechanical testing was performed at the rim. Currier et al[10] noted in various first generation HXLPE acetabular liners retrieved with up to 5.3 years in vivo that increased oxidation correlated with increased clinical fatigue damage at the rim with increasing in vivo time. Retrieval analysis by small punch testing of sequentially annealed (second-generation) liners up to 5 years in vivo time showed no deterioration of ultimate strength at the bearing surface with in vivo time[73]. In addition, sequentially

annealed liners had a lesser extent of delamination type of rim damage as compared to annealed cohorts. Mechanical testing of retrievals after long term implantation remains to be evaluated. Furthermore, literature reporting mechanical properties at the rim, the area of mechanical failure, is lacking.

2.7 Summary and Conclusions

HXLPE has demonstrated clear benefit in reducing wear rates and the incidence of osteolysis related the polyethylene wear. More studies are necessary to see the impact of HXLPE on overall revision rates. Concerns related to diminished mechanical properties induced by cross-linking, reports demonstrating fatigue related damage at the rim, along with increased propensity of oxidation at the rim in the HXLPE retrievals raise long term performance questions. Second generation sequentially annealed HXLPE liners have shown improved resistance to oxidation in short-term retrievals in comparison to the first-generation annealed counterparts. Like first generation HXLPE, second generation HXLPE have low wear rates. Vitamin E –diffused (E1) second generation HXLPE shows good short-term results but long-term results remain to be seen. More retrieval studies to analyze in vivo oxidation and degradation of mechanical properties are necessary to understand potential long term failures related to HXLPE in THA.

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Chapter 3

3 Thesis Outline and Brief Summary

In Chapters 1 and 2, the prevalence and clinical importance of THA was highlighted, and that the clinical performance of HXLPE in THA to date has been promising. High quality literature has demonstrated decreased wear rates, osteolysis, and polyethylene wear related revision rates. However, reports have emerged showing fractures and fatigue damage at the rim of the HXLPE acetabular liners. Given the diminished fatigue properties of HXLPE, along with evidence of oxidation at the rim, the study of retrieved HXLPE liners has become more important.

In this Master's, we will validate a specific methodology of polyethylene testing and hypothesize that the mechanical properties at the rim of the HXLPE acetabular liners will demonstrate deterioration with increasing in vivo time.

In chapter 4, various ways of testing mechanical properties of retrieved polyethylene liners will be highlighted. Furthermore, the mechanical testing modality used for determining mechanical properties in this project will be discussed in detail.

In chapter 5, the results from the initial testing of acetabular liners of a single design will be provided and discussed. These liners had similar in vivo time (< 12 weeks) but variable ex vivo (shelf storage times). This testing was performed to determine the effect of shelf oxidation on mechanical properties.

In Chapter 6, the results of mechanical properties of retrieved HXLPE acetabular liners with varying in vivo times will be presented and discussed.

Finally, in Chapter 7 the results of this thesis will be reviewed with a discussion of relevance and future research directions.

Chapter 4

4 Indentation testing of UHMWPE

Wear of conventional UHMWPE and the reaction of the body to generated wear particles in vivo has been a major player in osteolysis and loosening in THA[1,2]. In an effort to reduce wear and the subsequent osteolysis, highly cross-linked polyethylene (HXLPE) was developed in the 1990s[3]. Since the inception of HXLPE in THA, wear rates and the incidence of osteolysis have significantly decreased[4–7]. Furthermore, the revision THA rates related to polyethylene wear with HXLPE are lower than conventional UHMWPE[5,8,9].

Development of HXLPE to reduce wear rates has an unfortunate consequence of a compromise of the mechanical properties of polyethylene[3,10]. Formation of cross-linking requires irradiation of UHMWPE, which reduces the polyethylene's mechanical strength to failure[10]. In addition, concerns have developed regarding further degradation of mechanical properties with time in vivo as a result of oxidation[11–14]. Furthermore, numerous case reports have demonstrated fractures at the rim of HXLPE acetabular liners[15–18].

It has been demonstrated that irradiated annealed liners experience in vivo oxidation as time in vivo increases, particularly at the rim[19–21]. Moreover, cyclical stressing of polyethylene liners in vitro has been shown to promote oxidation in irradiated remelted acetabular liners [22]. The use of larger femoral heads to prevent dislocations have led to the use of thinner acetabular liners. Some liners also have unprotected rim designs. Also, as mentioned previously, HXLPE liners have diminished fatigue properties. All three factors have been shown to contribute to fractures at the rim.

We suspect that the diminished mechanical properties in HXLPE liners along with increasing oxidative damage at the rim with in vivo time plays a role in these mechanical failures. While the trends in oxidative damage at the rim with increasing in vivo time have been demonstrated, the mechanical deterioration in vivo is not as clear[19]. As the

number of THAs performed continues to rise, the study of the mechanical properties has become more important.

Gilbert et al[23] pioneered hardness testing of polyethylene using microindentation to study the surface mechanical properties of UHMWPE, as it relates to wear resistance and oxidation. It has been demonstrated that hardness increases with increasing oxidation[23,24]. Given this finding, indentation testing is the test of choice for determining the effect of in vivo oxidation on mechanical properties at the rim of HXLPE liners.

4.1 Indentation testing

4.1.1 Background

Indentation testing has been a part of material testing for decades. In a depth-sensing indentation (DSI) test, a hard indenter of a known tip geometry is loaded into a sample surface resulting in a deformation. Depending on the material under study, the deformation can be elastic, plastic or viscoelastic. The load and depth of the indentation is measured directly, and from these parameters, hardness of the material can be calculated[23]. Hardness is a measure of how mechanically resistant a material (test workpiece) is to the mechanical penetration of another, harder body (indenter). Various testing methods exist and vary according to the shape of the indenter and the testing technique. Hardness measurement can be defined as macro-, micro- or nano- scale according to the forces applied and displacements obtained.

After the indentation is produced by using a test force by an indenter, either the penetration depth or the size of the indentation is measured. A distinction is made with the hardness testing methods between depth measurement methods and optical measurement methods.

Depth measurement methods measure the residual depth of indentation left by the indenter. The Rockwell method is the only standardized depth measurement method. Optical measurement methods measure the residual size of indentation left by the

indenter. Standardized optical hardness testing methods are Brinell, Knoop and Vickers[25].

4.1.2 **Microhardness calculation**

As mentioned above, various testing methods can be employed to measure hardness by DSI. Vickers microhardness test is reliable for measuring microhardness of metals, polymers, and ceramics and will be employed in this master's project. In a Vickers microhardness test, a diamond indenter, in the form of a square-based pyramid with an angle of 136˚ is pressed into a flat test specimen using a known force F. The test force is maintained for 10-15 seconds and is removed. The applied load can vary from 1 gf (gram-force) to 120 kgf (kilogram-force). After the force is removed, the diagonal lengths of the indentation are measured with an optical microscope (Figure 4-1)[25].

The Vickers hardness (VH) is calculated using the equation below

$$VH = \frac{2F}{d^2}\sin\frac{136°}{2} = 1.854\ \frac{F}{d^2}$$

where $d = (d_1 + d_2) / 2$ is the mean diagonal length in mm and the unit of force is kgf. The VH is calculated in units of kgf/mm^2. VH is most commonly reported in its SI units of GPa by multiplying the values in kgf/mm^2 by 0.009807, a known constant[25].

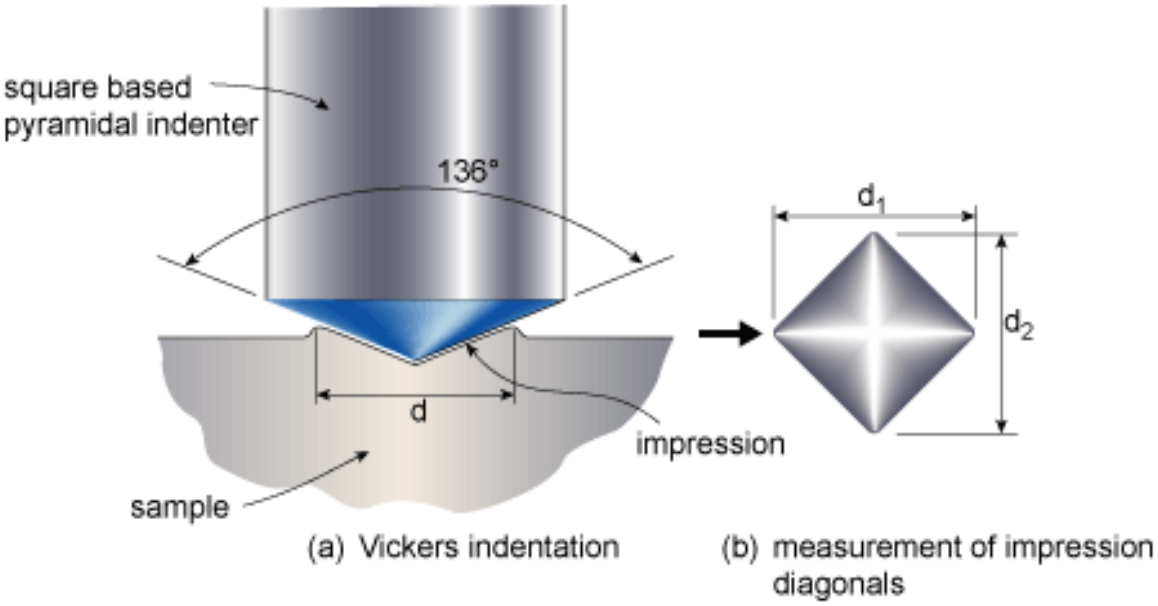

Figure 4-1 (a) Vickers indentation, where a hard tip indenter is loading a sample resulting in an impression. (b) d1 and d2 represent the diagonal lengths of the indent produced from the force applied. (Courtesy of TWI Ltd, Hardness Testing Part 1 - Job Knowledge 74 n.d. http://www.twi-global.com/technical-knowledge/job-knowledge/hardness-testing-part-1-074/ (accessed June 13, 2017))

4.1.3 **DSI testing for UHMWPE**

Both nanoindentation and microindentation testing has been used for UHMWPE and differs based on the size of indenter tip and indentation performed in the material. To perform such testing, samples are typically microtomed to obtain flat smooth surfaces prior to testing. Microindentation is less sensitive than nanoindentation to surface variations that may be induced from microtoming or due to general differences in topography and crystalline/amorphous content. Microindentation allows for larger loads, larger indent depths, and a greater volume of material is investigated. Nanoindentation can be used to test smaller volumes. Nanoindentation is more sensitive to surface variations and better accounts for surface mechanical properties [23].

Gilbert et al[26] used microindentation to determine microhardness and elastic modulus, and showed that microindentation is an effective way measuring micromechanical behavior of various UHMWPE materials[26]. The differences in behavior demonstrated

using microindentation between various UHMWPE materials (GUR 1020, 1050 and Hylamer) were shown to correlate with other macroscopic validated methods.

4.1.4 **DSI and oxidation of UHMWPE**

The effects of oxidation of UHMWPE on its mechanical properties has been investigated using DSI. DSI testing of UHMWPE retrieved and shelf aged tibial inserts have demonstrated a linear increase in hardness and elastic modulus with increasing oxidation (Figure 4-2)[27–29]. Oxidation of UHMWPE results in chain scissoring of the polymer chains resulting in increased crystallinity, which results in a stiffer and harder material[24].

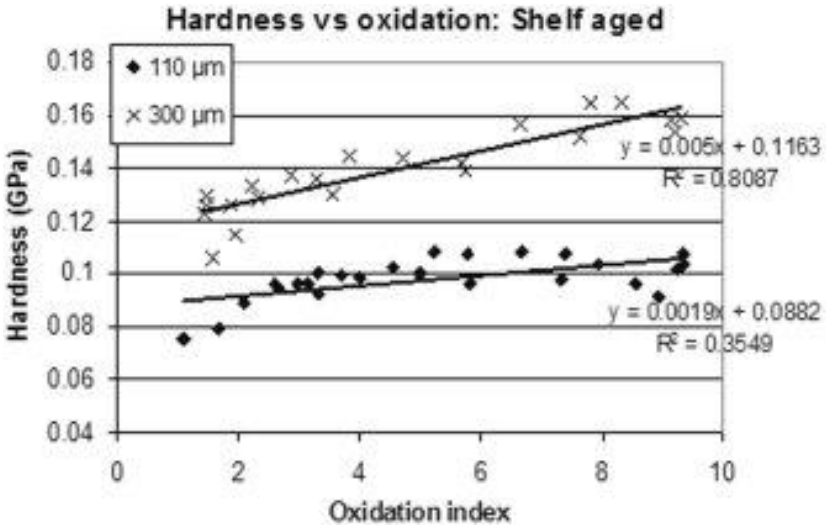

Figure 4-2 An increase in hardness is demonstrated with increasing oxidation in shelf aged tibial inserts. (Permission from Wernlé, J. D., & Gilbert, J. L. Micromechanics of Shelf-Aged and Retrieved UHMWPE Tibial Inserts: Indentation Testing, Oxidative Profiling, and Thickness Effects. J Biomed Mater Res Part B: Appl Biomater, 75, 113–121.)

4.1.5 **DSI and in vivo time**

The relation of DSI and in vivo time has not been extensively studied. One study recently demonstrated that hardness and elastic modulus at the bearing surface increased with increasing in vivo time in both conventional UHMWPE and HXLPE acetabular liners

(Figure 4-3)[30]. Elastic modulus, which defines the stiffness of a material has been shown to have a direct relationship with hardness[27]. However, it has been repeatedly shown that the bearing surface is well protected from oxidation relative to the rim[31]. Therefore, we expect a more significant increase in hardness at the rim with increasing in vivo time.

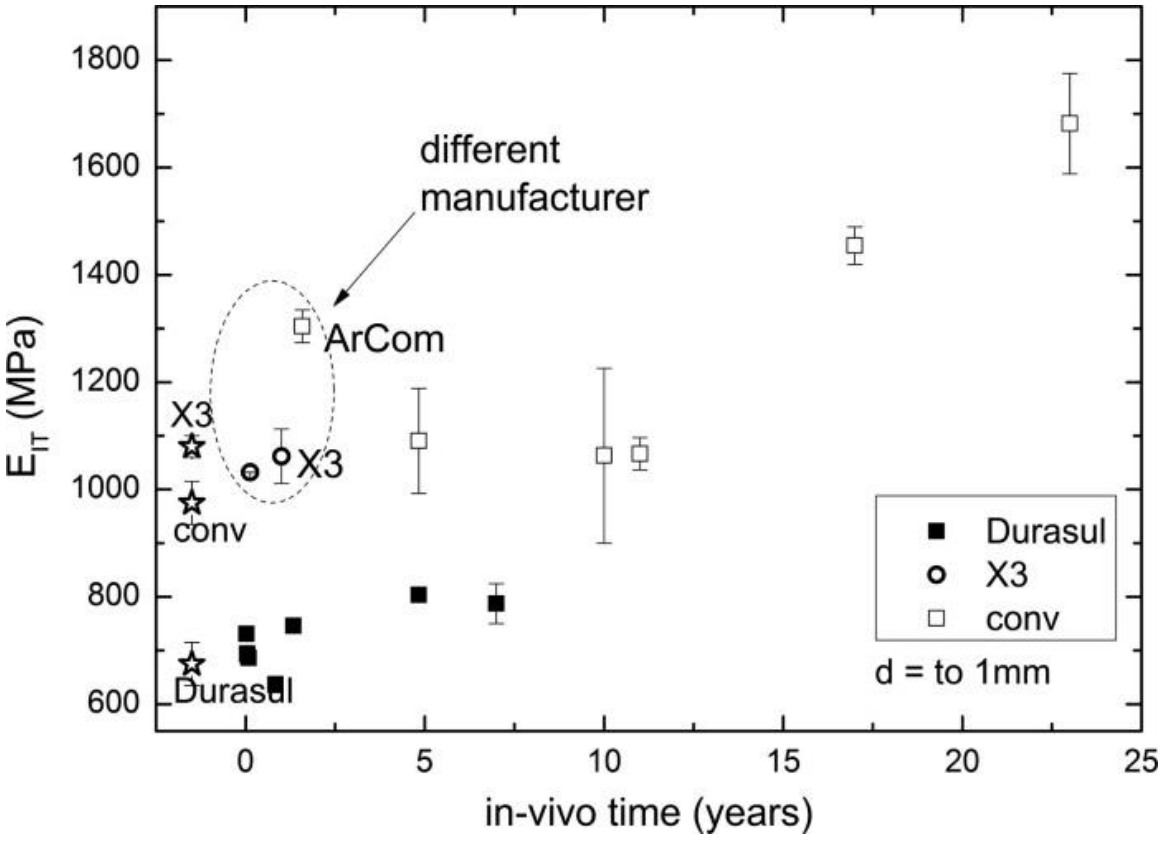

Figure 4-3 DSI testing results measuring modulus of elasticity (EIT) of various retrieved UHMWPE liners with varying in vivo time. (star symbol above represents control never implants samples from each polyethylene) (Permission from Laska, A., Archodoulaki, V.-M., & Duscher, B. (2016). Failure analysis of retrieved PE-UHMW acetabular liners. Journal of the Mechanical Behavior of Biomedical Materials, 61, 70–78.)

4.2 Summary

With reports demonstrating fractures at the rim of acetabular liners, the study of mechanical properties at the rim has become important. While there is clear evidence of

in vivo oxidation at the rim of the liners, no studies have been published measuring mechanical properties at the rim as a function of in vivo time. In this chapter, we have reviewed relevant literature that demonstrates DSI testing is an effective and validated method to measure hardness of UHMWPE. Hardness is proportional to elastic modulus of UHMWPE. Hardness has been shown to increase with increasing oxidation of UHMWPE. Therefore, DSI testing of the rim of the HXLPE acetabular liners should demonstrate increasing hardness with increasing time in vivo.

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Chapter 5

5 Impact of increasing shelf (ex vivo) time on hardness of irradiated remelted HXLPE acetabular liners – A validation study.

5.1 Introduction

Total hip arthroplasty (THA) has been termed “The operation of the century” for its excellent improvement in pain and function of patients with end-stage arthritis[1]. An ultra-high-molecular-weight polyethylene (UHMWPE) liner articulating against a metal femoral head has been the predominant bearing surface in THA. Despite the clinical success, the longevity of THA using conventional UHMWPE is limited due to polyethylene wear with resultant osteolysis and aseptic loosening[2]. This led to the development of highly cross-linked polyethylene (HXLPE) [3].

Since the routine adoption of HXLPE for THA in the early 2000s, a significant decline in polyethylene wear, osteolysis and wear related revisions has been reported[4–8]. However, irradiation and thermal treatment utilized in the manufacturing of HXLPE leads to reduced mechanical properties of polyethylene [3,9]. In addition, the presence of free radicals in irradiated annealed HXLPE predispose it to oxidation, further compromising its mechanical properties[10]. Even in irradiated HXLPE implants which have been remelted to eliminate the free radicals, retrieval studies have demonstrated evidence of oxidation[11].

With evidence of oxidation at the rim, decreased mechanical properties, and case reports demonstrating rim fractures of first-generation HXLPE (irradiated remelted and annealed) liners, the study of retrieved HXLPE acetabular liners to understand the decline of mechanical properties has become more important[10,12–14]. This is particularly important as younger patients are undergoing THA and increased implant longevity is necessary. One of the limitations in studying retrieved UHMWPE implants is that shelf oxidation can influence the accuracy of results of in vivo oxidation. Since oxidation has been shown to influence mechanical properties of UHMWPE, the study of mechanical properties must account for changes during the ex vivo time[15]. Kurtz et al[16]

describes three ways to deal with the issue of ex vivo aging when studying retrievals. (1) Perform the testing within a year of retrieval to minimize the effect of ex vivo aging. (2) Store the explanted polyethylene in a cryogenic freezer until testing is performed. (3) Store the component at room temperature nitrogen, depriving the material of additional oxygen during storage[16]. However, these conditions are not feasible in most retrieval labs and do not enable testing of majority of the implants. In this study, we attempt to identify the influence of ex vivo time on hardness measured by micro indentation of irradiated remelted liners at the rim.

5.2 Materials and methods

A preliminary review was performed to obtain a list of available highly cross-linked acetabular liners of a specific design (R3 XLPE, Smith and Nephew, Memphis, TN)). Twelve explants with short in vivo time (2 weeks – 5 months) and varying ex vivo time (4 months – 8 years) were selected for testing. Two never implanted acetabular liners with the same design served as controls. Institutional review board approval was obtained for the retrieval and patient chart access. For each retrieved implant patients age, gender, and reason for revision were obtained (Table 5-1).

Table 5-1 Gender, Age at revision, Time in vivo, Shelf time and Reason for revision for each tested retrieval is shown.

Patient Number	Gender	Age at Revision (years)	Time in vivo (weeks)	Time ex vivo (Years)	Reason for Revision
1	M	66	11	0.4	Periprosthetic Fracture
2	F	60	5	0.9	Infection
3	F	68	3	0.9	Infection
4	F	73	3 days	1.5	Wound Dehiscence
5	F	68	3	2.0	Infection
6	F	78	4	2.6	Periprosthetic Fracture
7	M	65	2	3.9	Infection
8	F	70	2	4.8	Periprosthetic Fracture
9	F	76	3	5.4	Infection
10	M	66	4	5.7	Periprosthetic Fracture
11	F	60	12	7.0	Infection
12	F	62	2 days	8.3	Leg Length Discrepancy

All tested liners underwent an identical sanitation protocol at our implant retrieval laboratory that included storage in 10% formalin solution and cleansing in 10% bleach solution. The liners were then stored in a closed cardboard box, wrapped in a gauze at room temperature in room air.

Micro indentation testing was performed at the rim of the acetabular liners. Micromet II, Vickers microhardness (Buehler Ltd, Lake Bluff, IL) tester was used perform the indentation of the liners. All testing was performed in an independent laboratory in a blinded fashion. The person performing the testing was unaware of the sample or clinical data. The liner was mounted in a resin to stabilize it during indentation testing. A load of

50 gram force (gf) was applied for 10s using a diamond indenter into the flat surface of the liner rim. After the indentation, diagonal lengths (d1 and d2) of the indents were measured using optical microscope (40x magnification) of the hardness tester (Figure 5-1). On each sample 8 to 10 measurements were made and the average hardness was calculated. The Vickers hardness (VH)was calculated using the equation below

$$VH = \frac{2F}{d^2}\sin\frac{136°}{2} = 1.854\ \frac{F}{d^2}$$

where $d = (d_1 + d_2) / 2$ is the mean diagonal length in mm and the unit of force is kgf. The VH was then converted from kgf/mm^2 to GPa by multiplying by 0.009807, a constant. The average VH and standard deviation was calculated for each sample.

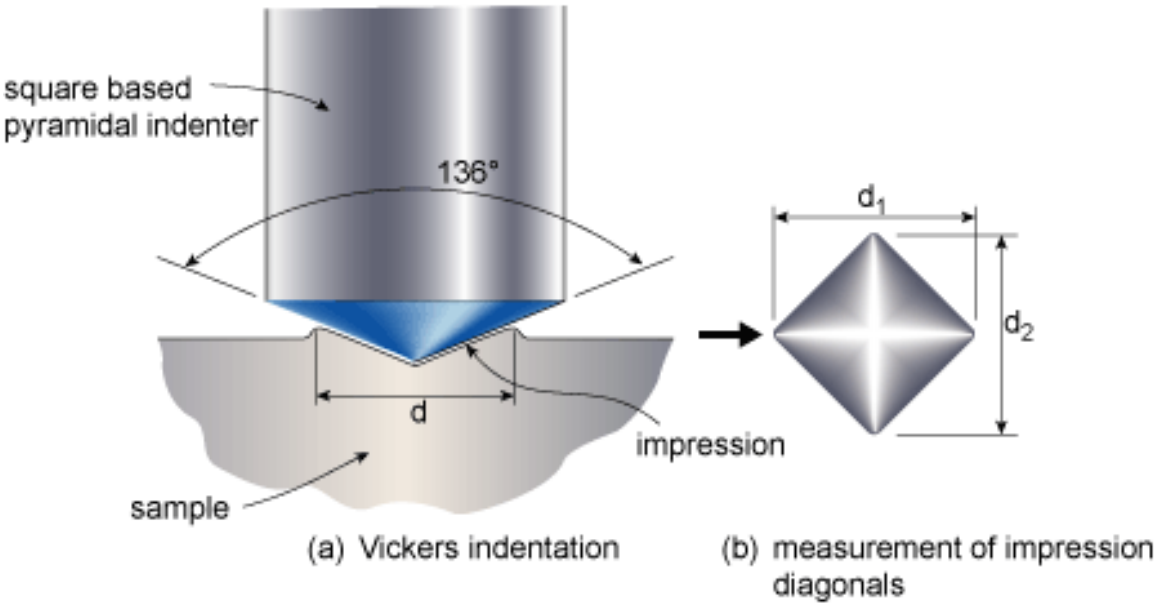

Figure 5-1 (a) Vickers indentation, where a hard tip indenter is loading a sample resulting in an impression. (b) d1 and d2 represent the diagonal lengths of the indent produced from the force applied. (Courtesy of TWI Ltd, Hardness Testing Part 1 - Job Knowledge 74 n.d. http://www.twi-global.com/technical-knowledge/job-knowledge/hardness-testing-part-1-074/ (accessed June 13, 2017))

5.3 Results

A total of 12 retrieved liners were tested, and included 25% (3/12) males and 75% (9/12) females. The mean age was 67.7 years (range 60-78 years). The in vivo time ranged from 2 days to 11 weeks. The reasons of revision included infection in 58.3% (7/12), periprosthetic fracture in 33.3% (4/12) and leg length discrepancy in 8.3% (1/12) of the cases. The shelf time ranged from 4.5 months to 8.3 years. The average VH results of the liners ranged from 0.042 - 0.050 GPa (Table 5-2). The VH of the control samples was 0.044 +/- 0.003 and 0.048 +/- 0.004 GPa. A regression analysis showed no correlation between shelf time and VH for the tested samples (Figure 5-2), with a p value of 0.385 and r^2 of 0.063.

Table 5-2 Shelf times (Ex vivo Time) and measured Vickers Hardness for control and experimental samples.

Patient Number	Ex Vivo Time (Years)	Avg. Hardness (GPa)	Stdev
Control 1	0.00	0.044	0.003
Control 2	0.00	0.048	0.004
1	0.4	0.042	0.003
2	0.9	0.045	0.005
3	0.9	0.043	0.004
4	1.5	0.049	0.003
5	2.0	0.042	0.005
6	2.6	0.052	0.006
7	3.9	0.050	0.002
8	4.8	0.049	0.004
9	5.4	0.049	0.003
10	5.7	0.044	0.002
11	7.0	0.044	0.004
12	8.3	0.048	0.005

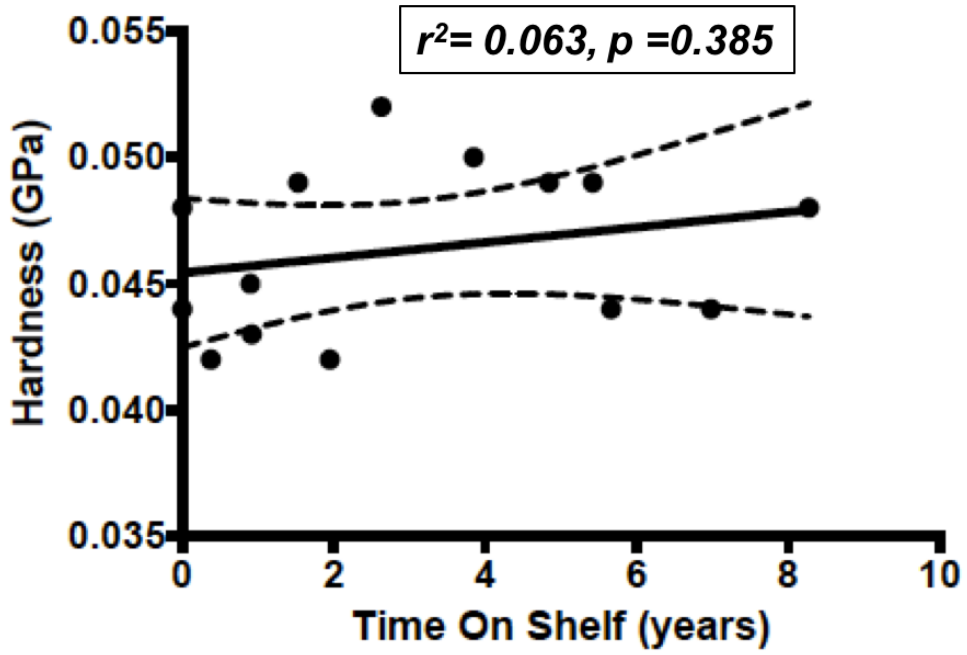

Figure 5-2 A linear regression analysis shows no significant correlation between hardness and shelf time of the tested liners.

5.4 Discussion

One of the challenges in oxidation and mechanical testing of retrieved hip UHMWPE liners is the potential impact of shelf oxidation of the tested samples. The study of in vivo oxidation of UHMWPE began in 1980s. Grood et al[17] showed that oxidation, and a resultant increase in crystallinity and density occurred with increasing in vivo time. Another important finding described in the same study was that the effects of shelf aging (ex vivo aging) on crystallinity was comparable to that of in vivo aging. Although the effect of ex vivo aging was not accounted for, a total aging time was used – this included in vivo time of retrieved implant added to the shelf time prior to testing of the implants. Furthermore, the implants tested in that study were conventional UHMWPE, gamma sterilized in air, and therefore contained free radicals.

The problem of shelf oxidation can be avoided by testing samples immediately after retrieval, storing them in subzero conditions or storing the samples at room temperature in nitrogen environment, minimizing exposure to oxygen. Some recent retrieval studies employ these techniques to account for shelf oxidation[18]. Many retrieval laboratories store the specimens at room temperature in a cardboard box, and are essentially exposed to room air. Therefore, the impact of shelf oxidation on mechanical properties is an important consideration for retrieval labs with these storage protocols. The results from this case series of 12 samples, which served similar in vivo time (<11 weeks) but variable shelf time (4 months – 8.3 years) showed no correlation between hardness at the rim and varying ex vivo time. Hardness testing was used as the testing modality because hardness has been shown to increase with increasing oxidation. In this series, the lack of correlation between hardness and ex vivo time may be due to the elimination of free radicals in irradiated remelted liners. While irradiated annealed liners have been shown to have significant increase in rim oxidation with in vivo time, irradiated remelted liners oxidize to much lesser degree[18]. In this study, only the rim of the liners were tested as the rim has been shown to have the greatest exposure to oxidative stress due to exposure to the synovial fluid[18–20]. Also, the mechanical properties due to in vivo oxidation are of more interest at the rim of the liners, given the reports of fractures at the rim. The decreased oxidation at the articular surface or/and back surface may have different impact on hardness. The results in our study apply to only a specific design of liners that were tested. It is also unknown how the in vivo exposure to lipids changes the polyethylene oxidation and mechanical properties.

Our study challenges the notion of deterioration of mechanical properties due to shelf oxidation in irradiated remelted first-generation liners of a single design. Our study has the following limitations. The sample numbers are small and only the rim of the liners was tested. Furthermore, impact of shelf oxidation on mechanical properties tested by other techniques may differ. We only tested liners which served less than 12 weeks in vivo. Therefore, the ex vivo mechanical stability may not be valid in liners which have served longer in vivo times. In addition, the clinical relevance of oxidation and deterioration in mechanical properties in still open to debate.

In conclusion, the hardness measured at the rim of a single type of irradiated remelted HXLPE liner showed no correlation with increasing shelf times. These findings potentiate the use of implants from retrieval laboratories with normal retrieval storage protocols. The impact of in vivo oxidation and stress on mechanical properties could be studied independently without accounting for shelf deterioration in these retrievals. More studies are necessary to understand the impact of shelf oxidation on different HXLPE formulations and designs, as well as different testing methodologies.

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Chapter 6

6 Impact of in vivo time on hardness at the rim of irradiated remelted HXLPE acetabular liners.

6.1 Introduction

Total hip arthroplasty (THA) has been termed “The operation of the century” for its excellent improvement in pain and function of patients with end-stage arthritis[1]. An ultra-high-molecular-weight polyethylene (UHMWPE) liner articulating against a metal femoral head has been the most commonly used bearing surface in THA. This is due to high failure rate of metal on metal articulation due to adverse soft tissue reactions, and high costs associated with use of ceramics. Despite the clinical success, the longevity of THA using conventional UHMWPE is limited due to polyethylene wear and the resultant osteolysis and aseptic loosening[2]. This led to the development of a highly cross-linked polyethylene (HXLPE) [3].

Since the routine adoption of HXLPE for THA in the early 2000s, a significant decline in polyethylene wear, osteolysis and wear related revisions has been reported[4–8]. However, irradiation and thermal treatment utilized in the manufacturing of HXLPE leads to reduced mechanical properties of polyethylene [3,9]. In addition, the presence of free radicals in irradiated annealed HXLPE predispose it to oxidation, further compromising its mechanical properties[10]. Even in irradiated HXLPE implants which have been remelted to eliminate the free radicals, retrieval studies have demonstrated evidence of oxidation[11]. Concerns related to oxidation and compromised mechanical properties of first-generation HXLPE liners have led to the introduction of second-generation HXLPE liners – which include sequentially annealed, vitamin-E containing, and mechanically annealed liners.

Retrieval studies have demonstrated that the rim of the first-generation HXLPE (irradiated remelted and annealed) liners oxidize in vivo[12]. Furthermore, oxidation of HXLPE has been shown to further decrease its ultimate tensile strength and elongation at break[13]. With evidence of oxidation at the rim, decreased mechanical properties of HXLPE and case reports demonstrating rim fractures of first-generation HXLPE liners,

the study of retrieved HXLPE acetabular liners to understand the decline of mechanical properties has become more important[10,14–16]. This is particularly important as younger patients are undergoing THA and increased implant longevity is necessary[17]. Moreover, revision THA presents a huge economic and clinical burden[18], particularly as the number of THA continue to rise[19].

A number of retrieval studies have investigated mechanical properties at the articular surface of first-generation irradiated annealed liners with increasing in vivo time and have demonstrated no significant decline[20,21]. However, no studies have investigated the mechanical properties at the rim, the site of in vivo oxidation and fractures. In this study, we hypothesize that hardness at the rim of retrieved first-generation irradiated remelted HXLPE acetabular liners will increase with in vivo time.

6.2 Materials and methods

A preliminary review was performed to obtain a list of available highly cross-linked acetabular liners of a specific design (R3 XLPE, Smith and Nephew, Memphis, TN). Ten explants with in vivo time ranging from 10 months to 4.3 years were selected for testing. Samples that sustained a damaged rim during the explantation were excluded. Two never implanted acetabular liners with the same design served as controls. Institutional review board approval was obtained for the retrieval study and patient chart access. For each retrieved implant patients age, gender, and reason for revision were obtained (Table 6-1).

Table 6-1 Gender, Age at revision, In vivo time, and Reason for revision for each tested retrieval is shown.

Sample	Gender	Age at Revision (years)	Time in vivo (years)	Reason for Revision
1	M	58	0.8	Infection
2	F	67	1.0	Instability
3	M	72	1.0	Instability
4	F	57	1.1	Aseptic Loosening
5	M	56	1.4	Aseptic Loosening
6	M	86	3.8	Instability
7	M	54	3.9	Infection
8	F	64	4.0	Instability
9	F	59	4.2	Instability
10	M	62	4.3	Infection

All tested liners underwent an identical sanitation protocol at our implant retrieval laboratory that included storage in 10% formalin solution and cleansing in 10% bleach solution. The liners were then stored in a closed cardboard box, wrapped in a gauze at room temperature in room air.

Micro indentation testing was performed at the rim of the acetabular liners. Micromet II, Vickers micro-hardness tester (Buehler Ltd, Lake Bluff, IL) was used to perform the indentation testing of the liner. All testing was performed in an independent laboratory in a blinded fashion. The person performing the testing was unaware of the sample or clinical data. The liner was mounted in a resin to stabilize it during indentation testing. A

load of 50 gram force (gf) was applied for 10s using a diamond indenter into the flat surface of the rim. After the indentation, diagonal lengths (d1 and d2) of the indents were measured using optical microscope (40x magnification) of the hardness tester (Figure 6-1). On each sample 8 to 10 measurements were made and the average hardness was calculated. The Vickers hardness (VH) was calculated using the equation below

$$VH = \frac{2F}{d^2}\sin\frac{136°}{2} = 1.854\ \frac{F}{d^2}$$

where $d = (d_1 + d_2) / 2$ is the mean diagonal length in mm and the unit of force is kgf. The VH was then converted from kgf/mm^2 to GPa by multiplying by 0.009807, a constant. The average VH and standard deviation was calculated for each sample. A regression analysis was then performed using SPSS to determine relationship between VH and time implanted.

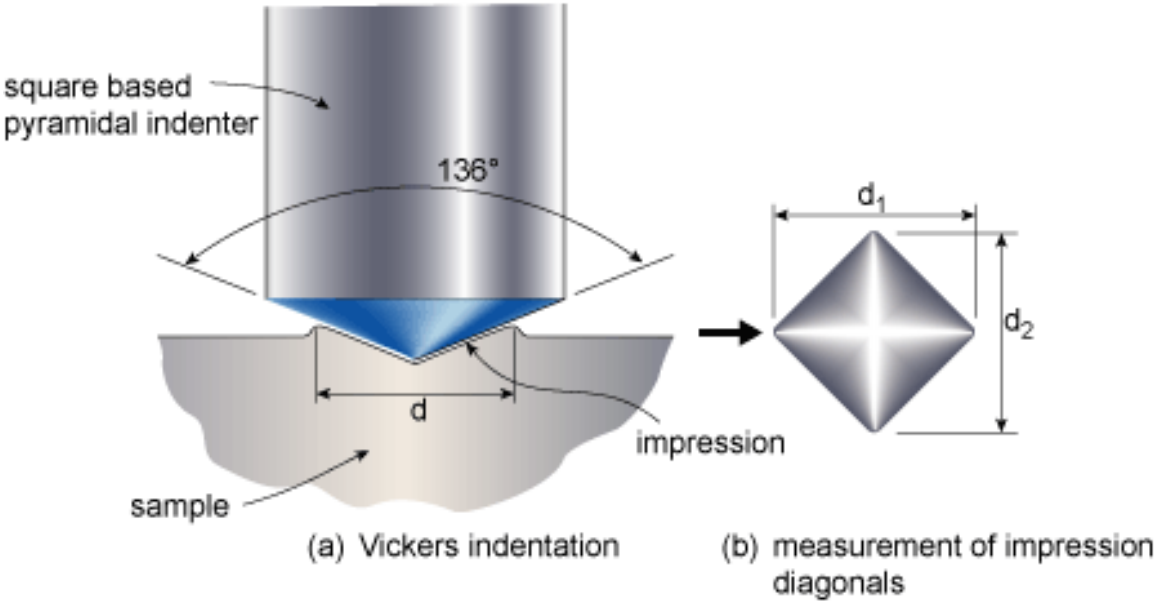

Figure 6-1 (a) Vickers indentation, where a hard tip indenter is loading a sample resulting in an impression. (b) d1 and d2 represent the diagonal lengths of the indent produced from the force applied. (Courtesy of TWI Ltd, Hardness Testing Part 1 - Job Knowledge 74 n.d. http://www.twi-global.com/technical-knowledge/job-knowledge/hardness-testing-part-1-074/ (accessed June 13, 2017))

6.3 Results

A total of 10 retrieved implants were tested, and included 60% (6/10) males and 40% (4/10) females. The mean age of the patients was 63.5 years (range 54-86 years). The time in vivo ranged from 0.8 – 4.3 years. The reasons for revision included infection in 30% (3/10), instability in 50% (5/10), and aseptic loosening in 20% (2/10) of the cases. The time on shelf, after explantation, ranged from 0.5 – 5.9 years. The VH for the test samples ranged from 0.038 – 0.045 GPa (Table 6-2). The VH for two control samples was 0.044 +/- 0.003 and 0.048 +/- 0.004 GPa. The regression analysis of VH as a function of time in vivo showed no significant correlation, $r^2 = 0.015$ and $p = 0.707$ (Figure 6-2).

Table 6-2 Implanted time (Time in vivo) and Vickers Hardness for control and experimental samples.

Sample	Time in vivo (years)	Vickers Hardness (Gpa)	Std Deviation
Control 1	0.0	0.044	0.003
Control 2	0.0	0.048	0.004
1	0.8	0.043	0.004
2	1.0	0.042	0.003
3	1.0	0.039	0.002
4	1.1	0.038	0.002
5	1.4	0.038	0.002
6	3.8	0.042	0.004
7	3.9	0.042	0.004
8	4.0	0.045	0.003
9	4.2	0.040	0.002
10	4.3	0.042	0.001

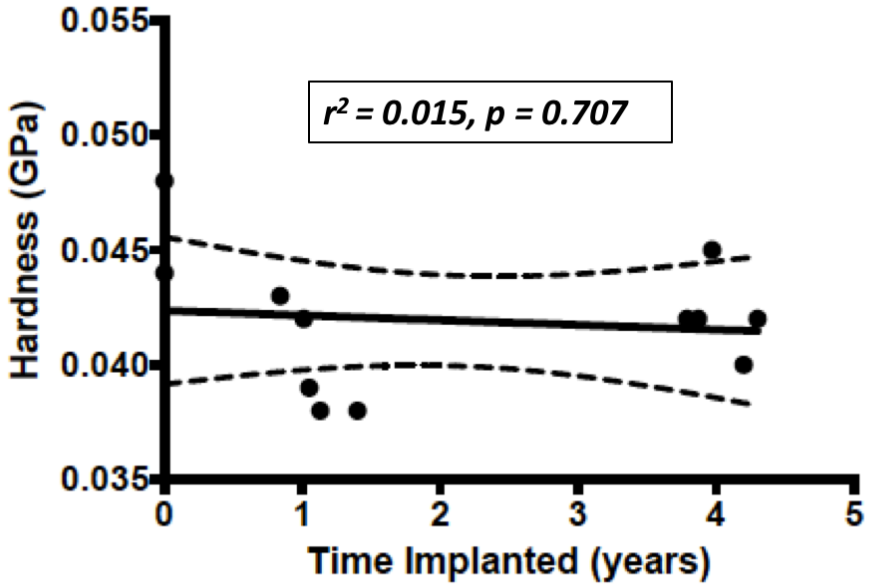

Figure 6-2 A linear regression analysis shows no significant correlation between hardness and time implanted of the tested liners.

6.4 Discussion

The improvements in wear characteristics due to crosslinking in HXLPE come at an expense of diminished mechanical properties. In addition, thermal treatment to eradicate free radicals leads to further deterioration fatigue crack propagation and fracture toughness[22]. Irradiated annealed first-generation liners, which contain residual free radicals demonstrate increasing in vivo oxidation with time, particularly at the rim[21]. Although to a lesser extent than irradiated annealed liners, irradiated remelted liners also exhibit measurable in vivo oxidation at the rim[11]. These factors in conjunction with reports of fractures at the rim of first-generation HXLPE liners make the study of mechanical properties in these liners important. Kurtz et al[21] showed that after intermediate implantation time, ranging from 0-8 years, irradiated annealed liners showed no correlation with in vivo time and ultimate tensile strength as measured by small punch testing. The testing of mechanical properties was carried out at the articulating surface. In

the same study, the oxidation index correlated exponentially with in vivo time at the rim ($R^2 = 0.48$; $p < 0.0001$). However, no mechanical properties were reported at the rim of the liners.

We demonstrate in this study findings like those of Kurtz et al[21], but at the rim of the liners. In our series, there was no correlation between time in vivo and hardness at the rim of irradiated remelted liners. Irradiated remelted liners, as opposed to annealed liners, have no detectable free radicals and therefore, may be relatively resistant in vivo oxidative deterioration. Although the tested samples had varying times on shelf, prior validation work (Chapter 5) that the time on shelf did not influence hardness in this design of liners up to 8 years on shelf.

Our study had some limitations. We had small numbers with relatively short time in vivo (0.8 - 4.3 years). Furthermore, implants studied in any retrieval study do not necessarily represent the full spectrum of in vivo biomechanics. The results of this study only apply to the single design of implants tested. We limited our study to a single design of liners, which had a flat rim surface. Although microtoming of samples can be performed to obtain flat surfaced specimens for indentation testing, microtoming can influence mechanical properties and lead to inaccurate results. No correlation to cup position and femoral component position was performed in this study. Furthermore, the mechanical testing technique used in this study is a novel setup and it is possible that hardness testing may not be sensitive enough to show degradation. The results of the study only apply to metal on polyethylene articulations and may not extrapolated to other bearing surface combinations.

Our study had the following strengths. This was the first retrieval study testing mechanical properties at the rim – the most commonly reported site of polyethylene fractures. We used a single design of liners and controlled for mechanical property variations that may exist within the various formulations of first-generation acetabular liners. We also demonstrate a relatively simple technique of testing mechanical properties, whereby the polyethylene liners do not need be sectioned or microtomed. The microtoming can influence mechanical properties of the polyethylene, as surface

variations induced from microtoming can influence hardness[23]. The samples were well preserved for further additional analysis after the indentation testing.

In conclusion, we demonstrate that the hardness at the rim of this specific design of irradiated remelted liners does not change with increasing time in vivo up to 4 years. The fractures at the rim of these liners is unlikely to be a result of worsening mechanical properties in vivo and likely a multifactorial issue as previously highlighted. More long term retrieval studies on various implants are necessary to monitor the in vivo performance of HXLPE acetabular liners.

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Chapter 7

7 Discussion

7.1 Discussion and Conclusions

Total hip arthroplasty (THA) has been termed “The operation of the century” for its excellent improvement in pain and function of patients with end-stage arthritis[1]. An UHMWPE has been the gold standard bearing surface in THA for its chemical inertness, lubricity, impact resistance, abrasion resistance, and low cost[2]. Wear of conventional UHMWPE resulting in osteolysis, aseptic loosening and ultimately, revision surgery has limited the longevity of the THA[3]. HXLPE was developed using radiation of the UHMWPE to improve wear characteristics of conventional UHMWPE[4] and has demonstrated excellent survivorship[5].

Irradiation and thermal treatment used in manufacturing of HXLPE results in decreased mechanical properties of polyethylene[6]. Moreover, the free radical production from irradiation predisposes it to oxidative deterioration, resulting in a further decline in mechanical properties[7]. Evidence of in vivo oxidation has been demonstrated at the rim of retrieved HXLPE liners[8]. In addition, case reports have been published reporting fractures at the rim[9]. These findings raise concerns related to in vivo decline of mechanical properties in these implants and warrants further study of mechanical properties. This is especially important given the increasing number of THA predicted to be performed in the future[10]. Moreover, implant longevity is crucial with evidence of increasing numbers of THA in younger patients[11]. In chapter 2, we reported the findings of our literature review on HXLPE. While retrieval studies have assessed mechanical properties at the articular surface of HXLPE[8], no studies have reported the mechanical properties at the rim – the site of maximal in vivo oxidation and fractures in HXLPE liners.

In this thesis, we set forth to determine the impact of in vivo time on mechanical properties at the rim of retrieved implants.

In Chapter 4, we discussed the modalities available and the rationale for using indentation testing to determine the mechanical properties in our studies. Micro indentation testing was selected for its simplicity of use, its prior validation in UHMWPE[12], its ability to test intact samples of liners and its correlation with oxidative deterioration[13].

It became evident through our literature review that ex vivo shelf oxidation can influence mechanical properties of our tested retrievals. The problem of shelf oxidation can be avoided by testing samples immediately after retrieval, storing them in subzero conditions or storing the samples at room temperature in nitrogen environment, minimizing exposure to oxygen[14]. In the majority of retrieval laboratories, the samples are stored at room temperature, and are exposed to room air. In chapter 5, the results of validation testing to determine the effects of shelf aging were reported. We demonstrated that implants with similar in vivo time (<12 weeks) showed no significant change in hardness at the rim with increasing shelf time up to 8.3 years.

In chapter 6, the results of our main study arm were reported. The hypothesis tested was that hardness at the rim of irradiated, remelted, retrieved HXLPE acetabular liners will increase with increasing in vivo time. The results demonstrated no significant change in hardness with increasing in vivo time up to 4.3 years, rejecting our proposed hypothesis.

In conclusion, we demonstrated that rim fractures in irradiated, remelted, HXLPE liners of this design are likely not due to in vivo deterioration of mechanical properties. This suggests that fractures result from other factors such as component positioning, thickness of liners, impingement, and potential patient factors. We demonstrated a relatively simple technique to measure mechanical properties at the flat surface of the rim of retrieved liners with preservation of the samples for further testing. We also showed that the storage protocols of retrieved HXLPE implants at room air may not result in significant mechanical deterioration. This study is the first one testing mechanical properties at the rim of the HXLPE liners. Retrieval studies with longer in vivo duration and including various designs are necessary to determine the impact of in vivo time on mechanical properties of HXLPE.

7.2 Future Directions

While irradiated, remelted retrievals of the tested design showed no changes mechanical properties up to 4.3 years of in vivo time, this may not apply to other designs and longer in vivo times. The next steps will involve testing of irradiated annealed liners, especially given the clear evidence of greater degree in vivo oxidation due to presence of free radicals in these liners. Correlation of oxidation indices and mechanical properties will be an important consideration to understand the impact of oxidation on mechanical properties. Furthermore, other manufacturing variables in resin stock, irradiation dose, and type of sterilization methods may impact mechanical properties differently with in vivo time. The impact of these variables on mechanical properties in vivo will add new information to the orthopaedic literature. In addition, determining the impact of clinical and surgeon factors on mechanical properties in vivo will be an important consideration.

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Appendix A: Ethics approval

Western Research

Research Ethics

Western University Health Science Research Ethics Board
HSREB Delegated Initial Approval Notice

Principal Investigator: Dr. Brent Lanting
Department & Institution: Schulich School of Medicine and Dentistry\Orthopaedic Surgery, London Health Sciences Centre

Review Type: Delegated
HSREB File Number: 108424
Study Title: Mechanical testing of retrieved acetabular liners from total hip arthroplasty

HSREB Initial Approval Date: October 17, 2016
HSREB Expiry Date: October 17, 2017

Documents Approved and/or Received for Information:

Document Name	Comments	Version Date
Western University Protocol	Received 2016/09/23	
Data Collection Form/Case Report Form	Implant data collection form - Received 2016/08/25	
Data Collection Form/Case Report Form	Demographic data collection form - Received 2016/08/25	

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above named study, as of the HSREB Initial Approval Date noted above.

HSREB approval for this study remains valid until the HSREB Expiry Date noted above, conditional to timely submission and acceptance of HSREB Continuing Ethics Review.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

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Curriculum Vitae

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Peer-Reviewed Publications

1. Percutaneous treatment of pelvic and acetabular fractures in the obese. Bates P, Gary JL, **Singh G**, Reinert CM, Starr AJ. Orthopedic Clinics of North America - January 2011 (Vol. 42, Issue 1, Pages 55-67)

Poster Presentations

1. Anatomic Delineation and MRI of the anterolateral ligament of the cadaveric knee. Bean G, **Singh, G**, Griffith B, Schmidt D.
2. Improve aftercare of Osteoporotic patients treated in the ER following fragility fracture: A Quality improvement project. **Singh G,** Volpini DM, Gray J, Toohey JS. In Implementation, pending data collection. 2015
3. Improve aftercare of Osteoporotic patients treated in the ER following fragility fracture: A Quality improvement project. **Singh G,** Volpini DM, Gray J, Toohey JS. In Implementation, pending data collection. 2016

Podium Presentations

1. Ethnic Differences in Perceptions towards Isolated Orthopaedic Injuries: a Pilot Study. **Singh G**, Zelle BC. Presented at Alamo Orthopaedic Society meeting 2016 and UTHSCSA Alumni Day 2016.