Apex Knee™ System Polyethylene

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INTRODUCTION

Highly crosslinked ultra high molecular weight polyethylene (UHMWPE) has become the current clinical standard for acetabular bearings in total hip arthroplasty (THA) components. The wear performance of highly crosslinked THA bearings from various manufacturers have generally been similar to the wear performance reported for *in vitro* hip simulator studies [1-5], with an approximate six to ten-fold reduction in the wear rates compared to conventional (gamma sterilized in inert gas or vacuum) components [6-13]. However, there have been reports of modular acetabular liner fractures, especially thin highly crosslinked liners, due to recurrent subluxation of the femoral head, impingement of the femoral neck, and/or notch-like design features at the rim [14-19]. This risk can be exacerbated by oxidation of the exposed rim of the liner [13, 20, 21].

The success of highly crosslinked UHMWPE in the hip naturally has lead to the development and testing of highly crosslinked UHMWPE for total knee arthroplasty (TKA). Consistent with hip simulator testing, wear rates in knee simulators decrease with increasing radiation dose, though the decrease is less dramatic [3, 22]. Subsequently many orthopaedic implant manufacturers have released highly crosslinked UHMWPE components for TKA.

The Apex Knee™ System consists of cobalt chrome femoral components and tibial base plates, and UHMWPE tibial inserts and patella resurfacing components. All tibial inserts and patellar components used in the Apex Knee™ System are machined from compression molded, calcium stearate-free UHMWPE, and sterilized using ethylene oxide (EtO), with no radiation crosslinking at any stage of the production, including sterilization. **This was a deliberate choice for the Apex Knee™ System based on both the long term excellent clinical results for non-irradiated UHMWPE and various concerns regarding highly crosslinked polyethylene as applied to TKA.**

Figure 1: Apex Knee System™ Femoral and Tibial Components

To date, the clinical literature regarding the performance of highly crosslinked TKA components is limited and not generally superior when compared to the clinical performance of gamma radiation sterilized, inert packaged “conventional” UHMWPE. The purpose of this paper is to review the most relevant literature in some detail and to contrast the rationale and results for highly crosslinked UHMWPE to both conventional, radiation sterilized UHMWPE, and to non-irradiated EtO sterilized UHMWPE. Relevant background information is included for completeness and to provide an historical perspective.

BRIEF HISTORY OF TKA UHMWPE

The majority of commercial knee replacement systems up until the mid-to-late 1990’s employed gamma radiation sterilization of the UHWMPE tibial components packaged and stored in air prior to surgical implantation. The combination of gamma irradiation, which creates free radicals in the polymer, and exposure to oxygen results in oxidation of the UHMWPE [23]. This oxidation, which begins during shelf storage of the components and continues *in vivo*, can result in embrittlement and degraded fatigue strength [24]. When combined with the high stresses that occur during gait and other normal activities, the degraded material properties can result in

catastrophic material failure, including pitting, delamination, and fracture [25]. In response to these observed failures, most manufacturers using gamma radiation sterilization of their UHMWPE components eliminated oxygen from their packaging, employing either vacuum or an inert gas such as nitrogen or argon. **Many manufacturers continue to offer gamma radiation sterilized UHMWPE components in inert packaging, now commonly referred to as "standard" or "conventional" polyethylene.** While the elimination of oxygen from the package prevents oxidation during shelf storage, unfortunately radiation-sterilized polyethylene is still susceptible to oxidation *in vivo* [26-28].

Going against the mainstream, some manufacturers changed to, or continued to use non-irradiated UHMWPE for TKA components; this requires sterilization using non-ionizing methods, most commonly ethylene oxide (EtO) or gas plasma. In contrast to gamma or electron beam irradiation, EtO or gas plasma sterilization does not result in free radical formation and maintains the inherent strength of the virgin UHMWPE [4]. Provided the material is never irradiated, EtO sterilized polyethylene maintains its resistance to oxidation both on the shelf [29, 30] and *in vivo* [31-33]. Non-irradiated, compression molded, EtO sterilized UHMWPE is used for all Apex Knee™ System polyethylene components. **It is important to distinguish non-irradiated, EtO sterilized UHMWPE from so-called "conventional" polyethylene, which has been sterilized using gamma radiation in inert packaging.**

There have been multiple attempts to enhance the UHMWPE used in TKA. Carbon fiber reinforcement was perhaps the most striking clinical failure of an "improved" UHMWPE [34]. Other failed attempts that reached clinical usage include heat-pressed UHWMPE [35, 36] and high crystalline UHMWPE (Hylamer-M, DePuy Orthopaedics, Warsaw, IN) [37]. More recently, a number of implant manufacturers have released highly crosslinked UHMWPE TKA components. Some of these materials include a chemical antioxidant, most commonly vitamin E. Based on the evaluation of explanted components, joint fluid particle measurement, and clinical survivorship to date, the *in vivo* performance of these various materials has largely been similar to that of "conventional" gamma-sterilized, inert-packaged UHMWPE (see below).

FACTORS THAT INFLUENCE WEAR PERFORMANCE OF UHMWPE IN TKA

The mechanics of total knee replacement are far different from the mechanics of total hip replacement. The geometry of the articular surfaces and the kinematic behavior of the knee are more complex than those of the hip joint. As a consequence, the material properties of the UHMWPE components are only one of many factors that can influence the wear performance of TKA:

- **Implant factors:**
  - **Congruity**: higher congruity generally results in higher contact areas and lower contact stresses [38];
  - **Kinematics**: wear can increase with adverse kinematics, such as excessive posterior translation of the femoral component with high flexion resulting in wear of the posterior edges of the tibial insert [39, 40];
  - **UHMWPE thickness**: stresses increase with decreasing thickness, especially for metal-backed inserts with a thickness of less than 6 mm [41];
  - **Locking mechanism**: backside wear can be elevated by inadequate capture of the UHMWPE insert to the tibial tray [42];
  - **Surface finish**: roughness of the femoral articular surface and/or the tibial tray surface supporting the insert can increase wear [43]; and
  - **Material**: inadequate strength of the UHMWPE can lead to gross material failure, such as pitting and delamination resulting from oxidation of gamma irradiated tibial inserts [24], or fracture of the posterior stabilized (PS) post of highly crosslinked inserts [44-46].
- **Surgical factors:**
  - **Alignment**: malalignment, such as excess posterior tibial slope, varus malalignment of the tibial component and/or valgus malalignment of the femoral component, can result in elevated wear of the UHMWPE insert [47-49]; and
  - **Soft tissue balancing**: improper soft tissues tensions and balancing can increase UHMWPE wear, such as either an excessively loose or excessively tight PCL with cruciate retaining TKA [39, 40].

- **Other factors**:
  - **Third body debris**: third body debris, such as bone cement particles, can result in elevated UHWMPE tibial insert wear [50]; and
  - **Functional demand**: higher levels of patient activity [51, 52], body mass [48], and high flexion range of motion (ROM) [53], especially for implants not designed to accommodate high flexion, can increase UHMWPE component wear.

EFFECTS OF RADIATION CROSSLINKING ON UHMWPE

Exposure of UHMWPE to ionizing radiation, typically by gamma or electron beam radiation, causes breaks in the long molecular chains and the formation of free radicals. These free radicals are groups of atoms with an odd (unpaired) number of electrons, and are highly reactive. Molecular crosslinks are created by the recombination of these breaks across adjacent molecular chains, neutralizing the corresponding free radicals. However, if oxygen is present, the free radicals can lead to oxidative degradation of the UHMWPE. The free radicals can react with oxygen and form peroxy free radicals; these highly reactive free radicals form hydroperoxides, which decay over time, and also create new free radicals that further fuel the oxidation process [54]. This oxidation can result in dramatic degradation of the material strength and fracture toughness [24].

"Conventional" UHMWPE can be considered to be lightly or moderately crosslinked, relative to virgin UHMWPE, due to the gamma irradiation used for sterilization. The radiation dose typically used for sterilization is in the range of 28-40 kGray (2.8-4.0 Mrad). For intentionally crosslinked materials, the supplemental radiation dose varies by manufacturer and formulation, but is typically in the range of 50-70 kGray (4-6 Mrad) for "moderately" crosslinked or 80-110 kGray (8-11 Mrad) for "highly" crosslinked UHMWPE [55]. The total radiation dose may be higher if the highly crosslinked UHMWPE is terminally sterilized using gamma radiation.

It has been clearly established that gamma-in-air sterilized UHMWPE components oxidize during shelf storage and *in vivo* service [31, 56-60]. This oxidation has been associated with higher wear rates in laboratory testing [61], and wear damage, cracking, delamination, and fracture in retrieved components [56, 62]. Gamma radiation in the presence of oxygen induces oxidation, primarily within about 0.5 mm of the surface (the diffusion depth of the oxygen), whereas the same irradiation induces crosslinking of the polymer in the absence of oxygen [63]. Artificial aging in the presence of oxygen reduces the crosslinking and increases the oxidation, with maximal effect on the surface and subsurface regions of the gamma irradiated UHMWPE.

On the other hand, radiation in the absence of oxygen increases the crosslinking of the UHMWPE and, in turn, can yield improved wear resistance in both hip and knee simulators [4, 22, 64]. Unfortunately, radiation crosslinking even in the absence of oxidation reduces critical mechanical properties, including elongation to break [65, 66], fatigue strength [30], and subsurface toughness [22]. Irradiation also results in residual free radicals that can oxidize (on the shelf and *in vivo*) and lead to markedly reduced wear performance [4, 32, 67-69]. The oxidation resistance of the irradiated UHMWPE can be improved by post irradiation heat treatment (annealing or remelting) [3, 64], but these processes have additional undesirable effects on the mechanical properties of the finished material [65, 70], with annealing being less detrimental than remelting [71]; however, oxidation can still occur *in vivo* [13, 72, 73].

STABILIZATION WITH VITAMIN E OR OTHER CHEMICAL ANTIOXIDANT

The addition of a chemical antioxidant is an alternative to heat treatment for stabilization of radiation crosslinked UHMWPE. Stabilization of irradiated UHMWPE is needed to avoid degradation of the material due to oxidation. Vitamin E (α-tocopherol) currently is the most commonly used chemical antioxidant for orthopaedic implants [74-76]. Pentaerythritol tetrakis (Covernox™, DePuy Orthopaedics, Warsaw, IN) is also in use, but little has been published to date regarding application of this chemical to UHMWPE orthopaedic implants.

UHMWPE is first generated in the powder form; this powder is subsequently consolidated into a solid form by compression molding or ram extrusion. Radiation crosslinking is usually performed after consolidation because crosslinking the powder would inhibit proper consolidation. Vitamin E can either be mixed with the UHMWPE powder prior to consolidation or it can be added by diffusion into the solid form after consolidation.

The advantage of mixing the vitamin E with the powder prior to consolidation is that the concentration of vitamin E will be more uniform through the bulk of the consolidated material. While vitamin E can be an effective antioxidant, vitamin E also blocks crosslinking [77], so the concentration must be low if it is added to the UHMWPE powder prior to consolidation (and irradiation). On the other hand, if it is added after consolidation via chemical diffusion, the concentration will not be uniform, with the concentration being greatest near the surface, and lower in the bulk [78]. Micheli *et al.* [79] have reported improved wear for radiation crosslinked, vitamin E-doped UHMWPE relative to conventional UHMWPE in a knee simulator.

"E-CIMA" UHMWPE was developed by the Cambridge Polymer Group and the Massachusetts General Hospital, and stands for vitamin E enhanced, cold-irradiated, mechanically annealed UHMWPE. The vitamin E is added to the UHWPE powder prior to consolidation. The vitamin E is effective at preventing oxidation due to accelerated aging, and the mechanical annealing may help regain some yield strength lost due to radiation crosslinking, but the ultimate tensile strength and elongation at break are inferior to highly crosslinked, thermally annealed UHWMPE [80].

Rationale for adding vitamin E to UHMWPE:

- Radiation crosslinking of UHMWPE can increase wear resistance but leaves the material susceptible to oxidation;
- Vitamin E is very effective at blocking oxidation [78];
- The addition of a chemical antioxidant to UHMWPE that has been radiation crosslinked can eliminate the need for heat treatment and thus avoid the strength reduction that occurs with high temperature annealing (remelting).

Concerns regarding vitamin E in UHMWPE:

- Vitamin E blocks crosslinking [77];
- Vitamin E (alone) decreases wear resistance, which must be countered with increased crosslinking [81];
- Applied via diffusion, the vitamin E concentration can be high near the surface, but lower in the bulk [78], which could become exposed with significant wear;
- If blended with the UHMWPE powder prior to consolidation (for uniform concentration through the bulk), crosslinking is hindered [77], and a higher radiation dose is needed for equivalent crosslinking even with a low concentration of vitamin E; and
- The clinical performance of vitamin E-stabilized UHMWPE is unproven to date.

In summary, chemical antioxidants such as vitamin E can be useful for preventing oxidation of irradiated UHMWPE. On the other hand, **if the UHMWPE has never been irradiated, there is no need for a chemical antioxidant**.

RETRIEVAL ANALYSES OF KNEE TIBIAL INSERTS

The analysis of clinical retrievals (explanted components) is a highly effective means of establishing the behavior of particular materials and designs, especially as the behavior relates to long-term clinical performance. The severe degradation of gamma-in-air sterilized UHMWPE tibial inserts was first recognized by the examination of explanted components. More recently, retrieved highly crosslinked tibial inserts have been analyzed and compared to those of "conventional" UHMWPE tibial inserts.

Williams *et al.* [33] analyzed retrieved non-irradiated, EtO sterilized knee tibial inserts, with an average implantation time of 115 months (range of 4 to 214 months); they found no evidence of oxidation or fatigue damage of those inserts, even after more than 15 years of *in vivo* service. The authors concluded that (emphasis added) "**The wear performance of the examined bearings sterilized with EtO was exceptional**; they had significantly longer *in vivo* durations than retrievals sterilized with gamma irradiated in air ($P < .01$), **the bearings that were gamma irradiated in air older than 3 years had a fatigue incidence of 80% whereas the bearings sterilized with EtO had none**, and the 22 unicompartmental implants sterilized with EtO were of designs known to exert exceptionally high contact stress on the polyethylene...**Ethylene oxide gas sterilized components revealed no significant subsurface oxidation either visually in the form of a white band or chemically as measured with Fourier transform infrared analysis.** The excellent resistance to oxidation of these retrievals sterilized with EtO most likely is attributable to the minimal presence of molecular free radicals."

More recently, Willie *et al.* [82] examined 41 Natural Knee II explanted tibial inserts of three types: 1) 10 ram extruded GUR 4150 gamma-in-air sterilized inserts, average 8.6 years *in vivo* (range 42-196 months), 7 of which were "Flat" (versus "Congruent" or "Ultracongruent"); 2) 18 gamma-in-nitrogen compression molded GUR 1020 inserts, average 4.4 years *in vivo* (range 4-158 months) ; and 3) 13 compression molded GUR 1050 Durasul™ highly crosslinked inserts, average 1.1 years *in vivo* (range 4-27 months). The highly crosslinked inserts outperformed the gamma-in-air inserts, but **there was no significant difference between the highly crosslinked and the "conventional" gamma-in-nitrogen inserts**.

Van Citters *et al.* [83] found measurable oxidation in explanted tibial inserts with four different highly crosslinked materials (X3, Prolong, Durasul, and XLK, in decreasing order of oxidation), which increased with time *in vivo*. The authors reported that (emphasis added) "**To date, no reduction in clinical wear rate has been demonstrated by using highly crosslinked polyethylene in the knee**". When asked, the lead author stated that they still have never seen wear through of non-irradiated, EtO sterilized tibial insert explants.

The study by Williams *et al.* [33] merits further consideration. Their findings were published in 1998, which means that the retrieved tibial inserts with over 15 years of *in vivo* service were implanted in the early 1980's (at the latest). Inarguably there has been significant progress in the field of knee arthroplasty since that time. Current generation TKA components have much improved articular geometries, with greater congruency, greater inherent stability, better restoration of healthy anatomy, and reduced potential for edge loading, all of which reduce the mechanical stresses in the UHMWPE bearing components relative to those historical designs. Despite the dated designs, the non-irradiated, EtO sterilized tibial components demonstrated "exceptional" wear performance. One must ask, **what problem is the industry attempting to fix by radiation crosslinking of UHMWPE tibial inserts?**

IN VIVO WEAR AND FRACTURE OF UHMWPE

The clinical results for highly cross-linked acetabular shell liners have been encouraging to date based on measured wear rates [17-26]. These reports focus on femoral head penetration (or wear) of the UHMWPE liner, measured using radiographs or Radiostereometric Analysis (RSA), with follow-up times ranging from two to five years. All of these studies report lower wear rates, as reflected by lower measured femoral head penetrations, for the highly crosslinked UHMWPE acetabular cup liners when compared to conventional UHMWPE liners of the same design. The measurement of wear rates in the knee *in vivo* is more difficult due to the more complex geometry of TKA components compared to the ball-and-socket geometry of THA. In place of RSA, several reports have been published in which UHMWPE particles were extracted and measured from synovial fluid samples taken from TKA patients as an indication of combined tibial and patellar component UHMWPE wear.

Minoda *et al.* [84] measured particles in the synovial fluid from 52 knees (total), 9-12 months post TKA, from five different implant groups: 1) posterior stabilized (PS) knees with "conventional" polyethylene (gamma-in-nitrogen, n=11); 2) mobile bearing knees with "conventional" polyethylene (n=11); 3) cobalt chrome "Medial Pivot" knees with EtO sterilized polyethylene (n=15); 4) alumina ceramic "Medial Pivot" knees with EtO sterilized polyethylene (n=11); and 5) cruciate retaining (CR) knees with Prolong highly crosslinked polyethylene (n=4):

Table 1: UHMWPE particle counts from various designs and materials [84]

TKA design	UHMWPE condition	Total particles (mean ± SE)
Mobile bearing	Gamma-inert	$1750 \pm 1020 \times 10^5$
PS with gamma-inert	Gamma-inert	$1160 \pm 570 \times 10^5$
Medial pivot	EtO sterilized	$570 \pm 282 \times 10^5$
Medial pivot (alumina)	EtO sterilized	$71 \pm 28.6 \times 10^5$
Cruciate retaining	Prolong highly crosslinked	$2.8 \pm 1.2 \times 10^5$

Unfortunately there were many confounding variables between groups, including different implant designs and manufacturers, and the report did not include statistical analysis (significance, or lack thereof).

In a single implant design study, Hinarejos *et al.* [85] measured particles from synovial fluid of Stryker Triathlon TKA patients 12 months post-op (17 patients in each group): conventional UHMWPE (gamma-in-nitrogen) and X3 highly crosslinked UHWMPE. There was no significant difference between the two groups in the concentration, size, or morphology of the UHWMPE particles. The authors concluded that the great variability between individuals in their study (emphasis added) "...suggests that ***in vivo*** **polyethylene wear depends on many factors and probably the type of polyethylene is not the most significant."**

UHMWPE TKA components can be subjected to considerable mechanical stresses, which can put locking mechanisms, posterior tibial insert condyles, PS posts, patellar component fixation pegs, and other critical design features at risk of severe wear or fracture. For example, there are numerous reports of fractures of the posts of conventional UHWMPE PS tibial inserts [86-93]. Highly crosslinked UHMWPE tibial inserts and patellar components are also at risk of mechanical failure; there are fewer reports in the literature, though there have been case reports of four PS tibial post fractures with X3 (Stryker Orthopaedics, Mahwah, NJ) highly crosslinked UHMWPE [44-46], one recent case report of two fractured XLK (DePuy, Warsaw, IN) tibial inserts [94], one case report of a fractured Durasul® (Zimmer, Warsaw, IN) patellar component [95], and one case report of a fractured E1® (Biomet, Warsaw, IN) vitamin E-stabilized tibial insert [96].

Of course not all failures are reported in the literature. A search of the US FDA Manufacturer and User Facility Device Experience (MAUDE)[1] database for "X3" brand knee components (FDA Product Code "JWH") in the two year period from September 1, 2011 to August 30, 2013 revealed Medical Device Reports (MDR's) on 10 X3 tibial inserts and 13 X3 patellar components revised for fracture of the UHMWPE. In addition, there were 8 MDR's over the same two year period for excessive wear of X3 tibial inserts. This finding is not limited to X3 highly crosslinked UHMWPE, a similar search of the MAUDE database for "Durasul" brand knee components in the thirteen year period from March 1, 2000 to February 28, 2013 revealed MDR's on 7 Durasul tibial inserts and 13 Durasul patellar components revised for fracture of the UHMWPE, and 5 MDR's for excessive wear of Durasul tibial inserts. A similar search of the MAUDE database for "E1" brand knee components (FDA Product Code "JWH") in the two year period from September 1, 2011 to December 31, 2013 revealed two MDR's on E1 tibial inserts revised for fracture of the UHMWPE (one of which corresponds to the case report from R. L. Barrack [96]) and two MDR's on E1 tibial inserts revised for excessive wear.

CLINICAL SURVIVAL OF TKA WITH HIGHLY CROSSLINKED UHMWPE

The ultimate test of any TKA is the long term clinical survivorship, with the endpoint of greatest interest being surgical revision for any reason. Published survivorship studies of TKA with highly crosslinked UHMWPE components include single implant design studies and one joint registry retrospective review of a large patient population with a variety of implants and materials.

Hodrick *et al.* reported a retrospective review of 200 Natural Knee II (Zimmer) TKA patients, of which 100 patients received conventional UHMWPE tibial inserts (gamma-irradiated in nitrogen, 82-101 months post-operative) and 100 received Durasul™ highly crosslinked UHMWPE tibial inserts (69-82 months post-operative) [97]. The highly crosslinked UHMWPE group had two patients with tibial radiolucencies and no revisions for tibial tray loosening and the conventional UHMWPE group had 20 patients with radiolucencies and three patients revised for tibial tray loosening. The tibial revision rates were not significantly different between the two groups and there were no cases of early catastrophic failure related to wear of the UHMWPE components in either of the two groups.

Minoda *et al.* [98] reported on 202 consecutive NexGen CR (Zimmer) TKA patients, the first 113 received conventional UHMWPE tibial inserts and the following 89 knees received Prolong™ highly crosslinked UHMWPE tibial inserts. Two years after surgery, there were no surgical revisions, and there were no significant differences in the Knee Society scores and range-of-motion between the two groups.

Inacio *et al.* [99] conducted a retrospective analysis of 62,177 primary TKA's in a United States joint registry on three bearing combinations: 1) conventional UHMWPE combined with cobalt chrome femoral components (n=49,055); 2) conventional UHMWPE combined with oxidized zirconium femoral components (n=1,066); and 3) highly crosslinked UHMWPE combined with cobalt chrome femoral components (n=7,618). The outcome of interest was surgical revision (for any reason), grouped by aseptic and septic revision. The authors reported

[1] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases, search results on file

that the risk of all-cause aseptic and septic revision with cobalt chrome-highly crosslinked UHMWPE TKA bearings was not significantly greater than the risk with cobalt chrome-conventional UHMWPE TKA bearings. Similarly, the risk of all-cause aseptic and septic revision with oxidized zirconium-conventional UHMWPE TKA bearings was not significantly greater than the risk with cobalt chrome-conventional UHMWPE TKA bearings. However, **the cobalt chrome-conventional UHMWPE TKA bearings had the lowest aseptic revision rate of the three groups (Figure 2)**, with 0.38 revisions per 100 observed years versus 0.52 revisions per 100 observed years for the cobalt chrome-highly crosslinked UHMWPE TKA bearings, and versus 0.67 revisions per 100 observed years for the oxidized zirconium-conventional UHWMPE TKA bearings.

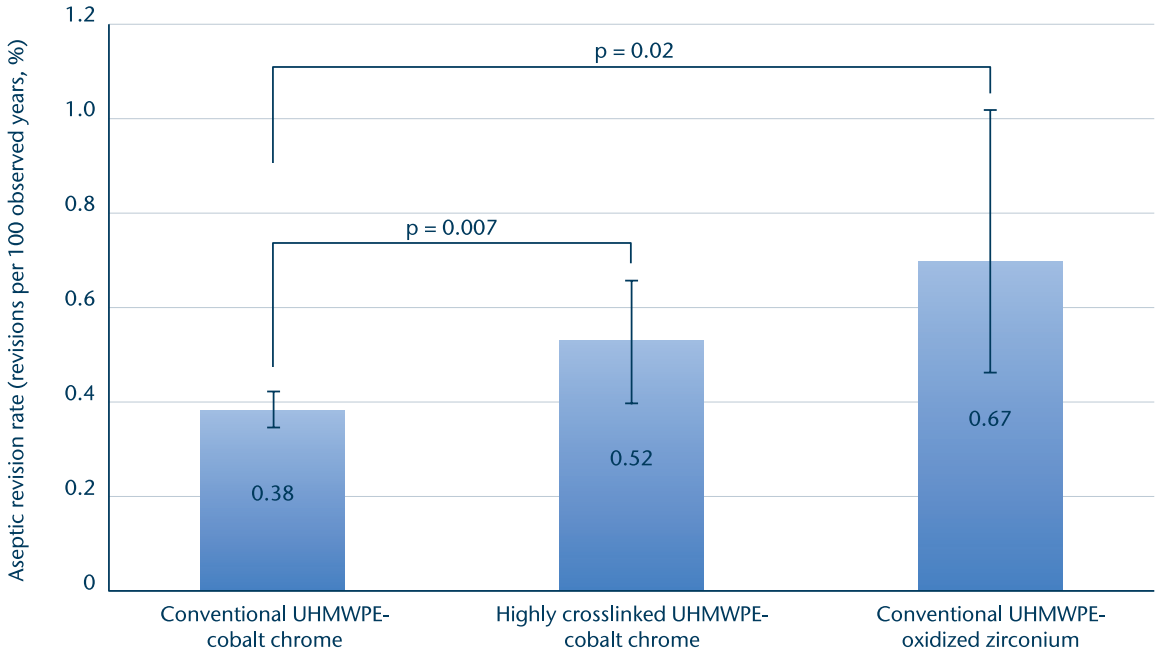

Figure 2: Aseptic revision rates, data extracted from Table 2 of Inacio *et al.* [99]

The report by Inacio *et al.* did not differentiate the various causes of aseptic revision, such as fracture, wear, or other material failure of a UHMWPE component versus, for instance, tibial insert exchange to address instability or limited range-of-motion. However, based on our searches of the FDA MDR database (above), it is reasonable to conclude that at least a portion of the TKA revisions in their registry were due to material failure of a highly crosslinked UHMWPE component.

CLINICAL SURVIVAL OF THE APEX KNEE SYSTEM

The clinical survivorship of the OMNI Apex Knee™ System in the United States is tracked using a combination of passive and active post-market surveillance. The study end-point is defined as surgical revision of any component for any reason, including both septic and aseptic revision. The passive surveillance includes any and all sources of reported Apex Knee™ System revisions, including FDA MDR's, medical professionals, sales agents, and third party sources such as literature, abstracts, and scientific meetings. As of year-end 2013, this database included over 25,000 TKA cases. This report does not account for non-reporting or competing events that preclude revision such as death. Although it cannot be assured that all APEX Knee System revisions are reported to OMNI, reports from all sources are investigated and included in the survivorship data.

The Kaplan-Meier survivorship estimate [100] as of year-end 2013 for the Apex Knee™ is above 99.3% at 7 years (Figure 3). The total number of surgical revisions was 89. The majority of the surgical revisions were related to superficial or deep infection (47 of the 89, or 53%). The primary reasons for aseptic revision were similar to those reported in the registries, including (from most frequent to least frequent) tibial insert exchanges for instability or limited ROM, femoral or tibial component loosening, periprosthetic bone fracture, and patellofemoral or other knee pain. To date, we are not aware of any revisions of the Apex Knee™ due to wear or fracture of a UHMWPE tibial insert or patellar component. It should be noted that the survivorship function at the far right of the Kaplan-Meier survival curve should be interpreted cautiously since there are fewer patients in the longest time periods and the survival estimates for those periods are not as accurate [101].

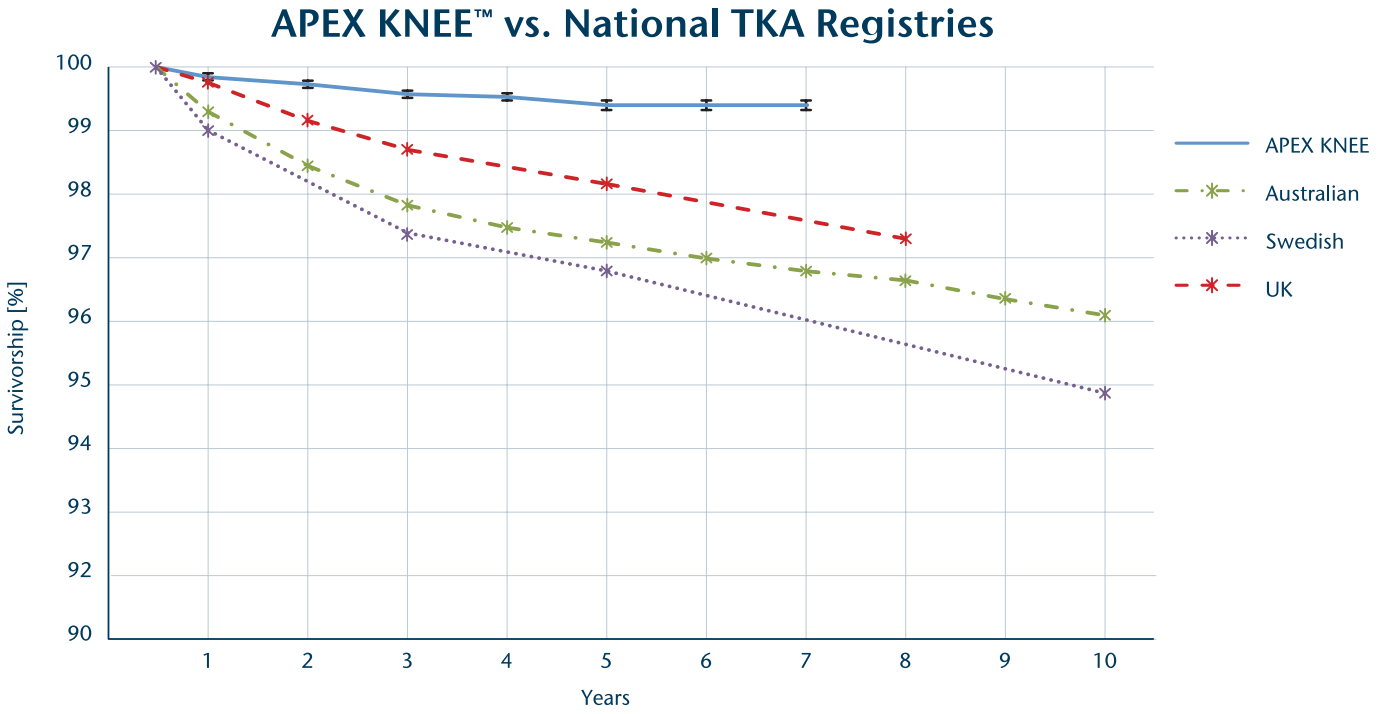

Figure 3: Kaplan-Meier Survivorship

Apex Knee™: all revisions, all types (cemented, cementless, and hybrid) fixed bearing TKA, 95% confidence interval using Greenwood's method [100]

UK National Joint Registry: all brands, all revisions, cemented fixed bearing TKA [102]

Swedish Knee Arthroplasty Register: all brands, all revisions, all types TKA [103]

Australian (AOA) National Joint Replacement Registry: all revisions, all types fixed bearing TKA [104]

Linear interpolation used between data points

All tibial inserts and patella implants in the Apex Knee™ System are machined from compression molded UHMWPE and have been since the product was first released in 2006. Ionizing radiation (gamma or electron beam) is not used at any stage in the manufacturing or sterilization of these UHMWPE components. The midterm survivorship of the Apex Knee™ System has been excellent and compares favorably to national registry data for other contemporary knee systems.

SUMMARY

Concerns regarding highly crosslinked UHMWPE in TKA:

- Reduction of fatigue strength [30], subsurface toughness [22], and elongation to break [65,66] due to radiation crosslinking;
- Oxidation *in vivo* that can lead to further strength reduction, which has been reported for various highly crosslinked UHMWPE formulations [13, 72, 73]; and
- Published case reports [44-46, 94-96] and FDA MDR's of surgical revision due to wear or fracture of highly crosslinked tibial inserts and patellar components.

Evidence-based selection of non-irradiated, compression molded UHMWPE for TKA:

- Lack of clinical performance advantage of highly crosslinked UHMWPE components compared to conventional (gamma-in-inert gas or gamma-in-vacuum sterilized) UHMWPE components from both single-design clinical and implant retrieval studies [82, 85, 97, 98], and from a registry survivorship study of a large collection of mixed implant data [99];
- Exceptional wear behavior of non-irradiated, EtO-sterilized tibial inserts from long term retrieval analysis [33]; and
- Excellent midterm survivorship of the Apex Knee System™ EtO-sterilized UHMWPE components.

REFERENCES

1. Affatato, S., Bordini, B., Fagnano, C., Taddei, P., Tinti, A., and Toni, A.: Effects of the sterilisation method on the wear of UHMWPE acetabular cups tested in a hip joint simulator. *Biomaterials*, **23**:1439-46, 2002.
2. Chiesa, R., Tanzi, M.C., Alfonsi, S., Paracchini, L., Moscatelli, M., and Cigada, A.: Enhanced wear performance of highly crosslinked UHMWPE for artificial joints. *J Biomed Mater Res*, **50**:381-87, 2000.
3. McKellop, H., Shen, F.W., Lu, B., Campbell, P., and Salovey, R.: Development of an extremely wear-resistant ultra high molecular weight polyethylene for total hip replacements. *J Orthop Res*, **17**:157-67, 1999.
4. McKellop, H., Shen, F.W., Lu, B., Campbell, P., and Salovey, R.: Effect of sterilization method and other modifications on the wear resistance of acetabular cups made of ultra-high molecular weight polyethylene. A hip-simulator study. *J Bone Joint Surg Am*, **82-A**:1708-25, 2000.
5. Ries, M.D., Scott, M.L., and Jani, S.: Relationship between gravimetric wear and particle generation in hip simulators: conventional compared with cross-linked polyethylene. *J Bone Joint Surg Am*, **83-A**:116-22, 2001.
6. Bragdon, C.R., Barrett, S., Martell, J.M., Greene, M.E., Malchau, H., and Harris, W.H.: Steady-state penetration rates of electron beam-irradiated, highly cross-linked polyethylene at an average 45-month follow-up. *J Arthroplasty*, **21**:935-43, 2006.
7. D'Antonio, J.A., Manley, M.T., Capello, W.N., Bierbaum, B.E., Ramakrishnan, R., Naughton, M., and Sutton, K.: Five-year experience with Crossfire highly cross-linked polyethylene. *Clin Orthop Relat Res*, **441**:143-50, 2005.
8. Rohrl, S., Nivbrant, B., Mingguo, L., and Hewitt, B.: *In vivo* wear and migration of highly cross-linked polyethylene cups a radiostereometry analysis study. *J Arthroplasty*, **20**:409-13, 2005.
9. Digas, G., Karrholm, J., Thanner, J., Malchau, H., and Herberts, P.: The Otto Aufranc Award. Highly cross-linked polyethylene in total hip arthroplasty: randomized evaluation of penetration rate in cemented and uncemented sockets using radiostereometric analysis. *Clin Orthop Relat Res*, **429**:6-16, 2004.
10. Geller, J.A., Malchau, H., Bragdon, C., Greene, M., Harris, W.H., and Freiberg, A.A.: Large diameter femoral heads on highly cross-linked polyethylene: minimum 3-year results. *Clin Orthop Relat Res*, **447**:53-9, 2006.
11. Heisel, C., Silva, M., dela Rosa, M.A., and Schmalzried, T.P.: Short-term *in vivo* wear of cross-linked polyethylene. *J Bone Joint Surg Am*, **86-A**:748-51, 2004.
12. Oonishi, H., Kim, S.C., Takao, Y., Kyomoto, M., Iwamoto, M., and Ueno, M.: Wear of highly cross-linked polyethylene acetabular cup in Japan. *J Arthroplasty*, **21**:944-9, 2006.
13. Kurtz, S.M., Austin, M.S., Azzam, K., Sharkey, P.F., Macdonald, D.W., Medel, F.J., and Hozack, W.J.: Mechanical properties, oxidation, and clinical performance of retrieved highly cross-linked crossfire liners after intermediate-term implantation. *J Arthroplasty*, **25**:614-623 e2, 2010.
14. Schroder, D.T., Kelly, N.H., Wright, T.M., and Parks, M.L.: Retrieved highly crosslinked UHMWPE acetabular liners have similar wear damage as conventional UHMWPE. *Clin Orthop Relat Res*, **469**:387-94, 2011.
15. Hara, D., Nakashima, Y., Yamamoto, T., Higashihara, S., Todo, M., Hirata, M., Akiyama, M., and Iwamoto, Y.: Late failure of annealed highly cross-linked polyethylene acetabular liner. *J Mech Behav Biomed Mater*, **28C**:206-212, 2013.
16. Halley, D., Glassman, A., and Crowninshield, R.D.: Recurrent dislocation after revision total hip replacement with a large prosthetic femoral head. A case report. *J Bone Joint Surg Am*, **86-A**:827-30, 2004.
17. Tower, S.S., Currier, J.H., Currier, B.H., Lyford, K.A., Van Citters, D.W., and Mayor, M.B.: Rim cracking of the cross-linked longevity polyethylene acetabular liner after total hip arthroplasty. *J Bone Joint Surg Am*, **89-A**:2212-17, 2007.
18. Waewsawangwong, W. and Goodman, S.B.: Unexpected failure of highly cross-linked polyethylene acetabular liner. *J Arthroplasty*, **27**:323 e1-4, 2012.
19. Blumenfeld, T.J., McKellop, H.A., Schmalzried, T.P., and Billi, F.: Fracture of a cross-linked polyethylene liner: a multifactorial issue. *J Arthroplasty*, **26**:666 e5-8, 2011.
20. Currier, B.H., Currier, J.H., Mayor, M.B., Lyford, K.A., Collier, J.P., and Van Citters, D.W.: Evaluation of oxidation and fatigue damage of retrieved Crossfire polyethylene acetabular cups. *J Bone Joint Surg Am*, **89**:2023-9, 2007.
21. Muratoglu, O.K., Wannomae, K.K., Rowell, S.L., Micheli, B.R., and Malchau, H.: *Ex vivo* stability loss of irradiated and melted ultra-high molecular weight polyethylene. *J Bone Joint Surg Am*, **92**:2809-16, 2010.
22. Akagi, M., Asano, T., Clarke, I.C., Niiyama, N., Kyomoto, M., Nakamura, T., and Hamanishi, C.: Wear and toughness of crosslinked polyethylene for total knee replacements: a study using a simulator and small-punch testing. *J Orthop Res*, **24**:2021-7, 2006.
23. Premnath, V., Harris, W.H., Jasty, M., and Merrill, E.W.: Gamma sterilization of UHMWPE articular implants: an analysis of the oxidation problem. Ultra High Molecular Weight Poly Ethylene. *Biomaterials*, **17**:1741-53., 1996.
24. Collier, J.P., Sperling, D.K., Currier, J.H., Sutula, L.C., Saum, K.A., and Mayor, M.B.: Impact of gamma sterilization on clinical performance of polyethylene in the knee. *J Arthroplasty*, **11**:377-89, 1996.
25. Muratoglu, O.K., Mark, A., Vittetoe, D.A., Harris, W.H., and Rubash, H.E.: Polyethylene damage in total knees and use of highly crosslinked polyethylene. *J Bone Joint Surg Am*, **85-A Suppl 1**:S7-S13, 2003.
26. Kurtz, S.M., Hozack, W.J., Purtill, J.J., Marcolongo, M., Kraay, M.J., Goldberg, V.M., Sharkey, P.F., Parvizi, J., Rimnac, C.M., and Edidin, A.A.: 2006 Otto Aufranc Award Paper: Significance of *in vivo* degradation for polyethylene in total hip arthroplasty. *Clin Orthop Relat Res*, **453**:47-57, 2006.

27. Wannomae, K.K., Bhattacharyya, S., Freiberg, A., Estok, D., Harris, W.H., and Muratoglu, O.: *In vivo* oxidation of retrieved cross-linked ultra-high-molecular-weight polyethylene acetabular components with residual free radicals. *J Arthroplasty*, **21**:1005-11, 2006.
28. Currier, B.H., Currier, J.H., Mayor, M.B., Lyford, K.A., Van Citters, D.W., and Collier, J.P.: *In vivo* oxidation of gamma-barrier-sterilized ultra-high-molecular-weight polyethylene bearings. *J Arthroplasty*, **22**:721-31, 2007.
29. Collier, J.P., Sutula, L.C., Currier, B.H., Currier, J.H., Wooding, R.E., Williams, I.R., Farber, K.B., and Mayor, M.B.: Overview of polyethylene as a bearing material: comparison of sterilization methods. *Clin Orthop Relat Res*, **333**:76-86, 1996.
30. Ries, M.D., Weaver, K., Rose, R.M., Gunther, J., Sauer, W., and Beals, N.: Fatigue strength of polyethylene after sterilization by gamma irradiation or ethylene oxide. *Clin Orthop Relat Res*, **333**:87-95, 1996.
31. Sutula, L., Currier, B.H., Currier, J.H., Farber, K.B., and Collier, J.P.: Relationship between sterilization methods, polyethylene resin types, and clinical performance. *Amer. Acad. of Orthop. Surg.*, Atlanta, 1996.
32. Sutula, L.C., Collier, J.P., Saum, K.A., Currier, B.H., Currier, J.H., Sanford, W.M., Mayor, M.B., Wooding, R.E., Sperling, D.K., Williams, I.R., and et al.: The Otto Aufranc Award. Impact of gamma sterilization on clinical performance of polyethylene in the hip. *Clin Orthop Relat Res*, **319**:28-40, 1995.
33. Williams, I.R., Mayor, M.B., and Collier, J.P.: The impact of sterilization method on wear in knee arthroplasty. *Clin Orthop Relat Res*, **356**:170-80, 1998.
34. Dannenmaier, W.C., Haynes, D.W., and Nelson, C.L.: Granulomatous reaction and cystic bony destruction associated with high wear rate in a total knee prosthesis. *Clin Orthop Relat Res*, **198**:224-30, 1985.
35. Mintz, L., Tsao, A.K., McCrae, C.R., Stulberg, S.D., and Wright, T.: The arthroscopic evaluation and characteristics of severe polyethylene wear in total knee arthroplasty. *Clin Orthop Relat Res*, 215-22, 1991.
36. Engh, G.A., Dwyer, K.A., and Hanes, C.K.: Polyethylene wear of metal-backed tibial components in total and unicompartmental knee prostheses. *J Bone Joint Surg Br*, **74**:9-17, 1992.
37. Ahn, N.U., Nallamshetty, L., Ahn, U.M., Buchowski, J.M., Rose, P.S., Lemma, M.A., and Wenz, J.F.: Early failure associated with the use of Hylamer-M spacers in three primary AMK total knee arthroplasties. *J Arthroplasty*, **16**:136-9, 2001.
38. Heim, C.S., Postak, P.D., and Greenwald, A.S.: Factors influencing the longevity of UHMWPE tibial components. *AAOS Instructional Course Lectures*, **45**:303, 1996.
39. Heesterbeek, P.: Mind the gaps! Clinical and technical aspects of PCL-retaining total knee replacement with the balanced gap technique: an academic essay in Medical Science. *Acta Orthop Suppl*, **82**:1-26, 2011.
40. Vail, T.P. and Lang, L.E.: Surgical techniques and instrumentation in total knee arthroplasty, in *Insall and Scott Surgery of the Knee*, W.N. Scott, Editor. 2012, Churchill Livingstone.
41. Bartel, D.L., Burstein, A.H., Toda, M.D., and Edwards, D.L.: The effect of conformity and plastic thickness on contact stresses in metal-backed plastic implants. *J Biomech Eng*, **107**:193-9, 1985.
42. Conditt, M.A., Thompson, M.T., Usrey, M.M., Ismaily, S.K., and Noble, P.C.: Backside wear of polyethylene tibial inserts: mechanism and magnitude of material loss. *J Bone Joint Surg Am*, **87**:326-31, 2005.
43. Galvin, A., Jennings, L.M., McEwen, H.M., and Fisher, J.: The influence of tibial tray design on the wear of fixed-bearing total knee replacements. *Proc Inst Mech Eng H*, **222**:1289-93, 2008.
44. Jung, K.A., Lee, S.C., Hwang, S.H., and Kim, S.M.: Fracture of a second-generation highly cross-linked UHMWPE tibial post in a posterior-stabilized Scorpio knee system. *Orthopedics*, **31**:1137-1139, 2008.
45. Jung, K.A., Lee, S.C., Hwang, S.H., and Kim, S.M.: Fractured polyethylene tibial post in a posterior-stabilized knee prosthesis presenting as a floating palpable mass. *J Knee Surg*, **22**:374-6, 2009.
46. Lim, H.C., Bae, J.H., Hwang, J.H., Kim, S.J., and Yoon, J.Y.: Fracture of a polyethylene tibial post in a Scorpio posterior-stabilized knee prosthesis. *Clin Orthop Surg*, **1**:118-21, 2009.
47. Srivastava, A., Lee, G.Y., Steklov, N., Colwell, C.W., Jr., Ezzet, K.A., and D'Lima, D.D.: Effect of tibial component varus on wear in total knee arthroplasty. *Knee*, **19**:560-3, 2012.
48. Ritter, M.A., Davis, K.E., Meding, J.B., Pierson, J.L., Berend, M.E., and Malinzak, R.A.: The effect of alignment and BMI on failure of total knee replacement. *J Bone Joint Surg Am*, **93**:1588-96, 2011.
49. Pang, H.N., Jamieson, P., Teeter, M.G., McCalden, R.W., Naudie, D.D., and Macdonald, S.J.: Retrieval analysis of posterior stabilized polyethylene tibial inserts and its clinical relevance. *J Arthroplasty*, **29**:365-8, 2014.
50. Zietz, C., Bergschmidt, P., Lange, R., Mittelmeier, W., and Bader, R.: Third-body abrasive wear of tibial polyethylene inserts combined with metallic and ceramic femoral components in a knee simulator study. *Int J Artif Organs*, **36**:47-55, 2013.
51. Lavernia, C.J., Sierra, R.J., Hungerford, D.S., and Krackow, K.: Activity level and wear in total knee arthroplasty: a study of autopsy retrieved specimens. *J Arthroplasty*, **16**:446-53, 2001.
52. Cerciello, S., Vasso, M., Felici, A., Corona, K., Palombi, A., and Schiavone Panni, A.: A review of sport recovery after total knee replacement. *J. Nov. Physiother.*, **S3**:1-5, 2013.
53. Paterson, N.R., Teeter, M.G., MacDonald, S.J., McCalden, R.W., and Naudie, D.D.: The 2012 Mark Coventry award: a retrieval analysis of high flexion versus posterior-stabilized tibial inserts. *Clin Orthop Relat Res*, **471**:56-63, 2013.
54. Oral, E. and Muratoglu, O.K.: Radiation cross-linking in ultra-high molecular weight polyethylene for orthopaedic applications. *Nucl Instrum Methods Phys Res B*, **265**:18-22, 2007.
55. Kurtz, S.M.: *The UHMWPE Handbook: Ultra High Molecular Weight Polyethylene in Total Joint Replacement and Medical Devices*. 2nd ed. 2009, San Diego, CA: Academic Press.

56. Otfinowski, J. and Dutka, J.: [Fracture of the acetabular cup as an early complication of total hip replacement]. *Chir Narzadow Ruchu Ortop Pol*, **56**:150-5, 1991.
57. Witkiewicz, H., Deng, M., Vidovszky, T., Bolander, M.E., Rock, M.G., Morrey, B.F., and Shalaby, S.W.: A differential scanning calorimetry study of retrieved orthopedic implants made of ultrahigh molecular weight polyethylene. *J Biomed Mater Res*, **33**:73-82, 1996.
58. Kurtz, S.M., Hozack, W., Marcolongo, M., Turner, J., Rimnac, C., and Edidin, A.: Degradation of mechanical properties of UHMWPE acetabular liners following long-term implantation. *J Arthroplasty*, **18**:68-78, 2003.
59. Willie, B.M., Ashrafi, S., Alajbegovic, S., Burnett, T., and Bloebaum, R.D.: Quantifying the effect of resin type and sterilization method on the degradation of ultrahigh molecular weight polyethylene after 4 years of real-time shelf aging. *J Biomed Mater Res*, **69A**:477-89, 2004.
60. Kurtz, S.M., Rimnac, C.M., Hozack, W.J., Turner, J., Marcolongo, M., Goldberg, V.M., Kraay, M.J., and Edidin, A.A.: *In vivo* degradation of polyethylene liners after gamma sterilization in air. *J Bone Joint Surg Am*, **87**:815-23, 2005.
61. Besong, A.A., Tipper, J.L., Ingham, E., Stone, M.H., Wroblewski, B.M., and Fisher, J.: Quantitative comparison of wear debris from UHMWPE that has and has not been sterilised by gamma irradiation. *J Bone Joint Surg Br*, **80**:340-4, 1998.
62. Birman, M.V., Noble, P.C., Conditt, M.A., Li, S., and Mathis, K.B.: Cracking and impingement in ultra-high-molecular-weight polyethylene acetabular liners. *J Arthroplasty*, **20**:87-92, 2005.
63. Shen, F.W. and McKellop, H.A.: Interaction of oxidation and crosslinking in gamma-irradiated ultrahigh molecular-weight polyethylene. *J Biomed Mater Res*, **61**:430-9, 2002.
64. Muratoglu, O.K., Bragdon, C.R., O'Connor, D.O., Jasty, M., and Harris, W.H.: A novel method of cross-linking ultra-high-molecular-weight polyethylene to improve wear, reduce oxidation, and retain mechanical properties. Recipient of the 1999 HAP Paul Award. *J Arthroplasty*, **16**:149-60, 2001.
65. Collier, J.P., Currier, B.H., Kennedy, F.E., Currier, J.H., Timmins, G.S., Jackson, S.K., and Brewer, R.L.: Comparison of cross-linked polyethylene materials for orthopaedic applications. *Clin Orthop Relat Res*, **414**:289-304, 2003.
66. McKellop, H.A., Shen, F.W., Campbell, P., and Ota, T.: Effect of molecular weight, calcium stearate, and sterilization methods on the wear of ultra high molecular weight polyethylene acetabular cups in a hip joint simulator. *J Orthop Res*, **17**:329-39., 1999.
67. Costa, L., Luda, M.P., Trossarelli, L., Brach del Prever, E.M., Crova, M., and Gallinaro, P.: *In vivo* UHMWPE biodegradation of retrieved prosthesis. *Biomaterials*, **19**:1371-85, 1998.
68. Edidin, A.A., Jewett, C.W., Kalinowski, A., Kwarteng, K., and Kurtz, S.M.: Degradation of mechanical behavior in UHMWPE after natural and accelerated aging. *Biomaterials*, **21**:1451-60, 2000.
69. Kurtz, S.M., Muratoglu, O.K., Evans, M., and Edidin, A.A.: Advances in the processing, sterilization, and crosslinking of ultra-high molecular weight polyethylene for total joint arthroplasty. *Biomaterials*, **20**:1659-88, 1999.
70. Kurtz, S.M., Villarraga, M.L., Herr, M.P., Bergstrom, J.S., Rimnac, C.M., and Edidin, A.A.: Thermomechanical behavior of virgin and highly crosslinked ultra-high molecular weight polyethylene used in total joint replacements. *Biomaterials*, **23**:3681-97, 2002.
71. Gencur, S.J., Rimnac, C.M., and Kurtz, S.M.: Fatigue crack propagation resistance of virgin and highly crosslinked, thermally treated ultra-high molecular weight polyethylene. *Biomaterials*, **27**:1550-7, 2006.
72. Rowell, S., Wannomae, K., Malchau, H., and Muratoglu, O.K.: Oxidative stability of a first generation highly cross-linked UHMWPE with up to 11 years *in vivo*. *AAHKS 23rd Annual Meeting*, American Association of Hip and Knee Surgeons, Dallas, TX, 2013.
73. Currier, B.H., Currier, J.H., Collier, J.P., Mayor, M.B., and Van Citters, D.W.: *In vivo* oxidation of highly cross-linked UHMWPE bearings. *56th Annual Meeting of the Orthopaedic Research Society*, 2011.
74. Oral, E., Rowell, S.L., and Muratoglu, O.K.: The effect of alpha-tocopherol on the oxidation and free radical decay in irradiated UHMWPE. *Biomaterials*, **27**:5580-7, 2006.
75. Oral, E. and Muratoglu, O.K.: Vitamin E diffused, highly crosslinked UHMWPE: a review. *Int Orthop*, **35**:215-23, 2011.
76. Oral, E., Wannomae, K.K., Hawkins, N., Harris, W.H., and Muratoglu, O.K.: Alpha-tocopherol-doped irradiated UHMWPE for high fatigue resistance and low wear. *Biomaterials*, **25**:5515-22, 2004.
77. Parth, M., Aust, N., and Lederer, K.: Studies on the effect of electron beam radiation on the molecular structure of ultra-high molecular weight polyethylene under the influence of alpha-tocopherol with respect to its application in medical implants. *J Mater Sci Mater Med*, **13**:917-21, 2002.
78. Oral, E., Wannomae, K.K., Rowell, S.L., and Muratoglu, O.K.: Diffusion of vitamin E in ultra-high molecular weight polyethylene. *Biomaterials*, **28**:5225-37, 2007.
79. Micheli, B.R., Wannomae, K.K., Lozynsky, A.J., Christensen, S.D., and Muratoglu, O.K.: Knee simulator wear of vitamin E stabilized irradiated ultrahigh molecular weight polyethylene. *J Arthroplasty*, **27**:95-104, 2012.
80. Wannomae, K.K., Micheli, B.R., Lozynsky, A.J., and Muratoglu, O.K.: A new method of stabilizing irradiated UHMWPE using vitamin E and mechanical annealing. *56th Annual Meeting of the Orthopaedic Research Society*, 2010.
81. Tipper, J.L., Beadling, A., Hussain, H., Russell, S., and Fisher, J.: Wear of vitamin E UHMWPEs under ideal and advers conditions. *5th UHMWPE International Meeting*, UHMWPE Lexicon, Philadelphia, PA, 2011.
82. Willie, B.M., Foot, L.J., Prall, M.W., and Bloebaum, R.D.: Surface damage analysis of retrieved highly crosslinked polyethylene tibial components after short-term implantation. *J Biomed Mater Res B Appl Biomater*, **85**:114-24, 2008.

83. Van Citters, D.W., Currier, J.H., Mayor, M.B., Currier, B.H., Carlson, E.M., Reinitz, S.D., Tomek, I.M., Kantor, S.R., Levine, R.A.C., Santa Maria, A.N., Wu, X., and Collier, J.P.: 1000 knee retrievals by tyhe numbers: important lessons learned, questions still to be answered. *American Acadamy of Orthopaedic Surgery*, AAOS, Chicago, IL, 2013.
84. Minoda, Y., Kobayashi, A., Iwaki, H., Iwakiri, K., Inori, F., Sugama, R., Ikebuchi, M., Kadoya, Y., and Takaoka, K.: *In vivo* analysis of polyethylene wear particles after total knee arthroplasty: the influence of improved materials and designs. *J Bone Joint Surg Am*, **91 Suppl 6**:67-73, 2009.
85. Hinarejos, P., Pinol, I., Torres, A., Prats, E., Gil-Gomez, G., and Puig-Verdie, L.: Highly crosslinked polyethylene does not reduce the wear in total knee arthroplasty: *in vivo* study of particles in synovial fluid. *J Arthroplasty*, **28**:1333-7, 2013.
86. Mariconda, M., Lotti, G., and Milano, C.: Fracture of posterior-stablized tibial insert in a Genesis knee prosthesis. *J Arthroplasty*, **15**:529-30, 2000.
87. Bal, B.S. and Greenberg, D.: Failure of a metal-reinforced tibial post in total knee arthroplasty. *J Arthroplasty*, **22**:464-7, 2007.
88. Chiu, Y.S., Chen, W.M., Huang, C.K., Chiang, C.C., and Chen, T.H.: Fracture of the polyethylene tibial post in a NexGen posterior-stabilized knee prosthesis. *J Arthroplasty*, **19**:1045-9, 2004.
89. Clarke, H.D., Math, K.R., and Scuderi, G.R.: Polyethylene post failure in posterior stabilized total knee arthroplasty. *J Arthroplasty*, **19**:652-7, 2004.
90. Hendel, D., Garti, A., and Weisbort, M.: Fracture of the central polyethylene tibial spine in posterior stabilized total knee arthroplasty. *J Arthroplasty*, **18**:672-4, 2003.
91. Mauerhan, D.R.: Fracture of the polyethylene tibial post in a posterior cruciate-substituting total knee arthroplasty mimicking patellar clunk syndrome: a report of 5 cases. *J Arthroplasty*, **18**:942-5, 2003.
92. Sands, K.C. and Silver, J.W.: Fracture of the polyethylene tibial post in a posterior stabilized PFC total knee arthroplasty. *Orthopedics*, **28**:1203-4, 2005.
93. Lachiewicz, P.F.: How to treat a tibial post fracture in total knee arthroplasty? A systematic review. *Clin Orthop Relat Res*, **469**:1709-15, 2011.
94. Teeter, M.G., McAuley, J.P., and Naudie, D.D.: Fracture of two moderately cross-linked polyethylene tibial inserts in a TKR patient. *Case Reports in Orthopedics*, **2014**:1-5, 2014.
95. Hambright, D.S., Watters, T.S., Kaufman, A.M., Lachiewicz, P.F., and Bolognesi, M.P.: Fracture of highly cross-linked all-polyethylene patella after total knee arthroplasty. *J Knee Surg*, **23**:237-40, 2010.
96. Barrack, R.L.: Retrieval analysis of an early fracture of a vitamin E-stabilized tibial liner in total knee arthroplasty. A case report. *J Bone Joint Surg Case Connect*, **3**:1-6, 2013.
97. Hodrick, J.T., Severson, E.P., McAlister, D.S., Dahl, B., and Hofmann, A.A.: Highly crosslinked polyethylene is safe for use in total knee arthroplasty. *Clin Orthop Relat Res*, **466**:2806-12, 2008.
98. Minoda, Y., Aihara, M., Sakawa, A., Fukuoka, S., Hayakawa, K., Tomita, M., Umeda, N., and Ohzono, K.: Comparison between highly cross-linked and conventional polyethylene in total knee arthroplasty. *Knee*, **16**:348-51, 2009.
99. Inacio, M.C., Cafri, G., Paxton, E.W., Kurtz, S.M., and Namba, R.S.: Alternative bearings in total knee arthroplasty: risk of early revision compared to traditional bearings: an analysis of 62,177 primary cases. *Acta Orthop*, **84**:145-52, 2013.
100. Kaplan, E.L. and Meier, P.: Nonparametric estimation from incomplete observations. *J Am Stat Assoc*, **53**:457-481, 1958.
101. Rich, J.T., Neely, J.G., Paniello, R.C., Voelker, C.C., Nussenbaum, B., and Wang, E.W.: A practical guide to understanding Kaplan-Meier curves. *Otolaryngol Head Neck Surg*, **143**:331-6, 2010.
102. Porter, M. *et al.*: *9th Annual Report*. National Joint Registry for England and Wales, 2012.
103. Robertsson, O. *et al.*: *Swedish Knee Arthroplasty Register Annual Report 2012*. Department of Orthopedics, Skane University Hospital, 2012.
104. Graves, S. *et al.*: *National Joint Replacement Registry Annual Report*. Australian Orthopaedic Association, 2012.

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