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Long-term biotribological evaluation of total hip and knee arthroplasty implants

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Abstract (English)

Total joint arthroplasty (TJA) is one of the clinically most successful and cost-effective surgical procedures being performed as a treatment for end-stage osteoarthritis. However, complications may occur due to biological responses triggered by polyethylene wear particles and metal ions released from the implant components. Originally, TJA was conceived as a procedure for elderly patients with moderate activity levels. Nevertheless, this procedure has now expanded to younger and more active patients, who generate more wear products due to their higher activity level. The purpose of the following doctoral thesis was to perform a series of pre-clinical tests in the field of biotribology in order to better understand the mechanisms that generate wear and evaluate if the implants in question are able to fulfill the demanding requirements of a long-term clinical performance. Two main research topics were defined, each one addressing a certain aspect of the implants: 1) backside wear on acetabular polyethylene liners and 2) biotribological behavior and metal ion release barrier function of zirconium nitride (ZrN) multilayer coated knee implants, designed for patients with metal ion hypersensitivity.

Backside wear due to micro-motion and poor conformity between the polyethylene liner and its acetabular shell may contribute to the overall amount of released wear particles and lead to aseptic loosening. Two research publications regarding this topic were performed with the purpose of understanding the wear process at the backside of polyethylene liners with a certain locking mechanism. As there are currently no studies nor standards to quantitatively measure the backside wear, a semi-quantitative optical analysis was developed in order to evaluate this type of wear. In the first research publication, a direct comparison between the backside wear of short-term in vitro wear simulated and retrieved acetabular liners with an equivalent life in service was done to obtain a first knowledge of the type of wear present at this non-articulating cup-insert fixation surface. In the second research publication, a long-term in vitro wear simulation was performed to analyze if this type of wear increases with time. The main finding of these two research publications was that most of the backside wear produced on the liners occurred during their insertion and removal from the acetabular shell rather than during their life in service and that there was no significant incremental progression of this type of wear through time (high cycle testing).

Regarding metal ion release, metal hypersensitivity became an important topic of research due to the adverse clinical results seen in patients with elevated cobalt values in blood. An alternative for such patients is the use of implants with a ZrN multilayer coating, which prevents the release of metal ions from the CoCrMo substrate material. The second part of this doctoral thesis was focused in the pre-clinical evaluation of total knee implants with such a ZrN multilayer coating. For the third and final research publication of the present thesis, a highly demanding activities knee wear simulation was performed for the first time on a ZrN multilayer coated knee implant with the purpose of comparing its wear characteristics and metal ion release barrier function against its clinically established uncoated version made out of CoCrMo. The results demonstrated that the ZrN multilayer coating significantly reduced the polyethylene wear rate and metal ion release from the

substrate material, even under such highly demanding conditions. Besides, the integrity of the ZrN multilayer coating was not impaired by failure modes such as delamination, surface disruption or flaking, resulting in a full functioning multilayer coating with long-term behavior.

In conclusion, this doctoral thesis demonstrates that the analyzed implants are able to maintain their good biotribological performance at the long-term, even under highly demanding conditions. Long-term in vitro tests that account for high demanding activities, need to be applied in future pre-clinical testing in order to evaluate and ensure the performance at the long-term of total joint arthroplasty implants in younger patients.

Zusammenfassung (Deutsch)

Die totale Gelenkarthroplastik (TJA) ist eines der klinisch erfolgreichsten und kostengünstigsten chirurgischen Verfahren zur Behandlung von Arthrose im Endstadium. Komplikationen können jedoch durch biologische Reaktionen auftreten, die durch Polyethylen-Verschleißpartikel und Metallionen aus den Implantatkomponenten ausgelöst werden. Ursprünglich wurde TJA als ein Verfahren für ältere Patienten mit überschaubarer Aktivität konzipiert. Dennoch wurden diese Verfahren inzwischen auf jüngere und aktivere Patienten ausgeweitet, die aufgrund ihrer höheren Aktivität mehr Verschleißprodukte erzeugen. Ziel der folgenden Doktorarbeit war es, eine Reihe von präklinischen Tests im Bereich der Biotribologie durchzuführen, um die Mechanismen besser zu verstehen, die zu Verschleiß führen und zu bewerten, ob die betreffenden Implantate die hohen Anforderungen an eine langfristige klinische Leistungsfähigkeit erfüllen können. Es wurden zwei Forschungsschwerpunkte definiert, die sich jeweils auf einen bestimmten Aspekt der Implantate beziehen: 1) „Backside Wear“ (Rückflächenverschleiß) am Acetabulum-Polyethylen-Inlay und 2) biotribologisches Verhalten und Metallionenfreisetzung Barrierefunktion von Zirkoniumnitrid (ZrN) Multilayer-beschichteten Knieimplantaten, die für Patienten mit Metallionenüberempfindlichkeit entwickelt wurden.

„Backside Wear“ aufgrund von Mikrobewegungen und mangelnder Übereinstimmung zwischen dem Polyethylen-Inlay und der zugehörigen Hüftpfanne kann die Gesamtmenge der freigesetzten Verschleißpartikel erhöhen und zu einer aseptischen Lockerung führen. Zwei Veröffentlichungen zu diesem Thema wurden mit der Zielsetzung durchgeführt, den Verschleißprozess an der Rückfläche des Polyethylen-Inlays mit einem bestimmten Fixationsmechanismus zu verstehen. Da es derzeit weder Studien noch Standards zur quantitativen Messung des „Backside Wear“ gibt, wurde eine semi-quantitative optische Analyse entwickelt, um diese Art von Verschleiß zu bewerten. In der ersten Veröffentlichung wurde ein direkter Vergleich zwischen dem „Backside Wear“ von kurzzeitig in vitro simulierten Hüft-Polyethylen-Inlays und Explantaten mit einer äquivalenten Lebensdauer in situ durchgeführt, um erste Erkenntnisse über die Art des Verschleißes an dieser nicht artikulierenden Oberfläche (Cup-Inlay-Fixation) zu erhalten. In der zweiten Veröffentlichung wurde eine langfristige In-vitro-Verschleißsimulation durchgeführt, um zu analysieren, ob diese Art von Verschleiß mit der Zeit zunimmt. Das Hauptergebnis dieser beiden Veröffentlichungen war, dass der größte Teil des „Backside Wear“ bei den Inlays während des Einsetzens und Entfernens aus der Hüftgelenkpfanne und nicht während ihrer Lebensdauer auftrat, und dass es keinen signifikanten Anstieg dieser Art von Verschleiß im Laufe der Zeit gab (Hochzyklische Tests).

Im Hinblick auf die Metallionenfreisetzung, wurde die Metallüberempfindlichkeit aufgrund der negativen klinischen Ergebnisse bei Patienten mit erhöhten Kobaltwerten im Blut zu einem wichtigen Forschungsthema. Eine Alternative für solche Patienten ist der Einsatz von Implantaten mit einer ZrN-Multilayer-Beschichtung, die die Freisetzung von Metallionen aus dem CoCrMo-Substratmaterial substantiell vermindert. Der zweite Teil dieser Dissertation befasste sich mit

präklinischen Tests von Knieimplantaten mit einer solchen ZrN-Multilayer-Beschichtung. Für die dritte und letzte Veröffentlichung der vorliegenden Arbeit wurde erstmals eine Knieverschleißsimulation mit Hochbelastungsaktivitäten an einem Multilayer-beschichteten ZrN-Knieimplantat mit dem Ziel durchgeführt, dessen Verschleißverhalten und Barrierefunktion gegen Metallionenfreisetzung mit seiner klinisch etablierten unbeschichteten Version aus CoCrMo zu vergleichen. Die Ergebnisse zeigten, dass die ZrN-Multilayer-Beschichtung die Polyethylenverschleißrate und die Metallionen-freisetzung aus dem Substratmaterial auch unter solchen anspruchsvollen Bedingungen deutlich reduziert. Außerdem wurde die Integrität der ZrN-Multilayer-Beschichtung nicht durch Versagensmodi wie Delamination, Oberflächenzerrüttung oder Schichtabplatzen beeinträchtigt, was einer voll funktionsfähigen Multilayer-Beschichtung mit Langzeitverhalten entspricht.

Zusammenfassend zeigt diese Dissertation, dass die untersuchten Implantate ihre gute biotribologische Leistungsfähigkeit auch unter sehr anspruchsvollen Bedingungen langfristig erhalten können. Langfristige In-vitro-Tests, die hohe Anforderungen stellen, sollten in zukünftigen präklinischen Tests angewendet werden, um die Leistungsfähigkeit von Implantaten für die Gelenkendoprothetik bei aktiven Patienten zu beurteilen und langfristig zu gewährleisten.

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List of abbreviations

µg/l	Microgram per liter
µm	Micrometer
µm/year	Micrometer per year
ASTM	American Society for Testing and Materials
CoCr	Cobalt chromium
CoCrMo	Cobalt chromium molybdenum alloy
DD	Deep Dish
g/l	Gram per liter
HDA	Highly demanding activities
ICP-MS	Inductively coupled plasma - mass spectrometry
IL-1ß	Interleukin 1 beta
IL-6	Interleukin 6
ISO	International Organization for Standardization
kg	Kilogram
kGy	Kilo Gray
mg	Milligram
mm	Millimeters
n	Number of samples
P-CupD_{Sym}	Plasmacup DC Symmetrical
P-CupS_{PW}	Plasmacup SC Posterior wall
P-Fit $_{Sym}$	Plasmafit Poly Symmetrical
Ref	Reference
STD	Conventional standard polyethylene
THA	Total hip arthroplasty
Ti6Al4V	Titanium -6 aluminum -4 vanadium alloy
TJA	Total joint arthroplasty
TKA	Total knee arthroplasty
TNF-α	Tumor necrosis factor alfa
UHMWPE	Ultra high molecular weight polyethylene
VitE	Highly cross-linked and vitamin E (0.1%) blended polyethylene
XPE	Highly cross-linked polyethylene
ZrN	Zirconium nitride

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1. Introduction

1.1 Background – Total joint arthroplasty

Total joint arthroplasty (TJA) is one of the clinically most successful and cost-effective surgical procedures being performed as a treatment for end-stage osteoarthritis, which has shown to relief pain and improve mobility in patients. During this procedure, the damaged articulation is resected and an artificial one is implanted. In case of total hip arthroplasty (THA), the four main components of a hip joint replacement are a metallic or ceramic ball, a metallic femoral stem, and an acetabular component formed by a liner made out of ultra high molecular weight polyethylene (UHMWPE), ceramic or metal and its metallic shell. Regarding the total knee arthroplasty (TKA), the three main components of a knee joint replacement are a metallic femoral component, a metallic tibia tray and an UHMWPE tibia liner.

In 2016, hip arthroplasty with 233 424 procedures and knee arthroplasty with 187 319 procedures were number six and fourteen among the most commonly performed inpatient procedures in Germany [1]. According to a study performed by Wengler et al. [2], the number of THA and TKA procedures performed in Germany increased approximately 11% and 22% respectively from 2005 to 2011 and is expected to keep growing during the next decades [3,4]. The general future demographic change to an older population as well as the increasing life expectancy were suggested as the main reasons for the increasing number of THA procedures [3]. However, non-demographic factors played a greater role in the changes of knee replacement case numbers [2].

In part due to its high survival rates greater than 90% at 10 years [5–9], TJA is nowadays more frequently performed in younger patients. A projection study performed by Kurtz et al. [10] showed that the patient population younger than 65 years represented 25 - 32% of the patients undergoing primary and revision TJA in 1993, this percentage increased to 40 - 46% in 2006 and is projected to be 52% for primary THA, 36% for revision THA, 55% for primary TKA and 62% for revision TKA by 2030. Thus, not only the aging of the population, but also the acceptance of TJA in young patients have contributed to the increasing number of primary TJA [11]. Consequently, the number of revision surgeries is also expected to increase and this could bring serious problems to the budget of the healthcare systems. For this reason, it is very important to research for new materials and implant designs that could assure a long-term performance and thus, reduce the need for a revision surgery.

1.2 Reasons for revision

Even though joint replacements are highly successful during their first decade of use, follow-up studies as well as registry data have shown a decrease in their survival rates during the second and third decade of clinical performance, where the survival rates can drop to 70 - 80% [12–17]. Moreover, studies have demonstrated that young patients have an enhanced risk of requiring a revision surgery starting the second decade after the primary procedure, especially young men who underwent a TKA [5,7,12,15,18] (Figure 1).

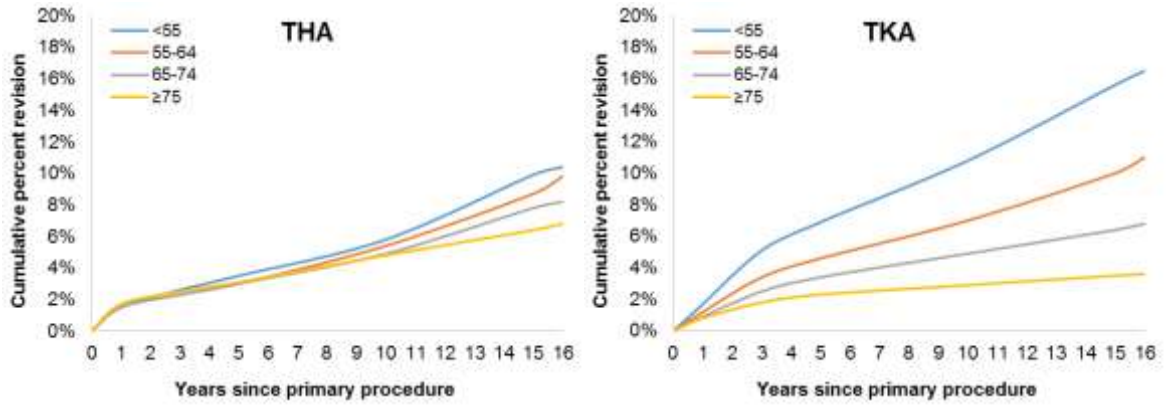

Figure 1: Cumulative percentage for revision of primary THA and TKA (with a primary diagnosis for osteoarthritis) classified by patient´s age. Adapted from the Australian National Joint Replacement Registry 2017 [12].

The most common causes for revision surgery in THA are aseptic loosening (55.2%) followed by dislocation (11.8%), while for TKA are aseptic loosening (29.8%) followed by septic loosening (14.8%) and wear (8.2%) [19]. Aseptic loosening is a direct consequence of wear particles from the UHMWPE liners. These wear particles trigger an inflammatory response mediated by macrophages and giant cells, who activate and liberate cytokines (interleukins IL-1ß, IL-6 and the TNF-α), which in turn produce inflammation, stimulate the osteoclasts and reduce the activity of the osteoblasts [20–22]. As a result, a periprostetic osetolysis occurs and so a loosening of the implant components. This inflammatory response is dependent on the amount of wear particles as well as their size and shape [22].

Originally, TJA was conceived as a procedure for elderly patients with moderate activity levels. Over the time, this procedure was expanded to younger and more active patients, who generate more wear on the UHMWPE liners due to their higher activity level. In order to reduce wear of the UHMWPE liners, and thus the incidence of revision resulting from oseteolysis, several improvements on the UHMWPE have been made through the last decades, which include a change to sterilization in an inert environment [23] and highly crosslinking of the UHMWPE [24–26]. Nevertheless, the long-term clinical performance of the highly-crosslinked UHMWPE is in question, as retrieval studies have demonstrated in vivo oxidation of this material due to cyclic loading and fluid absorption, which would increase its wear rates at the long-term [23,25,27–29]. More recently, antioxidants like α-tocopherol (vitamin E) are being added to the UHMPWE to prevent its oxidation and so maintain the low wear rates at the long-term [30–33]. However, there are currently no long-term in vivo results available and to date only in vitro studies are able to demonstrate its capabilities at the long-term.

Besides the UHMWPE wear debris, metal ion and particle release as well as metal hypersensitivity have become important research topics, as a relationship between cobalt and chromium blood levels and failure of implants has been demonstrated [34–40]. With the purpose of preventing cobalt ion release from the metallic implants, alternative materials such as ceramics, titanium or zirconium alloys or cobalt chromium alloys with a mono- or multilayer coating like titanium or zirconium nitride

have been developed [36,41]. However, retrieval studies have shown that some of these coatings might be susceptible to damage [42–44] and most of the available follow-up studies are restricted to their first decade of clinical performance [45–48]. As these implants are nowadays being used by younger and more active patients, it is important to perform adequate pre-clinical tests that can demonstrate their long-term performance accounting for such population.

1.3 Pre-clinical testing – Relevance of biotribology

Through the decades, research has been made with the purposes of increasing implant durability, reducing complications and improving the capacity of an implant to reproduce the native articulation. An ideal TJA implant should mimic normal physiology with respect to tribology, which means, the bearing couples should have a low coefficient of friction, high surface hardness with scratch resistance, generate a low volume of wear particles and the exposed surfaces should be non-cytotoxic and biocompatible [49]. Currently, the clinical lifespan of the implants is limited due to wear of the UHMWPE liners and subsequent loosening of the implants as well as to the adverse clinical reactions triggered by metallic wear debris. As a consequence, many patients outlive their implants and must undergo a costly and disruptive revision surgery. Considering that the number of TJA procedures is increasing, understanding the in vivo tribological process responsible of the damage caused to the implant components is highly important.

Implant biotribology is a function of the articulating surfaces, the surrounding environment and the applied load and motion [50]. As level walking is the most frequent activity performed by a TJA patient [51], one of the most important pre-clinical tests for total joint replacements is carried out using mechanical wear simulators under generic walking conditions, like the ISO 14242 for hip implants and ISO 14243 for knee implants. With these tests, the researcher is able to evaluate the wear and geometrical changes of the UHMWPE liners, analyze the surface of all the components and examine the test medium for wear products such as UHMWPE particles and metal ions.

However, a limitation of these tests is that they only simulate the short-term performance of an implant, as the 5 million cycles stipulated by the standards are equivalent to approximately 3 years of in vivo service [52]. Moreover, recent in vivo studies were able to measure the actual loads being applied at the knee [53] and hip articulations [54] during different daily life activities and have demonstrated that higher loads than those stated in the current standards are actually being applied on such articulations. These findings need to be applied in future pre-clinical testing in order to evaluate and ensure the performance at the long-term of total joint arthroplasty implants in younger patients.

1.4 Research questions, objectives and short summary of results

The main purpose of the present doctoral thesis was to perform a series of long-term biotribological pre-clinical tests in order to evaluate and understand the wear behavior of total hip and knee arthroplasty implants. Two main research topics were defined, each one addressing a certain aspect

of the implants. The first research topic was focused on evaluating the backside wear generated on acetabular liners at the short- and long-term performance, whereas the second topic was focused on evaluating multilayer-coated TKA implants, intended for patients with metal ion hypersensitivity, under pre-clinical tests accounting for young and dynamic patients.

In all the original research publications presented here, the author of this doctoral thesis contributed to the conception and design of the studies and performed the majority of the described tests. Moreover, she was fully responsible for the data collection, analysis and interpretation of results as well as drafting the manuscript and its further submission and revision process.

1.4.1 Publications I and II: Articulation and backside wear in acetabular liners

As previously stated, aseptic loosening due to polyethylene wear particles is the main reason for revision at the long-term in THA. Even though the origin of the wear particles occurs mainly at the articulation surface, another important source of wear particles occurs at the interface between the backside of the polyethylene liner in contact with the acetabular shell [55]. High backside wear has been associated with micro-motion between the liner and its acetabular shell due to an unstable locking mechanism and poor conformity between both components [56–58], and was implicated in the high rates of retroacetabular osteolysis observed in acetabular components with certain types of locking mechanisms [59–62].

For the first research publication of the present thesis, entitled “Backside wear analysis of retrieved acetabular liners with a press-fit locking mechanism in comparison to wear simulation in vitro” and published in BioMed Research International [63], the backside wear generated by a locking mechanism based on a press-fit cone in combination with a rough titanium inner surface at the rim of the metallic shell was investigated for the first time. By means of an optical analysis, in vitro tested and retrieved liners from different polyethylene materials and designs were examined with the following research objectives:

- to determine if there is micro-motion between the acetabular shell and polyethylene liner with the locking mechanism previously described
- to analyze the backside wear of polyethylene liners and determine the type of wear that occurs at this surface
- to compare the backside wear of polyethylene liners of different materials and designs
- to determine if a comparable backside wear could be observed between retrieved liners and in vitro tested liners of similar life in service

Plasmacup® and Plasmafit® polyethylene liners (Aesculap AG, Tuttlingen, Germany), both having the same locking mechanism between the liner and the acetabular shell previously described, were analyzed. Furthermore, three different polyethylene materials were analyzed for backside wear: conventional standard polyethylene (STD) packed under nitrogen atmosphere and sterilized by γ-irradiation (30 kGy); highly cross-linked polyethylene (XPE) by γ-irradiation (75 kGy) and sterilized

by ethylene oxide; and highly cross-linked and vitamin E (0.1%) blended polyethylene (VitE) which was cross-linked by an electron beam (80 kGy) and sterilized by ethylene oxide. The polyethylene liners were articulated in combination with acetabular shells made out of Ti6Al4V alloy and modular heads made out of ceramic or cobalt-chromium. A schematic presentation of the components is shown in Figure 2.

Figure 2: Schematic presentation of the different materials and designs investigated.

The in vitro tested liners (see Table 1) were subjected to artificial aging for two weeks according to ASTM 2003-02 and a hip wear simulation according to ISO 14242-1:2012(E) for 5 million cycles, which represents a mean life in service of 2.9 years [52]. On the other hand, the retrieved liners (n = 5) were all Plasmacup® models (STD = 1; XPE = 2; VitE = 2), were explanted during hip arthroplasty revisions in various hospitals in Germany and were in situ for a mean time of 13.1 months (from 0.5 to 37 months).

Table 1: Summary of in vitro tested implants. Obtained from Puente Reyna et al. [63].

In vitro group (n = 3 each)	Model	Polyethylene Material	Femoral Head	Head Diameter (mm)	Shell Diameter (mm)
P-Cup$D_{Sym\ VitE}$*	Plasmacup DC Symmetrical	VitE	CoCr	36	52
P-Cup$D_{Sym\ VitE}$	Plasmacup DC Symmetrical	VitE	Ceramic	36	52
P-Cup$D_{Sym\ XPE}$*	Plasmacup DC Symmetrical	XPE	CoCr	36	52
P-Fit $_{Sym\ VitE}$	Plasmafit Poly Symmetrical	VitE	Ceramic	36	50
P-Fit $_{Sym\ STD}$*	Plasmafit Poly Symmetrical	STD	CoCr	32	46
P-Fit $_{Sym\ STD}$	Plasmafit Poly Symmetrical	STD	Ceramic	32	46

As there are currently neither studies nor standards to quantitatively measure backside wear, a semi-quantitative optical analysis based on Hood et al. [64] was developed in order to analyze the backside wear of the polyethylene acetabular liners. The backside wear analysis was performed using a stereo light microscope up to a 25x magnification. Seven different zones in the polyethylene liners were defined on basis of their in situ orientation (Figure 3) and in each zone, a score between 0 and 3 was given for the following wear modes: pitting, scratching, burnishing, abrasion, embedded particles, deformation and delamination. A score of 0 meant no damage, 1 meant damage to less than 10% of the surface area, 2 meant damage to 10 - 50% of the surface area and 3 meant that

more than 50% of the area was damaged. This gave a total wear score of 21 per section and 147 for the entire liner. This analysis was performed twice on each liner by the author of this doctoral thesis (A. L. Puente Reyna) and the scores were averaged.

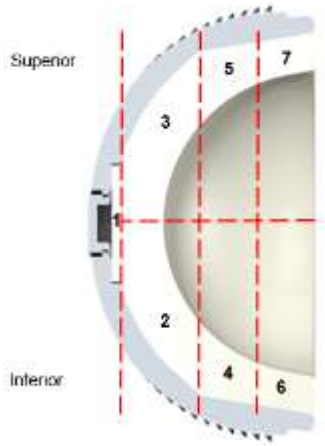

Figure 3: Sketch from a cross section of a P-Fit liner with its titanium alloy shell and backside sections for wear analysis. Adapted from Puente Reyna et al. [63].

The most common wear mode observed were small scratches at the fixation zone directly below the rough titanium inner surface of the shell, which were produced during the insertion and removal of the liner, rather than during its time in situ (Figure 4). As these small scratches were clearly seen, and the machining lines around them and at the pole of the liners were still clearly visible, it was concluded that the locking mechanism did not generate micro-motion and thus, that it did not produce significant wear at the backside of the polyethylene liners during its time in situ.

The total backside wear score for the in vitro tested liners ranged from 13.17 ± 0.75 to 21.83 ± 2.23, being 147 the maximum total backside wear score possible (Figure 5). The STD and XPE liners showed statistically higher total backside wear scores compared to the VitE liners and the total backside wear score was approximately the same for the in vitro and retrieved liners.

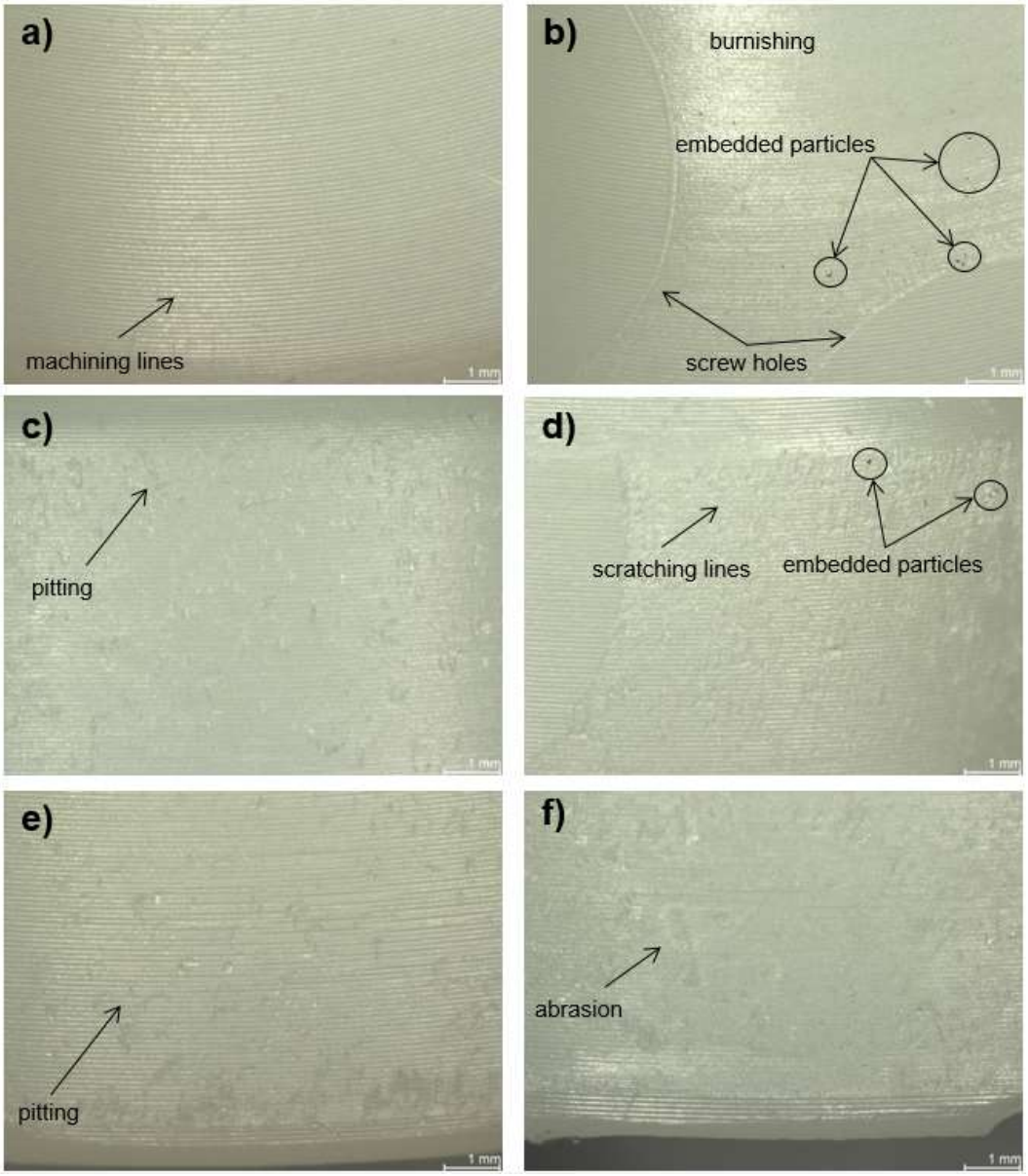

Figure 4: Photographs taken with a stereo light microscope from a P-Cup$S_{PW\,STD^*}$ retrieved liner after 37 months in situ; (a) Section 2: Machining lines clearly visible with no major wear marks; (b) Section 3: Screw holes visible but not palpable, with machining lines clearly visible and the periphery scratched and burnished with embedded particles; (c) Section 4: Pitting and machining marks still visible; (d) Section 5: Area with embedded particles and covered with scratches, machining marks partially visible; (e) Section 6: Small pitting visible; (f) Section 7: Area with abrasion marks. Adapted from Puente Reyna et al. [63].

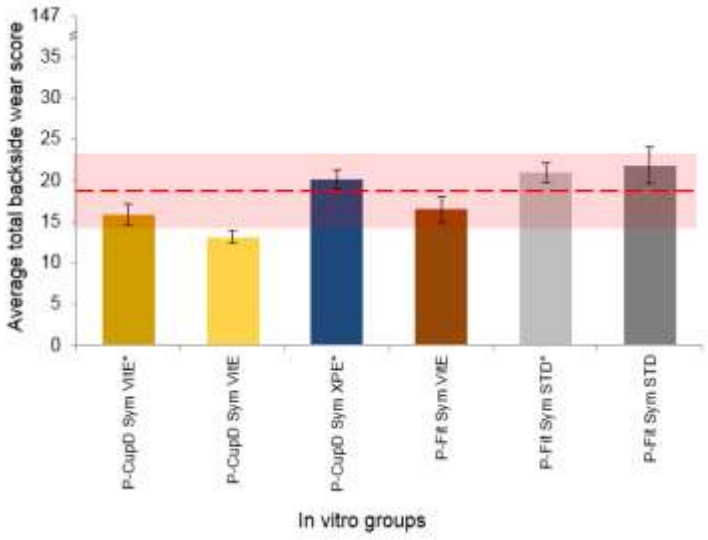

Figure 5: Summary of the average total backside wear score for in vitro tested liners. The dashed red line represents the average total backside wear score for the retrieved liners, while the red shadow shows the 95% confidence interval. The groups with "∗" were articulated against CoCr femoral heads and the others against ceramic femoral heads. Maximum total backside wear score possible = 147. Adapted from Puente Reyna et al. [63].

A limitation of this study was that the analyzed retrievals and the in vitro tested liners represented only the short-term performance of the locking mechanism in question. Since retrieval studies have demonstrated a correlation between backside damage and age in vivo for conventional and highly crosslinked polyethylene [65,66], it was important to perform a study where the long-term performance of the locking mechanism could be investigated. Moreover, as no long-term vitamin E blended polyethylene retrievals are available, only an in vitro study could provide this information.

In the second publication of this doctoral thesis, entitled "Articulation and backside wear analysis after long-term in vitro wear simulation of vitamin E stabilized polyethylene acetabular liners with a press-fit locking mechanism" and published in Traumatology and Orthopedics of Russia [67], a long-term in vitro hip wear simulation was performed with the following objectives:

- to determine what type of wear modes occur at the articulation and backside surfaces of vitamin E blended polyethylene liners at the long-term
- to quantify the wear rate at the articulation surface of this material
- to analyze if the backside wear increases with time (high cycle testing)

For this study, two weeks artificially aged VitE Plasmafit® polyethylene liners were used for the in vitro test. Hip wear simulation was performed according to ISO 14242-1:2014(E) for 20 million cycles, which represent a service life of approximately 12 years. Two different testing groups were defined: "Reference" liners, which correspond to the liners that were subjected only to axial load (n = 2), and "Wear simulated" liners (n = 6), which where subjected to axial load and movement. The wear simulation was stopped after 5, 10, 15 and 20 million cycles to perform an optical analysis of the articulation, and thus determine what type of wear modes were present. Furthermore, in order to

obtain a wear rate, the total femoral head penetration due to creep and wear of the polyethylene liners was assessed through a three-dimensional measuring machine at the end of the 20 million cycles. Finally, the same optical method previously described for the backside wear analysis was used with the purpose of analyzing this type of wear. For this study, two observers performed the analysis for this study (A. L. Puente Reyna and M. Holderied) and their scores were averaged.

The wear mode predominantly seen at the articulation area of the "Wear simulated" liners was burnishing of the surface with slight scratches. Besides, the wear area increased with time and the total head penetration was 107.4 ± 31.0 µm after 20 million cycles (Figure 6). On the other hand, the "Reference" liners showed no wear marks, as the machining lines were clearly seen through the whole test, and its total head penetration generated only by creep was 33.4 ± 7.8 µm (Figure 6). Taking into account an average of 1.76 million gait cycles per year for hip and knee arthroplasty patients [52], and that after approximately one year of implantation there is no considerable creep of the liner, the steady state wear rate of the vitamin E liners was approximately 7 µm/year.

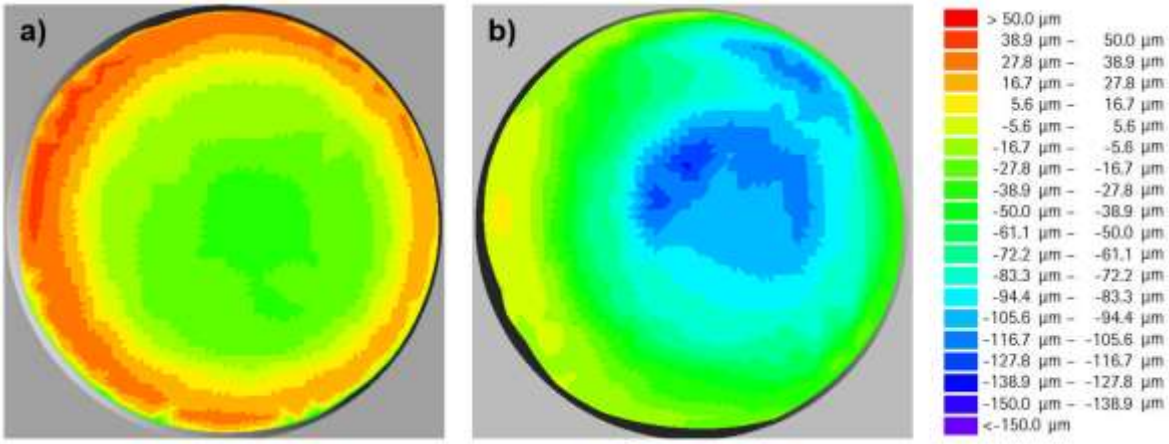

Figure 6: (a) Geometrical changes after 20 million cycles of a "Reference" liner subjected only to axial load (creep) and (b) a "Wear simulated" liner subjected to axial load and movement (creep and wear). Adapted from Puente Reyna et al. [67].

Regarding the backside wear analysis, the total average backside wear score of the "Wear simulated" liners (axial load and movement) was 22.00 ± 2.59 after 5 million cycles, increased to 31.92 ± 5.57 after 10 million cycles, but showed no further statistically significant increment after 15 and 20 million cycles. The "Reference" liners (subjected only to axial load) had statistically smaller scores than the "Wear simulated" liners after 5 and 20 million cycles. However, their wear modes and overall appearance were very similar to those seen in the "Wear simulated" liners. Comparable to the first publication, small scratches produced during insertion and removal were clearly seen at the rim (fixation) area and no considerable abrasion due to movement was observed, as the machining lines on the convex surface were always visible (Figure 7).

These results showed that there was little to no micro-motion between the liner and its acetabular shell in a long-term hip wear simulation. Furthermore, it was demonstrated that the main wear patterns at the backside of the liners were produced during their insertion and removal from the

acetabular shell rather than during their life in service, as a similar backside wear pattern was seen in the “Wear simulated” and “Reference” liners. Finally, the wear rate at the articulation surface was similar to that seen in vivo at a short- and mid-term on highly cross-linked polyethylene liners with and without vitamin E content [68–73] and was considerably below the reported osteolysis threshold wear rate of 100 µm/year [74].

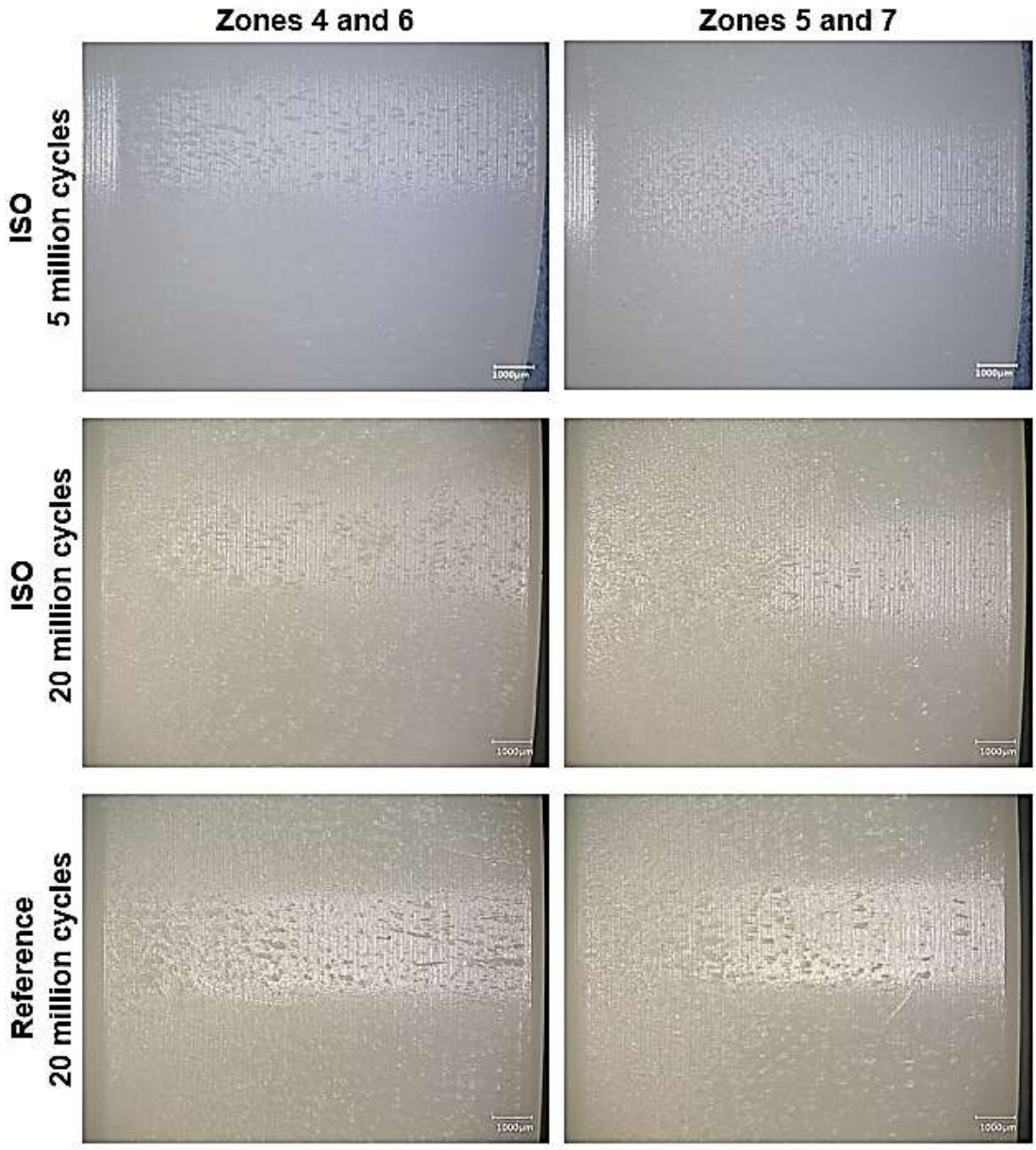

Figure 7: Representative images of backside zones 4 to 7 of a “Wear simulated” liner after 5 and 20 million cycles (axial load and movement) and a “Reference” liner after 20 million cycles (only axial load). Small scratches in the direction of insertion and removal were clearly seen. Even though the images correspond to the same “Wear simulated” liner, the color difference was due to a different white balance configuration of the microscope. Adapted from Puente Reyna et al. [67].

1.4.2 Publication III: Biotribological behavior and metal ion release barrier function of zirconium nitride multilayer coated knee implants

Regarding TKA, as this treatment is nowadays also being performed in heavier, younger and more active patients, it is important to perform pre-clinical tests that account for the activities performed by such population. During the second decade of clinical performance, UHMWPE tibial liners subjected to high contact stresses and oxidation suffer from a structural fatigue that will lead to delamination and cracking. The current ISO 14243-1:2009(E) wear test only simulates level walking and is not able to reproduce such long-term wear characteristics on the tibial liners. However, in vitro studies accounting for high demanding activities have been able to reproduce them [33,75–77] and should be used in future pre-clinical tests for evaluating new materials and implant designs in such demanding conditions at the long-term.

On the other hand, metal hypersensitivity has become an important topic of research due to the different adverse local tissue reactions and systemic complications seen in patients with elevated cobalt values in blood. An alternative for such patients is the use of knee implants with a zirconium nitride (ZrN) multilayer coating, which prevents the release of cobalt ions from the CoCrMo substrate material and reduces the wear rate of the UHMWPE liner when compared with an uncoated implant. The ZrN multilayer coating has a total thickness between 3.5 and 5.0 µm, is applied to CoCrMo knee implants and consists of a thin adhesive chromium layer, five alternating intermediate layers out of chromium nitride and chromium carbonitride and a final zirconium nitride shielding layer [78]. Even though ZrN multilayer coated knee implants have been in the market for almost a decade and pre-clinical tests under normal walking conditions have been made [78–82], the research question regarding if this material can withstand and fulfill its ion release barrier function and low wear rate when subjected to the daily activities of heavier, younger and more dynamic patients during the second or third decade of clinical performance remains open.

These additional aspects of the ZrN multilayer coating were addressed in the third research publication entitled “Metal ion release barrier function and biotribological evaluation of a zirconium nitride multilayer coated knee implant under high demanding activities wear simulation”, published at Journal of Biomechanics [83]. By means of a highly demanding activities knee wear simulation performed for the first time on ZrN multilayer coated knee implants, the objectives of this publication were:

- to determine if the wear rate on the polyethylene liners is reduced when articulated against ZrN multilayer coated components in comparison with uncoated ones
- to analyze the metal ion release of ZrN multilayer coated TKA implants in comparison with the clinically established uncoated ones
- to confirm that the ZrN multilayer coating keeps its integrity even under high demanding activities knee wear simulation

The wear tests were performed using medium size AS Columbus® DD (Aesculap AG, Tuttlingen, Germany) femoral and tibial components with a ZrN multilayer coating (ZrN group), in comparison with the clinically established cobalt chromium version Columbus® DD (CoCr group). UHMWPE liners (size T3, height 10 mm) machined from GUR 1020, packed under nitrogen atmosphere and sterilized by electron beam irradiation (30 ± 2 kGy) were used as gliding surfaces. A schematic representation of the implant components is shown in Figure 8. Wear simulation was performed on a load controlled knee wear simulator capable of reproducing the loads and movements of highly demanding activities (HDA). The applied load and motion profiles were based on in vivo measurements obtained from patients with instrumented implants [53] and normalized to represent a patient weight of 100 kg [76]. These profiles were applied in a combination of 40% stairs up, 40 % stairs down, 10% level walking, 8% chair raising and 2% deep squatting for 5 million cycles.

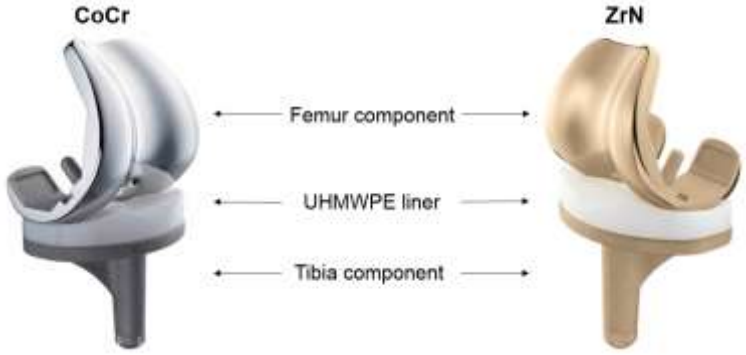

Figure 8: Schematic representation of the implant components of the CoCr and ZrN groups.

The simulation was run in new born calf serum with a protein concentration of 20 g/l. This test medium was changed every 0.5 million cycles and all the components were cleaned and analyzed according to ISO 14243-2:2009(E) and wear of the UHMWPE liners was determined gravimetrically. The liners were inspected optically for abrasive-adhesive wear modes with a stereo microscope and scanned before and after the test with a three-dimensional measuring machine in order to measure their geometrical deformation due to creep and wear. Furthermore, the test medium was analyzed for metal ion concentration of cobalt, chromium, molybdenum and zirconium after every 0.5 million cycles using ICP-MS according to ISO 17294-2.

The results showed a significant wear rate reduction in the ZrN group (1.01 ± 0.29 mg/million cycles) in comparison with the uncoated CoCr group (2.89 ± 1.04 mg/million cycles) ($p = 0.04$). Regarding the ZrN multilayer coating, the articulation surface of the ZrN coated femurs remained polished after the testing period, whereas the uncoated femurs showed characteristic wear scratches at the articulation surface (Figure 9). Furthermore, the metal ion release from the ZrN coated implants was reduced by up to three orders of magnitude in comparison with the CoCr implants (Figure 10) and the cobalt ion concentration remained below 1 µg/l starting the 2 million HDA cycles. These results demonstrated that the ZrN multilayer coating was able to keep its integrity even under a highly demanding activities knee wear simulation, as neither scratches nor delamination of the coating were seen.

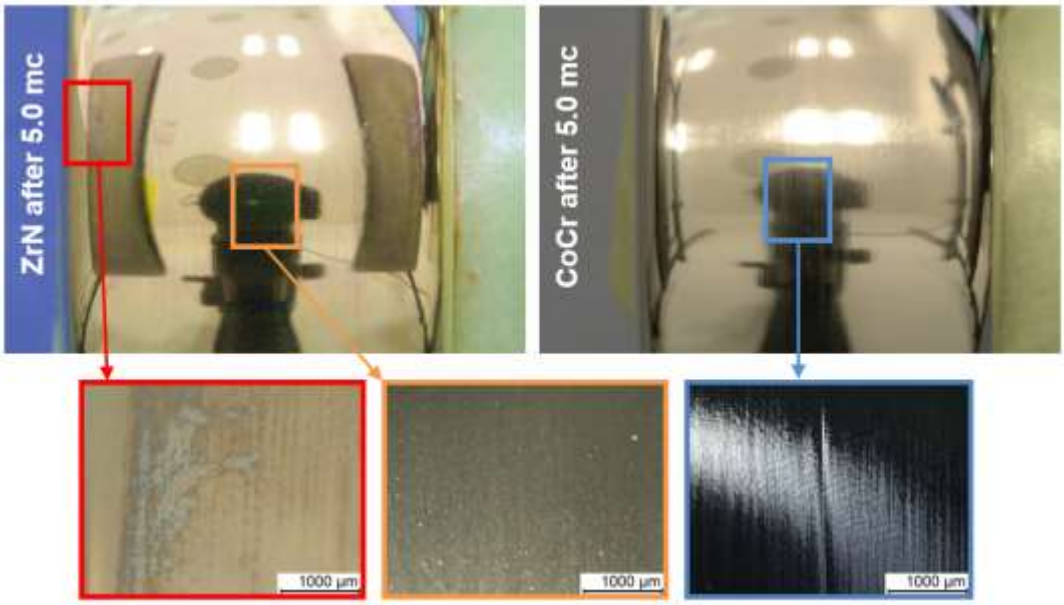

Figure 9: Wear characteristics of the femur components after 5 million HDA cycles. The ZrN femurs remained polished after the wear simulation, demonstrated by the clear reflection of the camera and lights, and neither scratches nor layer breakage were seen at the center of the articulation area. However, oxidation marks at the edges and in the articulation area were seen after 5 million HDA cycles (highlighted in red). On the other hand, slight scratches were seen at the articulation area of the CoCr femurs (highlighted in blue), demonstrated by the blurred reflection of the camera and lights. Obtained from Puente Reyna et al. [83].

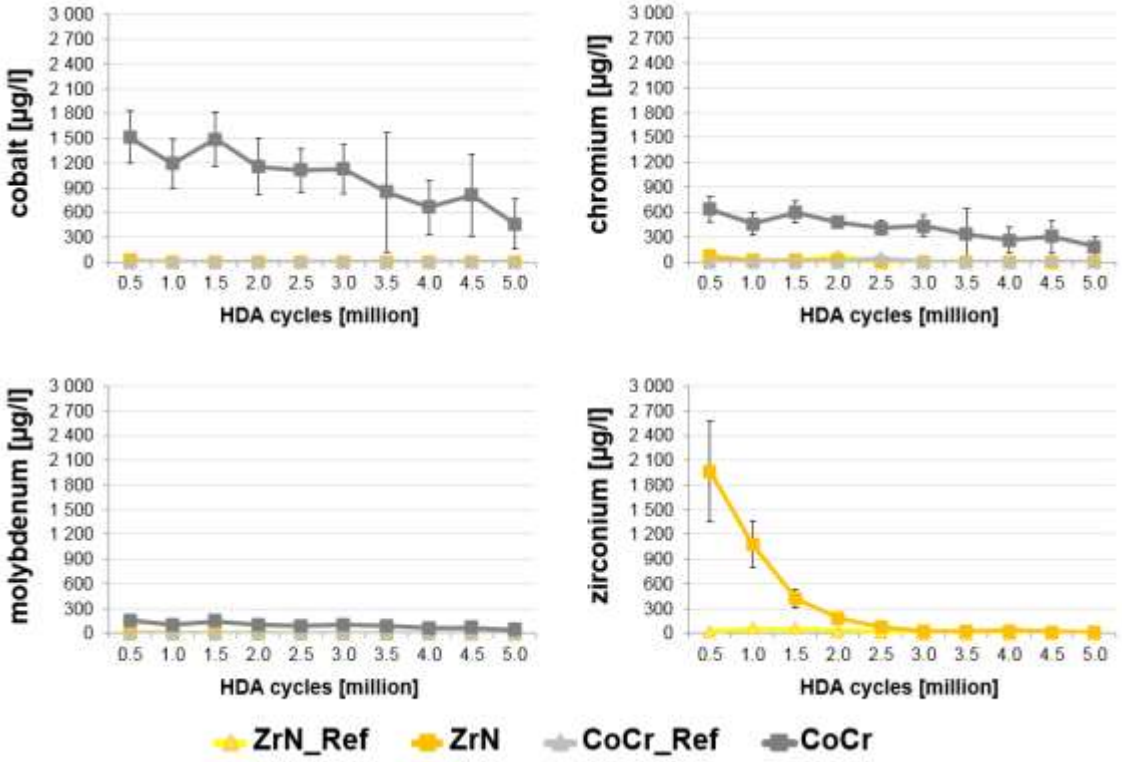

Figure 10: Metal ion concentration analysis of the ZrN and CoCr groups (subjected to axial load and movement) and their references (Ref = subjected just to axial load) during 5 million HDA cycles. The reference stations represent basic ion contamination of the environment and ion release by corrosion of the implant, whereas the wear testing groups additionally include the articulation-induced metal ion release. Obtained from Puente Reyna et al. [83].

1.5 Conclusions

Long-term in vitro tests that account for highly demanding activities, such as the ones here described, need to be applied in future pre-clinical tests in order to evaluate and ensure the performance at the long-term of total joint arthroplasty implants in younger and more active patients with higher life expectancy. This doctoral thesis demonstrated that the analyzed implants were able to maintain their good biotribological performance at the long-term, even under highly demanding conditions. In case of the highly-crosslinked and vitamin E blended polyethylene acetabular liners, no significant backside wear due to micro-motion with its acetabular shell was seen during the long-term in vitro wear simulation. Moreover, the wear rate generated at the articulation surface was two orders of magnitude below the osteolysis threshold. However, future long-term retrieval studies and registry data are needed in order to confirm the results from these pre-clinical tests. On the other hand, the results of the ZrN multilayer coated knee implants showed that they are able to significantly reduce the polyethylene wear rate and the metal ion release from the substrate material, even under highly demanding conditions. Besides, neither delamination nor disruption of the ZrN multilayer coating was seen, resulting in a full functioning multilayer coating with long-term behavior.

2. Publication I

Backside wear analysis of retrieved acetabular liners with a press-fit locking mechanism in comparison to wear simulation in vitro

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Research Article

Backside Wear Analysis of Retrieved Acetabular Liners with a Press-Fit Locking Mechanism in Comparison to Wear Simulation In Vitro

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Backside wear due to micromotion and poor conformity between the liner and its titanium alloy shell may contribute to the high rates of retroacetabular osteolysis and consequent aseptic loosening. The purpose of our study was to understand the wear process on the backside of polyethylene liners from two acetabular cup systems, whose locking mechanism is based on a press-fit cone in combination with a rough titanium conical inner surface on the fixation area. A direct comparison between in vitro wear simulator tests (equivalent to 3 years of use) and retrieved liners (average 13.1 months in situ) was done in order to evaluate the backside wear characteristics and behavior of these systems. Similar wear scores between in vitro tested and retrieved liners were observed. The results showed that this locking mechanism did not significantly produce wear marks at the backside of the polyethylene liners due to micromotion. In all the analyzed liners, the most common wear modes observed were small scratches at the cranial fixation zone directly below the rough titanium inner surface of the shell. It was concluded that most of the wear marks were produced during the insertion and removal of the liner, rather than during its time in situ.

1. Introduction

Aseptic loosening of the implant is the main reason for revision in total hip arthroplasty (THA), with over 50% of the cases [1–3]. The main stimulator of periprosthetic osteolysis and subsequent aseptic loosening is the particulate debris generated by the wear at the articulating surface between the acetabular polyethylene liners and the femoral heads [2, 4–6]. However, there are also other sources of particulate debris generation, such as wear due to impingement, the presence of third-body particles, or micromotion between an insert and its metallic acetabular shell, also known as backside wear [7]. Hence, different implant designs and materials used in hip arthroplasty have been developed in order to decrease the polyethylene wear particle generation.

Currently, the most widely used components in THA are the modular metal-backed acetabular components. Since their development in the 1970s [8], the modular components showed some advantages such as intraoperative flexibility, multiple options for screw placement, and the opportunity to exchange the polyethylene liner during revision surgeries without removing the metallic shell. However, these types of components also brought disadvantages, like an altered stress transmission and micro- and macromotion between the liner and its metallic shell. Creep and wear on the backside of the polyethylene liner are thus generated, therefore an additional

(a) (b)

FIGURE 1: (a) P-Cup and (b) P-Fit metallic shell with grit blasted rough titanium conical inner surface at the rim ① and milled-drilled smooth surface on the concave area ②.

source of particulate debris that increases the risk of osteolysis and eventual aseptic loosening of the prostheses [9–11].

Particularly high backside wear has been associated with micromotion between the liner and its shell due to an unstable locking mechanism and a poor conformity between both components [11–13]. This type of wear was implicated in the high rates of retroacetabular osteolysis observed in liners that were locked to their metallic shell by means of a titanium locking ring or using a hexagonal thin polyethylene rim at the base of the liner, which fitted to a complementary groove in the metallic shell [9, 14–16]. Moreover, if there is a dissociation of the liner from the shell, the debris generated at the articulating surface can migrate between the liner and the shell and the screw holes can act as conduits for a further migration of the debris into the pelvic bone stock with the risk of inducing osteolysis [17].

Different designs have been developed in order to reduce backside wear and prevent the migration of wear debris into the acetabular bone stock [18]. These designs include improving the locking mechanism between the liner and the shell, polishing the inner surface of the shell, or sealing the screw holes with modular caps. The purpose of our study was to understand more of the wear process on the backside of polyethylene liners from two acetabular cup designs with long- and short-term clinical history, whose locking mechanism is based on a press-fit cone in combination with a rough titanium inner surface at the rim of the metallic shell. A direct comparison between in vitro tested and retrieved liners was done in order to evaluate the backside wear characteristics and behavior.

2. Materials and Methods

An optical analysis of polyethylene liners from two different cup systems (Plasmacup® and Plasmafit®, Aesculap AG, Tuttlingen, Germany) was performed (Figure 1). Both cup designs present the same locking mechanism between the liner and the shell, which is based on a press-fit cone with a large surface area and through a contact with the base of the shell, which will be achieved after the load in service. A grit blasted rough titanium inner surface (Rz = 20–32 μm) along the rim of the shell intends to stabilize the liner to it. Furthermore, the conical fixation surface of the liners intends to form a seal against the migration of wear particles from the articulation joint. The screw drill holes of the Plasmacup (further referred to as P-Cup) are located in the cranial region of the shell. The Plasmafit liners (further referred to as P-Fit) analyzed did not have screw drill holes. The polyethylene liners of the two different cup systems can have either a symmetrical (Sym) or a posterior wall (PW) design. In the symmetrical design, the liners fit symmetrically in the shells, whereas the posterior wall liners contain a polyethylene hood that extends outside the shell in the luxation direction in order to increase luxation stability.

Liners from three different polyethylene materials were analyzed for backside wear. The conventional standard polyethylene liners (STD) were packed under nitrogen atmosphere and sterilized by gamma-irradiation (30 ± 2 kGy). The highly cross-linked polyethylene liners (XPE) were cross-linked by γ-irradiation (75 kGy) and sterilized by ethylene oxide. The highly cross-linked and Vitamin E (0.1%) blended polyethylene liners (VitE) were cross-linked by an electron beam (80 kGy) and sterilized by ethylene oxide. The polyethylene liners were tested in combination with acetabular shells made out of Ti6Al4V alloy and modular heads made out of ceramic or cobalt-chromium (Tables 1 and 2). Large femoral head and shell diameters were chosen, as these produce a high amount of wear at the articulation surface but with a low risk of luxation. Furthermore, as there is no worst case size reported for backside wear, we have chosen the most common clinically used diameters (32 and 36 mm). All the polyethylene liners for the in vitro wear tests were subjected to artificial aging according to ASTM F2003-02 at 70°C in pure oxygen at 5 bar for two weeks (Millipore Corp., 6700P05,

Table 1: Summary of in vitro tested implants.

In vitro group ($n = 3$ each)	Model	Polyethylene material	Femoral head	Head diameter (mm)	Shell diameter (mm)
P-CupD$_{\text{Sym VitE}}$*	Plasmacup DC symmetrical	VitE	CoCr	36	52
P-CupD$_{\text{Sym VitE}}$	Plasmacup DC symmetrical	VitE	Ceramic	36	52
P-CupD$_{\text{Sym XPE}}$*	Plasmacup DC symmetrical	XPE	CoCr	36	52
P-Fit$_{\text{Sym VitE}}$	Plasmafit Poly symmetrical	VitE	Ceramic	36	50
P-Fit$_{\text{Sym STD}}$*	Plasmafit Poly symmetrical	STD	CoCr	32	46
P-Fit$_{\text{Sym STD}}$	Plasmafit Poly symmetrical	STD	Ceramic	32	46

Table 2: Summary of retrieved implants and demographic data of patients.

Retrieval	Model	Polyethylene material	Femoral head	Head diameter (mm)	Shell diameter (mm)	Time in situ (months)	Gender (age in years at revision surgery)	Weight (kg)	Reason for revision
P-CupD$_{\text{Sym VitE}}$	Plasmacup DC symmetrical	VitE	Ceramic	32	50	11	F (74)	—	Luxation
P-CupD$_{\text{Sym XPE-1}}$	Plasmacup DC symmetrical	XPE	Ceramic	32	56	0.5	N/A (77)	—	Infection
P-CupD$_{\text{Sym XPE-2}}$	Plasmacup DC symmetrical	XPE	Ceramic	32	54	15	M (64)	92	Stem loosening
P-CupD$_{\text{PW VitE}}$	Plasmacup DC posterior wall	VitE	Ceramic	32	52	2	M (69)	109	Stem subsidence
P-CupS$_{\text{PW STD}}$*	Plasmacup SC posterior wall	STD	CoCr	32	58	37	M (69)	110	Stem fracture

Merck KgaA, Darmstadt, Germany). All liners were soaked prior to wear simulation in serum-based test medium until the incremental mass change over 24 h was less than 10% of the previous cumulative mass change to allow for saturated fluid absorption.

In vitro wear simulation was performed on a customized 6 + 2 (reference) stations servo hydraulic hip simulator (EndoLab GmbH, Thansau, Germany) with kinematic and load patterns according to ISO 14242-1:2012 (E). The liners were tested through 5 million cycles with a frequency of 1 Hz in a lubricant of newborn calf serum (Biochrom AG, Berlin, Germany) diluted with deionized water to achieve a target protein content of 30 g/L. The lubricant was incubated at 37°C, pH-stabilized with ethylene diamine tetraacetic acid, and replaced at intervals of 0.5 million cycles. Patricin was added to prevent fungal decay. Every 0.5 million cycles, the polyethylene liners were removed from the acetabular shell in order to perform gravimetric wear measurements and image documentation [18]. It is estimated that the 5 million cycles required in the ISO 14242-1:2012 (E) represent a mean in vivo service life of 2.9 years [19], as several studies that have estimated the gait cycles per year in patients before and after total hip or knee arthroplasty measured an average of 1.76 million gait cycles per year (range of 0.9–3.2 million gait cycles) [20–24].

Retrievals, all Plasmacup liners, were explanted during hip arthroplasty revisions in various hospitals in Germany for various reasons. P-CupD and P-CupS refer to Plasmacup DC and SC acetabular shells, which have no significant design difference. Three of the five explants that were harvested and sent to Aesculap stem from a prospective randomized study to investigate clinical and radiological differences in behavior of two different polyethylene types [25]. Between removal and optical analysis, these liners were cleaned through an ultrasonic bath in mild detergent, individually vacuum packed under nitrogen atmosphere, and stored on a freezer at −20°C. The two other liners were cleaned, individually packed under air atmosphere, and stored at room temperature. The mean survival time for all implants was 13.1 months (from 0.5 to 37 months). The liners were implanted between 2006 and 2014 and their reasons for removal were luxation (20%), infection (20%), and stem related reasons like loosening, fracture, and subsidence (60%).

The backside surface of the acetabular liners was inspected using a stereo light microscope (Leica MZ 16, Bensheim, Germany) up to a 25x magnification. Additional images

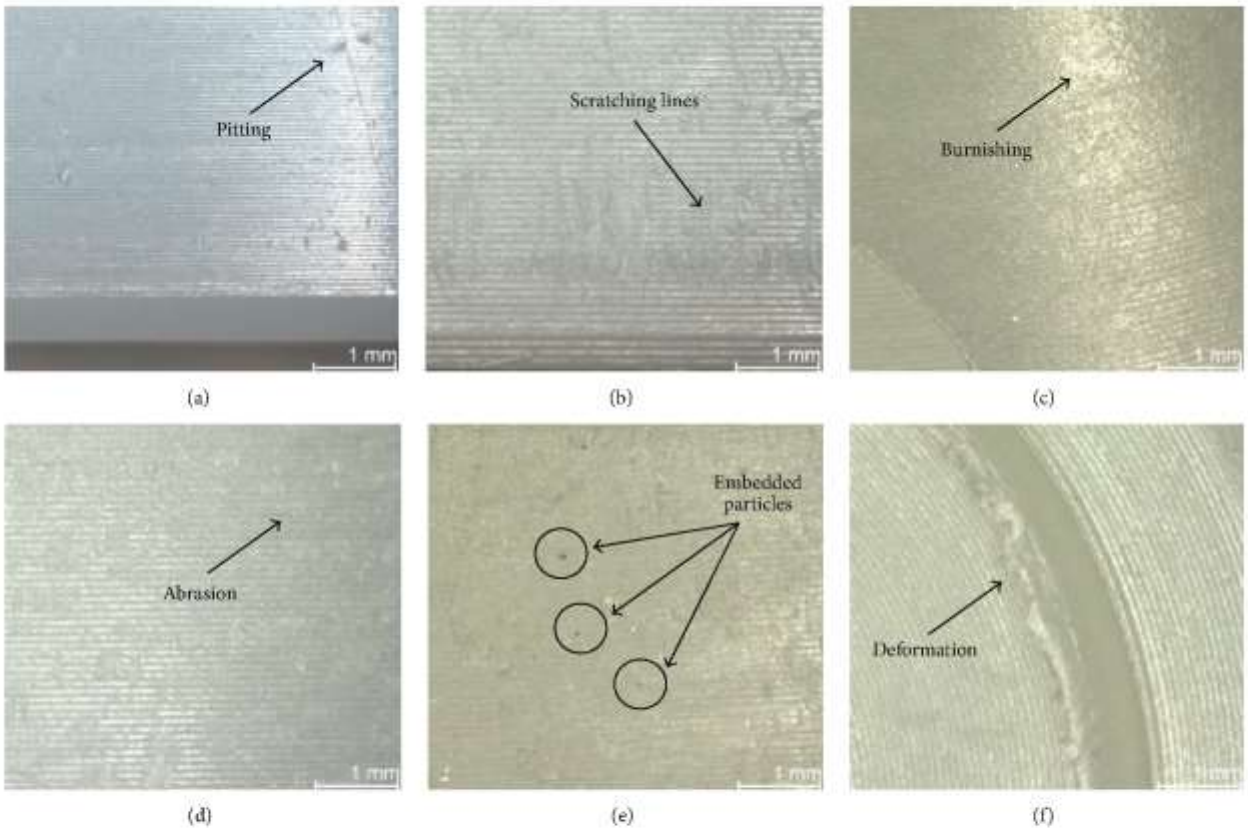

FIGURE 2: Images from each wear mode: (a) pitting, (b) scratching, (c) burnishing, (d) abrasion, (e) embedded particles, and (f) deformation. No image of delamination was taken, as this wear mode was not present in any of the inserts.

were obtained through Scanning Electron Microscope (SEM) (Zeiss EVO 50, Oberkochen, Germany) equipped with energy dispersive spectrometer (EDX) (Oxford Instruments X-Max, Wiesbaden, Germany) in order to analyze the composition of embedded particles. A semiquantitative method developed by Hood et al. [26] and modified for hip implants was used to assess the damage on the backside of the liners. Seven different modes of damage were defined (Figure 2). Deformation was used to describe the evidence of permanent deformation from the original shape due to cold flow and/or creep. Pitting described small circular indentations. Embedded particles were defined as particles embedded in the polyethylene and were recognized by the color and/or texture difference within the polyethylene surface. Scratching described straight lines that cut into the polyethylene. Burnishing described areas that had become highly polished and thus machining marks were worn off. Abrasion was defined as an area with roughened texture due to repeated rubbing. Finally, delamination described areas where a large section of polyethylene had been lost. Care was taken to differentiate the wear marks that were thought to have occurred during insertion and removal of the liner from the wear marks generated due to the liner's micromovement in service.

On basis of its in situ orientation, the backside section was divided by a superior/inferior line and 7 different sections were determined (Figure 3(a)). Sections 2 and 3 correspond to the convex surface below the milled-drilled area of the shell, whereas Sections 4 to 7 correspond to the rim below the rough titanium inner surface of the shell. Damage scores for the backside surface of each liner were determined. For each section, a score between 0 and 3 was given for each of the seven damage modes, giving a maximum possible damage score of 21 per section. Following Hood's method [26], a score of 0 meant no damage; a score of 1 meant damage to less than 10% of the surface area, 2 meant damage to 10–50% of the surface area, and 3 meant that more than 50% of the area had been damaged. The grading system also combined the severity of the damage with its extent. For example, if several large scratches cover less than 50% of the section, it would be graded as 3, the same grade that would be given if small scratches cover most of the area. Each component was given a total damage score based on the sum of the scores from all its seven sections. Thus, the maximum possible damage score was 147. In case of the in vitro tested liners, a total of three liners were analyzed per group and their scores were averaged.

Moreover, the presence of creep on the backside of the liner into the screw drill holes of the metallic acetabular shell was evaluated for the P-Cup liners. Applying the grading system used by Schroder et al. [27], the liners were divided into two sections (Figure 3(b)) and each was graded according to the presence of screw holes. A grade of 0 was given if no visual

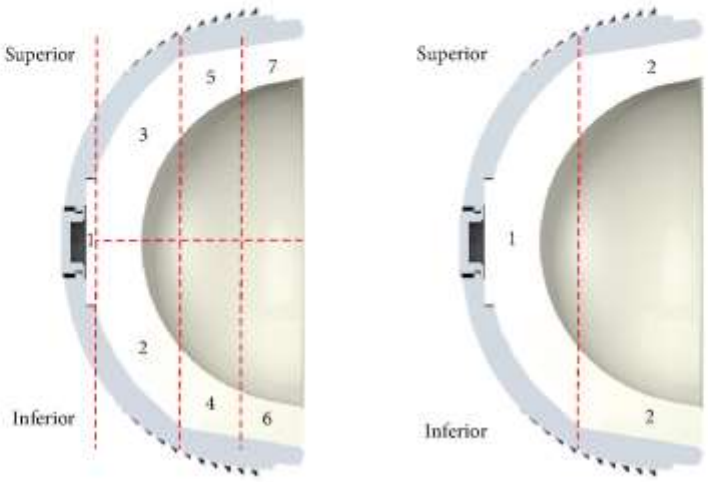

FIGURE 3: Sketch from a cross section of a P-Fit liner with its titanium alloy shell; (a) backside sections for wear analysis; (b) backside sections for screw indentation analysis.

evidence of creep was observed, a grade of 1 when visual evidence was observed but no palpable step could be felt, and a grade of 2 when both visual evidence and a palpable step were noted.

Two sets of observations were performed by one author (ALPR) in a time distance of one month and the scores were averaged. The intraobserver reliability of this method was between "substantial" and "almost perfect," with kappa measures ranging between 0.72 and 0.88 for retrieved liners and between 0.69 and 0.91 for in vitro tested liners.

To differentiate between the inserts' manufacturing materials (STD versus VitE and XPE versus VitE), the metallic shell model (P-Cup versus P-Fit), and the articulating femoral heads (CoCr versus ceramic) of the in vitro tested groups, an analysis of variance was carried out ($p = 0.05$) followed by a post hoc test (Scheffe $p = 0.05$). Prior to the analysis, the normal distribution (p-p plots) and the homogeneity of variance (Levene test) were verified (Statistica 10, StatSoft Europe GmbH, Hamburg, Germany). A p value less than 0.05 is considered as significant.

3. Results

3.1. General Results. The most common wear modes observed on the backside of in vitro tested and retrieved liners were scratching, abrasion, burnishing, and embedded particles (Table 3). Scratching, with an average score of 1.62 (±1.62) for in vitro tested liners and 1.36 (±0.83) for retrieved liners, had the highest score. No delamination and practically no deformation nor pitting was found in any of the in vitro tested and the retrieved liners. The highest score difference on the wear modes between the in vitro tested and the retrieved liners was found on the embedded particles, as in the in vitro tested liners just a few particles were found in comparison with the retrieved liners (score of 0.07 (±0.24) and 0.70 (±0.82), resp.). Scanning electron microscopy and EDX confirmed that the embedded particles were titanium particles (Figure 4).

TABLE 3: Average score per wear mode of all backside sections from in vitro and retrieved liners (maximum possible score per wear mode = 3).

Wear mode	In vitro	Retrievals
Pitting	0.00 (±1.04)	0.03 (±0.17)
Scratching	1.62 (±1.62)	1.36 (±0.83)
Burnishing	0.23 (±0.47)	0.13 (±0.41)
Abrasion	0.67 (±0.95)	0.32 (±0.65)
Embedded particles	0.07 (±0.24)	0.70 (±0.82)
Deformation	0.01 (±0.11)	0.03 (±0.17)
Delamination	0.00 (±0.00)	0.00 (±0.00)

3.2. In Vitro Wear Simulated Liners. After the 5 million gait cycles' simulation, the average total backside wear score for the in vitro tested liners ranged from 13.17 (±0.75) to 21.83 (±2.23). The maximum total backside wear score possible was 147. As it can be seen in Figure 5, regardless their design, liners manufactured with STD or XPE showed a statistically higher total backside wear score compared to the liners manufactured with VitE. In case of the P-CupD liners articulated against CoCr femoral heads, the XPE group had a significantly higher average total backside wear score, with 20.17 (±0.75), in comparison with the VitE group, which had 15.83 (±1.33) ($p = 0.0014$). In case of the P-Fit liners articulated against ceramic heads, the STD group had an average total backside wear score of 21.83 (±2.23) compared to 16.50 (±1.52) of the VitE group ($p = 0.0001$).

In a direct comparison between the liners' models, when these were manufactured with VitE and articulated against

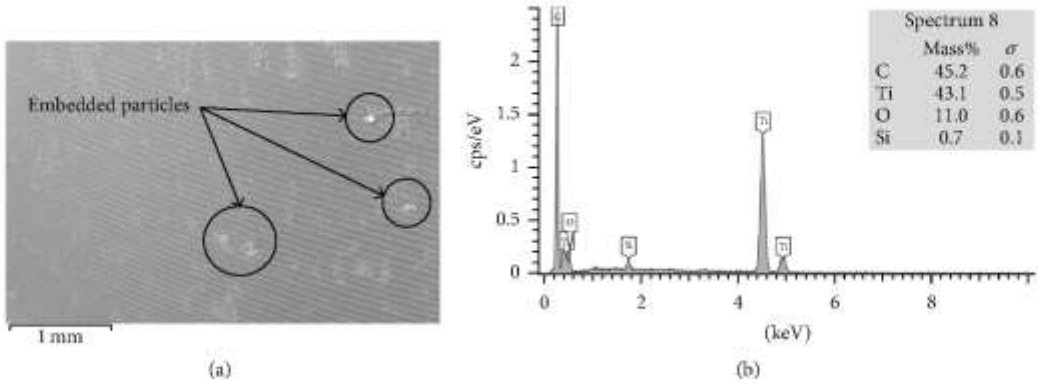

FIGURE 4: (a) SEM image with embedded particles in Section 5 from P-CupD$_{PW\ VitE}$ retrieval; (b) EDX analysis of the selected particle, which apparently consists of titanium alloy. The carbon spectrum corresponds to the surrounding polymer of the liner.

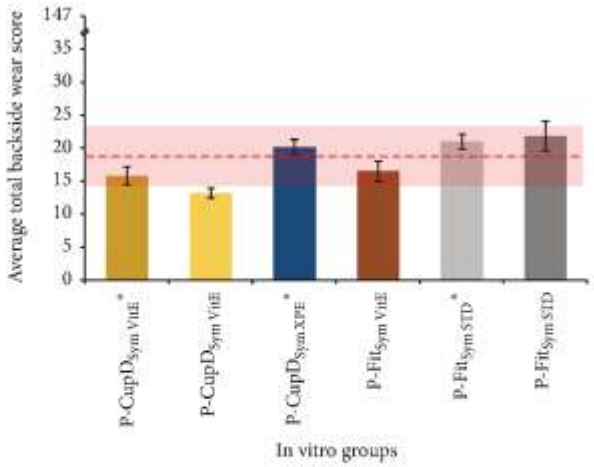

FIGURE 5: Summary of the average total backside wear score for in vitro tested liners. The dashed red line represents the average total backside wear score for the retrieved liners, while the red shadow shows the 95% confidence interval. The groups with "*" were articulated against CoCr femoral heads and the others against ceramic femoral heads. Maximum total backside wear score possible = 147.

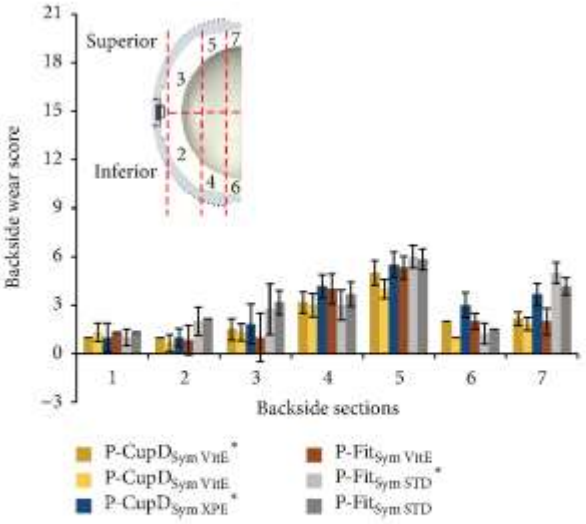

FIGURE 6: Backside wear score per backside section for in vitro wear tested liners. The groups with "*" were articulated against CoCr femoral heads and the others against ceramic femoral heads. Maximum backside wear score per zone = 21.

ceramic femoral heads, the P-Cup group (13.17 ± 0.75) showed a significantly lower average total backside wear score than the P-Fit group (16.50 ± 1.52) (p = 0.0215). However, no significant difference (p = 0.9755) was found if the liners were manufactured with XPE or STD and articulated against CoCr femoral heads (20.17 ± 0.75 for P-Cup versus 21.00 ± 1.15 for P-Fit). Finally, no statistically significant difference in the average total backside wear score was found regarding the material of the articulating femoral head. For the P-Cup liners with VitE, the group articulated against CoCr had an average total backside wear score of 15.83 (±1.33), while the group articulated against ceramic had 13.17 (±0.75) (p = 0.1049). In case of the P-Fit liners with STD, the group articulated against CoCr had an average total backside wear score of 21.00 ± 1.15, while the group articulated against ceramic had 21.83 (±2.23) (p = 0.9755).

The most damaged areas were Sections 4 through 7 (Figure 6), corresponding to the area against the roughened titanium surface of the acetabular metallic shell, with backside wear scores between 1.00 (±0.00) and 6.00 (±0.71) from a maximum score of 21. In these sections, the mode of wear mostly observed was multiple small scratches produced by the roughened inner surface during the repeated insertion and removal of the polyethylene liner in the acetabular shell (Figures 7(c), 7(e), and 8(a)). Section 5, corresponding to the limit between the roughened and milled-drilled section of the metallic acetabular shell on the superior orientation, showed the most wear marks overall, with a backside wear score between 4.00 (±0.58) and 6.00 (±0.71). It was observed that, in this section, the multiple scratches produced abrasion of the liner and the machining marks were not more seen in some areas of the section (Figures 7(d) and 8(b)). However,

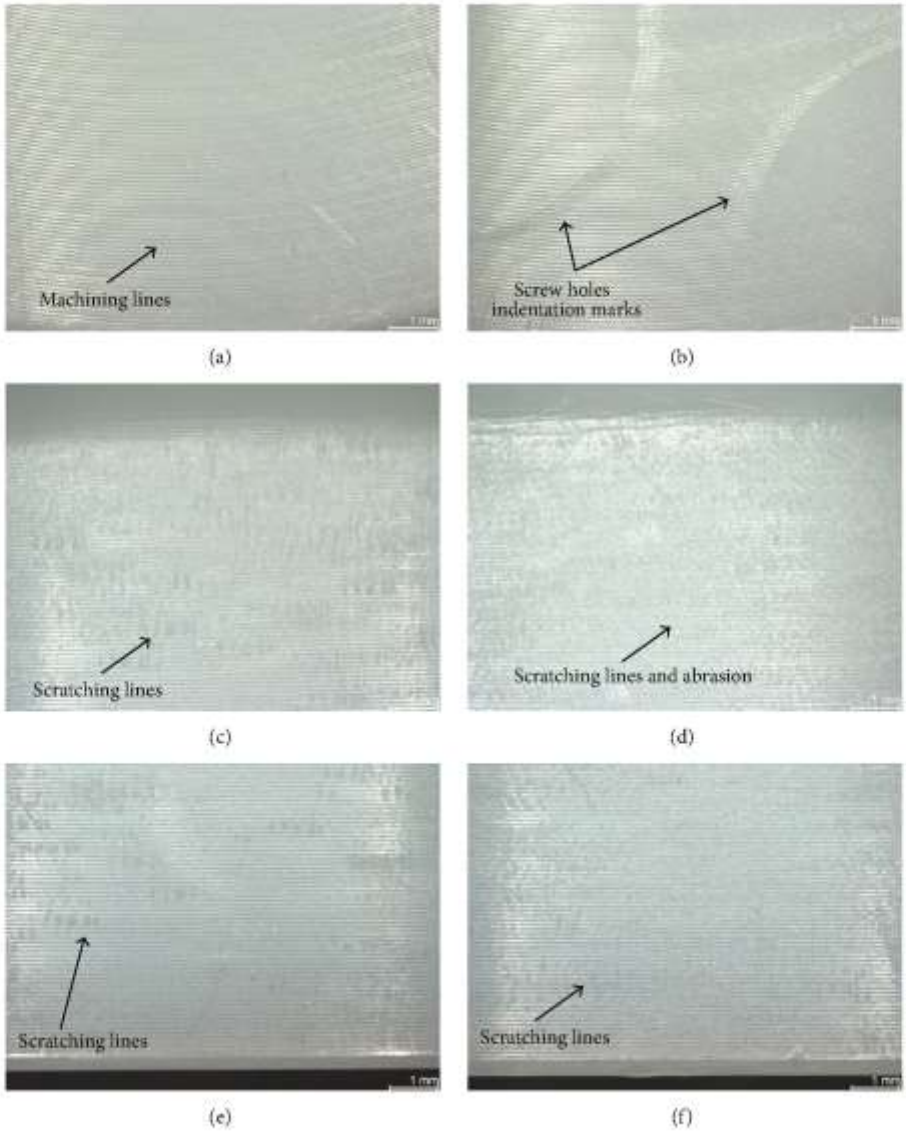

FIGURE 7: Photographs with microscope from in vitro wear tested liners. (a) P-CupD$_{\text{Sym VitE}}$ group, Section 2, machining lines clearly visible with no wear marks; (b) P-CupD$_{\text{Sym VitE}}$ group, Section 3, screw holes indentations marks and machining lines still visible; (c) P-CupD$_{\text{Sym VitE}}$* group, Section 4, small scratching lines; (d) P-CupD$_{\text{Sym VitE}}$*, Section 5, scratching lines and slight abrasion; screw hole is visible; (e) P-CupD$_{\text{Sym VitE}}$*, Section 6, small scratching lines; (f) P-CupD$_{\text{Sym VitE}}$*, Section 7, small scratching lines.

it was also observed that even if a section in the superior orientation was damaged, its corresponding inferior section could be almost free of wear (Figures 7(a), 7(b), 7(e), and 7(f)). In the sections under the milled-drilled acetabular inner surface, mainly in Section 3, only a few scratches and a slight flattening/burnishing were observed, having low backside wear scores between 1.00 (±0.00) and 2.75 (±1.56).

In all the P-Cup liners, creep due to the screw holes of the metallic acetabular shell was visible but not palpable (score of 1). Near the creep produced by the screw holes, several indentations were observed due to the repeated removal every 0.5 million cycles of the liners (Figures 7(b) and 8(c)). In both the area inside and outside the screw hole creep marks, the machining marks were still clearly visible over the milled-drilled surface. In some cases, particularly on the STD and XPE liners, the machining lines appeared to be slightly flattened or burnished.

3.3. Retrieved Liners. The average total backside wear score for the retrieved liners, whose implantation time varied from 0.5 to 37 months, ranged from 14.50 (±0.71) up to 29.00 (±1.41) (Figure 9). The maximum total backside wear score possible was 147. All the retrieved liners were P-Cup implants. In general, P-CupD liners showed less total average backside wear score, between 14.50 (±0.71) and 17.00 (±0.71), than the P-CupS liner, which had a score of 29.00 (±1.41). The two

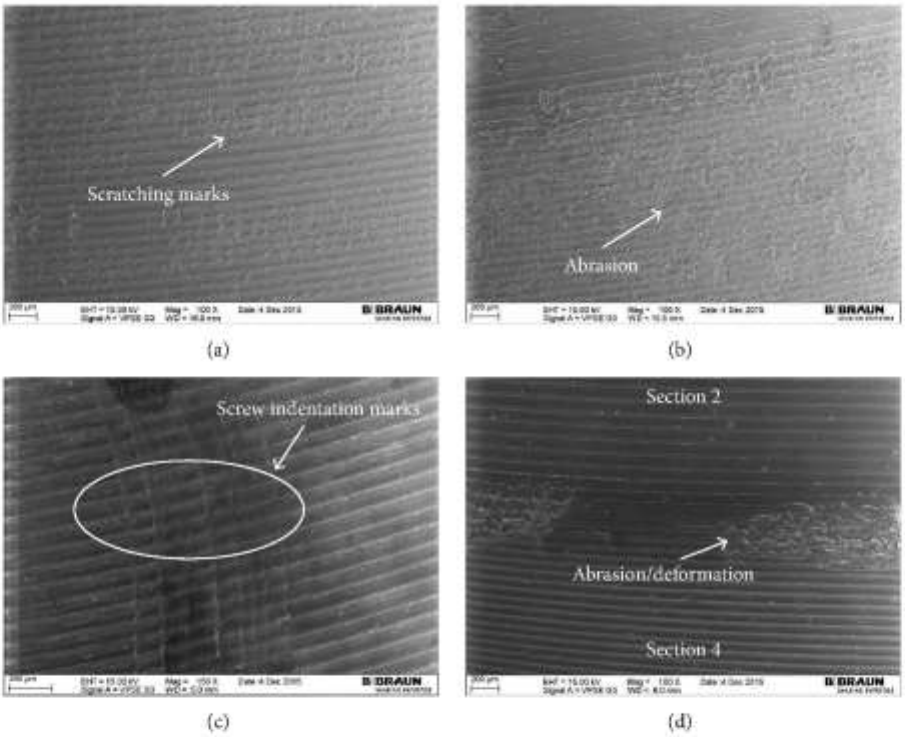

FIGURE 8: SEM images from the backside of the liners. (a) In vitro tested liners P- $Fit_{Sym\ VitE}$, Section 7 with scratches and visible machining marks; (b) in vitro tested liner P-$Fit_{Sym\ VitE}$, Section 5 with apparently considerable abrasion but with machining marks still visible; (c) in vitro tested liner P-$CupD_{Sym\ VitE}$, Section 3 with multiple screw indentations and clear machining lines on both sides of the hole; (d) retrieval P-$CupD_{PW\ VitE}$, edge between Sections 2 and 4 with small abrasion/deformation.

retrieved liners manufactured with Vitamin E, one P-Cup DC symmetrical and one P-Cup DC posterior wall, had a total average wear score of 17.00 (±0.71).

Figure 10 shows that the P-CupD liners had their highest wear score in Section 5, with an average backside wear score between 4.00 (±1.00) and 6.00 (±1.00). In case of the P-CupS liner, the highest score was found in Section 3, a superior located section, with a score of 9 (±1.00). The high score presented in this section was due to the presence of multiple embedded particles as well as a considerable scratching, abrasion, and moderate burnishing (Figure 11). Overall, the wear modes mostly seen were small scratches produced during the insertion and removal of the liner in the metallic shell (Sections 4–7), generating some degree of abrasion on Sections 5 and 7, and embedded particles (Figures 11(d) and 11(f)).

In all the P-CupD liners, no creep due to the screw holes could be seen in the section below the milled-drilled shell, whereas, below the roughened section, the screw hole could be seen but was not palpable. Regarding the P-CupS liner, the screw holes were visible but not palpable in both sections.

4. Discussion

The purpose of our study was to understand more of the wear process on the backside of polyethylene liners. This was done via optical analysis of the backside of two acetabular cup designs with long- and short-term clinical history, whose locking mechanism is based on a press-fit cone in combination with a rough titanium inner surface at the rim of the metallic shell. A direct comparison between in vitro tested and retrieved liners was done in order to evaluate the backside wear characteristics and behavior. To the best of our knowledge, this is the first study to analyze backside wear on acetabular liners with this particular locking mechanism.

Because of their nature, implant retrieval analysis studies are in general limited and imperfect in study design, as they usually deal with specimens that have been removed due to a clinical failure [28]. Moreover, there is often a broad heterogeneity among the analyzed specimens, such as implant size, articulation material, implant positioning, patient loads and activity level, and time in vivo. One of the biggest limitations of the current study was the limited number of retrievals available for analysis ($n = 5$).

On the other hand, the current study had the strength that all the liners were machined from a single resin depending on their group (GUR1020 for conventional PE, GUR1020X for highly cross-linked PE, or GUR1020E for highly cross-linked and Vitamin E blended PE). Furthermore, the in vitro tested liners within each group had the same batch number and all the liners underwent the same testing and handling procedures. Besides, the in vitro tested liners were selected from batches intended for commercial sale; thus, they had the same manufacturing procedure as the retrieved liners.

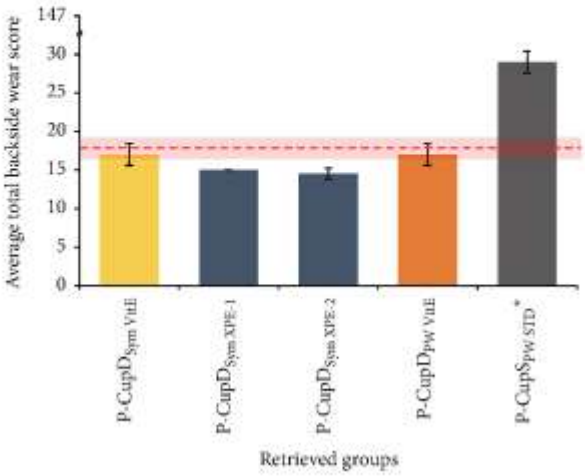

FIGURE 9: Summary of the total average wear score for retrieved liners. The dashed red line represents the total average backside wear score for the in vitro tested liners, while the red shadow shows the 95% confidence interval. The liner with "*" was articulated against a CoCr femoral head; the others were articulated against ceramic femoral heads. Maximum total backside wear score possible = 147.

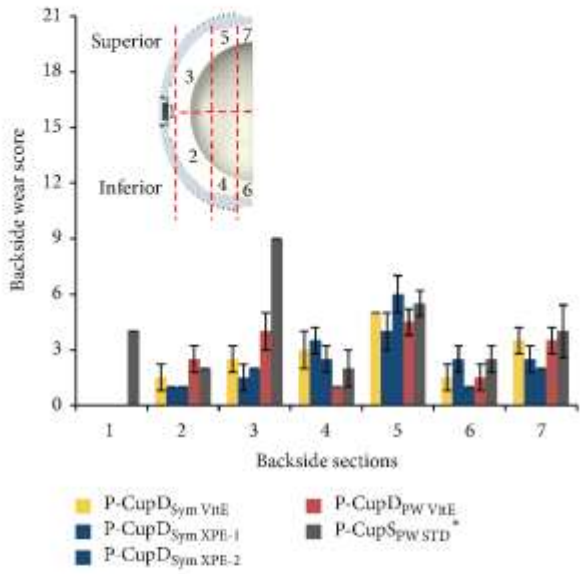

FIGURE 10: Wear score per backside section for retrieved liners. The liner with "*" was articulated against a CoCr femoral head; the others were articulated against ceramic femoral heads. Maximum backside wear score per zone = 21.

Moreover, the wear rates produced by the ISO hip simulator during 5 million cycles are in the clinically observed range for ceramic heads coupled with polyethylene liners [29] and represent approximately 2.9 years of in vivo service life [19–24], in comparison to the average 1.09 years of the retrieved liners (range from 2 weeks to 3 years).

Minimizing polyethylene wear is an important goal in the design of total joint replacements, as a mechanical wear of the polyethylene liner may lead to implant failure and the need for revision surgery [11]. Several locking mechanisms have been designed to prevent micromotion and backside wear, obtaining different results [8, 15, 16, 30]. The present study showed that the press-fit locking mechanism of the Plasmacup, which has proven itself successful in clinical practice since 1997 [31], and Plasmafit did not significantly influence the backside of the analyzed polyethylene liners, as most of the small wear marks were limited to the fixation area. In all the analyzed liners, the most common mode of wear observed was small scratches at the zone directly below the rough titanium inner surface of the shell. No major difference regarding the wear modes and patterns was observed among the different liner sizes. These scratches were produced during the insertion of the liner into the shell. In case of the in vitro tested liners, these were repeatedly removed and inserted every half million cycles through 5 million cycles due to the test protocol. For this reason, more scratches and several screw indentations marks (Figure 8(c)) were observed.

It could be observed that the total average backside wear score of the P-CupS$_{PW\ STD}$* retrieval was higher than the P-CupD retrievals and in vitro tested liners. This higher score was mainly influenced by the higher scores obtained in Sections 1 and 3, which had a high amount of embedded titan particles and a higher score on scratching and burnishing. The rest of the sections had a similar score to the other liners. Wear is influenced by several factors other than a liner or shell design, such as the experience of the surgeon, method of implantation, femoral head size and cup orientation [32], and the patient gait characteristics, activity level, weight, and postoperative range of motion [33]. For these reasons, different wear scores and wear patterns could be observed even within the same liner designs. Moreover, a previous in vitro wear simulation study from Grupp et al. [18] showed that Plasmacup liners machined with conventional PE and aged for two weeks had approximately seventeen times more cumulative wear than aged liners machined with Vitamin E. Thus, the reason for the higher backside wear score from this retrieval could be attributed to the manufacturing material, longer in situ time, the patient's weight and activity level, or damage produced during the fracture of the stem.

Several facts helped to determine the micromotion between the liner and the shell. First, the small scratches produced during insertion were clearly seen and no big abrasion due to movement was observed in most of the rim area. Second, the machining marks on the convex surface beneath the milled-drilled area of the metallic shell were still clearly visible in most of the in vitro tested and retrieved liners (Figures 7(a), 8(c), 8(d), and 11(a)). Third, even though the screw drill hole edges produced indentations, the machining lines in the periphery just appeared to be flattened and were not blurred (Figures 7(b) and 8(c)). Fourth, the P-CupD$_{Sym\ XPE-1}$ retrieved insert that was implanted just for two weeks had a total backside wear score similar to the rest of the retrieved P-CupD liners that were longer in situ and similar to the in vitro tested liners. This could demonstrate that most of the backside wear produced on the liners occurred during their insertion and not during the period

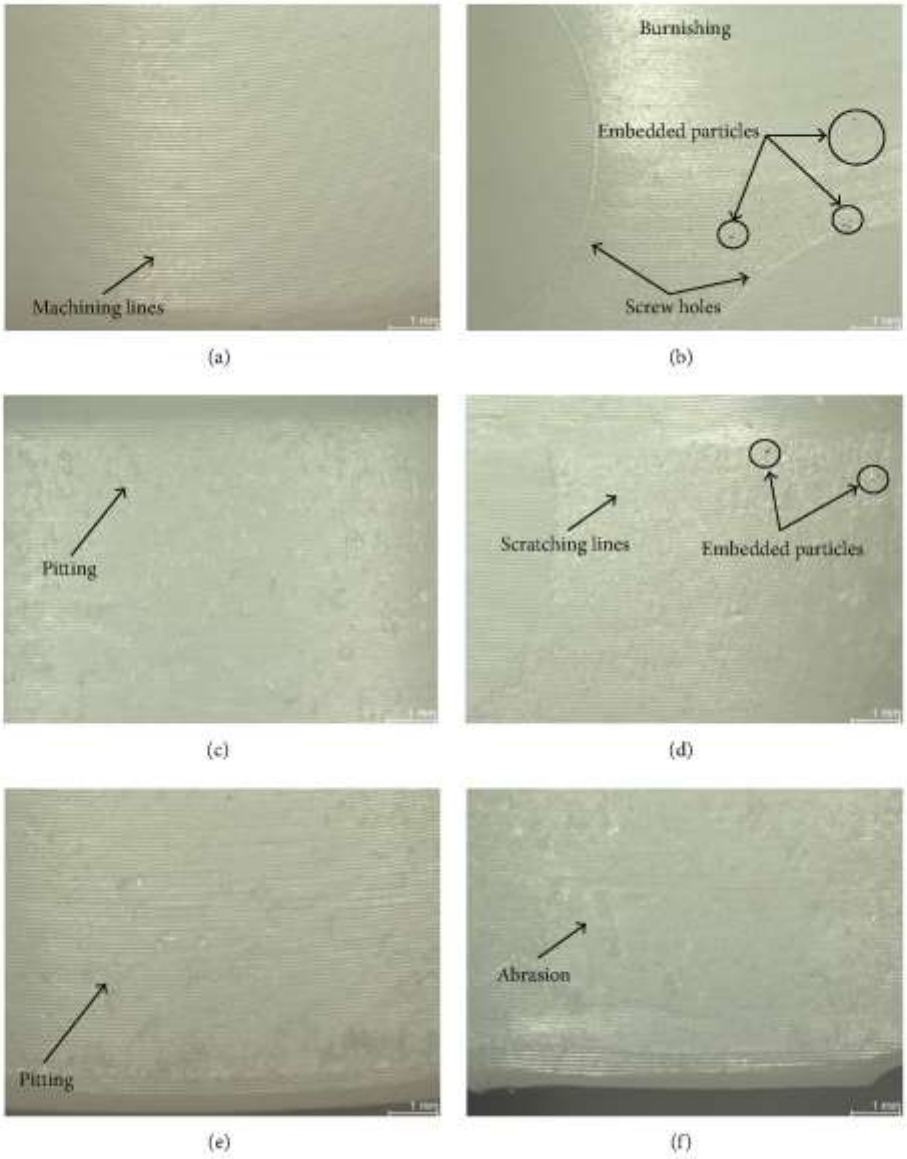

FIGURE 11: Photographs with microscope from P-Cup$S_{PW\ STD}$* retrieved liner after 37 months in situ; (a) Section 2: machining lines clearly visible with no major wear marks; (b) Section 3: screw holes visible but not palpable, with machining lines clearly visible and the periphery scratched and burnished with embedded particles; (c) Section 4: pitting and machining marks still visible; (d) Section 5: area with embedded particles and covered with scratches, machining marks partially visible; (e) Section 6: small pitting visible; (f) Section 7: area with abrasion marks.

in situ. Further studies should be done in order to quantify the backside wear produced solely during the insertion and removal of the liner. Finally, as mentioned before, the in vitro wear simulation study from Grupp et al. [18] showed a seventeen times difference in the cumulative wear between conventional PE and Vitamin E liners. However, even though our results also showed a higher backside wear score for the liners manufactured with conventional PE in comparison with those manufactured with VitE, this difference was not as high as that found in the previous study. The fact that the average total backside wear scores between the two materials were not as significantly different as the cumulative wear confirms that backside wear is produced during the insertion and removal of the liner and does not have a substantial contribution to overall wear.

The only zone where abrasion could be observed was at the edge along a small zone between the rim and the convex area (Figures 7(d), 8(b), 8(d), and 9(d)). However, a closer analysis with scanning electron microscopy (Figure 8(b)) confirmed that the machining marks were still visible. Several studies have proven through a heat-treatment of conventional PE liners that not all deep scratches necessarily mean loss of

material but small deformations or cold flow, as machining lines reappear after the mentioned treatment [34–36]. Deformation of the liner at the edge between the milled-drilled and roughened sections can be expected due to the change of surface characteristics in this zone.

Moreover, it was observed that the anatomically superior located zones had the higher backside wear scores, and, in some cases, its corresponding inferior zone had a considerably lower backside wear score (Figure 11). Kawaji et al. [9] performed a retrieval analysis of polyethylene liners for backside wear and also found that the most changed surface area was the superior-anterior quadrant followed by the superior-posterior quadrant. The reason for a higher wear score in these sections is the orientation of the axial joint load transmitted to the liner. Kligman et al. [11], who performed an optical analysis on retrieved hip liners, observed creep at the superior-lateral quadrant on the convex surface of the polyethylene liner and associated this creep and its location due to the cyclical axial loading, which is transmitted mostly to the superior-lateral part of the acetabulum. This orientation was also confirmed by Bergmann et al. [37], who measured the in vivo acting loads at the hip joint in four patients and determined the contact force vector in the hip joint.

Insufficient locking mechanism, the amount of micromotion, and the metal surface finish have been well accepted factors for backside wear [14]. Several studies have shown that suboptimal conformity between the shell and the liner could be the major influence factor on liner instability causing backside wear and subsequent osteolysis [3, 12, 14, 16]. The reason for this is that synovial fluid with debris particles from the articulation surface could occupy this empty backside space and a piston pumping mechanism generated during gait could push the debris solution into the iliac bone through the screw holes and create osteolysis [10, 16].

Proven that the locking mechanism and the liner-shell connection is stable, backside wear of polyethylene liners does not substantially contribute to the overall wear rate of polyethylene liners. Using three-dimensional finite element models, Kurtz et al. [12] showed that backside linear wear rates were three orders of magnitude less than the wear rate estimates at the articulating surface. Furthermore, the wear rates between two hole and eight hole cups designs were not substantially different. In another study with a different cup design, Krieg et al. [13] showed that only 2.8% of the rate of volumetric articular wear corresponded to the rate of backside volumetric change. As Krieg's study included creep and wear for the volumetric change, this might be the reason for their higher backside wear proportion found. Moreover, the so-called "monoblock" cups, whose polyethylene liners and cups are factory-preassembled into a single solid construct, theoretically eliminate backside wear of polyethylene liners. Nevertheless, a systematic review performed by Halma et al. [3] as well as a study by González Della Valle et al. [38] showed that there was no difference in the polyethylene wear rate between monoblock and modular acetabular components at intermediate-term follow-up.

Finally, midterm clinical studies have shown very good results of the Plasmacup system, with a low revision rate due to aseptic loosening at a minimum follow-up of eight years [31, 39]. As the retrievals from the present study were at an average of 13.1 months in situ, further long-term studies with a sufficiently large number of retrievals should be performed in the future in order to analyze the backside wear behavior in the long-term as well as in vitro tests with longer testing times.

5. Conclusion

In general, the total average backside wear score was approximately the same for in vitro tested and retrieved liners. The same wear modes of damage and their patterns were observed in both types of liners. More importantly, our observations confirmed the low backside wear of the liners and confirmed that the wear marks were mainly initiated during their insertion and removal rather than during their time in situ. Even though retrieval analysis may show different results among the specimens and may not always coincide with in vitro tests, they still help tracking the performance of implant materials and designs. Further tests with long-term in vivo retrievals and corresponding in vitro test periods could support the results observed, as the simulation and mean retrieval times of the current study were in the short-term range.

Competing Interests

Three of the authors (Ana Laura Puente Reyna, Christoph Schilling, and Thomas M. Grupp) are employees of Aesculap AG, Tuttlingen, a manufacturer of orthopaedic implants.

References

[1] P. Sadoghi, M. Liebensteiner, M. Agreiter, A. Leithner, N. Böhler, and G. Labek, "Revision surgery after total joint arthroplasty: a complication-based analysis using worldwide arthroplasty registers," *Journal of Arthroplasty*, vol. 28, no. 8, pp. 1329–1332, 2013.

[2] S. Glyn-Jones, G. E. R. Thomas, P. Garfjeld-Roberts et al., "The John Charnley Award: highly crosslinked polyethylene in total hip arthroplasty decreases long-term wear: a double-blind randomized trial," *Clinical Orthopaedics and Related Research*, vol. 473, no. 2, pp. 432–438, 2014.

[3] J. J. Halma, H. C. Vogely, W. J. Dhert, S. M. Van Gaalen, and A. De Gast, "Do monoblock cups improve survivorship, decrease wear, or reduce osteolysis in uncemented total hip arthroplasty?" *Clinical Orthopaedics and Related Research*, vol. 471, no. 11, pp. 3572–3580, 2013.

[4] H. C. Amstutz, P. Campbell, N. Kossovsky, and I. C. Clarke, "Mechanism and clinical significance of wear debris-induced osteolysis," *Clinical Orthopaedics and Related Research*, no. 276, pp. 7–18, 1992.

[5] P. A. Revell, N. Al-Saffar, and A. Kobayashi, "Biological reaction to debris in relation to joint prostheses," *Proceedings of the Institution of Mechanical Engineers H*, vol. 211, no. 2, pp. 187–197, 1997.

[6] S. M. Kurtz, H. A. Gawel, and J. D. Patel, "History and systematic review of wear and osteolysis outcomes for first-generation

highly crosslinked polyethylene," *Clinical Orthopaedics and Related Research*, vol. 469, no. 8, pp. 2262–2277, 2011.

[7] T. M. Wright and S. B. Goodman, "What are the wear mechanisms and what controls them?" in *Implant Wear in Total Joint Replacement: Clinical and Biologic Issues, Material and Design Considerations*, pp. 176–185, American Academy of Orthopaedic Surgeons, 2001.

[8] V. G. Williams II, L. A. Whiteside, S. E. White, and D. S. McCarthy, "Fixation of ultrahigh-molecular-weight polyethylene liners to metal- backed acetabular cups," *The Journal of Arthroplasty*, vol. 12, no. 1, pp. 25–31, 1997.

[9] H. Kawaji, A. Koistinen, R. Korhonen et al., "Back-side wear in HexLoc cups clinico-radiological, immunohistopathological, finite element, and retrieval analysis studies," *Journal of Long-Term Effects of Medical Implants*, vol. 24, no. 4, pp. 319–332, 2014.

[10] A. Gonzalez Della Valle and T. P. Sculco, "Complications of acetabular modularity," *Business Briefing: US Orhopaedics Review*, pp. 25–28, 2006.

[11] M. Kligman, B. D. Furman, D. E. Padgett, and T. M. Wright, "Impingement contributes to backside wear and screw-metallic shell fretting in modular acetabular cups," *Journal of Arthroplasty*, vol. 22, no. 2, pp. 258–264, 2007.

[12] S. M. Kurtz, J. A. Ochia, C. B. Hovey, and C. White, "Frontside vs Backside wear in an acetabular component with multiple screw holes," in *Proceedings of the 45th Annual Meeting, Orthopaedic Research Society*, Anaheim, Calif, USA, 1999.

[13] A. H. Krieg, B. M. Speth, and P. E. Ochsner, "Backside volumetric change in the polyethylene of uncemented acetabular components," *The Journal of Bone & Joint Surgery—British Volume*, vol. 91, no. 8, pp. 1037–1043, 2009.

[14] J. J. Nieuwenhuis, J. D. W. Malefijt, J. C. Hendriks, T. Gosens, and M. Bonnet, "Unsatisfactory results with the cementless Omnifit acetabular component due to polyethylene and severe osteolysis," *Acta Orthopaedica Belgica*, vol. 71, no. 3, pp. 294–302, 2005.

[15] P. C. Noble, S. K. Durrani, M. M. Usrey, K. B. Mathis, and N. V. Bardakos, "Constrained cups appear incapable of meeting the demands of revision THA," *Clinical Orthopaedics and Related Research*, vol. 470, no. 7, pp. 1907–1916, 2012.

[16] C. C. Powers, H. Ho, S. E. Beykirch et al., "A comparison of a second- and a third-generation modular cup design," *The Journal of Arthroplasty*, vol. 25, no. 4, pp. 514–521, 2010.

[17] C. Khalily, M. G. Tanner, V. G. Williams, and L. A. Whiteside, "Effect of locking mechanism on fluid and particle flow through modular acetabular components," *The Journal of Arthroplasty*, vol. 13, no. 3, pp. 254–258, 1998.

[18] T. M. Grupp, M. Holderied, M. A. Mulliez et al., "Biotribology of a vitamin E-stabilized polyethylene for hip arthroplasty—influence of artificial ageing and third-body particles on wear," *Acta Biomaterialia*, vol. 10, no. 7, pp. 3068–3078, 2014.

[19] J. Schwiesau, C. Schilling, C. Kaddick et al., "Definition and evaluation of testing scenarios for knee wear simulation under conditions of highly demanding daily activities," *Medical Engineering & Physics*, vol. 35, no. 5, pp. 591–600, 2013.

[20] A. A. J. Goldsmith, D. Dowson, B. M. Wroblewski et al., "Comparative study of the activity of total hip arthroplasty patients and normal subjects," *The Journal of Arthroplasty*, vol. 16, no. 5, pp. 613–619, 2001.

[21] B. B. Seedhom and N. C. Wallbridge, "Walking activities and wear of prostheses," *Annals of the Rheumatic Diseases*, vol. 44, no. 12, pp. 838–843, 1985.

[22] M. Silva, E. F. Shepherd, W. O. Jackson, F. J. Dorey, and T. P. Schmalzried, "Average patient walking activity approaches 2 million cycles per year: pedometers under-record walking activity," *The Journal of Arthroplasty*, vol. 17, no. 6, pp. 693–697, 2002.

[23] T. P. Schmalzried, E. S. Szuszczewicz, M. R. Northfield et al., "Quantitative assessment of walking activity after total hip or knee replacement," *The Journal of Bone & Joint Surgery—American Volume*, vol. 80, no. 1, pp. 54–59, 1998.

[24] B. B. Seedhom, D. Dowson, and V. Wright, "Wear of solid phase formed high density polyethylene in relation to the life of artificial hips and knees," *Wear*, vol. 24, no. 1, pp. 35–51, 1973.

[25] Longterm-Evaluation of Vitelene® against Standard (VITAS), ClinicalTrials.gov, https://www.clinicaltrials.gov/ct2/show/NCT01713062?term=VITAS+Aesculap&rank=1.

[26] R. W. Hood, T. M. Wright, and A. H. Burstein, "Retrieval analysis of total knee prostheses: a method and its application to 48 total condylar prostheses," *Journal of Biomedical Materials Research*, vol. 17, no. 5, pp. 829–842, 1983.

[27] D. T. Schroder, N. H. Kelly, T. M. Wright, and M. L. Parks, "Retrieved highly crosslinked UHMWPE acetabular liners have similar wear damage as conventional UHMWPE," *Clinical Orthopaedics and Related Research*, vol. 469, no. 2, pp. 387–394, 2011.

[28] K. French, R. Moore, H. Gawel et al., "Retrieval analysis of Harris-Galante I and II acetabular liners in situ for more than 10 years," *Acta Orthopaedica*, vol. 83, no. 4, pp. 366–373, 2012.

[29] C. Kaddick and M. A. Wimmer, "Hip simulator wear testing according to the newly introduced standard ISO 14242," *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, vol. 215, no. 5, pp. 429–442, 2001.

[30] K. Corten, R. W. McCalden, Y. Teo, K. D. Charron, S. J. MacDonald, and R. B. Bourne, "Midterm results of 506 solid trispiked reflection cementless acetabular components for primary total hip arthroplasty," *Journal of Arthroplasty*, vol. 26, no. 8, pp. 1350–1356, 2011.

[31] U. Ochs, T. Ilchmann, B. G. Ochs et al., "EBRA migration patterns of the plasmacup with ceramic or polyethylene inserts: a randomised study," *Zeitschrift für Orthopädie und Unfallchirurgie*, vol. 145, supplement 1, pp. S20–S24, 2007.

[32] A. D. Heiner, K. M. Kruger, N. M. Tikekar, J. J. Callaghan, J. J. Lannutti, and T. D. Brown, "THA retrievals: the need to mark the anatomic orientation of the femoral head," *The Journal of Arthroplasty*, vol. 30, no. 6, pp. 1089–1094, 2015.

[33] M. Yamaguchi, Y. Hashimoto, T. Akisue, and T. W. Bauer, "Polyethylene wear vector in vivo: a three-dimensional analysis using retrieved acetabular components and radiographs," *Journal of Orthopaedic Research*, vol. 17, no. 5, pp. 695–702, 1999.

[34] K. Knahr, M. Pospischill, P. Köttig, W. Schneider, and H. Plenk Jr., "Retrieval analyses of highly cross-linked polyethylene acetabular liners four and five years after implantation," *The Journal of Bone & Joint Surgery—British Volume*, vol. 89, no. 8, pp. 1036–1041, 2007.

[35] O. K. Muratoglu, E. S. Greenbaum, C. R. Bragdon, M. Jasty, A. A. Freiberg, and W. H. Harris, "Surface analysis of early retrieved acetabular polyethylene liners: a comparison of conventional and highly crosslinked polyethylenes," *Journal of Arthroplasty*, vol. 19, no. 1, pp. 68–77, 2004.

[36] W. Schneider and P. Köttig, "Analysis of early retrieved acetabualar cups of highly crosslinked polyethylene," in *Proceedings of the 12th Annual Meeting of the European Orthopaedic Research Society*, Lausanne, Switzerland, 2002.

[37] G. Bergmann, G. Deuretzbacher, M. Heller et al., "Hip contact forces and gait patterns from routine activities," *Journal of Biomechanics*, vol. 34, no. 7, pp. 859–871, 2001.

[38] A. González Della Valle, E. Su, A. Zoppi, T. P. Sculco, and E. A. Salvati, "Wear and periprosthetic osteolysis in a match-paired study of modular and nonmodular uncemented acetabular cups," *The Journal of Arthroplasty*, vol. 19, no. 8, pp. 972–977, 2004.

[39] S. Lakemeier, G. Aurand, N. Timmesfeld, T. J. Heyse, S. Fuchs-Winkelmann, and M. D. Schofer, "Results of the cementless Plasmacup in revision total hip arthroplasty: a retrospective study of 72 cases with an average follow-up of eight years," *BMC Musculoskeletal Disorders*, vol. 11, article 101, 2010.

3. Publication II

Articulation and backside wear analysis after long-term in vitro wear simulation of vitamin E stabilized polyethylene acetabular liners with a press-fit locking mechanism

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Articulation and Backside Wear Analysis after Long-Term *in vitro* Wear Simulation of Vitamin E Stabilized Polyethylene Acetabular Liners with a Press-Fit Locking Mechanism

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Abstract

A previous retrieval study analyzed the backside wear of short-term implanted liners against in vitro tested liners of similar life in service and showed comparable results among both groups, with no significant backside wear due to micro-motion.

The purpose — to obtain a picture of the overall wear (articulation and backside surfaces) of 0.1% vitamin E blended polyethylene liners, with a locking mechanism based on a press-fit cone in combination with a rough titanium conical inner surface in the fixation area, under a 20 million cycles hip wear simulation.

Materials and Methods. A semi-quantitative method was used in order to assess the damage on the backside of the liners and a 3D measuring machine to assess the creep and wear at the articulation surface.

Results. The total average backside wear score was 22.00±2.59 from a maximum total score of 147 after 5 million cycles (mc), increased to 31.92±5.57 after 10 mc, but showed no further increment after 15 and 20 mc. The reference liners (subjected only to axial load) showed similar wear scores and modes as the liners under wear simulation (axial load and movement). Small scratches produced during insertion and removal were clearly seen at the rim (fixation) area and no considerable abrasion was observed. The machining marks on the convex surface were always visible. Regarding the articulation surface, a steady state wear rate of 7 µm/year was measured.

Conlusion. These results determined that most of the backside wear produced on the liners occurred during their insertion and removal rather than during their life in service. Moreover, the wear at the articulation surface was similar to that seen in vivo at short- and mid-term on highly cross-linked polyethylene liners with and without vitamin E content.

Keywords: total hip arthroplasty, wear simulation, vitamin E, backside wear.

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Анализ износа артикулирующей и тыльной поверхностей после долгосрочного *in vitro* моделирования износа стабилизированных витамином Е полиэтиленовых вкладышей с пресс-фит блокированием

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Реферат

Предыдущие исследования были посвящены износу тыльной поверхности кратковременно имплантированных вкладышей в сравнении со вкладышами, тестируемыми *in vitro*, в течение равного количества времени. В результате были продемонстрированы сравнимые результаты в обеих группах, при этом не было отмечено существенного износа тыльной поверхности вследствие микроподвижности.

Цель исследования — получить данные об общем износе (артикулирующей поверхности и тыльной поверхности) полиэтиленовых вкладышей, стабилизированных 0,1% витамином Е, которые блокировали за счет пресс-фит посадки в шероховатой титановой внутренней поверхности чашки. Условия моделирования износа составляли 200 миллионов циклов движений тазобедренного сустава.

Материал и методы. Для оценки степени повреждения тыльной поверхности вкладышей использовали полуколичественный метод. Степень износа сочленяющихся поверхностей определяли с использованием 3D координатно-измерительного прибора.

Результаты. Общий средний показатель износа тыльной поверхности вкладышей составил 22,00±2,59, максимальный общий показатель составил 147 после 5 млн циклов. Авторы наблюдали увеличение среднего показателя до 31,92±5,57 через 10 млн циклов, при этом, дальнейшего увеличения показателей через 15 и 20 млн циклом не отмечали. Контрольные вкладыши (подверженные только аксиальной нагрузке) продемонстрировали схожие показатели и модели износа как вкладыши, подверженные моделированию износа (аксиальная нагрузка и движение). Небольшие царапины, нанесенные во время установки и удаления вкладышей, были четко видны в области фиксации, при этом значимого абразивного истирания не было отмечено. Всегда были видны риски на выпуклой поверхности вкладышей. Скорость износа сочленяющихся поверхностей составила 7 мкм/год.

Выводы. Результаты исследования продемонстрировали, что основной объем износа тыльной стороны вкладышей происходит в процессе их установки и удаления, нежели в период функционирования протеза. Более того, объем износа артикулирующей поверхности был идентичен объему износа, который отмечали *in vivo* при кратко- и среднесрочной имплантации вкладышей из кросс-линк полиэтилена с высокими поперечными связями без или с добавлением витамина Е.

Ключевые слова: тотальное эндопротезирование тазобедренного сустава, моделирование износа, витамин Е, износ тыльной стороны вкладыша.

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Introduction

Aseptic loosening as a consequence of wear generated particulate debris remains the principal reason for revision in total hip arthroplasty at the long-term [1]. The main source of particulate debris, and thus the most studied, is at the articulation surface. However, the wear produced at the interface between the liner and the metallic acetabular component, known as backside wear, gained importance after high revision rates due to retroacetabular osteolysis were seen on retrieved liners showing high backside wear [2–6]. When there is an unstable locking mechanism and a poor conformity between the liner and the acetabular shell, wear is produced at this non-articulating surface as a result of micro-motions between both components [7–9]. Therefore, a secure locking mechanism should be able to decrease the backside wear to values that do not substantially contribute to the overall wear rate of polyethylene liners [9, 10].

A previous retrieval study analyzed the backside wear of acetabular liners with a locking mechanism based on a press-fit cone with a large surface area in combination with a grit blasted rough titanium inner surface along the rim of the acetabular shell [11]. In the study, the backside wear of short-term retrievals made out of conventional standard polyethylene (CPE), highly cross-linked polyethylene (XLPE) and highly cross-linked and vitamin E (0.1%) blended polyethylene was analyzed and compared with their corresponding *in vitro* tested liners of equivalent life in service, showing similar results among both groups and no significant backside wear due to micro-motion.

A limitation of the study was that the analyzed retrieved liners were only for an average of 13.1 months *in situ* and the *in vitro* test simulated approximately 2.9 years of *in vivo* service life. As retrieval studies from other acetabular cup designs have demonstrated a significant correlation between backside damage and age *in vivo* for CPE and XLPE liners [12, 13], it is important to investigate if the backside wear increases on vitamin E blended polyethylene liners with the mentioned locking mechanism through time. To date, no long-term retrievals of vitamin E blended polyethylene are available, therefore, only *in vitro* studies can provide information regarding their performance at the long-term.

Objectives

The purpose of our study was to obtain a picture of the overall wear (articulation and backside surfaces) of 0.1% vitamin E blended polyethylene liners with a press-fit locking mechanism under a 20 million cycles hip wear simulation, equivalent to approximately 11.4 years in vivo service [14]. More specifically, our purposes were to analyze the backside wear of the liners, which wear modes can be expected and if this type of wear increases with time.

Materials and Methods

In vitro wear simulation

In vitro wear simulation was performed on a customized 6 + 2 (reference) stations servohydraulic hip simulator (EndoLab GmbH, Thansau, Germany) with kinematic and load patterns according to ISO 14242-1:2014(E). Acetabular cups (Plasmafit® Poly Cup, size 50, Aesculap AG, Tuttlingen, Germany) made out of Ti6Al4V alloy and without screw drill holes were used in combination with highly cross-linked (electron beam, 80 kGy), vitamin E (0.1%) blended and EO sterilized polyethylene liners (Plasmafit® Poly Insert, size 36 mm, Aesculap AG, Tuttlingen, Germany). Modular heads of 36 mm (taper 12/14) made out of zirconia toughened alumina ceramic (BIOLOX® delta, Aesculap AG, Tuttlingen, Germany) were used for the articulation.

Prior wear simulation, all the polyethylene liners were subjected to artificial aging according to ASTM F2003-02 in a heat-conditioning chamber at 70°C in pure oxygen and at 5 bar for two weeks (BM400, Memmert GmbH + Co. KG, Schwabach, Germany). Afterwards, the polyethylene liners were soaked in serum-based test medium until the incremental mass change over 24 hours was less than 10% of the previous cumulative mass change (34 days) in order to allow for saturated fluid absorption according to ISO 14242-2:2016(E).

Wear simulation was performed for 20 million cycles at a frequency of 1 Hz in a test medium at 37°C consisting of newborn calf serum (Biowest SAS, Nuaille, France) diluted with deionized water in order to achieve a protein concentration of 30 g/l. Ethylene diamine tetraacetic acid and Amphotericin B were added to the test medium in order to stabilize the *p*H and prevent fungal decay, respectively. The test medium was replaced at 0.5 million cycles intervals and all the components were cleaned with deionized water and mild soap without removing the polyethylene liners from the acetabular cup in order to reduce potential backside wear produced by the constant removing and insertion of the liner. Only every 5 million cycles the polyethylene liners were removed from the acetabular cups and cleaned according to ISO 14242-2:2016(E). After every 0.5 million cycles, the component sets were rotated across stations to minimize the effect of inter-station kinematic variability. For the different analysis, two groups were defined: "Reference" liners (n = 2) subjected only to axial load; and "Wear simulated" liners (n = 6) subjected to axial load and movement.

Wear at the articulation surface and geometrical changes

Optical analysis of the articulation surface of the polyethylene liners was performed after 5, 10, 15 and 20 million cycles using a digital microscope (VHX-5000, Keyence Corporation, Osaka, Japan) with a 30- and 50-fold magnification. Plastic deformation due to creep and wear was assessed by means of a three-dimensional measuring machine (UMM850, Carl Zeiss AG, Oberkochen, Germany) in a tactile measuring mode (1500 points per scan). The geometrical changes were displayed vertically to the transversal plane of the polyethylene liners with a pseudo-color mode.

Optical backside wear analysis

Optical analysis of the backside surface of the polyethylene liners was performed after 5, 10, 15 and 20 million cycles using the digital microscope previously mentioned with a 50-fold magnification. A semi-quantitative method developed by Hood et al. [15] and modified for hip implants was used to assess the damage on the backside of the liners. The detailed description of the modified method is given in the previously performed study [11] and will be briefly summarized in the following. On basis of its *in situ* orientation, the backside section was divided by a superior / inferior line and 7 different sections were determined (Figure 1).

For each section, a score between 0 and 3 was given for each of the seven different wear modes (deformation, pitting, embedded particles, scratching, burnishing, abrasion and delamination), giving a maximum possible damage score of 21 per section. A score of 0 meant no damage; a score of 1 meant damage to less than 10% of the surface area, 2 meant damage to 10 —

50% of the surface area and 3 meant that more than 50% of the area had been damaged. Each component was given a total damage score based on the sum of the scores from all its seven sections. The maximum possible damage score was 147.

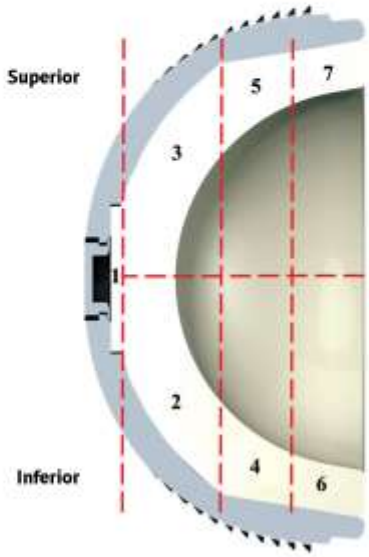


Fig. 1. Sketch from a cross-section of a Plasmafit® liner with its titanium alloy shell and the corresponding sections for backside wear analysis [11]

The optical analysis was performed by two of the authors (ALPR, MH) and their scores were averaged. Both observers were blinded to previous results at the time of new scoring and to the results of the other observer. The inter-observer reliability of this method was "substantial", with kappa measures ranging between 0.62 and 0.72.

Statistics

To differentiate the average total backside wear scores after 5, 10, 15 and 20 million cycles of the "Wear simulated" and "Reference" liners, an analysis of variance was carried out ($p = 0.05$) followed by a post hoc test (Scheffe $p = 0.05$). To differentiate between the "Wear simulated" and "Reference" liners at 5, 10, 15 and 20 million cycles, an analysis of variance ($p = 0.05$) was carried out followed by a post hoc test (HSD Test for unequal N, $p = 0.05$). Prior to analysis, the normal distribution (p-p plots) and the homogeneity of variance (Levene Test) were verified (Dell Statistica R13, Dell Inc., Hamburg, Germany). A p value less than 0.05 was considered as significant.

Results

Wear at the articulation surface and geometrical changes

Optical analysis of the wear patterns at the articulation surface of the "Wear simulated" liners showed an increment in the total wear area through the 20 million cycles (Figure 2). The wear modes seen at the articulation area during the whole test were burnishing and slight scratches. After the first 5 million cycles, even though there was burnishing of the surface, the machining marks at the pole of the articulation surface could still be slightly seen. However, these were erased through the rest of the wear simulation and were not seen at the end of the test. The superior side of the liner showed high burnishing since the first 5 million cycles, whereas the inferior side showed practically no wear marks after the first 5 million cycles, but showed burnishing of the surface through time. Regarding the "Reference" liners that underwent just to axial load, no burnishing nor scratches were seen through the entire simulation, as the machining marks were always clearly visible (Figure 3).

The 3D analysis performed on the "Wear simulated" liners after 20 million cycles showed a total head penetration generated by creep and wear of 107.4±31.0 μm, whereas the "Reference" liners had a total head penetration only by creep of 33.4±7.8 μm (Figure 4). Hence, approximately one third of the total head penetration of the "Wear simulated" liners was a result of plastic deformation.

Optical backside wear analysis

After 5 million cycles, the "Wear simulated" liners had a total average backside wear score of 22.00±2.59 (from a maximum total score of 147), which was statistically lower than the scores at 10 million cycles (31.92±5.57, $p < 0.001$), 15 million cycles (27.50±2.58, $p = 0.005$), and 20 million cycles (30.00±2.52, $p < 0.001$). Moreover, there was a statistical decrease in the total average backside wear score from 10 to 15 million cycles ($p = 0.04$), but there was no statistical change from 15 to 20 million cycles ($p = 0.41$). The reason for the decrease in the total average backside wear score will be discussed in the following section.

On the other hand, the "Reference" liners subjected only to axial load had a total average backside wear score of 16.50±2.52 after 5 million cycles, which was also statistically lower than the scores at 10 million cycles (26.75±2.63, $p < 0.001$), 15 million cycles (27.25±1.26, $p < 0.001$), and 20 million cycles (24.00±1.41, $p = 0.002$). They did not have any significant change from 10 to 15 million cycles ($p = 0.99$) nor from 15 to 20 million cycles ($p = 0.23$). Finally, there was a statistical difference between the total backside wear score of the "Wear simulated" liners and the "Reference" at 5 and 20 million cycles ($p = 0.009$ and $p = 0.003$, respectively), but not at 10 and 15 million cycles ($p = 0.17$ and $p = 0.88$, respectively) (Figure 5).

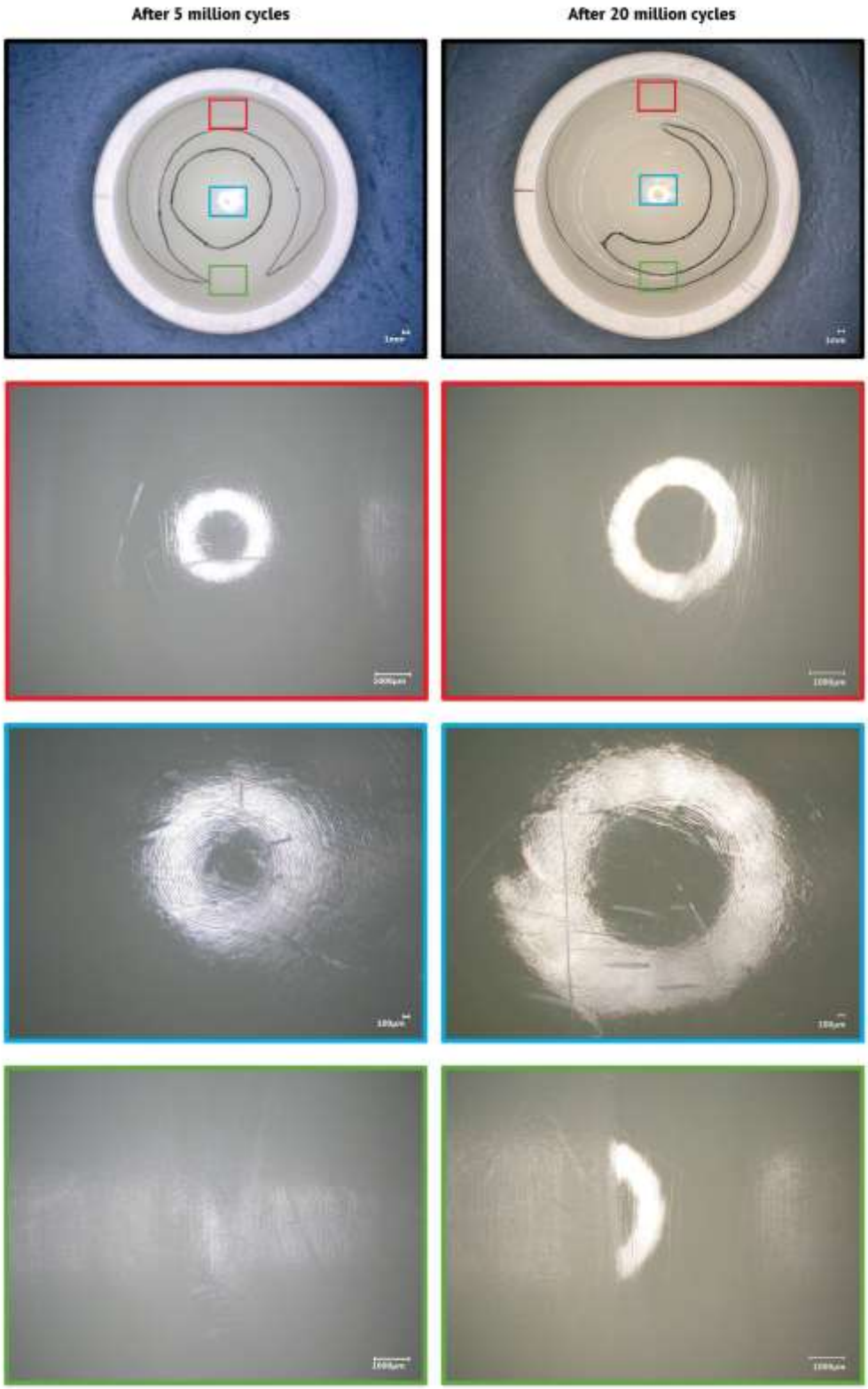


Fig. 2. Wear patterns at the articulation surface of a "Wear simulated" liner (subjected to axial load and movement) after 5 and 20 million cycles showing polishing and slight scratches. Black: overview of the wear areas; red: superior side of the liner in anatomical position; blue: wear at the pole; green: wear at the inferior side

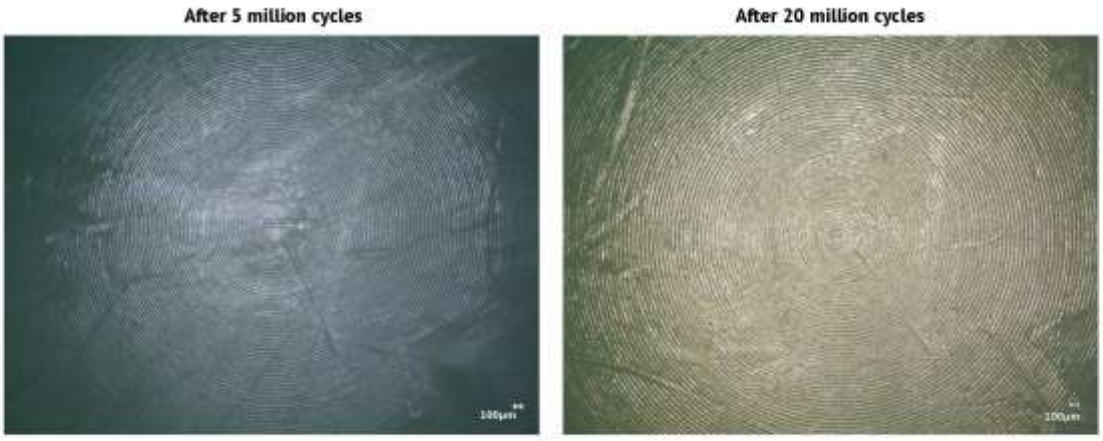


Fig. 3. Articulation surface of a "Reference" liner subjected just to axial load after 5 (left) and 20 (right) million cycles with machining marks still visible

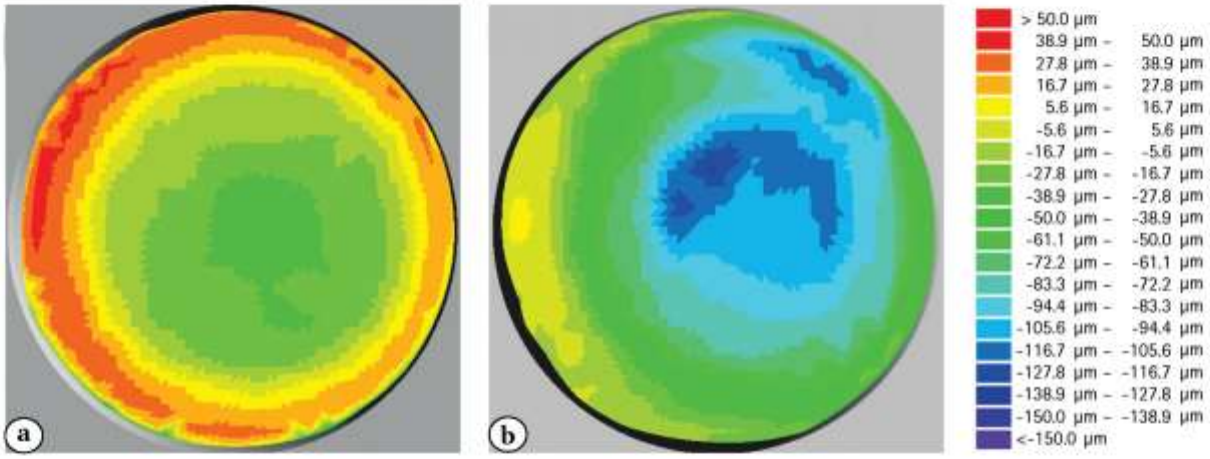


Fig. 4. Geometrical changes after 20 million cycles of a "Reference" liner subjected only to axial load (creep) (a) and a "Wear simulated" liner subjected to axial load and movement (creep and wear) (b)

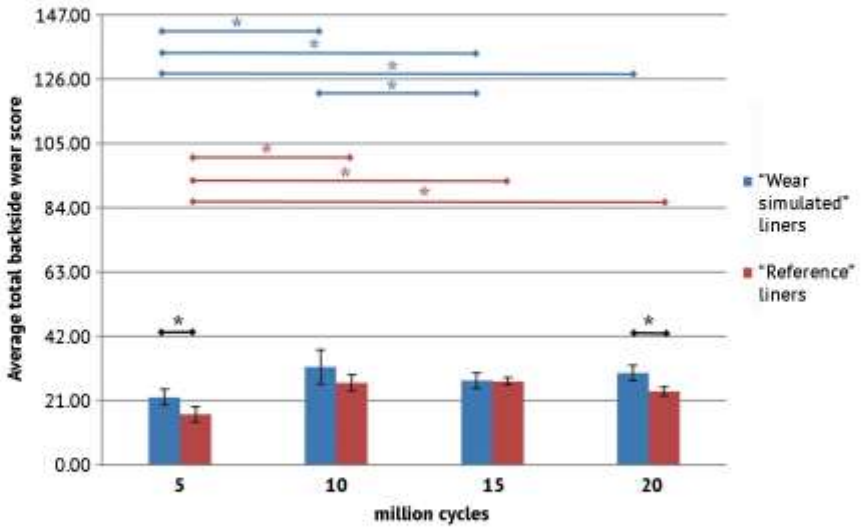


Fig. 5. Average total backside wear score of the "Wear simulated" liners (subjected to axial load and movement) and "Reference" liners (only axial load) after 5, 10, 15 and 20 million cycles. Maximum total backside wear score possible = 147.
* Indicates statistical difference ($p < 0.05$)

The most common wear mode overall seen after 5, 10 and 15 million cycles was scratching, followed by burnishing. However, after 20 million cycles, scratching, burnishing and abrasion had approximately the same weight regarding their wear score. Moreover, the number of embedded particles increased through the wear simulation (Figure 6).

When analyzing the wear per sections, those in contact with the milled-drilled smooth acetabular inner surface (sections 1 to 3) had the lowest backside wear score (between 2.00±0.00 and 4.00±0.71 from a maximum score of 21) (Figure 7). In these sections, the main wear mode seen was slight burnishing, as the machining marks appeared flattened. After every 5 million cycles, the machining marks appeared to be more flattened, but were still clearly visible after 20 million cycles. Same tendency was seen on the "Reference" liners (Figure 8).

Regarding the rim of the liners, the highest wear scores were seen in sections 4 and 5, with values ranging from 4.17±0.52 to 7.33±0.68. In these sections, the most observed wear mode were small scratches. However, as the test went on, the number of scratches increased and the surface showed abrasion marks.

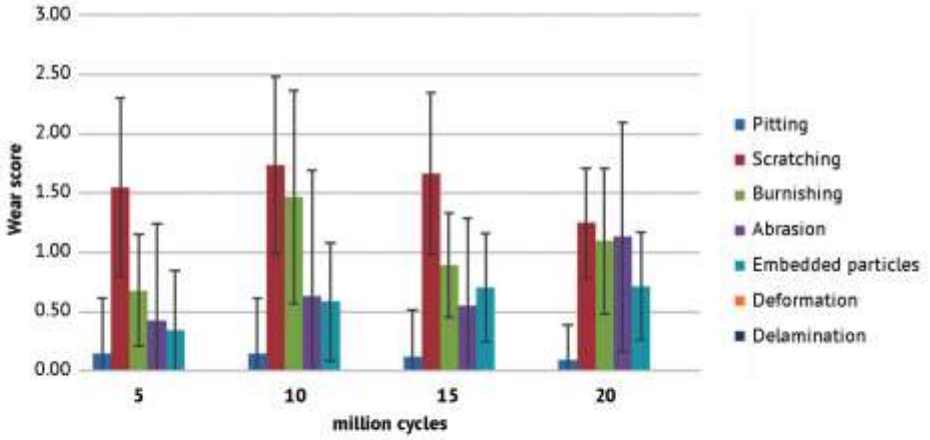


Fig. 6. Average score per wear mode of all backside sections of the "Wear simulated" liners after 5, 10, 15 and 20 million cycles. Maximum possible score per wear mode = 3

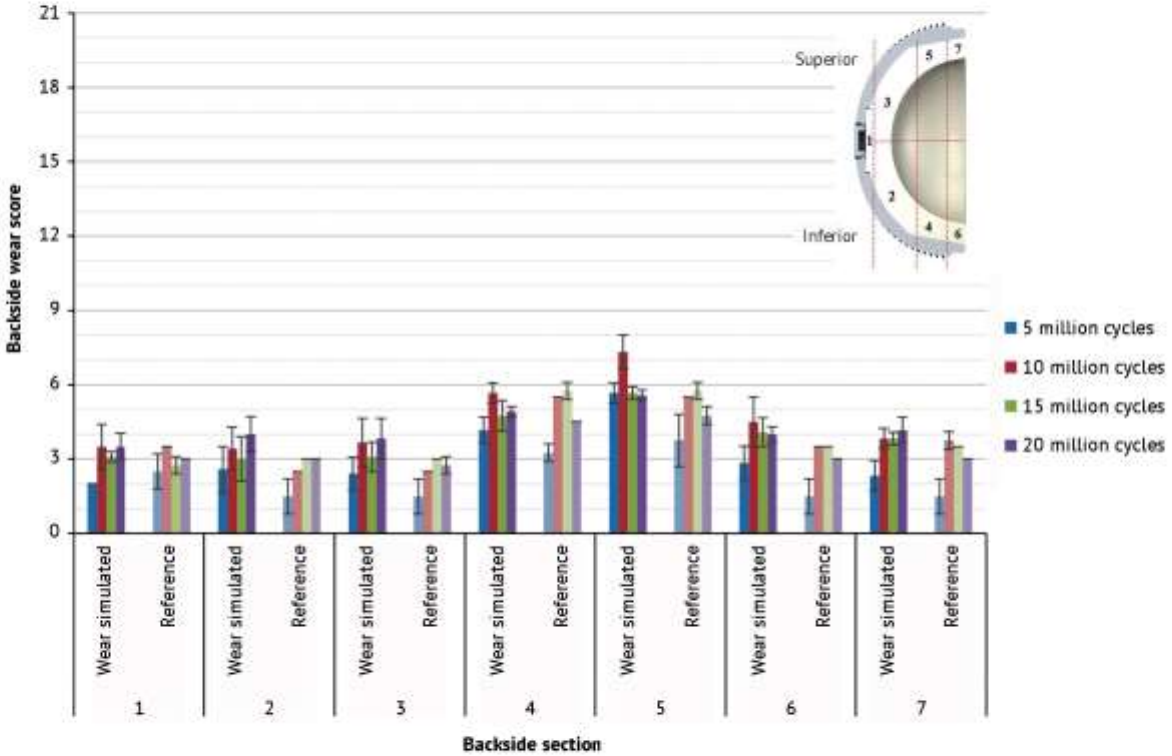


Fig. 7. Backside wear score per backside section for the "Wear simulated" (axial load and movement) and "Reference" liners (only axial load) after 5, 10, 15 and 20 million cycles. Maximum backside wear score per zone = 21

In sections 6 and 7, the surface also showed mainly small scratches and their number also increased through the test, but no abrasion in these zones was seen. The same tendency was seen in the "Reference" liners (Figure 9).

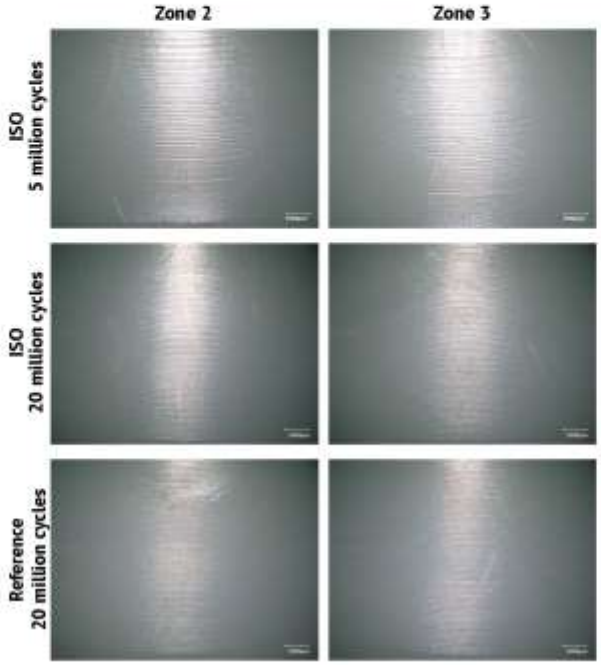
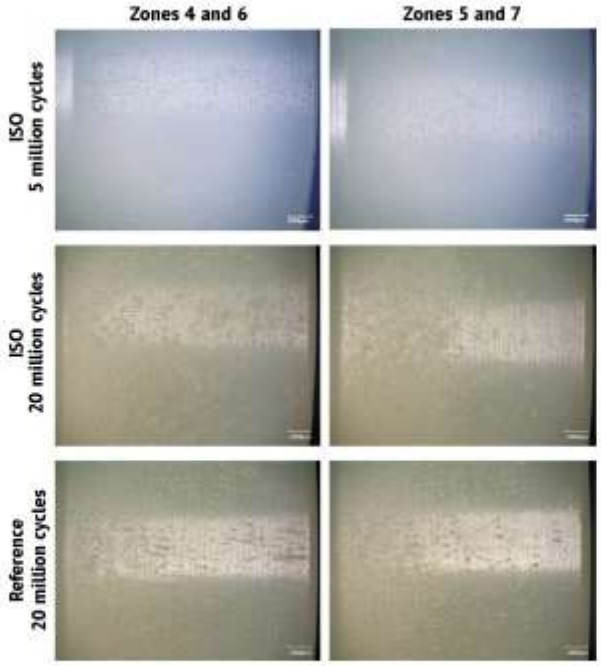


Fig. 8. Representative images of backside zones 2 and 3 of a "Wear simulated" liner after 5 and 20 million cycles (axial load and movement) and a "Reference" liner after 20 million cycles (only axial load). Machining marks were always visible



Discussion

The purpose of our study was to obtain a picture of the overall wear (articulation and backside surfaces) of 0.1% vitamin E blended polyethylene liners with a press-fit locking mechanism under a 20 million cycles hip wear simulation, equivalent to approximately 11.4 years *in vivo* service [14]. More specifically, our purposes were to analyze the backside wear of the liners, which wear modes can be expected and if this type of wear increases with time. To the authors knowledge, this is the first study to analyze the backside wear of vitamin E liners in a long-term *in vitro* wear simulation.

As highly cross-linked polyethylene with vitamin E content (either blended or diffused) is a relatively new material, there are currently no long-term follow-up studies available to compare the results obtained in the current *in vitro* study. Nevertheless, short-term follow-up studies have shown a similar performance between XLPE liners with and without vitamin E content [16, 17]. Vitamin E does not provide additional wear resistance to the polyethylene after highly cross-linking, but prevents its oxidation, and thus it is expected to maintain its excellent wear characteristics through time. For this reason, *in vivo* results of XLPE liners can be used as a reference to compare the vitamin E liner results of the present *in vitro* study.

During its *in vivo* service time, the most common method to measure the wear of polyethylene liners is through measurement of the femoral head penetration by means of x-ray images. The highest head penetration occurs during the first year after surgery and is mainly due to creep, which then decreases through time. Follow-up studies have shown an average head penetration between 30 and 50 µm on XLPE liners during the first year after surgery [18, 19]. The reference liners subjected just to axial load of the current *in vitro* study showed a total head penetration similar to those values. Taking into account an average of 1.76 million gait cycles per year for hip and knee arthroplasty patients [14], and that after approximately one year of implantation there is no considerable creep of the liner, the steady state wear rate of the vitamin E liners from our study was approximately 7 µm/year. This wear rate is similar to that found in several mid- and long-term follow-up (7 to 13 years) studies of XLPE

Fig. 9. Representative images of backside zones 4 to 7 of a "Wear simulated" liner after 5 and 20 million cycles (axial load and movement) and a "Reference" liner after 20 million cycles (only axial load). Small scratches in the direction of insertion and removal were clearly seen. Even though the images correspond to the same "Wear simulated" liner, the color difference was due to a different white balance configuration of the microscope

liners, where steady state wear rates between 1 and 10 μm/year have been found [19–22], and is considerably below the osteolysis threshold wear rate of 100 μm/year [23]. Short-term follow-up studies of XLPE liners with vitamin E content also show similar wear rates as those from XLPE previously mentioned [16, 17, 24, 25]. However, this excellent wear characteristics of the XLPE at the long-term are in question, as studies have demonstrated *in vivo* oxidation of annealed XLPE by means of cyclic fatigue loading and fluid absorption, whereas remelting of XLPE leads to a reduction of its mechanical properties [26–30]. Deterioration of the wear properties of vitamin E blended highly cross-linked polyethylene liners as a consequence of material oxidation is not expected to occur in the long-term, as previous in vitro studies have demonstrated oxidation resistance of this material even after severe artificial aging [31, 32].

Regarding the backside wear of our *in vitro* study, a total average backside wear score of 22 from a maximum of 147 was seen after the first 5 million cycles. After this time, small scratches were seen at the rim of the liner, which were produced during its insertion and removal from the acetabular shell. Nevertheless, the machining lines of the liners were still clearly visible in the rim areas without scratches as well as below the milled-drill smooth surface of the acetabular shell. This demonstrated that there was no micromotion of the liner that could produce burnishing or abrasion on it. The significant increment in the backside wear score seen after 10 million cycles was because of the second insertion and removal of the liner, as this produced more scratches and embedded particles from the rough titanium shell. However, there was no further significant increment in the total average backside wear scores after 15 and 20 million cycles. Furthermore, the machining lines in the rest of the liner just appeared to be more flattened through the test, but were still clearly visible.

Even though a structured method was applied, the visual analysis is based on appreciation and thus, changes in the type of microscope, light, magnification, observer and time lapse between scoring can influence the results. The facts that the observers were blinded to the previous results and that the time lapse between measuring points was approximately 3 months might be the reasons for the statistical drop in total backside wear scores registered from the 10 to 15 million cycles measuring points. The observers did not saw a clear change in the type and degree of wear as from the 5 to 10 million cycles analysis, but they did not had the previous results to influence their scoring. Regardless of the scores, the same wear modes and patterns were seen in the current *in vitro* study and in our previous retrieval study [11]. A previous study from Pang et al. [33] showed that visual backside damage scoring may not completely correspond with true volumetric wear, as no difference in damage scores were seen between XLPE and CPE liners, but there was three times more penetration in the CPE liners than in the XLPE liners.

Despite the limitations of the visual analysis because of its subjective nature, it was effective to describe the extent of the backside wear and how it developed through time. For example, it was seen that the superior sections of the liner had higher backside wear scores as their counterpart, which correlates to the direction of the joint forces and might also be the reason why the "Wear simulated" liners (subjected to axial load and movement in anatomical position) had a statistical difference with the "Reference" liners (subjected only to axial load), as in the later ones the force was equally distributed. Besides, it was the only tool available in order to measure the backside wear of the liners in a semi-quantitative manner. For instance, it was also pursued to measure the geometrical changes at the backside of the inserts with the 3D measuring machine used for the measurement at the articulation surface, but the backside wear was so low, that no quantitative results could be obtained with such method.

Proven that there is a secure locking mechanism and that there is no severe backside wear, it has been shown that this type of wear does not induce acetabular osteolysis. A retrieval study from Yamaguchi et al. [34] found no correlation between backside deformation and acetabular osteolysis, but a significant association between pelvic or femoral osteolysis and linear wear at the articulation surface. On the other hand, Akbari et al. [12] found no backside wear on CPE liners retrieved due to osteolysis, only partial flattening of the machining marks as in our current *in vitro* study. Furthermore, all the osteolytic cysts found at surgery were peripheral. Moreover, Bali et al. [13] suggested that XLPE is more resistant to backside damage than CPE, as a similar backside damage score was found on XLPE liners with different locking mechanism, contrary to the CPE, which had different scorings depending on the locking mechanism.

Studies have already shown that backside wear is considerable low compared with the wear at the articulation surface. For instance, Kurtz et al. [9] demonstrated that the backside linear and volumetric wear rates were three orders of magnitude less than wear estimates at the articulating surface, which was attributed to the difference in maximum sliding distances at the articulating surface (measured in mm) versus the back surface (measured in μm). Moreover, Krieg et al. [35] showed that the rate of backside volumetric change (predominantly creep) was only 2.8% of the rate of volumetric articular wear. Although some data suggest that a functional locking mechanism at the acetabular shell-liner interface is a major factor to reduce backside wear, other aspects concerning the

acetabular socket design have to be considered when evaluating the properties of an implant for clinical application [13]. It is evident that the clinical outcome is not only dependent on the amount of backside wear but also on the amount and type of wear particles which migrate behind the acetabular shell through the screw holes inducing aseptic loosening. Here, the significance of micro-pumping mechanisms and the application of screw holes promoting osteolysis in cementless cups is controversially discussed in the literature and needs to be investigated in the future [36–38]. The acetabular socket design of the present study lacks of screw hole drills, and thus reduces the potential migration of backside wear particles behind the acetabular shell through these screw holes.

In summary, two facts from the present study demonstrated that wear occurred predominantly at the articulation surface in the long-term *in vitro* wear simulation. First, there was increased burnishing through the test at the articulation area of the "Wear simulated" liners (subjected to axial load and movement), whereas the "Reference" liners (subjected just to axial load) showed no wear at all. Second, the backside wear of the "Wear simulated" liners, even though it was statistically different at 5 and 20 million cycles, was similar to that of the "Reference" liners, demonstrating that most of the backside wear was produced during their insertion and removal from the acetabular shell. As the wear rate found at the articulation surface of the *in vitro* tested vitamin E liners is one to two orders of magnitude lower than the osteolysis threshold, no acetabular osteolysis as a consequence of backside wear can be expected. Regarding its clinical performance at the long-term, the Danish Hip Arthroplasty Register from 2014 [39] reported a survival rate of 94.1% at 10 years for all reasons of cup revision and 99.3% at 10 years with aseptic loosening as endpoint for the previous model of the acetabular system here described, which has the same locking mechanism as the one in the present study. Long-term retrievals or follow-up studies will be needed in order to validate the current *in vitro* results.

Conclusions

The present study showed that wear at the articulation surface was far below the osteolysis threshold on highly cross-linked and 0.1% vitamin E blended polyethylene liners and confirmed that there was little to no micro-motion at its interface between the acetabular shell in a long-term hip wear simulation. Furthermore, it was demonstrated that most of the backside wear produced on the liners occurred during their insertion and removal rather than during their life in service and that there was no significant increment of this type of wear through time. Finally, long-term retrieval analysis will be needed in order to validate this *in vitro* results.

Declaration

Competing interests: Four of the authors (ALPR, MH, CS, TMG) are employees of Aesculap AG Tuttlingen, a manufacturer of orthopaedic implants. One of the authors (MJ) is an advising surgeon of Aesculap R&D projects and is receiving institutional research funding in correlation with Aesculap R&D projects.

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References

1. Sadoghi P., Liebensteiner M., Agreiter M., Leithner A., Böhler N., Labek G. Revision surgery after total joint arthroplasty: a complication-based analysis using worldwide arthroplasty registers. *J Arthroplasty.* 2013;28(8):1329-1332. DOI: 10.1016/j.arth.2013.01.012.
2. Nieuwenhuis J.J., Malefijt J. de W., Hendriks J.C., Gosens T., Bonnet M. Unsatisfactory results with the cementless Omnifit acetabular component due to polyethylene and severe osteolysis. *Acta Orthop Belg.* 2005;71(3):294-302.
3. Noble P.C., Durrani S.K., Usrey M.M., Mathis K.B., Bardakos N.V. Constrained cups appear incapable of meeting the demands of revision THA. *Clin Orthop Relat Res.* 2012;470(7):1907-1916. DOI: 10.1007/s11999-011-2212-4.
4. Powers C.C., Ho H., Beykirch S.E., Huynh C., Hopper R.H. Jr., Engh C.A. Jr., Engh C.A. A comparison of a second- and a third-generation modular cup design: is new improved? *J Arthroplasty.* 2010;25(4):514-521. DOI: 10.1016/j.arth.2009.02.018.
5. Wasielewski R.C., Jacobs J.J., Arthurs B., Rubash H.E. The acetabular insert-metal backing interface: an additional source of polyethylene wear debris. *J Arthroplasty.* 2005;20(7):914-922. DOI: 10.1016/j.arth.2005.04.033.
6. Kawaji H., Koistinen A., Korhonen R., Lappalainen R., Lohman M., Soininen A. et al. Back-side wear in HexLoc cups clinico-radiological, immunohistopathological, finite element, and retrieval analysis studies. *J Long Term Eff Med Implants.* 2014;24(4):319-331.-
7. Kurtz S.M., Ochoa J.A., White C.V., Srivastav S., Cournoyer J. Backside nonconformity and locking restraints affect liner/shell load transfer mechanisms and relative motion in modular acetabular components for total hip replacement. *J Biomech.* 1998;31(5):431-437.
8. Kligman M., Furman B.D., Padgett D.E., Wright T.M. Impingement contributes to backside wear and screw-metallic shell fretting in modular acetabular cups. *J Arthroplasty.* 2007;22(2):258-264. DOI: 10.1016/j.arth.2005.01.025.
9. Kurtz S.M., Ochoa J.A., Hovey C.B., White C.V. Simulation of initial frontside and backside wear rates in a modular acetabular component with multiple screw holes. *J Biomech.* 1999;32(9):967-976.
10. Khalily C., Tanner M.G., Williams V.G., Whiteside L.A. Effect of locking mechanism on fluid and particle flow through modular acetabular components. *J Arthroplasty.* 1998;13(3):254-258.
11. Puente Reyna A.L., Jäger M., Floerkemeier T., Frecher S., Delank K.S., Schilling C., Grupp T.M. Backside wear analysis of retrieved acetabular liners with a press-

fit locking mechanism in comparison to wear simulation in vitro. *Biomed Res Int.* 2016;2016:8687131. DOI: 10.1155/2016/8687131.
12. Akbari A., Roy M.E., Whiteside L.A., Katerberg B.J., Schnettgoecke D.J. Minimal backside surface changes observed in retrieved acetabular liners. *J Arthroplasty.* 2011;26(5):686-692. DOI: 10.1016/j.arth.2010.07.012.
13. Bali K., McCalden R.W., Naudie D.D., MacDonald S.J., Teeter M.G. Backside Wear Is Not Dependent on the Acetabular Socket Design in Crosslinked Polyethylene Liners. *Clin Orthop Relat Res.* 2016;474(2):374-382. DOI: 10.1007/s11999-015-4471-y.
14. Schwiesau J., Schilling C., Kaddick C., Utzschneider S., Jansson V., Fritz B. et al. Definition and evaluation of testing scenarios for knee wear simulation under conditions of highly demanding daily activities. *Med Eng Phys.* 2013;35(5):591-600. DOI: 10.1016/j.medengphy.2012.07.003.
15. Hood R.W., Wright T.M., Burstein A.H. Retrieval analysis of total knee prostheses: a method and its application to 48 total condylar prostheses. *J Biomed Mater Res.* 1983;17(5):829-842. DOI: 10.1002/jbm.820170510.
16. Nebergall A.K., Greene M.E., Laursen M.B., Nielsen P.T., Malchau H., Troelsen A. Vitamin E diffused highly cross-linked polyethylene in total hip arthroplasty at five years: a randomised controlled trial using radiostereometric analysis. *Bone Joint J.* 2017;99-B(5):577-584. DOI: 10.1302/0301-620X.99B5.37521.
17. Sillesen N.H., Greene M.E., Nebergall A.K., Huddleston J.I., Emerson R., Gebuhr P. et al. 3-year follow-up of a long-term registry-based multicentre study on vitamin E diffused polyethylene in total hip replacement. *Hip Int.* 2016;26(1):97-103. DOI: 10.5301/hipint.5000297.
18. Hagio K., Saito M., Okawa T., Moriyama S., Nakamura Y., Naito M. Polyethylene wear associated with 26- and 32-mm heads in total hip arthroplasty: a multicenter, prospective study. *J Arthroplasty.* 2016;31(12):2805-2809. DOI: 10.1016/j.arth.2016.05.063.
19. Nebergall A.K., Greene M.E., Rubash H., Malchau H., Troelsen A., Rolfson O. Thirteen-year evaluation of highly cross-linked polyethylene articulating with either 28-mm or 36-mm femoral heads using radiostereometric analysis and computerized tomography. *J Arthroplasty.* 2016;31(9 Suppl):269-276. DOI: 10.1016/j.arth.2016.02.076.
20. Lee J.H., Lee B.W., Lee B.J., Kim S.Y. Midterm results of primary total hip arthroplasty using highly cross-linked polyethylene: minimum 7-year follow-up study. *J Arthroplasty.* 2011;26(7):1014-1049. DOI: 10.1016/j.arth.2011.03.015.
21. Glyn-Jones S., Thomas G.E., Garfjeld-Roberts P., Gundle R., Taylor A., McLardy-Smith P., Murray D.W. The John Charnley Award: Highly crosslinked polyethylene in total hip arthroplasty decreases long-term wear: a double-blind randomized trial. *Clin Orthop Relat Res.* 2015;473(2):432-438. DOI: 10.1007/s11999-014-3735-2.
22. Johanson P.E., Digas G., Herberts P., Thanner J., Kärrholm J. Highly crosslinked polyethylene does not reduce aseptic loosening in cemented THA 10-year findings of a randomized study. *Clin Orthop Relat Res.* 2012;470(11):3083-3093. DOI: 10.1007/s11999-012-2400-x.
23. Dumbleton J.H., Manley M.T., Edidin A.A. A literature review of the association between wear rate and osteolysis in total hip arthroplasty. *J Arthroplasty.* 2002;17(5):649-661.
24. Shareghi B., Johanson P.E., Kärrholm J. Wear of Vitamin E-Infused Highly Cross-Linked Polyethylene at Five Years. *J Bone Joint Surg Am.* 20176;99(17):1447-1452. DOI: 10.2106/JBJS.16.00691.
25. Scemama C., Anract P., Dumaine V., Babinet A., Courpied J.P., Hamadouche M. Does vitamin E-blended polyethylene reduce wear in primary total hip arthroplasty: a blinded randomised clinical trial. *Int Orthop.* 2017 Jun;41(6):1113-1118. DOI: 10.1007/s00264-016-3320-2.
26. Oral E., Wannomae K.K., Hawkins N., Harris W.H., Muratoglu O.K. Alpha-tocopherol-doped irradiated UHMWPE for high fatigue resistance and low wear. *Biomaterials.* 2004;25(24):5515-5522. DOI: 10.1016/j.biomaterials.2003.12.048.
27. Oral E., Muratoglu O.K. Vitamin E diffused, highly crosslinked UHMWPE: a review. *Int Orthop.* 2011; 35(2):215-223. DOI: 10.1007/s00264-010-1161-y.
28. Muratoglu O.K., Wannomae K.K., Rowell S.L., Micheli B.R., Malchau H. Ex vivo stability loss of irradiated and melted ultra-high molecular weight polyethylene. *J Bone Joint Surg Am.* 2010;92(17):2809-2816. DOI: 10.2106/JBJS.I.01017.
29. Kurtz S.M., Hozack W.J., Purtill J.J., Marcolongo M., Kraay M.J., Goldberg V.M. et al. 2006 Otto Aufranc Award Paper: significance of in vivo degradation for polyethylene in total hip arthroplasty. *Clin Orthop Relat Res.* 2006;453: 47-57. DOI: 10.1097/01.blo.0000246547.18187.0b.
30. Wannomae K.K., Bhattacharyya S., Freiberg A., Estok D., Harris W.H., Muratoglu O. In vivo oxidation of retrieved cross-linked ultra-high-molecular-weight polyethylene acetabular components with residual free radicals. *J Arthroplasty.* 2006;21(7):1005-1011.
31. Grupp T.M., Holderied M., Mulliez M.A., Streller R., Jäger M., Blömer W., Utzschneider S. Biotribology of a vitamin E-stabilized polyethylene for hip arthroplasty - Influence of artificial ageing and third-body particles on wear. *Acta Biomater.* 2014;10(7):3068-3078. DOI: 10.1016/j.actbio.2014.02.052.
32. Popoola O.O., Mimnaugh K., Orozco-Villasenor D.A., Peiserich M. Vitamin E-grafted crosslinked ultrahigh-molecular weight polyethylene (VE-HXPE) inhibits fluid absorption and has long term oxidative stability. *Biotribology.* 2015;4:12-17. DOI: 10.1016/j.biotri.2015.09.006.
33. Pang H.N., Naudie D.D., McCalden R.W., MacDonald S.J., Teeter M.G. Highly crosslinked polyethylene improves wear but not surface damage in retrieved acetabular liners. *Clin Orthop Relat Res.* 2015;473(2):463-468. DOI: 10.1007/s11999-014-3858-5.
34. Yamaguchi M., Bauer T.W., Hashimoto Y. Deformation of the acetabular polyethylene liner and the backside gap. *J Arthroplasty.* 1999;14(4):464-469.
35. Krieg A.H., Speth B.M., Ochsner P.E. Backside volumetric change in the polyethylene of uncemented acetabular components. *J Bone Joint Surg Br.* 2009;91(8):1037-1043. DOI: 10.1302/0301-620X.91B8.21850.
36. Taniguchi N., Jinno T., Takada R., Koga D., Ando T., Okawa A., Haro H. Do screws and screw holes affect osteolysis in cementless cups using highly crosslinked polyethylene? A 7 to 10-year follow-up case-control study. *Orthop Traumatol Surg Res.* 2018 Jan 30. pii: S1877-0568(18)30023-9. DOI: 10.1016/j.otsr.2017.12.009.
37. Urban R.M., Hall D.J., Della Valle C., Wimmer M.A., Jacobs J.J., Galante J.O. Successful long-term fixation and progression of osteolysis associated with first-generation cementless acetabular components retrieved post mortem. *J Bone Joint Surg Am.* 2012;94(20):1877-1885. DOI: 10.2106/JBJS.J.01507.

38. Schmalzried T.P., Brown I.C., Amstutz H.C., Engh C.A., Harris W.H. The role of acetabular component screw holes and/or screws in the development of pelvic osteolysis. *Proc Inst Mech Eng H.* 1999;213(2): 147-153.

39. Dansk Hoftealloplastik Register: National Årsrapport 2014 [Danish Hip Arthroplasty Register: National Annual Report 2014]. Available at: http://danskhoftealloplastikregister.dk/wp-content/uploads/2015/11/DHR-årsrapport-2014.pdf. (in Danish).

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4. Publication III

Metal ion release barrier function and biotribological evaluation of a zirconium nitride multilayer coated knee implant under highly demanding activities wear simulation

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Metal ion release barrier function and biotribological evaluation of a zirconium nitride multilayer coated knee implant under highly demanding activities wear simulation

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ABSTRACT

Total knee arthroplasty is a well established treatment for degenerative joint disease, which is also performed as a treatment in younger and middle-aged patients who have a significant physical activity and high life expectancy. However, complications may occur due to biological responses to wear particles, as well as local and systemic hypersensitivity reactions triggered by metal ions and particles such as cobalt, chromium and molybdenum. The purpose of the study was to perform a highly demanding activities (HDA) knee wear simulation in order to compare the wear characteristics and metal ion release barrier function of a zirconium nitride (ZrN) coated knee implant, designed for patients with suspected metal ion hypersensitivity, against an uncoated knee implant made out of CoCrMo. The load profiles were applied for 5 million HDA cycles, which represent 15–30 years of in vivo service depending on the activity level of the patient. Results showed a significant wear rate reduction for the coated group (1.01 ± 0.29 mg/million cycles) in comparison with the uncoated group (2.89 ± 1.04 mg/million cycles). The zirconium nitride coating showed no sign of scratches nor delamination during the wear simulation, whereas the uncoated femurs showed characteristic wear scratches in the articulation areas. Furthermore, the metal ion release from the coated implants was reduced up to three orders of magnitude in comparison with the uncoated implants. These results demonstrate the efficiency of zirconium nitride coated knee implants to reduce wear as well as to substantially reduce metal ion release in the knee joint.

1. Introduction

Total knee arthroplasty (TKA) is a well established treatment for degenerative joint disease with good clinical results. Currently, there is an increasing demand on the performance and longevity of these implants, as this treatment is also performed in heavier, younger and middle-aged patients who have a significant physical activity and high life expectancy (Carr et al., 2012; Dennis, 2006; Kurtz et al., 2009; Pradhan et al., 2006). However, complications may occur due to a biological response to polyethylene wear particles, which may lead to osteolysis and aseptic loosening. Moreover, as up to 13% of the general population show allergic cutaneous reactions to metals such as nickel (Ni), cobalt (Co) or chromium (Cr) (Schäfer et al., 2001; Thyssen et al., 2007; Thyssen and Menné, 2010; Uter et al., 2014; Warshaw et al., 2015), they have an enhanced risk of not tolerating knee implants made out of these materials. Furthermore, studies have indicated potential patho-mechanisms for aseptic implant loosening secondary to metal hypersensitivity (Mitchelson et al., 2015; Rakow et al., 2016; Schiavone et al., 2011).

Metal ion and particle release as well as metal hypersensitivity have become important subjects in total joint replacement, as a relation between the cobalt and chromium blood levels and failure of implants has been demonstrated (Hart et al., 2011; Luetzner et al., 2007; van der Straeten et al., 2013). In several studies, patients with a failed total hip replacement (THR) had significantly higher blood levels of both cobalt and chromium compared to patients with a well-functioning implant (Hart et al., 2011; van

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der Straeten et al., 2013), while a total knee replacement (TKR) study showed that patients with implants had higher metal ion blood levels than patients without (Luetzner et al., 2007). Furthermore, patients with poor-functioning implants (pain, recurrent effusions, reduced range of motion, eczema, loosening, etc.) showed higher metal sensitivity than those with well-functioning implants, and the latter group showed higher metal sensitivity than the general population (Hallab et al., 2001; Thomas et al., 2015). In vitro and in vivo studies have shown that high metal ion concentrations are toxic and known to interfere with biological functions (Catelas et al., 2011; Friesenbichler et al., 2014; Posada et al., 2015; Tower, 2010). Some adverse local tissue reactions (ALTR) against metal debris include delayed hypersensitivity, osteolysis, pseudotumor formation, metallosis and local soft tissue reactions such as inflammation and necrosis (Friesenbichler et al., 2014; Jacobs et al., 2014; Kwon et al., 2016; Kwon, 2016; Mistry et al., 2016). When comparing the effects of Co and Cr ions on macrophages, it has been demonstrated that both induce tumor necrosis factor alpha (TNF-α) release and macrophage mortality, but Co is more toxic than Cr (Catelas et al., 2011) and it activates the toll-like receptor 4 (TLR-4), inducing inflammation similar to that observed during sepsis (Lawrence et al., 2014; Rachmawati et al., 2013).

Despite the good clinical history and biocompatibility of cobalt-chromium alloys, they show electrochemical and bio-corrosion as well as abrasive wear that produce ion and particle release in the intra-articular joint space. Under physiological conditions, cobalt corrodes faster than chromium and tends to remain mobile, allowing the ions to reach and enter remote organs (Posada et al., 2015; Urban et al., 2004). In order to avoid metallic ion release, several alternative materials have been developed, including ceramics; non-sensitizing metals such as titanium or zirconium alloys; or CoCrMo alloys with a mono- or multi-layer coating such as titanium or zirconium nitride (Bader et al., 2008; Thomas et al., 2016). Several case reports have demonstrated good results after management of metallic knee implant complications associated with hypersensitivity with any of the previous alternatives (Mitchelson et al., 2015). However, these implants must not only achieve their ion release barrier function, but should also have good tribological properties in order to withstand the high performance and long-term expectance of young patients. Thus it is important to perform adequate pre-clinical tests that account for high demanding activities of such patients (Jaber et al., 2015; Schwiesau et al., 2013a; Zietz et al., 2015).

For the current study, a zirconium nitride (ZrN) multilayer coated knee implant, designed for patients with suspected metal ion hypersensitivity, was subjected to a highly demanding activities knee wear simulation developed by Schwiesau et al. (2014) in order to evaluate its performance at the long-term on young and dynamic patients. The objectives of our study were to analyze the wear at the polyethylene gliding surface when articulating against a ZrN coated implant and compare it with the clinically stablished implant made out of CoCrMo, to evaluate the integrity of the ZrN multilayer coating and its metal ion release barrier function through the whole wear simulation.

2. Materials and methods

Medium size AS Columbus® DD Knee System (Aesculap AG, Tuttlingen, Germany) femoral (size F4L) and tibial (size T3) components with a ZrN surface were used for wear simulation, in comparison with the clinically established cobalt chromium version Columbus® DD. Four total knee assemblies AS Columbus® DD (ZrN group) and eight Columbus® DD (CoCr group) were tested (Table 1). The AS multilayer coating system, with a total thickness between 3.5 and 5 μm, is applied to CoCr28Mo6 alloy components (material composition according to ISO 5832-12:2007) using the physical vapor deposition (PVD) method and consists of a thin adhesive chromium bond layer, five alternating intermediate layers out of chromium nitride (CrN) and chromium carbonitride (CrCN), and a final zirconium nitride (ZrN) shielding layer (Reich et al., 2010). Ultra-high-molecular-weight polyethylene (UHMWPE) gliding surfaces (Columbus® DD, size T3, high 10 mm) machined from GUR 1020, packed under nitrogen atmosphere and sterilized by electron beam irradiation (30 ± 2 kGy) were used for both knee systems. Prior to wear simulation, all the polyethylene gliding surfaces were soaked in serum-based test medium at 37 °C for at least 46 days to allow fluid absorption saturation.

Table 1
Total knee assemblies from the ZrN coated group and the uncoated CoCr group subjected to HDA knee wear simulation for 5 million HDA cycles and their references subjected just to axial load for soak control.

	Specimens under HDA knee wear simulation	Reference specimens (loaded soak control)
ZrN coated implants	ZrN_1 to 3	ZrN_Ref_1
CoCr uncoated implants	CoCr_1 to 6	CoCr_Ref_1 to 2

2.1. In vitro wear simulation

Wear simulation was performed on a load controlled 3 + 1 station knee wear simulator (EndoLab GmbH, Thansau, Germany) capable of reproducing loads and movements of highly demanding activities (HDA). The applied load and motion profiles were based on in vivo measurements obtained from 8 patients with instrumented implants (Bergmann et al., 2014). These profiles were normalized to represent a patient weight of 100 kg, converted to the coordinate system described in ISO 14243-1:2009(E), and set up for a left side implantation with a 60% (medial) and 40% (lateral) load distribution (Schwiesau et al., 2014). The load profiles (Fig. 1) were applied for 5 million HDA cycles (mc) in a combination of 40% stair ascending, 40% stair descending, 10% level walking, 8% chair raising and 2% deep squatting. For walking, stair ascending and stair descending, the cycle time was set to 1 s (1 Hz) and for chair raising and deep squatting the cycle time was set to 2 s (0.5 Hz). A loop of 800 cycles chair rising, 1000 cycles level walking, 200 cycles deep squatting, 4000 cycles stair ascending and 4000 stair descending was repeated 500 times. Taking into account a mean of 172 stair ascending steps per day in an average arthroplasty patient and 448 steps in the most active one (Morlock et al., 2001), this profile distribution represents a realistic implant in vivo service time between 15 and 30 years (172 steps per day × 365 days × 30 years = 1,883,400 stair ascending cycles) (Schwiesau et al., 2013a).

The total knee assemblies were fixed with PMMA and mounted in sets of three wear test stations (axial load and movement) and a parallel reference station submitted only to axial load for soak control. This means, the ZrN and CoCr groups were tested one after another and each group underwent a total of 5 million HDA cycles. The component sets were rotated across stations after each million cycles to minimize the effect of inter-station kinematic variability. The simulation was performed under a test medium consisting of newborn calf serum (Biochrom AG, Berlin, Germany) diluted with deionized water to achieve a protein content of 20 g/l. Ethylene diamine tetraacetic acid was added to stabilize pH and Amphotericin B to prevent fungal decay. The test medium was changed every 0.5 million HDA cycles and all the components were cleaned

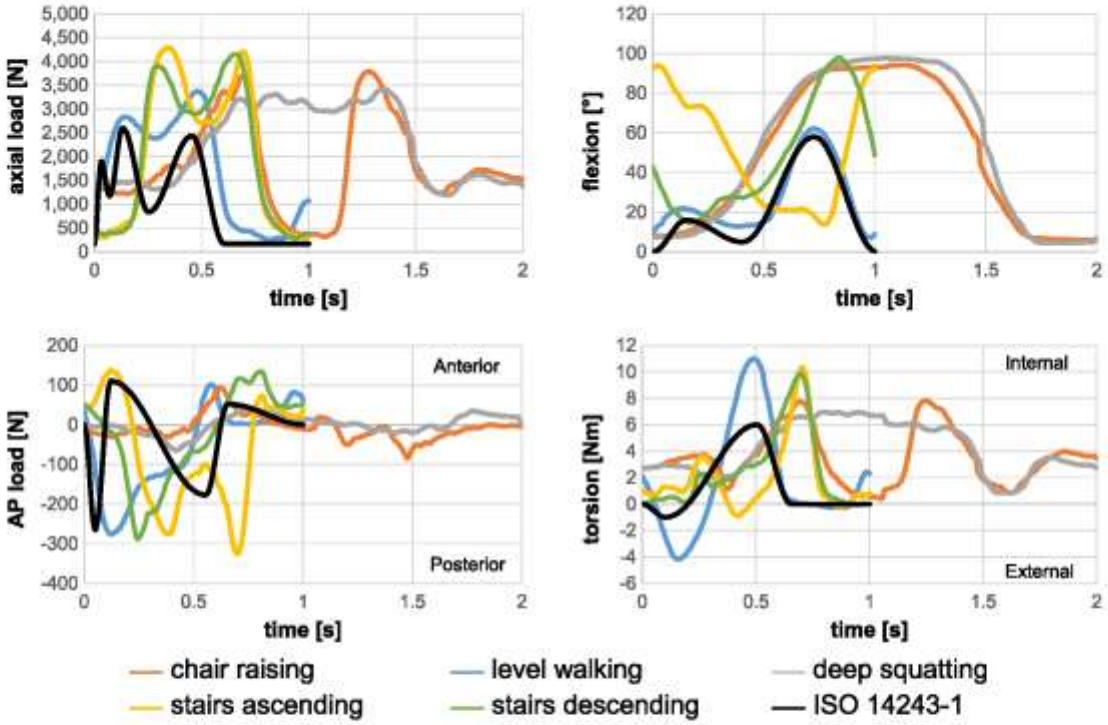

Fig. 1. Axial load, flexion angle, anterior-posterior load (AP load), and rotational torque applied during the simulation of the different high demanding activities (chair raising, level walking, deep squatting, stairs ascending, and stairs descending) in comparison with the ISO 14243-1:2009(E) profile. Figure adapted from Schwiesau et al. (2014).

according to ISO 14243-2:2009(E). At 0.5, 1, 2, 3, 4 and 5 million HDA cycles, wear of the polyethylene inserts was determined gravimetrically using an analytical balance (Sartorious CPA225D, Göttingen, Germany) to a precision of 0.01 mg, taking air buoyancy and serum absorption into account.

2.2. Optical and geometrical wear surface analysis

At 0.5, 1, 2, 3, 4, and 5 million HDA cycles, all bearing surfaces were inspected with a stereo microscope (Leica MZ 16, Bensheim, Germany). In order to asses the geometrical deformation of the UHMWPE gliding surfaces due to creep and wear, the specimens were scanned before and after the test by means of a 3D measuring machine using a tactile mode and a resolution of less than 3.5 μm (Zeiss UMM850, Oberkochen, Germany). The scans were superimposed, the geometrical changes were calculated (Zeiss Holos 2.4.12, Oberkochen, Germany), and the results were displayed in pseudo-colors in a plane transversal view.

2.3. Metal ion concentration analysis

To measure the metal ion release in the test medium through the entire wear simulation, serum samples from each simulator station were taken after every 0.5 million HDA cycles. The metal ion concentration values found in the reference stations represent the environment contamination as well as implant corrosion, whereas those from the wear testing stations include the articulation-induced metal ion release. After pressure digestion with microwave heating, the testing medium was analyzed by inductively coupled plasma mass spectrometry (ICP-MS) according to ISO 17294-2 with a detection limit of 0.1 μg/l for the element concentration of cobalt (Co), chromium ($\Sigma Cr^{III} + Cr^{VI}$), molybdenum (Mo) and zirconium (Zr).

2.4. Statistics

To differentiate the cumulative wear, wear rate and penetration depth between the ZrN and CoCr groups, an analysis of variance was carried out ($p < 0.05$) followed by a post hoc test (HSD Test for unequal N, $p < 0.05$). Prior to the analysis, the normal distribution (p-p plots) and the homogeneity of variance (Levene test) were verified (Dell Statistica R13, Dell Inc., Hamburg, Germany).

3. Results

3.1. In vitro wear simulation

A statistical decrease (3.1-fold) in the cumulative gravimetric wear was found in the ZrN group (4.60 ± 1.25 mg) in comparison with the CoCr group (14.27 ± 5.45 mg) ($p = 0.04$). Moreover, the wear rate of the ZrN group was 1.01 ± 0.29 mg/mc and was also statistically lower (2.8-fold) in comparison with the CoCr group, which had a wear rate of 2.89 ± 1.04 mg/mc ($p = 0.04$). The loaded soak control specimens used as reference had approximately the same weight gain, with 9.64 mg for the ZrN_Ref specimen and 11.16 ± 0.70 mg for the CoCr_Ref specimens (Fig. 2).

3.2. Optical and geometrical wear surface analysis

After 5 million HDA cycles, the polyethylene gliding surfaces from the ZrN group appeared to be mainly polished as a result of adhesive-abrasive wear with slight scratches and striated patterns (Fig. 3), whereas those from the CoCr group showed polishing and slight scratches, but with more striated patterns (Fig. 4). The 3D analysis of the polyethylene gliding surfaces showed that the medial compartment of the ZrN group had more penetration depth due to creep and wear than the lateral compartment (215.7 ± 11.2 μm

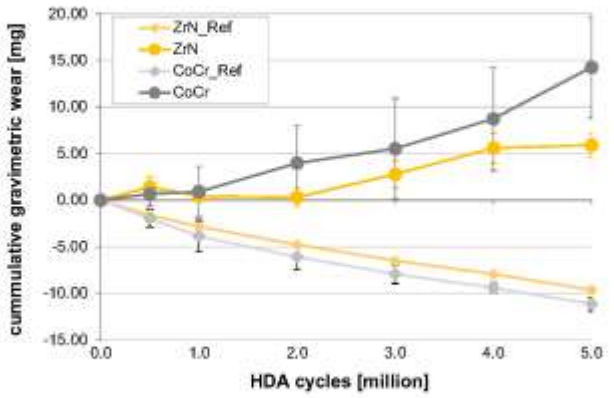

Fig. 2. Wear behavior of the polyethylene gliding surfaces from the ZrN and CoCr groups after 5 million HDA wear cycles.

and 86.1 ± 0 μm respectively) (Fig. 5). The same pattern was seen in CoCr group but with statistically higher penetration depths: 283.6 ± 22.7 μm in the medial compartment ($p = 0.004$) and 173.6 ± 31.9 μm in the lateral compartment ($p = 0.006$). The reference specimens from both groups had approximately the same penetration, being 50 μm in the lateral compartment and 60 μm in the medial compartment.

After 3.0 million HDA cycles, the femur components of the ZrN group started to show oxidation marks in their articulation surface, particularly at the internal and external edges and directly on the surface in contact with the polyethylene gliding surface. At 5.0 million HDA cycles, the lateral and medial condyles of all the ZrN femurs presented oxidation marks (Fig. 6) and the articulation areas showed a light yellow color, whereas the rest of the femur presented a slightly darker yellow color. No scratches nor layer breakage of the ZrN multilayer coating were visible. On the other hand, the femurs from the CoCr group showed slight scratches on the surface directly in contact with the polyethylene gliding surface.

3.3. Metal ion concentration analysis

Metal ion concentration analysis showed a reduction of up to three orders of magnitude on the release of cobalt, chromium and molybdenum ions in the coated ZrN group in comparison with the uncoated CoCr group. Moreover, their values were similar to those found on the reference station (ZrN_Ref), corresponding to basic contamination of the environment and corrosion of the implant (Fig. 7). During the 5 million HDA cycles, the cobalt, chromium and molybdenum values of the CoCr group tend to decrease linearly, starting with 1515.0 ± 311.8 μg/l, 634 ± 150.4 μg/l, and 155.3 ± 37.2 μg/l respectively at the first 0.5 million HDA cycles and ending with 461.7 ± 307.4 μg/l, 182.1 ± 15.7 μg/l and 41.1 ± 25.5 μg/l respectively at 5 million HDA cycles. On the other hand, the ZrN group started with a cobalt concentration of 21.0 ± 17.8 μg/l in the first 0.5 million HDA cycles and ended with 0.4 ± 0.2 μg/l at 5 million HDA cycles; chromium went from 64.4 ± 46 μg/l to 6.5 ± 2.3 μg/l, and molybdenum went from 9.2 ± 4.4 μg/l to 0.7 ± 0.2 μg/l. In case of the ZrN multilayer coating, the zirconium ion concentration values decreased exponentially starting with 1963.9 ± 615 μg/l and ending with 18.4 ± 4.5 μg/l at 5 million HDA cycles.

The Co/Cr ratio of the released ions from the CoCr group showed a similar ratio to that found in the composition of the CoCr alloy according to ISO 5832-12:2007 (Fig. 8), whereas the Co/Cr ratio of the ZrN group was 0.3 or lower during the whole test, indicating a higher release of chromium than cobalt.

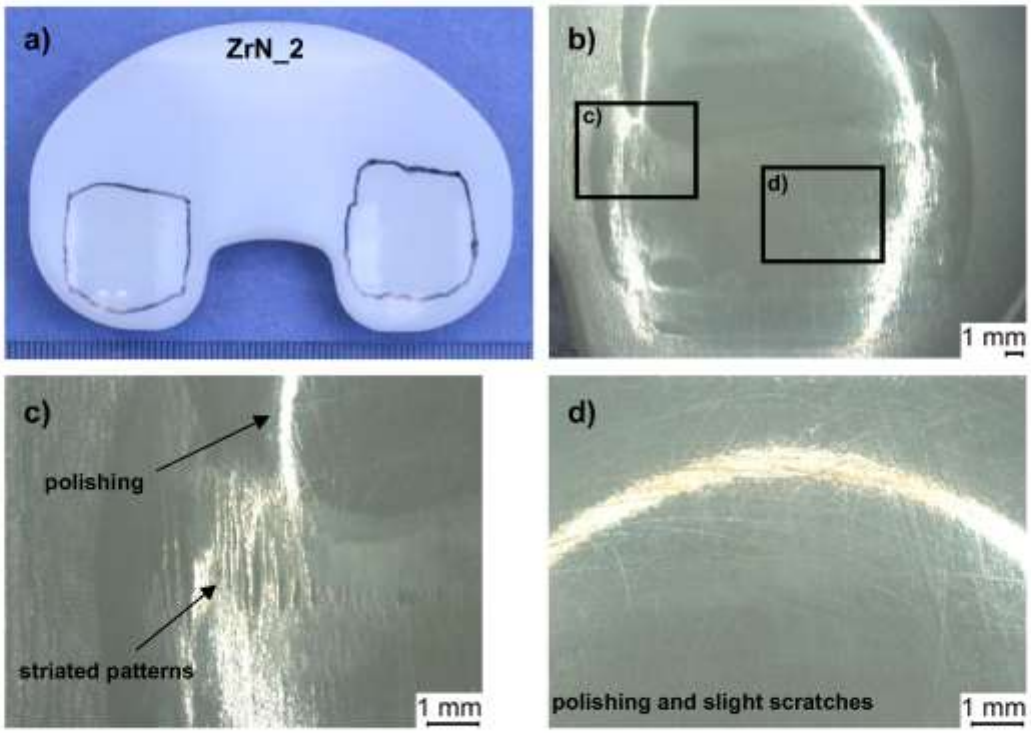

Fig. 3. Characteristic wear patterns of the polyethylene gliding surface of the ZrN group after 5 million HDA cycles. (a) Overview of the wear areas; (b) wear area in articulation with the medial condyle showing polishing, scratches and striated patterns; (c) striated patterns seen in the internal position and polishing in the rest of the area; (d) polishing and slight scratches seen at the center of the articulation area.

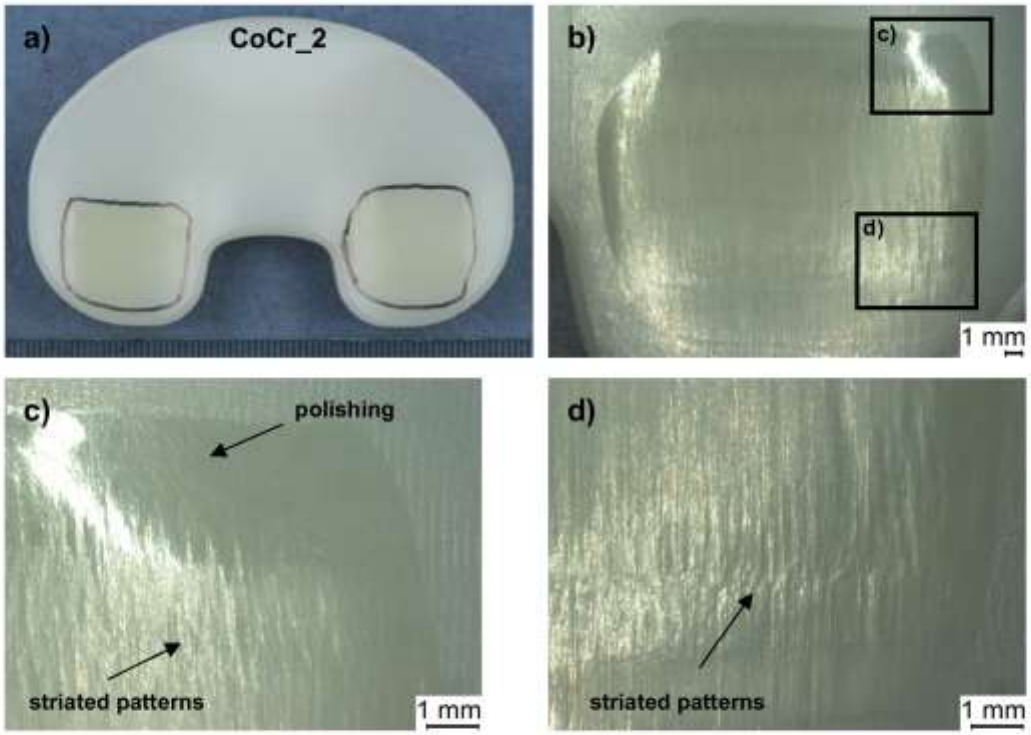

Fig. 4. Characteristic wear patterns of the polyethylene gliding surface of the CoCr group after 5 million HDA cycles. (a) Overview of the wear areas; (b) wear area in articulation with the medial condyle showing polishing, scratches and striated patterns; (c) polishing in the most anterior area and striated patterns in the rest of the area; (d) striated patterns seen at the external side of the articulation area.

4. Discussion

The objective of our study was to perform a highly demanding activities knee wear simulation in order to compare the wear characteristics and metal ion release barrier function of a ZrN coated knee implant, designed for patients with suspected metal ion hypersensitivity, against an uncoated knee implant made out of CoCrMo. Previous studies performed solely under walking condition (Affatato et al., 2011; Grupp et al., 2013a, 2013b, 2014; Reich et al., 2010) have already demonstrated the good tribological properties of the ZrN multilayer coating as well as its ion release barrier function, however, to the authors knowledge, this is the first study to analyze the metal ion release and wear performance of a ZrN coated knee implant through an entire HDA wear simulation.

As TKA patients are getting younger, heavier and more active (Carr et al., 2012; Pradhan et al., 2006), it is important to perform adequate pre-clinical testing which can simulate the range of activities performed by this group of patients, and thus, the long-term wear characteristics seen on polyethylene tibial inserts during the second decade of clinical performance, such as delamination and cracking (Grupp et al., 2017; Schwiesau et al., 2013b, 2014; Zietz et al., 2015). Studies have shown that it is possible to create the structural material fatigue and subsurface delamination seen in vivo by performing 5 million HDA cycles, as this test can simulate between 15 and 30 years of in vivo usage (depending on the activity level of the patient), in comparison with the 3 years of usage simulated by the ISO 14243-1:2009(E) (Schwiesau et al., 2013a).

Our results showed a significant polyethylene wear rate reduction and a smaller variation among the samples of the ZrN group in comparison with the uncoated group, which is in accordance with previous studies performed solely under level walking simulation (Grupp et al., 2013a; Reich et al., 2010). The smaller variation seen in the ZrN group might rely on its the lower sliding friction against the polyethylene liner and the higher scratch resistance of the coating, which generate a more uniform counterpart bearing than the CoCrMo alloy. Only one study involving an oxidized zirconium femoral component articulating against a non-cross-linked UHMWPE under a wear simulation accounting for athletically active patients was found and also showed a significant reduction on the wear rate in comparison with its CoCrMo version (17 mg/mc vs 12 mg/mc) (Ezzet et al., 2012). Studies performed under HDA simulation using the same knee system design as in our study (Columbus®) but with a different gliding surface (CR instead of DD) have shown wear rates of approximately 5.5 mg/mc for artificially aged vitamin E stabilized polyethylene inserts and 12 mg/mc for artificially aged standard polyethylene inserts against CoCrMo (Grupp et al., 2017; Schwiesau et al., 2014). By modifying the loading profile to account for obese patients or applying a stair climbing profile, studies have shown wear rates ranging from approximately 6 to 33 mg/mc on UHMWPE inserts and from 1 to 8 mg/mc on highly cross-linked polyethylene inserts from different knee systems (Abdel-Jaber et al., 2015; Benson et al., 2002; Essner et al., 2005, 2011; Jaber et al., 2015; Schaerer et al., 2010; Tozzi et al., 2014). The overall low wear rate seen in the current study might have two reasons. First, the polyethylene inserts were not artificially aged, as doing so might have produced delamination before the end of the test and the resistance of the ZrN coating could not have been assessed on the full 5 million HDA cycles test duration. Secondly, the deep dish (DD) design of the gliding surface generates lower wear rates than curved designs as a result of its high form fit (Grupp et al., 2009).

According to retrieval studies, the estimated linear penetration of UHMWPE inserts is between 10 and 100 μm/year (Argenson and O'Connor, 1992; Gill et al., 2006; Psychoyios et al., 1998). The

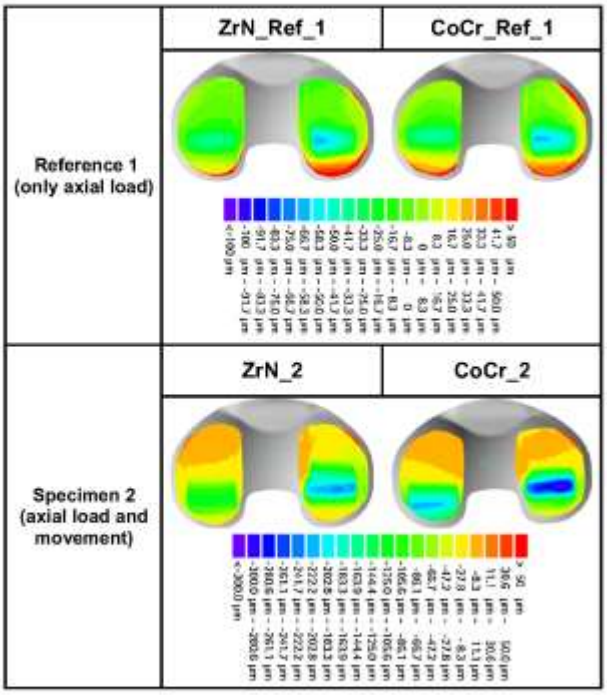

Fig. 5. Geometrical changes after 5 million HDA wear cycles of the polyethylene gliding surfaces from the ZrN and CoCr groups. The geometrical changes of the reference specimens were due to creep (only axial load was applied), whereas the changes in the testing specimens were due to creep and wear (axial load and movement were applied). The green and blue areas from the ZrN_2 and CoCr_2 specimens represent the wear areas marked in Figs. 3a and 4a respectively, while the yellow and orange areas represent plastic deformation.

results from both analyzed groups fit in this range and have a similar penetration pattern as seen in other studies (Grupp et al., 2017; Schwiesau et al., 2014). The CoCr group from the current study showed significantly more penetration depth than the ZrN group, while the reference specimens from both groups had approximately the same penetration depth just due to polyethylene creep. This confirms that the uncoated group generated significantly more wear than the ZrN group.

The optical analysis of the polyethylene gliding surfaces showed that, after 5 million HDA cycles, those from the ZrN group had a more polished surface than those from the CoCr, which showed more striated patterns. A reason for this might be the presence of slight scratches seen at the articulation areas of the CoCr femurs, which were not present at the beginning of the test. These slight scratches are typical for CoCrMo femur components articulating with polyethylene gliding surfaces (Kretzer et al., 2014; Lakdawala et al., 2005; Malikian et al., 2014; Muratoglu et al., 2004; Que et al., 2000). On the other hand, the ZrN femurs remained polished and showed no scratches through the whole test. The darker yellowish color of the ZrN femur outside the articulation area might be due to the overall oxidation of the femurs, as it is known that zirconium has more affinity to oxygen than to nitrogen and the color of zirconium alloys varies depending on the amount of oxygen and nitrogen they contain (Brown et al., 1993; Cheng and Zheng, 2006; Ferreira et al., 2006; Milošev et al., 1996, 1997; Niyomsoan et al., 2002; Reddy et al., 2007). In situ change of color from ZrN coated implants is known, but no adverse effects have been reported nor found.

Attention to elevated metal ion concentrations started after adverse clinical results appeared with metal on metal (MoM) bearings in hip arthroplasty (Gross and Liu, 2013; Rakow et al., 2016; Underwood et al., 2011). As all cobalt-chromium implanted into the body will suffer a degradation process based on tribo- and bio-corrosion and will release metal ions and particles into the joint intra-articular space (Bundy, 1994; Friesenbichler et al., 2014; Garrett et al., 2010; Gilbert et al., 2015; Hallab et al., 2001; Mitchelson et al., 2015), this concern has also turned to TKA. It is thought that the dissociated metal species have a greater influence on the local and systemic adverse effects than particles, as the latter are mainly internalized by phagocytic cells, whereas the metallic ions have a high mobility within the human body (Bader et al.,

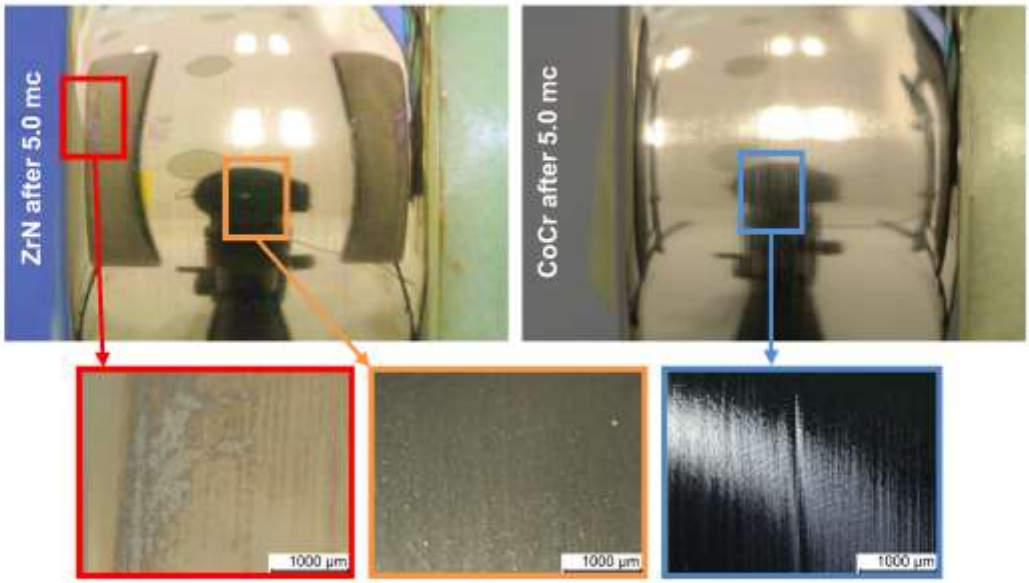

Fig. 6. Wear characteristics of the femur components after 5 HDA million cycles. The ZrN femurs remained polished after the wear simulation, demonstrated by the clear reflection of the camera and lights, and no scratches nor layer breakage were seen at the center of the articulation area. However, oxidation marks at the edges and articulation area after 5 million HDA cycles (highlighted in red) were seen. On the other hand, slight scratches were seen at the articulation area of the CoCr femurs (highlighted in blue), demonstrated by the blurred reflection of the camera and lights.

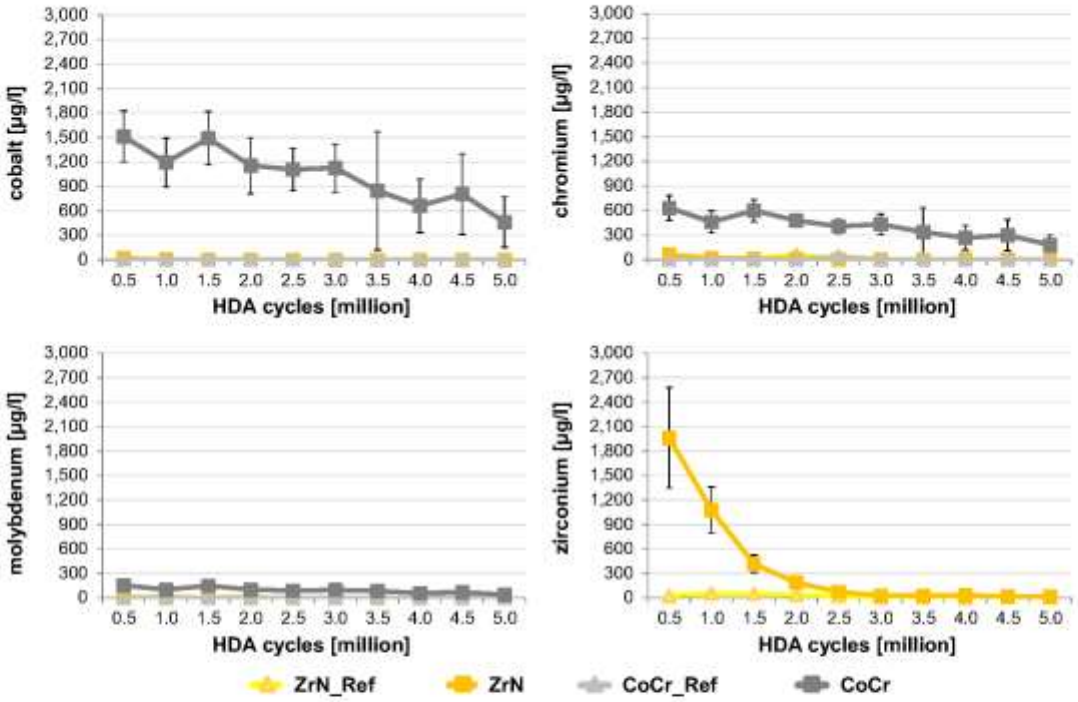

Fig. 7. Metal ion concentration analysis of the ZrN and CoCr groups (subjected to axial load and movement) and their references (Ref = subjected just to axial load) during 5 million HDA cycles. The reference stations represent basic contamination of the environment and corrosion of the implant, whereas the wear testing groups include the articulation-induced metal ion release.

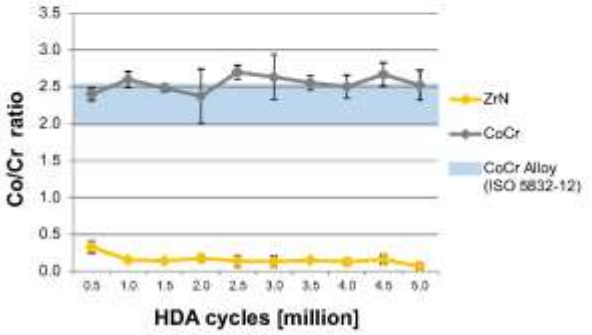

Fig. 8. Co/Cr ratio of the metal ion concentrations found in the test serum through the entire test in comparison with the range of CoCr ratio from the substrate material according to ISO 5832-12:2007.

2008; Garrett et al., 2010; Jacobs et al., 1998; Rakow et al., 2016). For this reason, it is important that a TKA coating fulfills its ion release barrier function. The metal ion analysis from the current study confirms that there was no damage in the ZrN coating, as the values of the ZrN testing stations were very similar to their reference and were up to three orders of magnitude smaller than those in the CoCr group. Moreover, the Co value, which is the most clinically relevant ion (Catelas et al., 2011; Hannemann et al., 2013; Posada et al., 2015; Tower, 2010) and is only located in the substrate material, remained under 1.0 µg/l after 2 million HDA cycles. A limitation of our study was the usage of stainless steel in the simulator fittings containing Cr, Ni and Mo, which may have contributed to the ion release. The higher ion release found during the first million cycles can be explained due to the running in phase, a process where the bearing counterparts build up a characteristic wear patch that increases conformity between them and a surface polishing of the as-manufactured components occurs, leading afterwards to a steady state phase (Kretzer et al., 2014). Furthermore, the ZrN multilayer coating is a porous structure rather than a completely impermeable one, which would explain the small Co and Cr ion release detected during the first million cycles. During this initial time, the implant starts to corrode and ions from the substrate material are released, showing similar values to those from the reference station. A previous study performed by Thomas et al. (2016) measured the metal ion release from uncoated CoCrMo discs, TiN and ZrN coated discs in different fluids such as cell culture, distilled water and artificial sweat and also confirmed that the ZrN coating had the least liberation of Co ions. The zirconium ion release should not be of concern, as a study from Dalal et al. (2012) demonstrated that cobalt alloy particles produced higher toxicity and inflammatory responses than zirconium alloy particles.

Regarding its performance in vivo, studies have shown that the complications produced due to metal ion hypersensitivity disappear after patients have changed to ZrN coated prostheses (Thomas et al., 2016; Thomsen et al., 2011). Besides, patch tests performed on patients with and without metal ion hypersensitivity have shown no allergic reaction to ZrN (Thomas et al., 2016). Moreover, a retrospective study comparing ZrN coated and uncoated knee implants after 5 years of implantation showed that the pro-inflammatory interleukin IL-8 and anti-inflammatory IL-10 were highly upregulated in patients with an uncoated knee, whereas in patients with ZrN coated implants were not (Schinkel, 2015). Finally, a randomized study comparing uncoated and ZrN coated implants after midterm follow up showed an excellent survival rate for both groups (100% for ZrN vs 98.1% for CoCrMo) and no coating related adverse aspects with the ZrN multilayer coated implants were reported after the 5-year follow up (Beyer et al., 2016). However, long term results are still necessary in order to confirm the good performance of ZrN coated implants in the second decade of usage.

In conclusion, the results from the current study showed that the ZrN coated implants significantly reduced wear at the polyethylene gliding surfaces in comparison with the clinically stablished uncoated CoCrMo implants. Moreover, the ZrN multilayer coating was able to keep its integrity even under a highly demanding activities knee wear simulation, as no scratches nor delamination of the coating were seen. Finally, the cobalt ion release reduction of up to three orders of magnitude in comparison with the uncoated implants confirmed that the ZrN multilayer coating is a secure barrier against the diffusion of this clinically relevant ion.

Declaration

Competing interests: five of the authors (ALPR, BF, JS, CS, TMG) are employees of Aesculap AG Tuttlingen a manufacturer of orthopaedic implants. Two of the authors (BS, PT) have received institutional research funding.

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Ethical approval

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References

Abdel-Jaber, S., Belvedere, C., Leardini, A., Affatato, S., 2015. Wear simulation of total knee prostheses using load and kinematics waveforms from stair climbing. J. Biomech. 48, 3830–3836.
Affatato, S., Spinelli, M., Lopomo, N., Grupp, T.M., Marcacci, M., Toni, A., 2011. Can the method of fixation influence the wear behaviour of ZrN coated unicompartmental mobile knee prostheses? Clin. Biomech. (Bristol, Avon) 26, 152–158.
Argenson, J.N., O'Connor, J.J., 1992. Polyethylene wear in meniscal knee replacement. A one to nine-year retrieval analysis of the Oxford knee. J. Bone Joint Surgery Br. 74, 228–232.
Bader, R., Bergschmidt, P., Fritsche, A., Ansorge, S., Thomas, P., Mittelmeier, W., 2008. Alternative Werkstoffe und Losungen in der Knieendoprothetik fur Patienten mit Metallallergie. Der Orthopade 37, 136–142.
Benson, L.C., Desjardins, J.D., Harman, M.K., LaBerge, M., 2002. Effect of stair descent loading on ultra-high molecular weight polyethylene wear in a force-controlled knee simulator. Proc. Inst. Mech. Eng. Part H 216, 409–418.
Bergmann, G., Bender, A., Graichen, F., Dymke, J., Rohlmann, A., Trepczynski, A., Heller, M.O., Kutzner, I., 2014. Standardized loads acting in knee implants. PloS One 9, e86035.
Beyer, F., Lutzner, C., Kirschner, S., Lutzner, J., 2016. Midterm results after coated and uncoated TKA: a randomized controlled study. Orthopedics 39, S13–S17.
Brown, R., Alias, M.N., Fontana, R., 1993. Effect of composition and thickness on corrosion behavior of TiN and ZrN thin films. Surf. Coat. Technol. 62, 467–473.
Bundy, K.J., 1994. Corrosion and other electrochemical aspects of biomaterials. Crit. Rev. Biomed. Eng. 22, 139–251.
Carr, A.J., Robertsson, O., Graves, S., Price, A.J., Arden, N.K., Judge, A., Beard, D.J., 2012. Knee replacement. The Lancet 379, 1331–1340.
Catelas, I., Wimmer, M.A., Utzschneider, S., 2011. Polyethylene and metal wear particles: characteristics and biological effects. Semin. Immunopathol. 33, 257–271.
Cheng, Y., Zheng, Y.F., 2006. A study of ZrN/Zr coatings deposited on NiTi alloy by PIID technique. IEEE Trans. Plasma Sci. 34, 1105–1108.
Dalal, A., Pawar, V., McAllister, K., Weaver, C., Hallab, N.J., 2012. Orthopedic implant cobalt-alloy particles produce greater toxicity and inflammatory cytokines than titanium alloy and zirconium alloy-based particles in vitro, in human osteoblasts, fibroblasts, and macrophages. J. Biomed. Mater. Res. Part A 100, 2147–2158.
Dennis, D.A., 2006. Trends in total knee arthroplasty. Orthopedics 29, S13–S16.
Essner, A., Herrera, L., Hughes, P., Kester, M., 2011. The influence of material and design on total knee replacement wear. J. Knee Surg. 24, 9–17.
Essner, A., Zeng, H., Yau, S.S., Wang, A., Dumbleton, J.H., Manley, M.T., 2005. Stair climbing knee wear simulation: sequentially crosslinked and annealed UHMWPE. Society for Biomaterials Annual Meeting Transactions 30.
Ezzet, K.A., Hermida, J.C., Steklov, N., D'Lima, D.D., 2012. Wear of polyethylene against oxidized zirconium femoral components effect of aggressive kinematic conditions and malalignment in total knee arthroplasty. J. Arthroplasty 27, 116–121.
Ferreira, S.C., Ariza, E., Rocha, L.A., Gomes, J.R., Carvalho, P., Vaz, F., Fernandes, A.C., Rebouta, L., Cunha, L., Alves, E., Goudeau, P., Rivière, J.P., 2006. Tribocorrosion behaviour of ZrOxNy thin films for decorative applications. Surf. Coat. Technol. 200, 6634–6639.
Friesenbichler, J., Sadoghi, P., Maurer-Ertl, W., Szkandera, J., Glehr, M., Ogris, K., Wolf, M., Weger, C., Leithner, A., 2014. Serum metal ion concentrations in paediatric patients following total knee arthroplasty using megaprostheses. BioMed Res. Int. 2014, 817257.
Garrett, S., Jacobs, N., Yates, P., Smith, A., Wood, D., 2010. Differences in metal ion release following cobalt-chromium and oxidized zirconium total knee arthroplasty. Acta Orthopaedica Belgica 76, 513–520.
Gilbert, J.L., Sivan, S., Liu, Y., Kocagoz, S., Arnholt, C., Kurtz, S.M., 2015. Direct In Vivo inflammatory cell-induced corrosion of CoCrMo alloy orthopedic implant surfaces. J. Biomed. Mater. Res. Part A 103, 211–223.
Gill, H.S., Waite, J.C., Short, A., Kellett, C.F., Price, A.J., Murray, D.W., 2006. In vivo measurement of volumetric wear of a total knee replacement. Knee 13, 312–317.
Gross, T.P., Liu, F., 2013. Incidence of adverse wear reactions in hip resurfacing arthroplasty: a single surgeon series of 2,600 cases. Hip Int.: J. Clin. Exp. Res. Hip Pathol. Therapy 23, 250–258.
Grupp, T.M., Fritz, B., Kutzner, I., Schilling, C., Bergmann, G., Schwiesau, J., 2017. Vitamin E stabilised polyethylene for total knee arthroplasty evaluated under highly demanding activities wear simulation. Acta Biomater. 48, 415–422.
Grupp, T.M., Giurea, A., Miehlke, R.K., Hintner, M., Gaisser, M., Schilling, C., Schwiesau, J., Kaddick, C., 2013a. Biotribology of a new bearing material combination in a rotating hinge knee articulation. Acta Biomater. 9, 7054–7063.
Grupp, T.M., Saleh, K.J., Mihalko, W.M., Hintner, M., Fritz, B., Schilling, C., Schwiesau, J., Kaddick, C., 2013b. Effect of anterior-posterior and internal-external motion restraint during knee wear simulation on a posterior stabilised knee design. J. Biomech. 46, 491–497.
Grupp, T.M., Schroeder, C., Kyun Kim, T., Miehlke, R.K., Fritz, B., Jansson, V., Utzschneider, S., 2014. Biotribology of a mobile bearing posterior stabilised knee design – effect of motion restraint on wear, tibio-femoral kinematics and particles. J. Biomech. 47, 2415–2423.
Grupp, T.M., Stulberg, D., Kaddick, C., Maas, A., Fritz, B., Schwiesau, J., Bloemer, W., 2009. Fixed bearing knee congruency – influence on contact mechanics, abrasive wear and kinematics. Int. J. Artif. Organs 32, 213–223.
Hallab, N., Merritt, K., Jacobs, J.J., 2001. Metal sensitivity in patients with orthopaedic implants. J. Bone Joint Surg. 83-A, 428–436.
Hannemann, F., Hartmann, A., Schmitt, J., Lutzner, J., Seidler, A., Campbell, P., Delaunay, C.P., Drexler, H., Ettema, H.B., Garcia-Cimbrelo, E., Huberti, H., Knahr, K., Kunze, J., Langton, D.J., Lauer, W., Learmonth, I., Lohmann, C.H., Morlock, M., Wimmer, M.A., Zagra, L., Gunther, K.P., 2013. European multidisciplinary consensus statement on the use and monitoring of metal-on-metal bearings for total hip replacement and hip resurfacing. Orthopaed. Traumatol., Surg. Res.: OTSR 99, 263–271.
Hart, A.J., Sabah, S.A., Bandi, A.S., Maggiore, P., Tarassoli, P., Sampson, B., Skinner, A.J., 2011. Sensitivity and specificity of blood cobalt and chromium metal ions for predicting failure of metal-on-metal hip replacement. J. Bone Joint Surg. Br. 93, 1308–1313.
ISO 5832-12:2007. Implants for Surgery - Metallic Materials - Part 12: Wrought Cobalt-chromium-molybdenum Alloy.
Jaber, S.A., Taddei, P., Tozzi, S., Sudanese, A., Affatato, S., 2015. In vitro effects on mobile polyethylene insert under highly demanding daily activities: stair climbing. Int. Orthop. 39, 1433–1440.
Jacobs, J.J., Cooper, H.J., Urban, R.M., Wixson, R.L., Della Valle, C.J., 2014. What do we know about taper corrosion in total hip arthroplasty? J. Arthroplasty 29, 668–669.
Jacobs, J.J., Gilbert, J.L., Urban, R.M., 1998. Corrosion of metal orthopaedic implants. J. Bone Joint Surg. Am. 80, 268–282.
Kretzer, J.P., Reinders, J., Sonntag, R., Hagmann, S., Streit, M., Jeager, S., Moradi, B., 2014. Wear in total knee arthroplasty–just a question of polyethylene?: Metal ion release in total knee arthroplasty. Int. Orthop. 38, 335–340.
Kurtz, S.M., Lau, E., Ong, K., Zhao, K., Kelly, M., Bozic, K.J., 2009. Future young patient demand for primary and revision joint replacement: national projections from 2010 to 2030. Clin. Orthop. Relat. Res. 467, 2606–2612.
Kwon, Y.-M., 2016. Evaluation of the painful dual taper modular neck stem total hip arthroplasty: do they all require revision? J. Arthroplasty 31, 1385–1389.
Kwon, Y.-M., Khormaee, S., Liow, M.H.L., Tsai, T.-Y., Freiberg, A.A., Rubash, H.E., 2016. Asymptomatic pseudotumors in patients with taper corrosion of a dual-taper modular femoral stem: MARS-MRI and metal ion study. J. Bone Joint Surg. Am. 98, 1735–1740.
Lakdawala, A., Todo, S., Scott, G., 2005. The significance of surface changes on retrieved femoral components after total knee replacement. J. Bone Joint Surg. Br. 87, 796–799.
Lawrence, H., Deehan, D., Holland, J., Kirby, J., Tyson-Capper, A., 2014. The immunobiology of cobalt: demonstration of a potential aetiology for inflammatory pseudotumours after metal-on-metal replacement of the hip. Bone Joint J. 96-B, 1172–1177.
Luetzner, J., Krummenauer, F., Lengel, A.M., Ziegler, J., Witzleb, W.C., 2007. Serum metal ion exposure after total knee arthroplasty. Clin. Orthop. Relat. Res. 461, 136–142.

Malikian, R., Maruthainar, K., Stammers, J., Cannon, S.R., Carrington, R., Skinner, J.A., Maruthainar, N., Dowd, G., Briggs, T.W., Blunn, G.W., 2014. In vivo roughening of retrieved total knee arthroplasty femoral components. Knee 21, 278–282.
Milošev, I., Strehblow, H.-H., Gaberšček, M., Navinšek, B., 1996. Electrochemical oxidation of ZrN Hard (PVD) coatings studied by XPS. Surf. Interface Anal. 24, 448–458.
Milošev, I., Strehblow, H.-H., Navinseka, B., 1997. Comparison of TiN, ZrN and CrN hard nitride coatings: electrochemical and thermal oxidation. Thin Solid Films 303, 246–254.
Mistry, J.B., Chughtai, M., Elmallah, R.K., Diedrich, A., Le, S., Thomas, M., Mont, M.A., 2016. Trunnionosis in total hip arthroplasty: a review. J. Orthopaed. Traumatol.: Off. J. Italian Soc. Orthopaed. Traumatol. 17, 1–6.
Mitchelson, A.J., Wilson, C.J., Mihalko, W.M., Grupp, T.M., Manning, B.T., Dennis, D. A., Goodman, S.B., Tzeng, T.H., Vasdev, S., Saleh, K.J., 2015. Biomaterial hypersensitivity: is it real? Supportive evidence and approach considerations for metal allergic patients following total knee arthroplasty. BioMed Res. Int. 2015, 137287.
Morlock, M., Schneider, E., Bluhm, A., Vollmer, M., Bergmann, G., Müller, V., Honl, M., 2001. Duration and frequency of every day activities in total hip patients. J. Biomech. 34, 873–881.
Muratoglu, O.K., Burroughs, B.R., Bragdon, C.R., Christensen, S., Lozynsky, A., Harris, W.H., 2004. Knee simulator wear of polyethylene tibias articulating against explanted rough femoral components. Clin. Orthop. Relat. Res., 108–113
Niyomsoan, S., Grant, W., Olson, D.L., Mishra, B., 2002. Variation of color in titanium and zirconium nitride decorative thin films. Thin Solid Films 415, 187–194.
Posada, O.M., Tate, R.J., Grant, M.H., 2015. Effects of CoCr metal wear debris generated from metal-on-metal hip implants and Co ions on human monocyte-like U937 cells. Toxicol. In Vitro: Int. J. Publ. Assoc. BIBRA 29, 271–280.
Pradhan, N.R., Gambhir, A., Porter, M.L., 2006. Survivorship analysis of 3234 primary knee arthroplasties implanted over a 26-year period: a study of eight different implant designs. Knee 13, 7–11.
Psychoyios, V., Crawford, R.W., O'Connor, J.J., Murray, D.W., 1998. Wear of congruent meniscal bearings in unicompartmental knee arthroplasty: a retrieval study of 16 specimens. J. Bone Joint Surg. Br. 80, 976–982.
Que, L., Topoleski, L.D.T., Parks, N.L., 2000. Surface roughness of retrieved CoCrMo alloy femoral components from PCA artificial total knee joints. J. Biomed. Mater. Res. (New York) 53, 111–118.
Rachmawati, D., Bontkes, H.J., Verstege, M.I., Muris, J., von Blomberg, B.M.E., Scheper, R.J., van Hoogstraten, I.M.W., 2013. Transition metal sensing by Toll-like receptor-4: next to nickel, cobalt and palladium are potent human dendritic cell stimulators. Contact Dermatitis 68, 331–338.
Rakow, A., Schoon, J., Dienelt, A., John, T., Textor, M., Duda, G., Perka, C., Schulze, F., Ode, A., 2016. Influence of particulate and dissociated metal-on-metal hip endoprosthesis wear on mesenchymal stromal cells in vivo and in vitro. Biomaterials 98, 31–40.
Reddy, G.L.N., Ramana, J.V., Kumar, S., Kumar, S.V., Raju, V.S., 2007. Investigations on the oxidation of zirconium nitride films in air by nuclear reaction analysis and backscattering spectrometry. Appl. Surf. Sci. 253, 7230–7237.
Reich, J., Hovy, L., Lindenmaier, H.-L., Zeller, R., Schwiesau, J., Thomas, P., Grupp, T. M., 2010. Praklinische Ergebnisse beschichteter Knieimplantate fur Allergiker. Der Orthopade 39, 495–502.
Schaerer, C., Mimnaugh, K., Popoola, O., Seebeck, J., 2010. Wear of UHMWPE tibial inserts under simulated obese patient conditions. Annual Meeting of the Orthopaedic Research Society 56th, 2329.
Schäfer, T., Böhler, E., Ruhdorfer, S., Weigl, L., Wessner, D., Filipiak, B., Wichmann, H. E., Ring, J., 2001. Epidemiology of contact allergy in adults. Allergy 56, 1192–1196.
Schiavone, P.A., Vasso, M., Cerciello, S., Maccauro, G., 2011. Metallosis following knee arthroplasty: a histological and immunohistochemical study. Int. J. Immunopathol. Pharmacol. 24, 711–719.
Schinkel, C., 2015. Retrospective multicentric study of 5-year results of a cemented, allergy-coated and uncoated TKA. Annual Meeting of the American Academy of Orthopaedic Surgeons, Las Vegas, NV, USA.
Schwiesau, J., Fritz, B., Kutzner, I., Bergmann, G., Grupp, T.M., 2014. CR TKA UHMWPE wear tested after artificial aging of the vitamin E treated gliding component by simulating daily patient activities. BioMed Res. Int. 2014, 567374.
Schwiesau, J., Schilling, C., Kaddick, C., Utzschneider, S., Jansson, V., Fritz, B., Blomer, W., Grupp, T.M., 2013a. Definition and evaluation of testing scenarios for knee wear simulation under conditions of highly demanding daily activities. Med. Eng. Phys. 35, 591–600.
Schwiesau, J., Schilling, C., Utzschneider, S., Jansson, V., Fritz, B., Blomer, W., Grupp, T.M., 2013b. Knee wear simulation under conditions of highly demanding daily activities–influence on an unicompartmental fixed bearing knee design. Med. Eng. Phys. 35, 1204–1211.
Thomas, B., Kulichova, D., Wolf, R., Summer, B., Mahler, V., Thomas, P., 2015. High frequency of contact allergy to implant and bone cement components, in particular gentamicin, in cemented arthroplasty with complications: usefulness of late patch test reading. Contact Dermatitis 73, 343–349.
Thomas, P., Weik, T., Roider, G., Summer, B., Thomsen, M., 2016. Influence of surface coating on metal ion release: evaluation in patients with metal allergy. Orthopedics 39, S24–S30.
Thomsen, M., Rozak, M., Thomas, P., 2011. Pain in a chromium-allergic patient with total knee arthroplasty: disappearance of symptoms after revision with a special surface-coated TKA – a case report. Acta Orthopaedica 82, 386–388.
Thyssen, J.P., Linneberg, A., Menne, T., Johansen, J.D., 2007. The epidemiology of contact allergy in the general population–prevalence and main findings. Contact Dermatitis 57, 287–299.
Thyssen, J.P., Menné, T., 2010. Metal allergy – a review on exposures, penetration, genetics, prevalence, and clinical implications. Chem. Res. Toxicol. 23, 309–318.
Tower, S.S., 2010. Arthroprosthetic cobaltism: neurological and cardiac manifestations in two patients with metal-on-metal arthroplasty: a case report. J. Bone Joint Surg. Am. 92, 2847–2851.
Tozzi, S., Modena, E., Falcioni, S., Sudanese, A., Affatato, S., Taddei, P., 2014. The effects of contact area and applied load on the morphology of in vitro worn ultra-high molecular weight knee prostheses: a micro-Raman and gravimetric study. J. Raman Spectrosc. 45, 781–787.
Underwood, R., Matthies, A., Cann, P., Skinner, J.A., Hart, A.J., 2011. A comparison of explanted Articular Surface Replacement and Birmingham Hip Resurfacing components. J. Bone Joint Surg. Br. 93, 1169–1177.
Urban, R.M., Tomlinson, M.J., Hall, D.J., Jacobs, J.J., 2004. Accumulation in liver and spleen of metal particles generated at nonbearing surfaces in hip arthroplasty. J. Arthroplasty 19, 94–101.
Uter, W., Gefeller, O., Geier, J., Schnuch, A., 2014. Contact sensitization to cobalt–multifactorial analysis of risk factors based on long-term data of the Information Network of Departments of Dermatology. Contact Dermatitis 71, 326–337.
van der Straeten, C., Grammatopoulos, G., Gill, H.S., Calistri, A., Campbell, P., de Smet, K.A., 2013. The 2012 Otto Aufranc Award: the interpretation of metal ion levels in unilateral and bilateral hip resurfacing. Clin. Orthop. Relat. Res. 471, 377–385.
Warshaw, E.M., Maibach, H.I., Taylor, J.S., Sasseville, D., DeKoven, J.G., Zirwas, M.J., Fransway, A.F., Mathias, C.G.T., Zug, K.A., DeLeo, V.A., Fowler, J.F., Marks, J.G., Pratt, M.D., Storrs, F.J., Belsito, D.V., 2015. North American contact dermatitis group patch test results, 2011-2012. Dermatitis: Contact, Atopic, Occupation., Drug 26, 49–59.
Zietz, C., Reinders, J., Schwiesau, J., Paulus, A., Kretzer, J.P., Grupp, T., Utzschneider, S., Bader, R., 2015. Experimental testing of total knee replacements with UHMW-PE inserts: impact of severe wear test conditions. J. Mater. Sci. - Mater. Med. 26, 134.

5. References

[1] Statistisches Bundesamt. Fallpauschalenbezogene Krankenhausstatistik (DRG-Statistik) Diagnosen, Prozeduren, Fallpauschalen und Case Mix der vollstationären Patientinnen und Patienten in Krankenhäusern - 2016 2017;Fachserie 12 Reihe 6.4.

[2] Wengler A, Nimptsch U, Mansky T. Hip and knee replacement in Germany and the USA: Analysis of individual inpatient data from German and US hospitals for the years 2005 to 2011. Dtsch Arztebl Int 2014;111(23-24):407–16.

[3] Pilz V, Hanstein T, Skripitz R. Projections of primary hip arthroplasty in Germany until 2040. Acta Orthop 2018;89(3):308–13.

[4] Pabinger C, Lothaller H, Portner N, Geissler A. Projections of hip arthroplasty in OECD countries up to 2050. Hip Int 2018:1120700018757940.

[5] Bayliss LE, Culliford D, Monk AP, Glyn-Jones S, Prieto-Alhambra D, Judge A, Cooper C, Carr AJ, Arden NK, Beard DJ, Price AJ. The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: A population-based cohort study. The Lancet 2017;389(10077):1424–30.

[6] Civinini R, Carulli C, Matassi F, Lepri AC, Sirleo L, Innocenti M. The Survival of Total Knee Arthroplasty: Current Data from Registries on Tribology: Review Article. HSS J 2017;13(1):28–31.

[7] Corbett KL, Losina E, Nti AA, Prokopetz JJZ, Katz JN. Population-based rates of revision of primary total hip arthroplasty: A systematic review. PloS ONE 2010;5(10):e13520.

[8] Kandala N-B, Connock M, Pulikottil-Jacob R, Sutcliffe P, Crowther MJ, Grove A, Mistry H, Clarke A. Setting benchmark revision rates for total hip replacement: Analysis of registry evidence. BMJ 2015;350:h756.

[9] Pabinger C, Berghold A, Boehler N, Labek G. Revision rates after knee replacement. Cumulative results from worldwide clinical studies versus joint registers. Osteoarthr Cartil 2013;21(2):263–68.

[10] Kurtz SM, Lau E, Ong K, Zhao K, Kelly M, Bozic KJ. Future young patient demand for primary and revision joint replacement: national projections from 2010 to 2030. Clin Orthop Relat Res 2009;467(10):2606–12.

[11] Sharkey PF, Lichstein PM, Shen C, Tokarski AT, Parvizi J. Why are total knee arthroplasties failing today--has anything changed after 10 years? J Arthroplasty 2014;29(9):1774–78.

[12] Australian Orthopaedic Association National Joint Replacement Registry: Hip, Knee & Shoulder Arthroplasty: 2017 Annual Report 2017.

[13] National Joint Registry for England, Wales, Northern Ireland and the Isle of Man: NJR 14th Annual Report 2017.

[14] Callaghan JJ, Templeton JE, Liu SS, Pedersen DR, Goetz DD, Sullivan PM, Johnston RC. Results of Charnley total hip arthroplasty at a minimum of thirty years. A concise follow-up of a previous report. J Bone Joint Surg Am 2004;86-A(4):690–95.

[15]Long WJ, Bryce CD, Hollenbeak CS, Benner RW, Scott WN. Total knee replacement in young, active patients: long-term follow-up and functional outcome: a concise follow-up of a previous report. J Bone Joint Surg Am 2014;96(18):e159.

[16]Mäkelä K, Eskelinen A, Pulkkinen P, Paavolainen P, Remes V. Cemented total hip replacement for primary osteoarthritis in patients aged 55 years or older: Results of the 12 most common cemented implants followed for 25 years in the Finnish Arthroplasty Register. J Bone Joint Surg Br 2008;90(12):1562–69.

[17]Martin CT, Callaghan JJ, Gao Y, Pugely AJ, Liu SS, Warth LC, Goetz DD. What Can We Learn From 20-year Followup Studies of Hip Replacement? Clin Orthop Relat Res 2016;474(2):402–07.

[18]Wainwright C, Theis JC, Garneti N, Melloh M. Age at hip or knee joint replacement surgery predicts likelihood of revision surgery. J Bone Joint Surg Br 2011;93(10):1411–15,.

[19]Sadoghi P, Liebensteiner M, Agreiter M, Leithner A, Böhler N, Labek G. Revision surgery after total joint arthroplasty: A complication-based analysis using worldwide arthroplasty registers. J Arthroplasty 2013;28(8):1329–32.

[20]Hallab NJ, Jacobs JJ. Biologic Effects of implant debris. Bull NYU Hosp Jt Dis 2009;67(2):182–88.

[21]Ingham E, Fisher J. The role of macrophages in osteolysis of total joint replacement. Biomaterials 2005;26(11):1271–86.

[22]Catelas I, Wimmer MA, Utzschneider S. Polyethylene and metal wear particles: characteristics and biological effects. Semin immunopathol 2011;33(3):257–71.

[23]Berry DJ, Currier BH, Mayor MB, Collier JP. Gamma-irradiation sterilization in an inert environment: A partial solution. Clin Orthop Relat Res 2012;470(7):1805–13.

[24]MacDonald DW, Higgs G, Parvizi J, Klein G, Hartzband M, Levine H, Kraay M, Rimnac CM, Kurtz SM. Oxidative properties and surface damage mechanisms of remelted highly crosslinked polyethylenes in total knee arthroplasty. Int Orthop 2013;37(4):611–15.

[25]Rowell SL, Reyes CR, Malchau H, Muratoglu OK. In Vivo Oxidative Stability Changes of Highly Cross-Linked Polyethylene Bearings: An Ex Vivo Investigation. J Arthroplasty 2015;30(10):1828–34.

[26]Ansari F, Ries MD, Pruitt L. Effect of processing, sterilization and crosslinking on UHMWPE fatigue fracture and fatigue wear mechanisms in joint arthroplasty. J Mech Behav Biomed Mater 2016;53:329–40.

[27]Muratoglu OK, Wannomae KK, Rowell SL, Micheli BR, Malchau H. Ex vivo stability loss of irradiated and melted ultra-high molecular weight polyethylene. J Bone Joint Surg Am 2010;92(17):2809–16.

[28]Wannomae KK, Bhattacharyya S, Freiberg A, Estok D, Harris WH, Muratoglu O. In vivo oxidation of retrieved cross-linked ultra-high-molecular-weight polyethylene acetabular components with residual free radicals. J Arthroplasty 2006;21(7):1005–11.

[29]Kop AM, Pabbruwe MB, Keogh C, Swarts E. Oxidation of Second Generation Sequentially Irradiated and Annealed Highly Cross-Linked X3™ Polyethylene Tibial Bearings. J Arthroplasty 2015;30(10):1842–46.

[30]Bracco P, Oral E. Vitamin E-stabilized UHMWPE for total joint implants: A review. Clin Orthop Relat Res 2011;469(8):2286–93.

[31]Lerf R, Zurbrügg D, Delfosse D. Use of vitamin E to protect cross-linked UHMWPE from oxidation. Biomaterials 2010;31(13):3643–48.

[32]Grupp TM, Holderied M, Mulliez MA, Streller R, Jager M, Blomer W, Utzschneider S. Biotribology of a vitamin E-stabilized polyethylene for hip arthroplasty - Influence of artificial ageing and third-body particles on wear. Acta Biomat 2014;10(7):3068–78.

[33]Grupp TM, Fritz B, Kutzner I, Schilling C, Bergmann G, Schwiesau J. Vitamin E stabilised polyethylene for total knee arthroplasty evaluated under highly demanding activities wear simulation. Acta Biomat 2017;48:415–22.

[34]Mitchelson AJ, Wilson CJ, Mihalko WM, Grupp TM, Manning BT, Dennis DA, Goodman SB, Tzeng TH, Vasdev S, Saleh KJ. Biomaterial hypersensitivity: is it real? Supportive evidence and approach considerations for metal allergic patients following total knee arthroplasty. BioMed Res Int 2015;2015:137287.

[35]Thomas P, Helm C von der, Schopf C, Mazoochian F, Frommelt L, Gollwitzer H, Schneider J, Flaig M, Krenn V, Thomas B, Summer B. Patients with intolerance reactions to total knee replacement: combined assessment of allergy diagnostics, periprosthetic histology, and peri-implant cytokine expression pattern. BioMed Res Int 2015;2015:910156.

[36]Thomas P, Weik T, Roider G, Summer B, Thomsen M. Influence of Surface Coating on Metal Ion Release: Evaluation in Patients With Metal Allergy. Orthopedics 2016;39(3 Suppl):S24-30,.

[37]Thomsen M, Rozak M, Thomas P. Pain in a chromium-allergic patient with total knee arthroplasty: disappearance of symptoms after revision with a special surface-coated TKA--a case report. Acta Orthop 2011;82(3):386–88.

[38]Hart AJ, Sabah SA, Bandi AS, Maggiore P, Tarassoli P, Sampson B, A Skinner J. Sensitivity and specificity of blood cobalt and chromium metal ions for predicting failure of metal-on-metal hip replacement. J Bone Joint Surg Br 2011;93(10):1308–13.

[39]Luetzner J, Krummenauer F, Lengel AM, Ziegler J, Witzleb WC. Serum metal ion exposure after total knee arthroplasty. Clinical orthopaedics and related research 2007;461:136–42.

[40]van der Straeten C, Grammatopoulos G, Gill HS, Calistri A, Campbell P, Smet KA de. The 2012 Otto Aufranc Award: The interpretation of metal ion levels in unilateral and bilateral hip resurfacing. Clin Orthop Relat Res 2013;471(2):377–85.

[41]Bader R, Bergschmidt P, Fritsche A, Ansorge S, Thomas P, Mittelmeier W. Alternative Werkstoffe und Losungen in der Knieendoprothetik fur Patienten mit Metallallergie. Orthopade 2008;37(2):136–42.

[42]Lapaj L, Wendland J, Markuszewski J, Mroz A, Wisniewski T. Retrieval analysis of titanium nitride (TiN) coated prosthetic femoral heads articulating with polyethylene. J Mech Behav Biomed Mater 2015;55:127–39.

[43] Heyse TJ, Davis J, Haas SB, Chen DX, Wright TM, Laskin RS. Retrieval analysis of femoral zirconium components in total knee arthroplasty: preliminary results. J Arthroplasty 2011;26(3):445–50.

[44] Burnell CD, Brandt JM, Petrak MJ, Bourne RB. Posterior condyle surface damage on retrieved femoral knee components. J Arthroplasty 2011;26(8):1460–67.

[45] Beyer F, Lutzner C, Kirschner S, Lutzner J. Midterm Results After Coated and Uncoated TKA: A Randomized Controlled Study. Orthopedics 2016;39(3 Suppl):S13-7.

[46] Innocenti M, Matassi F, Carulli C, Nistri L, Civinini R. Oxidized zirconium femoral component for TKA: A follow-up note of a previous report at a minimum of 10 years. Knee 2014;21(4):858–61.

[47] Hofer JK, Ezzet KA. A minimum 5-year follow-up of an oxidized zirconium femoral prosthesis used for total knee arthroplasty. Knee 2014;21(1):168–71.

[48] Bergschmidt P, Bader R, Ganzer D, Hauzeur C, Lohmann C, Ruther W, Tigani D, Rani N, Prats FL, Zorzi C, Madonna V, Rigotti S, Benazzo F, Rossi SMP, Kundt G, Bloch HR, Mittelmeier W. Ceramic femoral components in total knee arthroplasty - two year follow-up results of an international prospective multi-centre study. Open Orthop J 2012;6:172–78.

[49] Grieco PW, Pascal S, Newman JM, Shah NV, Stroud SG, Sheth NP, Maheshwari AV. New alternate bearing surfaces in total hip arthroplasty: A review of the current literature. J Clin Orthop Trauma 2018;9(1):7–16.

[50] Ngai V, Wimmer MA. Variability of TKR knee kinematics and relationship with gait kinetics: Implications for total knee wear. BioMed Res Int 2015;2015:284513.

[51] Morlock M, Schneider E, Bluhm A, Vollmer M, Bergmann G, Müller V, Honl M. Duration and frequency of every day activities in total hip patients. J Biomech 2001;34(7):873–81.

[52] Schwiesau J, Schilling C, Kaddick C, Utzschneider S, Jansson V, Fritz B, Blömer W, Grupp TM. Definition and evaluation of testing scenarios for knee wear simulation under conditions of highly demanding daily activities. Med Eng Phy 2013;35(5):591–600.

[53] Bergmann G, Bender A, Graichen F, Dymke J, Rohlmann A, Trepczynski A, Heller MO, Kutzner I. Standardized loads acting in knee implants. PloS ONE 2014;9(1):e86035.

[54] Bergmann G, Bender A, Dymke J, Duda G, Damm P. Standardized Loads Acting in Hip Implants. PloS ONE 2016;11(5):e0155612.

[55] Wright TM, Goodman SB. Implant wear in total joint replacement: Clinical and biologic issues, material and design considerations: symposium, Oakbrook, Illinois, October 2000. What are the wear mechanisms and what controls them? Rosemont, Ill.: American Academy of Orthopaedic Surgeons; 2001.

[56] Kligman M, Furman BD, Padgett DE, Wright TM. Impingement contributes to backside wear and screw-metallic shell fretting in modular acetabular cups. J Arthroplasty 2007;22(2):258–64.

[57] Kurtz SM, Ochoa JA, Hovey CB, White C. Frontside vs Backside wear in an acetabular component with multiple screw holes. Anaheim, California, USA; 1999.

[58] Krieg AH, Speth BM, Ochsner PE. Backside volumetric change in the polyethylene of uncemented acetabular components. J Bone Joint Surg Br 2009;91(8):1037–43.

[59]Kawaji H, Koistinen A, Korhonen R, Lappalainen R, Lohman M, Soininen A, Gomez-Barrena E, Konttinen YT, Ylinen P, Tallroth K. Back-side wear in HexLoc cups clinico-radiological, immunohistopathological, finite element, and retrieval analysis studies. J Long Term Eff Med Implants 2014;24(4):319–31.

[60]Nieuwenhuis JJ, Waal Malefijt J de, Hendriks JCM, Gonens T, Bonnet M. Unsatisfactory results with the cementless Omnifit acetabular component due to polyethylene and severe osteolysis. Acta Orthop Belg 2005;71(3):294–302.

[61]Noble PC, Durrani SK, Usrey MM, Mathis KB, Bardakos NV. Constrained cups appear incapable of meeting the demands of revision THA. Clin Orthop Relat Res 2012;470(7):1907–16.

[62]Powers CC, Ho H, Beykirch SE, Huynh C, Hopper RH, Engh CA, Engh CA. A comparison of a second- and a third-generation modular cup design: Is new improved? J Arthroplasty 2010;25(4):514–21.

[63]Puente Reyna AL, Jäger M, Floerkemeier T, Frecher S, Delank K-S, Schilling C, Grupp TM. Backside Wear Analysis of Retrieved Acetabular Liners with a Press-Fit Locking Mechanism in Comparison to Wear Simulation In Vitro. BioMed Res Int 2016;2016:8687131.

[64]Hood RW, Wright TM, Burstein AH. Retrieval analysis of total knee prostheses: A method and its application to 48 total condylar prostheses. J Biomed Mater Res 1983;17:829–42.

[65]Akbari A, Roy ME, Whiteside LA, Katerberg BJ, Schnettgoecke DJ. Minimal backside surface changes observed in retrieved acetabular liners. J Arthroplasty 2011;26(5):686–92,.

[66]Bali K, McCalden RW, Naudie DDR, MacDonald SJ, Teeter MG. Backside Wear Is Not Dependent on the Acetabular Socket Design in Crosslinked Polyethylene Liners. Clin Orthop Relat Res 2016;474(2):374–82

[67]Puente Reyna AL, Holderied M, Jäger M, Schilling C, Grupp TM. Articulation and backside wear analysis after long-term in vitro wear simulation of vitamin E stabilized polyethylene acetabular liners with a press-fit locking mechanism. Travmatol. ortop. Ross. 2018;24(2):29–40.

[68]Nebergall A, Greene M, Laursen M, Nielsen P, Malchau H, Troelsen A. Vitamin E diffused highly cross-linked polyethylene in total hip arthroplasty at five years: a randomised controlled trial using radiostereometric analysis. Bone Joint J 2017;99-B(5):577–84.

[69]Shareghi B, Johanson P, Karrholm J. Wear of Vitamin E-Infused Highly Cross-Linked Polyethylene at Five Years. J Bone Joint Surg Am 2017;99(17):1447–52.

[70]Scemama C, Anract P, Dumaine V, Babinet A, Courpied J, Hamadouche M. Does vitamin E-blended polyethylene reduce wear in primary total hip arthroplasty: A blinded randomised clinical trial. Int Orthop 2017;41(6):1113–18.

[71]Nebergall AK, Greene ME, Rubash H, Malchau H, Troelsen A, Rolfson O. Thirteen-Year Evaluation of Highly Cross-Linked Polyethylene Articulating With Either 28-mm or 36-mm Femoral Heads Using Radiostereometric Analysis and Computerized Tomography. J Arthroplasty 2016;31(9 Suppl):269–76.

[72]Lee JH, Lee BW, Lee BJ, Kim SY. Midterm results of primary total hip arthroplasty using highly cross-linked polyethylene: minimum 7-year follow-up study. J Arthroplasty 2011;26(7):1014–19.

[73] Glyn-Jones S, Thomas GER, Garfjeld-Roberts P, Gundle R, Taylor A, McLardy-Smith P, Murray DW. The John Charnley Award: Highly crosslinked polyethylene in total hip arthroplasty decreases long-term wear: a double-blind randomized trial. Clin Orthop Relat Res 2015;473(2):432–38.

[74] Dumbleton JH, Manley MT, Edidin AA. A literature review of the association between wear rate and osteolysis in total hip arthroplasty. J Arthroplasty 2002;17(5):649–61.

[75] Zietz C, Reinders J, Schwiesau J, Paulus A, Kretzer JP, Grupp T, Utzschneider S, Bader R. Experimental testing of total knee replacements with UHMW-PE inserts: impact of severe wear test conditions. J Mater Sci Mater Med 2015;26(3):134.

[76] Schwiesau J, Fritz B, Kutzner I, Bergmann G, Grupp TM. CR TKA UHMWPE wear tested after artificial aging of the vitamin E treated gliding component by simulating daily patient activities. BioMed Res Int 2014;2014:567374.

[77] Schwiesau J, Schilling C, Utzschneider S, Jansson V, Fritz B, Blomer W, Grupp TM. Knee wear simulation under conditions of highly demanding daily activities--influence on an unicompartmental fixed bearing knee design. Med Eng Phys 2013;35(8):1204–11.

[78] Reich J, Hovy L, Lindenmaier H-L, Zeller R, Schwiesau J, Thomas P, Grupp TM. Praklinische Ergebnisse beschichteter Knieimplantate fur Allergiker. Orthopade 2010;39(5):495–502.

[79] Affatato S, Spinelli M, Lopomo N, Grupp TM, Marcacci M, Toni A. Can the method of fixation influence the wear behaviour of ZrN coated unicompartmental mobile knee prostheses? Clin Biomech (Bristol, Avon) 2011;26(2):152–58.

[80] Grupp TM, Giurea A, Miehlke RK, Hintner M, Gaisser M, Schilling C, Schwiesau J, Kaddick C. Biotribology of a new bearing material combination in a rotating hinge knee articulation. Acta Biomater 2013;9(6):7054–63.

[81] Grupp TM, Saleh KJ, Mihalko WM, Hintner M, Fritz B, Schilling C, Schwiesau J, Kaddick C. Effect of anterior-posterior and internal-external motion restraint during knee wear simulation on a posterior stabilised knee design. J Biomech 2013;46(3):491–97.

[82] Grupp TM, Schroeder C, Kyun Kim T, Miehlke RK, Fritz B, Jansson V, Utzschneider S. Biotribology of a mobile bearing posterior stabilised knee design--effect of motion restraint on wear, tibio-femoral kinematics and particles. J Biomech 2014;47(10):2415–23.

[83] Puente Reyna AL, Fritz B, Schwiesau J, Schilling C, Summer B, Thomas P, Grupp TM. Metal ion release barrier function and biotribological evaluation of a zirconium nitride multilayer coated knee implant under highly demanding activities wear simulation. J Biomech 2018;79:88–96.

6. List of publications

Original research publications

Puente Reyna AL, Jäger M, Floerkemeier T, Frecher S, Delank K-S, Schilling C, et al. Backside Wear Analysis of Retrieved Acetabular Liners with a Press-Fit Locking Mechanism in Comparison to Wear Simulation In Vitro. Biomed Res Int 2016; 2016:8687131.

Puente Reyna AL, Holderied M, Jäger M, Schilling C, Grupp TM. Articulation and backside wear analysis after long-term in vitro wear simulation of vitamin E stabilized polyethylene acetabular liners with a press-fit locking mechanism. Travmatol ortop Ross 2018; 24(2):29–40.

Puente Reyna AL, Fritz B, Schwiesau J, Schilling C, Summer B, Thomas P, et al. Metal ion release barrier function and biotribological evaluation of a zirconium nitride multilayer coated knee implant under highly demanding activities wear simulation. J Biomech 2018; 79:88–96.

Attended conferences as presenter author

VI. Münchener Symposium für Experimentelle Orthopädie, Unfallchirurgie und Muskuloskelettale Forschung, July 15 - 16, 2016, Munich, Germany
Oral Presentation: Backside wear analysis of in vitro tested and retrieved liners with a press-fit locking mechanism

23rd Congress of the European Society of Biomechanics, July 2 - 5, 2017, Seville, Spain
Poster Presentation: Zirconium nitride ceramic multilayer coating evaluated under high demanding activities knee wear simulation

25th Annual Meeting of the European Orthopaedic Research Society, September 13 - 15, 2017, Munich, Germany
Oral Presentation: Biotribology and metal ion release of a zirconium nitride ceramic multilayer coating under high demanding activities knee wear simulation

8th World Congress of Biomechanics, July 8 -12, 2018, Dublin, Ireland
Poster Presentation: Backside wear analysis after long-term in-vitro wear simulation of acetabular liners with a press-fit locking mechanism

7. Curriculum

Ana Laura Puente Reyna, born on June 20th, 1988 in Monterrey, Mexico

Education

09.2015 – present	Doctor degree in Human Biology candidate at the Department of Orthopaedic Surgery, Physical Medicine and Rehabilitation, Campus Grosshadern, Ludwig-Maximilians-University Munich, Germany.
09.2012 – 11.2014	Master Degree in Biomedical Engineering at the Fachhochschule Aachen, Jülich, Germany. (Note: 1,3)
08.2006 – 05.2011	Bachelor Degree in Biomedical Engineering at the “Instituto Tecnologico y de Estudios Superiores de Monterrey” (ITESM), Excellence Scholarship, Monterrey, Mexico. (Note: 93/100)
10.2009 – 03.2010	Exchange student at the Technical University of Munich with DAAD Scholarship, Munich, Germany.
09.2003 – 06.2006	High School at “Instituto Regiomontano A. C.”, Monterrey, Mexico. (Note: 98/100). Best of the Class.

Experience

09.2015 – present	Research Engineer / Doctor degree candidate in the Front End Innovation and Materials Department at B. Braun-Aesculap Division, Tuttlingen, Germany.
03.2014 – 10.2014	Master student in the Front End Innovation and Materials / Biomechanical Research Laboratory Department at B. Braun-Aesculap Division, Tuttlingen, Germany. Title: “Pressure mapping within the intervertebral disc under different boundary conditions” (Note: 1,3)
10.2013 – 02.2014	Internship in the Knee Arthroplasty / Orthopaedic Research Department at B. Braun-Aesculap Division, Tuttlingen, Germany.
06.2011 – 08.2012	Technical Service Engineer at Lifetec SA de CV, Monterrey, Mexico
01.2011 – 05.2011	Internship in the Technological Development Department at Hospital San Jose – Tec de Monterrey, Monterrey, Mexico.
03.2010 – 07.2010	Internship in the Research and Development Orthopedics Department / Biomechanical Research Laboratory at B. Braun-Aesculap Division, Tuttlingen, Germany.