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Vitamin E-blended highly cross-linked polyethylene liners in total hip arthroplasty: a randomized, multicenter trial using virtual CAD-based wear analysis at 5-year follow-up

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Abstract

Background Progressive oxidation of highly cross-linked ultra-high molecular weight (UHMPWE-X) liners is considered to be a risk factor for material failure in THA. Antioxidants such as vitamin E (alpha-tocopherol) (UHMWPE-XE) were supplemented into the latest generation of polyethylene liners. To prevent inhomogenous vitamin E distribution within the polymer, blending was established as an alternative manufacturing process to diffusion. The purpose of the present study was to investigate the in vivo wear behavior of UHMWPE-XE in comparison with conventional UHMWPE-X liners using virtual CAD-based radiographs.

Methods Until now, 94 patients from a prospective, randomized, controlled, multicenter study were reviewed at 5-year follow-up. Of these, 51 (54%) received UHMWPE-XE and 43 (46%) UHMWPE-X liners. Anteroposterior pelvic radiographs were made immediately after surgery and at 1 and 5 years postoperatively. The radiographs were analyzed using the observer-independent analysis software RayMatch® (Raylytic GmbH, Leipzig, Germany).

Results The mean wear rate was measured to be 23.6 µm/year (SD 13.7; range 0.7–71.8 µm). There were no significant differences between the two cohorts (UHMWPE-X: 23.2 µm/year vs. UHMWPE-XE: 24.0 µm/year, $p=0.73$). Cup anteversion significantly changed within the 1st year after implantation independent from the type of polyethylene liner [UHMWPE-X: 18.2–23.9° ($p=0.0001$); UHMWPE-XE: 21.0–25.5° ($p=0.002$)]. No further significant changes of cup anteversion in both groups were found between year 1 and 5 after implantation [UHMWPE-X ($p=0.46$); UHMWPE-XE ($p=0.56$)].

Conclusion The present study demonstrates that the addition of vitamin E does not adversely affect the midterm wear behavior of UHMWPE-X. The antioxidative benefit of vitamin E is expected to become evident in long-term follow-up. Cup anteversion increment by 5° within the 1st year is likely a result of the released hip flexion contracture resulting in an enhanced posterior pelvic tilt. Therefore, a reassessment of target values in acetabular cup placement might be considered.

Keywords Total hip arthroplasty · CAD-based wear analysis · UHMWPE-XE · Particle-induced osteolysis

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Introduction

Ultra-high molecular weight polyethylene (UHMWPE) was considered to be the gold standard for acetabular liners in total hip arthroplasty for a long time [1–3]. However, polyethylene wear debris-induced periprosthetic osteolysis remains one of the main causes for aseptic loosening in THA [2, 3]. The introduction of radiation cross-linking of polyethylene liners resulted in enhanced wear resistance (UHMWPE-X) [4–6]. Progressive oxidation of UHMPWE-X was considered to be another risk factor for material failure in THA [7]. In vitro studies demonstrated that stabilization of UHMWPE-X with antioxidants such as vitamin E (alpha-tocopherol) (UHMWPE-XE) increases resistance to oxidative stress [8]. However, vitamin E addition reduces cross-linking capacity of polyethylene [9–11] and particularly concentrations above 0.3 wt% (mass fraction) in the irradiated surface are considered to impair wear characteristics [12]. On the other hand, a defined amount of vitamin E (ranging between 0.1 and 1.0 wt%) in the unirradiated bulk extends the oxidative stability of UHMWPE-XE blends [13]. For clinical application, two different manufacturing processes were used to integrate vitamin E into UHMWPE:

The first method rests upon the diffusion of vitamin E into UHMWPE after radiation cross-linking. Cross-linking is not warped due to absence of vitamin E during consolidation. However, inhomogeneity of vitamin E content in the polyethylene liner due to diffusion process requires post-irradiation thermal treatment [10, 14, 15].

The alternative method is based on blending of vitamin E with UHMWPE resin powder prior to consolidation resulting in homogenous distribution of vitamin E in the polyethylene liner [16–18]. It is not yet proven whether these features have a positive effect on in vivo wear behavior and long-term implant survival.

A reliable and accurate measurement of low wear rates using conventional radiographs remains challenging [19]. Although the radiostereometric analysis (RSA) is widely accepted as the gold standard to measure the micromotions of implant components [20], traditional RSA requires the insertion of tantalum beads into the bone [21]. In 2012, a report about two new RSA methods which supersede marker beads using phantom devices was published. Both new RSA methods [scanned models (MB-RSA) and computer-generated geometrical shape models (EGS-RSA)] were validated as accurate and precise as the former gold standard for evaluation of polyethylene wear [22, 23]. Another well-established technique to assess wear and implant position is EBRA (Einzel-Bild-Roentgen-Analyse) [24, 25], a semiautomatic, graphical-based method evaluating standard anteroposterior radiographs without requiring additional means at exposure (e.g. markers) [26]. However, all graphical-based methods such as EBRA, ROMAN (Roentgen monogrammetric analysis) and HAS (hip analysis suite) do not reach the level of precision like RSA [27]. A recently developed innovative wear analysis system was used in this study. It is based on virtual computer-aided design (CAD)-based radiographic images without the need for a reference sphere. This method was validated for analysis of in vivo polyethylene wear [28].

In this prospective multicenter study, the 5-year in vivo wear behavior of UHMWPE-XE versus UHMWPE-X was evaluated by virtual CAD-based X-rays [29].

Materials and methods

In 2011, the VITAS (Vitelene® against Standard UHMWPE-X) study was established (PI second author) as a prospective, randomized, multicenter study to compare vitamin E-blended UHMWPE-XE (Vitelene®, sponsor: Aesculap AG, Tuttlingen, Germany) with UHMWPE-X. Six different orthopaedic departments in Germany participated and recruited 400 patients between 2011 and 2015. The follow-up period is scheduled up to 15 years. Patients of both genders with the indication for a primary cementless total hip arthroplasty due to hip osteoarthritis were recruited for this trial. Exclusion criteria were significant increased anesthetic risk (ASA IV), tumors, drug or alcohol abuse as well as immunosuppressive therapy, infections, fractures, previous surgeries at the affected hip, poor bone quality and relevant deformities (leg length differences > 30 mm, offset reductions > 30 mm). Informed written consent according to the Declaration of Helsinki was obtained from every patient prior to surgery. The study was approved by the local ethics committee (#11-4845-BO) and registered on Clinicaltrials.gov (#NCT01713062).

Implants and intervention

Vitelene® is a vitamin E-blended highly cross-linked polyethylene liner. It is produced by compression molding technique from a compound of 0.1% vitamin E and polyethylene polymers. Subjects were randomly assigned to obtain either a Vitelene® liner or a conventional UHMWPE-X (remelted, cross-linking by γ-irradiation [75 kGy], sterilization: ethylene oxide) liner. The acetabular component was a cementless fixed Plasmacup DC® (Aesculap). It is a hemispheric cup with a microporous titanium coating (Plasmapore®). The type of femoral stem and the surgical approach was defined by the orthopaedic surgeon, but limited to four different stem types (Metha®, Excia®, Bicontact®, TRJ®, all Aesculap). To evade effects of different head materials, Al_2O_3 ceramic heads (Biolox® Ceramtec, Plochingen, Germany) with 32

or 36 mm diameter were regularly used. Postoperatively, all patients received physiotherapy and were mobilized 1 day after surgery. The further postoperative treatment schedule was left over to the study centers. The amount of weight bearing was dependent on individual decision of each surgeon and varied from full weight bearing immediately after surgery down to 20 kg weight bearing for 6 weeks.

Wear analysis

The 5-year wear analysis of 94 patients of the multicenter study (VITAS) was performed using the innovative software RayMatch® (Raylytic, Leipzig, Germany). The software enables to measure highly precise radiographic parameters and femoral head penetration. For this analysis, CAD data of the prosthetic components are crucial and were provided by the manufacturer of the prosthetic components (Aesculap AG, Tuttlingen, Germany). For method validation, virtual pelvis X-rays of 21 patients from 2 study centers (Vitelene® cohort with vitamin E: 12 patients, UHMWPE-X cohort without vitamin E: 9 patients) were made 1 and 5 years after surgery [27]. The radiographic images were analyzed to determine polyethylene wear, cup inclination and cup anteversion. The software works completely automatically and is independent from any other factors (e.g. investigators experiences, X-ray technique, type of implant, etc.). It is based on the creation of virtual images of the prosthetic components via computer simulation. In a first step, voxels with an isotropic edge length of 0.15 mm are discretized. Attenuation coefficients are assigned to the voxels depending on the prosthetic material. The simulation model consists of a projection surface (simulating the detector), an X-ray emitter (simulating the X-ray tube) and the prosthetic component. Emanating from an X-ray source, vectors are calculated reaching the pixels on the projection surface. The next step is to determine the resulting intensity of the radiation along the vectors using the Lambert–Beer law. The calculated intensity per virtual pixels constitutes grey values creating a realistic simulated image of the prosthesis. In the next step, the simulated image ("digitally reconstructed radiograph", DRR) is compared with the real image by creating gradient-based difference images. Subsequently, the accordance of DRR and real images is determined utilizing a cross-correlation. The position and the alignment of the implant components is adjusted iteratively in all six directions aiming at a maximum accordance with the real image. The data processing was performed by powerful hardware (PC with Intel® Core™ i5-4570 CPU and graphic card Nvidia® GTX1080). The mean absolute error of 4.0 µm with a standard deviation of 7.1 µm was attributed to different positions in space. Summing up, the RayMatch® method is equal to the most accurate method (RSA) without the disadvantage of the insertion of tantalum beads compared to the traditional RSA [27, 28] (Figs. 1, 2).

The cup inclination (CupInc) was measured as the angle between the cup surface and a horizontal reference line using a 2D–3D registration between the patient-specific cup CAD model and the X-ray. The cup anteversion (CupAnt) was measured as the angle between the cup surface against the cup symmetry axis in the frontal plane using a 2D–3D registration between the patient-specific cup CAD model and the X-ray. The hip implant wear (HIW) was measured between the hip cup and the hip head at the specified follow-up time point using a 2D–3D registration between the patient-specific cup and head CAD model and the X-ray. The parameter is determined in micrometers and expressed as the average wear rate per year.

Statistical analysis

For descriptive statistics of the data, means and standard deviations (SD) are provided. The Shapiro–Wilk test was used to test for normality of the sample. The Student's *t* test

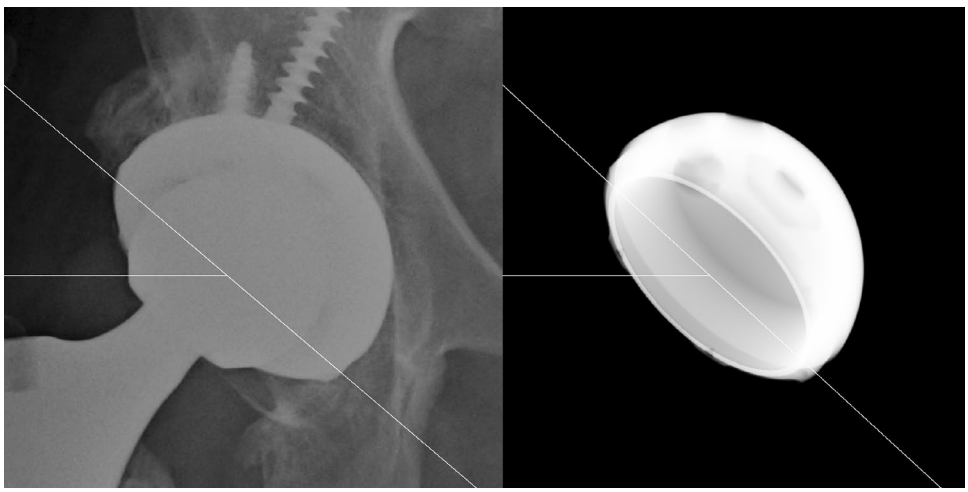

Fig. 1 Standard digital X-ray (left) and CAD (computer-aided design) cup model

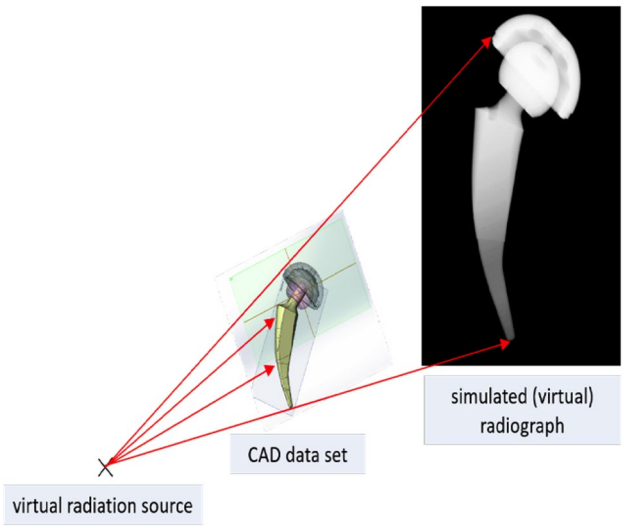

Fig. 2 Creation of virtual images of the prosthetic components via computer simulation. The simulation model consists of a projection surface (simulating the detector), an X-ray emitter (simulating the X-ray tube) and the prosthetic component. Emanating from an X-ray source, vectors are calculated reaching the pixels on the projection surface

was used for comparison of paired samples with a normal distribution of pre- and postoperative means. In cases of not normally distributed means, the Wilcoxon signed-rank test was used. p values < 0.05 were considered significant. The software SPSS®19 (SPSS Inc. Headquarters, Chicago, Illinois, USA) was used to carry out statistical analysis.

Results

From 400 included probands, 84 left the study. In ten patients (2.5%), revision surgery was necessary, of which seven occurred in UHMWPE-X group. The reasons for revision were postoperative hemorrhage ($n=3$), stem loosening (2), periprosthetic fracture (2), aseptic cup loosening (1), periprosthetic infection (1) or dislocation (1). At a minimum follow-up of 5 years, reasonable X-rays for wear analysis (postoperative, 1- and 5-year follow-up X-rays) were available from 94 patients. Among the 94 patients, no significant differences in any demographic characteristics between the UHMWPE-X ($n=43$) and UHMWPE-XE groups ($n=51$) were noted. In the UHMWPE-X group, gender ratio was 22–28 (male to female) and 31–37 in the UHMWPE-XE group, respectively. The mean age at the time of surgery was 62.3 years (range 34–75 years) and did not differ between the groups ($p=0.22$) as it was for the BMI (mean 28.5, range 18–41, $p=0.26$ between groups). In all patients, the diameter of the femoral modular head was 32 mm. Due to poor X-ray quality in one of the study centers, the HIW could not be analyzed in 12 images (UHMWPE-XE $n=8$; UHMWPE-X $n=4$). Therefore, the images of 82 patients were evaluated for femoral head penetration. In 35 (UHMWPE-X: $n=17$; UHMWPE-XE: $n=18$) of these patients, a Metha® short stem was applied. In 42 patients (UHMWPW-X: $n=21$; UHMWPE-XE: $n=21$), a Bicontact® straight stem was used. Four patients (UHMWPE-X: $n=2$; UHMWPE-XE: $n=2$) received a Excia® T stem system and in one case (UHMWPE-X) a trochanter preserving TRJ® stem was used. In total, mean femoral head penetration was similar between both cohorts (UHMWPE-X = 116 µm; UHMWPE-XE = 120 µm; $p=0.73$). The mean femoral head penetration was 23.2 µm/year (range 0.7–71.8 µm) in the UHMWPE-X group and 24.0 µm/year (range 0.7–67.8 µm) in the UHMWPE-XE group at 5-year follow-up. In the 1st year, no femoral head penetration was detected in both groups. Using four different stem types, there were no significant differences in wear rates between the cohorts [Metha® 24.6 µm/year (0.7–71.8); TRJ® 32.3 µm/year; Bicontact® 22.2 µm/year (0.7–61.9) and Excia® 25.8 µm/year (13.1–38.2)]. Within the two major subgroups, no significant difference could be identified using the two inlay types [Metha®: UHMWPE-X vs. UHMWPE-XE: 24.1 µm/year (0.7–71.8) vs. 25.4 (8.1–67.8) ($p=0.81$); Bicontact®: UHMWPE-X versus UHMWPE-XE: 23.3 µm/year (6.2–61.5) vs. 21.5 µm/year (0.7–41.8) ($p=0.65$)] (Tables 1, 2).

From surgery to 5-year follow-up, the cup inclination changed from 40.9° (range 29.9–52.7°) to 41.2° (range 29.1–54.1°) in the UHMWPE-X group ($p=0.82$) and from 39.5° (range 28.9°–52.2°) to 39.8° (range 28.4°–53.3°) in the UHMWPE-XE group ($p=0.77$) (Tables 3, 4).

The postoperatively measured cup anteversion significantly increased within the 1st year after implantation independent from the type of polyethylene liner, from 18.2° (range 7.3°–33.2°) to 23.9° (range 10.3°–44.2°) in the UHMWPE-X group ($p=0.0001$) and from 21.0° (range 6.0°–37.4°) to 25.5° (range 10.9°–46.1°) in the

Table 1 Descriptive statistical analysis for hip implant wear (HIW) in µm/year in the UHMWPE-X group ($n=39$)

FU	n	Mean wear rate (µm/year)	Median	SD	Max	Min
1 year	39	0.0	0.0	0.0	0.0	0.0
5 year	39	23.2	17.9	15.4	71.8	0.7

SD standard deviation, *Max* maximum, *Min* minimum

Table 2 Descriptive statistical analysis for hip implant wear (HIW) in the UHMWPE-XE group ($n=43$)

FU	n	Mean wear rate (µm/year)	Median	SD	Max	Min
1 year	43	0.0	0.0	0.0	0.0	0.0
5 years	43	24.0	23.8	12.0	67.0	0.7

Table 3 Descriptive statistical analysis for cup inclination (CupInc) in the UHMWPE-X ($n=43$)

FU	n	Mean	Median	SD	Max	Min
Post-Op	43	40.9°	40.7°	5.5	52.7°	29.9°
1 year	43	41.7°	40.9°	5.0	55.4°	31.4°
5 years	43	41.2°	40.8°	4.7	54.1°	29.1°

Table 4 Descriptive statistical analysis for cup inclination (CupInc) in the UHMWPE-XE group ($n=51$)

FU	n	Mean	Median	SD	Max	Min
Post-OP	51	39.5°	39.0°	5.4	52.2°	28.9°
1 year	51	40.2°	40.6°	6.8	53.3°	26.7°
5 years	51	39.8°	39.3°	6.1	53.3°	26.4°

Table 5 Descriptive statistical analysis for cup anteversion (CupAnt) in the UHMWPE-X group ($n=43$)

Examination period	Measurements (n)	Mean	Median	SD	Max	Min
Post-OP	43	18.2°	18.6°	6.0	33.2°	7.3°
1 year	43	23.9°	24.1°	7.1	44.2°	10.3°
5 years	43	22.8°	22.9°	8.1	40.1°	9.4°

Table 6 Descriptive statistical analysis for cup anteversion (CupAnt) in the UHMWPE-XE group ($n=51$)

FU	n	Mean	Median	SD	Max	Min
Post-OP	51	21.0°	20.8°	7.2	37.4°	6.0°
1 year	51	25.5°	26.3°	7.1	46.1°	10.9°
5 years	51	26.1°	27.5°	8.0	51.0°	12.0°

UHMWPE-XE group ($p=0.002$), respectively. From year 1 to year 5 after implantation, no further significant changes of cup anteversion in both groups were found (UHMWPE-X, $p=0.46$; UHMWPE-XE, $p=0.56$) (Tables 5, 6).

Discussion

Strong efforts have been made to improve material properties and to reduce wear of polyethylene in THA [2, 8, 9, 35]. Cross-linking of conventional polyethylene was a milestone to improve wear characteristics in THA. Since then, a precise measurement of low wear rates became challenging in conventional radiographs making it difficult for comparative studies. Especially in short and midterm follow-up, semi-automatic methods such as EBRA, ROMAS and HAS [27] have specific disadvantages and are inferior to RSA [28]. We used a novel, non-invasive and investigator independent wear analysis technique. In our study, the two cohorts (UHMWPE-X vs. UHMWPE-XE) showed no significant differences in wear rates within 5-year follow-up. The stem design had no significant impact on the wear behavior of the polyethylene inlay. In both groups, the polyethylene wear was substantially below the threshold for osteolysis induction of 100 µm/year [30]. This fits with most reports in the literature about vitamin E-supplemented polyethylene liners. Apart from Scemama et al. [31], no author described significant differences between vitamin E-supplemented and conventional polyethylene liners [31–36]. In Table 7, there is an overview about the current data in the literature.

Interestingly, the anteversion of the acetabular cup increased within the 1st year after implantation independent from the material of the acetabular liner (+5.7° UHMWPE-X vs. +5.1° UHMWPE-XE; $p=0.42$). It is known

Table 7 Our data compared to the literature

Study	Radiographic measurement	Type of manufacturing	Minimal follow-up (year)	Monoblock cup	Wear
Our study	CAD-based	Blended	5	O	UHMWPE-XE > UHMWPE-X
Salemyr et al. [32]	RSA	Diffused	2	O	UHMWPE-XE < UHMWPE-X
Nebergall et al. [33]	RSA	Diffused	5	O	UHMWPE-XE < UHMWPE-X
Galea et al. [34]	RSA	Diffused	2&5	O	UHMWPE-XE = UHMWPE-X
Shareghi et al. [35]	RSA	Diffused	3	O	UHMWPE-XE < UHMWPE-X
Sillesen et al. [43]	Software-based	Diffused	5	O	UHMWPE-XE < UHMWPE-X
Scemama et al. [31]	RSA	Blended	3	x	UHMWPE-XE < UHMWPE*

CAD computer-aided design, *RSA* radiostereometry, *UHMWPE-X* highly cross-linked ultra-high molecular weight polyethylene, *UHMWPE-XE* vitamin E-supplemented highly cross-linked ultra-high molecular weight polyethylene

*Significant difference

that permanent and stable osseointegration of titanium cups occurs during the early postoperative period [37, 38]. Therefore, a migration of the cup towards flexion must be taken into consideration in the analysis of our results. Yet, there is no gold standard for measuring the acetabular anteversion [39]. Due to automated measurement, the RayMatch® technique has the advantage to be non-dependent on investigators' experience [28]. However, the RayMatch® technique does not take differences in the pelvic tilt into account. In conventional two-dimensional radiographs, the variation of pelvic tilt may lead to an incorrect measurement of the acetabular orientation [40]. For inclination, the error is vanishingly small [41], but anteversion is highly susceptible to changes in pelvic tilt [42].

A major strength of our study is the design as a prospective, randomized multicenter trial. To our knowledge, this is the second report on in vivo wear behavior of vitamin E-blended polyethylene in total hip arthroplasty. The application of the recently validated, virtual computer-aided design (CAD)-based analysis tool ensures a reliable, observer-independent measurement of radiographic parameters. However, our study has several limitations. Of the 400 patients included, 84 patients have withdrawn their consent to participate in the study. Furthermore, among the 94 patients who were examined at 5-year follow-up, 12 cases could not be analyzed regarding HIW due to inadequate image quality.

In summary, there was no significant difference in midterm wear behavior between UHMWPE-X and UHMWPE-XE.

Conclusion

The addition of vitamin E does not significantly affect wear behavior of UHMWPE-X at 5-year follow-up. At 10-year follow-up, we expect superior wear behavior of UHMWPE-XE due to reduced oxidative embrittlement. Interestingly, cup anteversion increased by nearly 5° within the 1st year after implantation and is expected to be functional. Therefore, a reassessment of target values in acetabular cup placement might be considered.

Author contribution All authors ensured that they had furnished a substantial contribution to the article and that they are in agreement with form and contents of the manuscript.

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Availability of data and materials All patient-related data were collected by file research from the archives of the participating centers.

Compliance with ethical standards

Ethics approval and consent to participate The study was approved by the local ethics committee (11-4845-BO). The study was registered on Clinicaltrials.gov. The trial registration number is NCT01713062.

Consent to publish All patients consented to publish personal data in an anonymised form.

Conflict of interest The authors declare they have no conflict of interest.

Patient confidentiality Data were protected according to the U.S. Health Insurance Portability and Accountability Act (HIPAA).

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